

# Measles

**CLINICAL MANIFESTATIONS:** Measles is an acute viral disease characterized by fever, cough, coryza, and conjunctivitis, followed by a maculopapular rash beginning on the face and spreading cephalocaudally and centrifugally. During the prodromal period, a pathognomonic enanthema (Koplik spots) may be present. Complications of measles, including otitis media, bronchopneumonia, laryngotracheobronchitis (croup), and diarrhea, occur commonly in young children and immunocompromised hosts. Acute encephalitis, which often results in permanent brain damage, occurs in approximately 1 of every 1000 cases. In the postelimination era, death, predominantly resulting from respiratory and neurologic complications, has occurred in 1 to 3 of every 1000 cases reported in the United States. Case-fatality rates are increased in children younger than 5 years, pregnant women, and immunocompromised children, including children with leukemia, human immunodeficiency virus (HIV) infection, and severe malnutrition (including vitamin A deficiency). Sometimes the characteristic rash does not develop in immunocompromised patients. Individuals with incomplete immunity from immunization with inactivated measles vaccine may have an atypical presentation with some but not all symptoms following exposure to wild-type measles.

Subacute sclerosing panencephalitis (SSPE) is a rare degenerative central nervous system disease characterized by behavioral and intellectual deterioration and seizures that occurs 7 to 11 years after wild-type measles virus infection, occurring at a rate of 4 to 11 per 100 000 measles cases, with higher rates if measles occurs before 2 years of age. Widespread measles immunization has led to the virtual disappearance of SSPE in the United States.

**ETIOLOGY:** Measles virus is an enveloped RNA virus with 1 serotype, classified as a member of the genus *Morbillivirus* in the *Paramyxoviridae* family.

**EPIDEMIOLOGY:** The only natural host of measles virus is humans. 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; the attack rate in a susceptible individual exposed to measles is 90%. Population immunity of greater than 95% is needed to stop ongoing transmission. In temperate areas, the peak incidence of infection usually occurs during late winter and spring. In the prevaccine era, most cases of measles in the United States occurred in preschool- and young school-aged children, and few people remained susceptible by 20 years of age. Following implementation of routine childhood vaccination in the United States at age 12 to 15 months, the age of peak measles incidence during epidemics in the United States shifted to 6 to 12 months. This susceptibility approximates the time at which transplacentally acquired maternal antibodies no longer are present if the mother has vaccine-induced immunity. The childhood and adolescent immunization program in the United States began with licensure of the measles vaccine in 1963 and has resulted in a greater than 99% decrease in the reported incidence of measles, with interruption of endemic disease transmission being declared in 2000.

From 1989 to 1991, the incidence of measles in the United States increased because of low immunization rates in preschool-aged children, especially in urban areas, and because of primary vaccine failures after one measles vaccine dose. Following improved coverage in preschool-aged children and implementation of a routine second dose of measles-mumps-rubella (MMR) vaccine for children, the incidence of measles declined to extremely low levels (<1 case per 1 million population). In 2000, an independent panel of internationally recognized experts reviewed available data and unanimously agreed that measles no longer was endemic (defined as continuous, year-round transmission) in the United States. Compared with earlier postelimination years (2001–2008), when the annual median number of cases reported was 56 cases/year (range, 37–140), a median of 130 measles cases were reported annually (range, 55–667) during 2009–2014. In 2011, 2013, and 2014, the numbers of reported cases were 220, 187, and 667, respectively; these larger numbers of cases were attributable to an increase in the number of importations and/or spread from importations. The median number of measles outbreaks (defined as 3 or more cases linked in time and space) that occurred during 2009–2014 was 10 per year (range, 4–23) and was higher than the annual median number of outbreaks that occurred in earlier postelimination years (median, 4 outbreaks per year; range, 2–10 outbreaks). Of the 1264 cases reported during 2009–2014, 1204 (95%) were import associated (including 275 [22%] directly imported cases), and 60 (5%) cases were of an unknown source; among 1173 cases in US residents, 74% were in unvaccinated people, 16% were in people with unknown vaccination status (83% of those were adults), and 10% were in vaccinated people (with  $\geq 1$  dose of a measles-containing vaccine). During the same period, among 917 cases in vaccine-eligible US residents, 65% were in people reported as having a philosophical or religious objection to vaccination. In 2015, 188

people from 24 states and the District of Columbia were reported to have measles. This large, multistate measles outbreak was linked to an amusement park in California. The outbreak likely started from a traveler who became infected overseas with measles, then visited the amusement park while infectious; however, no source was identified. In 2016, 86 people from 16 states were reported to have measles, and in 2017, 120 people from 15 states and the District of Columbia were reported to have measles.

Progress continues toward global control and regional measles elimination. In 2016, there were 89 780 measles deaths globally, marking the first year measles deaths have fallen below 100 000 per year. Measles vaccination resulted in an 84% drop in measles deaths between 2000 and 2016 worldwide. In 2016, approximately 85% of the world's children received one dose of measles vaccine by their first birthday through routine health services, up from 72% in 2000. During 2000–2016, measles vaccination prevented an estimated 20.4 million deaths. All World Health Organization (WHO) regions have established goals to eliminate measles by 2020. Resuming progress toward 2020 milestones and elimination goals will require countries and their partners to raise the visibility of measles elimination, address barriers to measles vaccination, and make substantial and sustained additional investments in strengthening health systems.

Inadequate response to vaccine (ie, primary vaccine failure) occurs in as many as 7% of people who have received a single dose of vaccine at 12 months or older. Most cases of measles in previously immunized children seem to be attributable to primary vaccine failures, but waning immunity after immunization (ie, secondary vaccine failure) may be a factor in some cases. Primary vaccine failure was the main reason a 2-dose vaccine schedule was recommended routinely for children and high-risk adults.

Patients infected with wild-type measles virus are contagious from 4 days before the rash through 4 days after appearance of the rash. Immunocompromised patients who may have prolonged excretion of the virus in respiratory tract secretions can be contagious for the duration of the illness. Patients with SSPE are not contagious.

The **incubation period** generally is 8 to 12 days from exposure to onset of symptoms. In family studies, the average interval between appearance of rash in the index case and subsequent cases is 14 days, with a range of 7 to 21 days. In SSPE, the mean incubation period of 84 cases reported between 1976 and 1983 was 10.8 years.

**DIAGNOSTIC TESTS:** Measles virus infection can be confirmed by: (1) detection of measles viral RNA by reverse transcriptase-polymerase chain reaction (RT-PCR); (2) detection of measles-specific immunoglobulin (Ig) M; (3) a fourfold increase in measles IgG antibody concentration in paired acute and convalescent serum specimens (collected at least 10 days apart); or (4) isolation of measles virus in cell culture. Detection of IgM in serum samples by enzyme immunoassay has been the preferred method for case confirmation; however, as the incidence of disease decreases, the positive predictive value of IgM detection also decreases. For this reason, detection of viral RNA in blood; throat, nasal, and posterior nasopharyngeal swab specimens; bronchial lavage samples; or urine samples (respiratory samples are preferred specimens, and sampling more than 1 site may increase sensitivity) is playing an increasing role in case confirmation, especially in countries that have achieved measles elimination. A serum sample as well as a throat swab specimen should be obtained from any patient in whom measles infection is suspected. Additionally, it is ideal to obtain a urine sample, because sampling from all 3 sites will increase the likelihood of establishing a diagnosis. State public health laboratories and the Measles Laboratory at the Centers for Disease Control and Prevention (CDC) can perform RT-PCR

assays to detect measles RNA. Isolation of measles virus in cell culture is not recommended for routine case confirmation (ie, clinical diagnosis), because isolation can take up to 2 weeks to complete. However, viral isolates are important for monitoring the genetic characteristics of circulating measles viruses.

Ideally, both a serum sample for IgM detection and serum and throat swab samples for RNA detection should be taken at first contact with a suspected case. The sensitivity of measles IgM assays varies by timing of specimen collection, immunization status of the patient, and the assay method itself. Up to 20% of assays for IgM may have a false-negative result in the first 72 hours after rash onset. If the measles IgM result is negative and the patient has a generalized rash lasting more than 72 hours, a second serum specimen should be obtained, and the measles IgM test should be repeated. Measles IgM is detectable for at least 1 month after rash onset in unimmunized people but might be absent or present only transiently in people immunized with 1 or 2 vaccine doses. Therefore, a negative IgM test result should not be used to rule out the diagnosis in immunized people.

Detection of viral RNA by RT-PCR provides a relatively rapid and sensitive method for case confirmation. It is important to collect samples for RNA detection as soon as possible after rash onset, because viral shedding declines with time after rash. Specimen timing and quality greatly influence the results of RT-PCR testing, so a negative result should not be the only criterion used to rule out a case of measles. Another advantage of collecting samples for molecular detection of the virus is that these samples can also be used to genotype the virus. Genotype information is used to help identify patterns of importation and transmission. For example, analysis by CDC scientists showed that the measles virus type in the 2015 outbreak (B3) was identical to the virus type that caused the large measles outbreak in the Philippines in 2014. Genome sequencing can be used to differentiate between wild-type and vaccine virus infection in suspected cases with a history of recent vaccination.

In populations with high vaccine coverage, such as those in the United States, comprehensive serologic and virologic testing generally is not available locally and requires submitting specimens to state public health laboratories or the CDC. Individuals with a febrile rash illness who are seronegative for measles IgM and have negative RT-PCR assay results for measles should be tested for rubella using the same specimens. All cases of suspected measles should be reported immediately to the local or state health department without waiting for results of diagnostic tests. Measles is on the list of nationally notifiable diseases that should be reported to the CDC within 24 hours.

**TREATMENT:** No specific antiviral therapy is available. Measles virus is susceptible in vitro to ribavirin, which has been given by the intravenous and aerosol routes to treat severely affected and immunocompromised children with measles. However, no controlled trials have been conducted, and ribavirin is not licensed by the US Food and Drug Administration for treatment of measles.

**Vitamin A.** Vitamin A treatment of children with measles in resource-limited countries has been associated with decreased morbidity and mortality rates. Low serum concentrations of vitamin A also have been found in children in the United States, and children with more severe measles illness have lower vitamin A concentrations. The WHO currently recommends vitamin A for all children with acute measles, regardless of their country of residence. Vitamin A for treatment of measles is administered once daily for 2 days, at the following doses:

- 200 000 IU for children 12 months or older;
- 100 000 IU for infants 6 through 11 months of age; and
- 50 000 IU for infants younger than 6 months.
- An additional (ie, a third) age-specific dose should be given 2 through 4 weeks later to children with clinical signs and symptoms of vitamin A deficiency.

Even in countries where measles is not usually severe, vitamin A should be given to all children with severe measles (eg, requiring hospitalization). Parenteral and oral formulations of vitamin A are available in the United States.

**ISOLATION OF THE HOSPITALIZED PATIENT:** In addition to standard precautions, airborne transmission precautions are indicated for 4 days after the onset of rash in otherwise healthy children and for the duration of illness in immunocompromised patients. Exposed susceptible patients should be placed on airborne precautions from day 5 after first exposure until day 21 after last exposure.<sup>1</sup>

**CONTROL MEASURES:**

**Evidence of Immunity to Measles.**<sup>2</sup> Evidence of immunity to measles includes any of the following:

1. Documentation of age-appropriate vaccination with a live measles virus-containing vaccine:
  - ◆ preschool-aged children: 1 dose administered after the first birthday;
  - ◆ school-aged children (grades K-12): 2 doses; the first dose administered after the first birthday and the second dose administered at least 28 days after the first dose;
2. Laboratory evidence of immunity;
3. Laboratory confirmation of disease; or
4. Born before 1957.

**Care of Exposed People.**

**Use of Vaccine.** Available data suggest that measles vaccine, if administered within 72 hours of measles exposure to susceptible individuals, will provide protection or disease modification in some cases. Measles vaccine should be considered in all exposed individuals who are vaccine eligible and who have not been vaccinated or have received only 1 dose of vaccine (the second measles vaccine dose can be administered  $\geq 28$  days after the first measles vaccine dose). If the exposure does not result in infection, the vaccine should induce protection against subsequent measles exposures. Immunization is the intervention of choice for control of measles outbreaks in schools and child care centers and for vaccine-eligible people 12 months and older and has been used starting at 6 months of age with good efficacy in previous measles epidemics in the United States.

**Use of Immune Globulin.** Immune Globulin (IG) can be administered either intramuscularly (IGIM) or intravenously (IGIV) within 6 days of exposure to prevent or modify measles in people who do not have evidence of measles immunity. The recommended dose of IGIM is 0.50 mL/kg (the maximum dose by volume is 15 mL). IGIV is the recommended IG preparation for pregnant women without evidence of measles immunity and

<sup>1</sup>Centers for Disease Control and Prevention. Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2011;60(RR-7):1–45

<sup>2</sup>Centers for Disease Control and Prevention. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013 summary: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-4):1–34

for severely immunocompromised hosts,<sup>1</sup> regardless of immunologic or vaccination status, including patients with severe primary immunodeficiency; patients who have received a bone marrow transplant, until at least 12 months after finishing all immunosuppressive treatment, or longer in patients who have developed graft-versus-host disease; patients on treatment for acute lymphoblastic leukemia, within and until at least 6 months after completion of immunosuppressive chemotherapy; individuals who have received a solid organ transplant; people with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS) who have severe immunosuppression; and patients younger than 12 months whose mothers received biologic response modifiers during pregnancy. IGIV is recommended for these groups because they may be at higher risk of severe measles and complications, and people who weigh >30 kg will receive less than the recommended dose with IGIM preparations. IGIV is administered at a dose of 400 mg/kg. For patients who already are receiving IGIV at regularly scheduled intervals, the usual dose of 400 mg/kg should be adequate for measles prophylaxis after exposures occurring within 3 weeks of receiving IGIV. For people routinely receiving Immune Globulin Subcutaneous (IGSC) therapy, administration of at least 200 mg/kg for 2 consecutive weeks before measles exposure should be sufficient. IG is not indicated for household or other close contacts who have received 1 dose of vaccine at 12 months or older unless they are severely immunocompromised (as defined previously).

For children who receive IGIM for modification or prevention of measles after exposure, measles vaccine (if not contraindicated) should be administered 6 months after IGIM administration, provided the child is at least 12 months of age. Intervals vary between administration of IGIV or other biologic products and measles-containing vaccines (see Table 1.13, p 40).

**HIV Infection.**<sup>1</sup> HIV-infected children who are exposed to measles require prophylaxis on the basis of immune status and measles vaccine history. HIV-infected children who have serologic evidence of immunity or who received 2 doses of measles vaccine after initiation of combination antiretroviral therapy (cART) with no or moderate immunosuppression (see Human Immunodeficiency Virus Infection, p 459) should be considered immune and will not require any additional measures to prevent measles. Asymptomatic mildly or moderately immunocompromised HIV-infected patients without evidence of immunity to measles should receive IGIM at a dose of 0.5 mL/kg (maximum 15 mL), regardless of immunization status. Severely immunocompromised patients (including HIV-infected people with CD4+ T-lymphocyte percentages <15% [all ages] or CD4+ T-lymphocyte counts <200/mm<sup>3</sup> [age >5 years] and those who have not received MMR vaccine since receiving cART) who are exposed to measles should receive IGIV prophylaxis, 400 mg/kg, after exposure to measles regardless of vaccination status, because they may not be protected by the vaccine. Some experts would include all HIV-infected people, regardless of immunologic status or MMR vaccine history, as needing IGIV prophylaxis. HIV-infected children who have received IGIV within 3 weeks of exposure do not require additional passive immunization.

**Health Care Personnel.** To decrease health care-associated infection, immunization programs should be established to ensure that all people who work or volunteer in health

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<sup>1</sup>Centers for Disease Control and Prevention. Prevention of measles, rubella, congenital rubella syndrome, and mumps, 2013 summary: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2013;62(RR-4):1–34

**Table 3.39. Recommendations for Measles Immunization<sup>a</sup>**

Category	Recommendations
Unimmunized, no history of measles (12 through 15 mo of age)	MMR or MMRV vaccine is recommended at 12 through 15 mo of age; a second dose is recommended at least 28 days after the first dose (or 90 days for MMRV) and usually is administered at 4 through 6 y of age
Children 6 through 11 mo of age in epidemic situations <sup>b</sup> or before international travel	Immunize with MMR vaccine, but this dose is not considered valid, and 2 valid doses administered on or after the first birthday are required. The first valid dose should be administered at 12 through 15 mo of age; the second valid dose is recommended at least 28 days later and usually is administered at 4 through 6 y of age. MMRV should not be administered to children <12 mo of age.
Students in kindergarten, elementary, middle, and high school who have received 1 dose of measles vaccine at 12 mo of age or older	Administer the second dose
Students in college and other postsecondary institutions who have received 1 dose of measles vaccine at 12 mo of age or older	Administer the second dose
History of immunization before the first birthday	Dose not considered valid; immunize (2 doses)
History of receipt of inactivated measles vaccine or unknown type of vaccine, 1963–1967	Dose not considered valid; immunize (2 doses)
Further attenuated or unknown vaccine administered with IG	Dose not considered valid; immunize (2 doses)
Allergy to eggs	Immunize; no reactions likely (see text for details)
Neomycin allergy, nonanaphylactic	Immunize; no reactions likely (see text for details)
Severe hypersensitivity (anaphylaxis) to neomycin or gelatin	Avoid immunization
Tuberculosis	Immunize (see Tuberculosis, p 829); if patient has untreated tuberculosis disease, start antituberculosis therapy before immunizing
Measles exposure	Immunize or give IG, depending on circumstances (see Care of Exposed People, p 541)
HIV infected	Immunize (2 doses) unless severely immunocompromised (see text, p 542); administration of IG if exposed to measles is based on degree of immunosuppression and measles vaccine history (see text, p 542)
Personal or family history of seizures	Immunize; advise parents of slightly increased risk of seizures
Immunoglobulin or blood recipient	Immunize at the appropriate interval (see Table 1.13, p 40)

MMR indicates measles-mumps-rubella vaccine; MMRV, measles-mumps-rubella-varicella vaccine; IG, Immune Globulin; HIV, human immunodeficiency virus.

<sup>a</sup>See text for details and recommendations for use of MMRV vaccine.

<sup>b</sup>See Outbreak Control (p 550).

care facilities (including students) have presumptive evidence of immunity to measles (see Immunization in Health Care Personnel, p 97).

**Measles Vaccine Recommendations** (see Table 3.39 for summary).

**Use of MMR Vaccine.** The only measles vaccine licensed in the United States is a live further-attenuated strain prepared in chicken embryo cell culture. Measles vaccines provided through the Expanded Programme on Immunization in resource-limited countries meet the WHO standards and usually are comparable with the vaccine available in the United States. Measles vaccine is available in combination formulations, which include measles-mumps-rubella (MMR) and measles-mumps-rubella-varicella (MMRV) vaccines. Single-antigen measles vaccine no longer is available in the United States. Measles-containing vaccine in a dose of 0.5 mL is administered subcutaneously. Measles-containing vaccines can be administered simultaneously with other immunizations in a separate syringe at a separate site (see Simultaneous Administration of Multiple Vaccines, p 35).

Serum measles antibodies develop in approximately 95% of children immunized at 12 months of age and 98% of children immunized at 15 months of age. Protection conferred by a single dose is durable in most people. A small proportion (5% or less) of immunized people may lose protection after several years. For measles control and elimination, 2 doses of vaccine are required. More than 99% of people who receive 2 doses (separated by at least 28 days, and the first dose administered on or after the first birthday) develop serologic evidence of measles immunity. The second dose provides protection to those failing to respond to their primary measles immunization and, therefore, is not a booster dose. Immunization is not deleterious for people who already are immune. Immunized people do not shed or transmit measles vaccine virus.

Improperly stored vaccine may fail to protect against measles. Since 1979, an improved stabilizer has been added to the vaccine that makes it more resistant to heat inactivation. For recommended storage of MMR and MMRV vaccines, see the manufacturers' package labels. MMRV vaccine must be stored frozen between  $-58^{\circ}\text{F}$  and  $+5^{\circ}\text{F}$ .

**Age of Routine Immunization.** The first dose of MMR vaccine should be administered at 12 through 15 months of age. Delays in administering the first dose contributed to large outbreaks in the United States from 1989 to 1991. The second dose is recommended routinely at school entry (ie, 4 through 6 years of age) but can be administered at any earlier age (eg, during an outbreak or before international travel), provided the interval between the first and second MMR doses is at least 28 days. Catch-up second dose immunization should occur for all school children (elementary, middle, high school) who have received only 1 dose, including at the adolescent visit at 11 through 12 years of age and beyond. If a child receives a dose of measles vaccine before 12 months of age, this dose is not counted toward the required number of doses; the universally recommended 2 doses are still required in the US beginning at 12 through 15 months of age and separated by at least 28 days.

**Use of MMRV Vaccine.**<sup>1,2</sup>

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<sup>1</sup>Centers for Disease Control and Prevention. Use of combination measles, mumps, rubella, and varicella vaccine: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2010;59(RR-3):1-12

<sup>2</sup>American Academy of Pediatrics, Committee on Infectious Diseases. Prevention of varicella: update of recommendations for use of quadrivalent and monovalent varicella vaccines in children. *Pediatrics*. 2011;128(3):630-632



- MMRV vaccine is indicated for simultaneous immunization against measles, mumps, rubella, and varicella among children 12 months through 12 years of age; MMRV vaccine is not indicated for people outside this age group. See *Varicella-Zoster Infections*, p 869, for recommendations for use of MMRV vaccine for the first dose.
- Children with HIV infection also should not receive MMRV vaccine because of lack of safety data of the quadrivalent vaccine in children infected with HIV.
- MMRV vaccine may be administered with other vaccines recommended at 12 through 15 months of age and before or at 4 through 6 years of age ([https://redbook.solutions.aap.org/SS/Immunization\\_Schedules.aspx](https://redbook.solutions.aap.org/SS/Immunization_Schedules.aspx)).
- At least 28 days should elapse between a dose of measles-containing vaccine, such as MMR vaccine, and a dose of MMRV vaccine. However, the recommended minimal interval between MMRV vaccine doses is 90 days.
- Febrile seizures occur in 7 to 9 per 10 000 children receiving the first dose of MMRV vaccine at 12 through 23 months of age and in 3 to 4 per 10 000 children receiving the first dose of MMR and varicella vaccines administered separately at the same visit at 12 through 23 months of age. Thus, 1 additional febrile seizure is expected to occur per approximately 2300 to 2600 children 12 through 23 months of age immunized with a first-dose MMRV vaccine, compared with separate MMR and monovalent varicella vaccines. The period of risk for febrile seizures is from 5 to 12 days following receipt of the vaccine. Febrile seizures do not predispose to epilepsy or neurodevelopmental delays later in life and have no lasting medical consequence. The benefit of using MMRV instead of MMR and monovalent varicella vaccines separately is that the quadrivalent product results in 1 fewer injection. The American Academy of Pediatrics recommends that for the first dose of measles, mumps, rubella, and varicella vaccines at ages 12 through 47 months, either MMR and varicella vaccines or MMRV vaccine be used. Pediatricians should discuss risks and benefits of the vaccine choices with the parents or caregivers. For the first dose of measles, mumps, rubella, and varicella vaccines at ages 48 months and older and for dose 2 at any age (15 months through 12 years), use of MMRV vaccine generally is preferred over separate injections of MMR and varicella vaccines to minimize the number of injections. Children 4 through 6 years of age who received MMRV did not have an increased risk of febrile seizures when compared with children of the same age who received separate injections of MMR and varicella vaccine. However, it might be prudent to administer separate MMR and varicella vaccines to children with a personal or family history of febrile seizures or epilepsy, because the risk of febrile seizures is higher in this group.

*Colleges and Other Institutions for Education Beyond High School.* Colleges and other educational institutions should require that all entering students have documentation of evidence of measles immunity (see *Evidence of Immunity to Measles*, p 541). Students without documentation of measles immunity should receive MMR vaccine on entry, followed by a second dose 28 days later, if not contraindicated.

*Immunization During an Outbreak.* During an outbreak, MMR vaccine should be offered to all people exposed or in the outbreak setting who lack evidence of measles immunity. During a community-wide outbreak that affects infants, MMR vaccine has been shown to be efficacious and may be recommended for infants 6 through 11 months of age (see *Outbreak Control*, p 550). However, because of the presence of maternal antibody in some children, seroconversion rates after MMR immunization are lower in children immunized before the first birthday than in children immunized on or after the first birthday.

For this reason, doses received prior to the first birthday should not count toward the recommended 2-dose series. Children immunized before their first birthday should be reimmunized with MMR or MMRV vaccine at 12 through 15 months of age (at least 28 days after the initial measles immunization) and again at school entry (4 through 6 years of age).

**International Travel.** People traveling internationally (any country outside of the United States) should be immune to measles prior to travel. Infants 6 through 11 months of age should receive 1 dose of MMR vaccine before departure, and then they should receive a second dose of measles-containing vaccine at 12 through 15 months of age (at least 28 days after the initial measles immunization) and a third dose at 4 through 6 years of age. Children 12 through 15 months of age should receive their first dose of MMR vaccine before departure and again by 4 through 6 years of age. Children 12 months or older who have received 1 dose and are traveling to areas where measles is endemic or epidemic should receive their second dose before departure, provided the interval between doses is 28 days or more.

**International Adoptees.** The US Department of State requires that internationally adopted children 10 years and older receive several vaccines, including MMR, before entry into the United States. Internationally adopted children who are younger than 10 years are exempt from Immigration and Nationality Act regulations pertaining to immunization of immigrants before arrival in the United States (see *Children Who Received Immunizations Outside the United States or Whose Immunization Status is Unknown or Uncertain*, p 100); adoptive parents are required to sign a waiver indicating their intention to comply with US immunization recommendations after their child's arrival in the United States.

**Health Care Personnel.**<sup>1</sup> Adequate presumptive evidence of immunity to measles for people who work in health care facilities is: (1) documented administration of 2 doses of live-virus measles vaccine with the first dose administered at  $\geq 12$  months of age and the second dose at least 28 days after the first; (2) laboratory evidence of immunity or laboratory confirmation of disease; or (3) birth before 1957. Birth before 1957 is not a guarantee of measles immunity, and therefore, facilities should consider vaccinating unimmunized personnel born before 1957 who lack laboratory evidence of immunity with 2 doses of MMR vaccine at the appropriate interval (see *Immunization in Health Care Personnel*, p 97). For recommendations during an outbreak, see *Outbreak Control* (p 550).

**Adverse Events.** A body temperature of 39.4°C (103°F) or higher develops in approximately 5% to 15% of vaccine recipients, usually between 6 and 12 days after receipt of MMR vaccine; fever generally lasts 1 to 2 days but may last as long as 5 days. Most people with fever otherwise are asymptomatic. Transient rashes have been reported in approximately 5% of vaccine recipients. Recipients who develop fever and/or rash are not considered contagious. Febrile seizures 5 to 12 days after immunization occur in 1 in 3000 to 4000 people immunized with MMR vaccine. Transient thrombocytopenia occurs in 1 in 22 000 to 40 000 people after administration of measles-containing vaccines, specifically MMR (see *Thrombocytopenia*, p 548). There is no evidence that reimmunization increases the risk of adverse events in people already immune to these diseases. Data indicate that only people who are not immune to the viruses in MMR tend to have adverse

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<sup>1</sup>Centers for Disease Control and Prevention. Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(RR-07):1-45

effects. Thus, events following a second dose of MMR vaccine would be expected to be substantially lower than after a first dose, because most people who received a first dose would be immune.

Rates of most local and systemic adverse events for children immunized with MMRV vaccine are comparable with rates for children immunized with MMR and varicella vaccines administered concomitantly. However, recipients of a first dose of MMRV vaccine have a greater rate of fever 102°F (38.9°C) or higher than do recipients of MMR and varicella administered concomitantly (22% vs 15%, respectively), and measles-like rash is observed in 3% of recipients of MMRV vaccine and 2% of recipients of MMR and varicella vaccines administered concomitantly.

The reported frequency of central nervous system conditions, such as encephalitis and encephalopathy, after measles immunization is less than 1 per million doses administered in the United States. Because the incidence of encephalitis or encephalopathy after measles immunization in the United States is lower than the observed incidence of encephalitis of unknown cause, some or most of the rare reported severe neurologic disorders may be related temporally, rather than causally, to measles immunization. Multiple studies, as well as an Institute of Medicine (now called the National Academy of Medicine) Vaccine Safety Review, refute a causal relationship between autism and MMR vaccine or between inflammatory bowel disease and MMR vaccine. The original 1998 study claiming such a relationship was retracted by the publishing journal in 2010, and the lead author has had his medical license revoked in Great Britain.

**Seizures.** Risk of febrile seizures following receipt of MMR and MMRV vaccines at 12 through 23 months of age is discussed earlier in the chapter (see Use of MMRV Vaccine, p 544). Children with histories of seizures or children whose first-degree relatives have histories of seizures may be at a slightly increased risk of a seizure and should nevertheless be immunized with separate MMR and varicella vaccines, because the benefits of immunization greatly outweigh the risks of a febrile seizure.

**Subacute Sclerosing Panencephalitis.** Measles vaccine, by protecting against measles, decreases significantly the possibility of developing SSPE. Vaccine-strain measles virus has never been confirmed in a case of SSPE.

### **Precautions and Contraindications.**

**Febrile Illnesses.** Children with minor illnesses, such as upper respiratory tract infections, may be immunized. Fever is not a contraindication to immunization. However, if other manifestations suggest a more serious illness, immunization should be deferred until the illness has resolved.

**Allergic Reactions.** Hypersensitivity reactions occur rarely and usually are minor, consisting of wheal-and-flare reactions or urticaria at the injection site. Reactions have been attributed to trace amounts of neomycin or gelatin or some other component in the vaccine formulation. Anaphylaxis is rare. Measles vaccine is produced in chicken embryo cell culture and does not contain significant amounts of egg white (ovalbumin) cross-reacting proteins. Children with egg allergy are at low risk of anaphylactic reactions to measles-containing vaccines (including MMR and MMRV). Skin testing of children for egg allergy is not predictive of reactions to MMR vaccine and is not recommended before administering MMR or other measles-containing vaccines. People with allergies to chickens or feathers are not at increased risk of reaction to the vaccine.

People who have had a significant hypersensitivity reaction after the first dose of measles vaccine should: (1) be tested for measles immunity, and if immune, should not

receive a second dose; or (2) receive evaluation and possible skin testing before receiving a second dose. People who have had an immediate anaphylactic reaction to previous measles immunization should not be reimmunized but should be tested to determine whether they are immune.

People who have experienced anaphylactic reactions to gelatin or topically or systemically administered neomycin should receive measles vaccine only in settings where such reactions can be managed and after consultation with an allergist or immunologist. Most often, however, neomycin allergy manifests as contact dermatitis, which is not a contraindication to receiving measles vaccine.

**Thrombocytopenia.** Rarely, MMR vaccine can be associated with thrombocytopenia within 2 months of immunization, with a temporal clustering 2 to 3 weeks after immunization. On the basis of case reports, the risk of vaccine-associated thrombocytopenia may be higher for people who previously experienced thrombocytopenia, especially if it occurred in temporal association with earlier MMR immunization. The decision to immunize these children should be based on assessment of immunity after the first dose and the benefits of protection against measles, mumps, and rubella in comparison with the risks of recurrence of thrombocytopenia after immunization. The risk of thrombocytopenia is higher after the first dose of vaccine than after the second dose. There have been no reported cases of thrombocytopenia associated with receipt of MMR vaccine that have resulted in hemorrhagic complications or death in otherwise healthy people.

**Recent Administration of IG.** IG preparations interfere with the serologic response to measles vaccine for variable periods, depending on the dose of IG administered. Suggested intervals between IG or blood-product administration and measles immunization are provided in Table 1.13 (p 40). If vaccine is administered at intervals shorter than those indicated, as may be warranted if the risk of exposure to measles is imminent, the child should be reimmunized at or after the appropriate interval for immunization (and at least 28 days after the earlier immunization) unless serologic testing indicates that measles-specific antibodies were produced.

MMR vaccine should be administered at least 2 weeks before planned administration of IG, blood transfusion, or other blood products because of the theoretical possibility that antibody will neutralize vaccine virus and interfere with successful immunization; if IG must be administered within 14 days after administration of MMR or MMRV, these vaccines should be administered again after the interval specified in Table 1.13 (p 40).

**Tuberculosis.** Tuberculin skin testing is not a prerequisite for measles immunization. Antituberculosis therapy should be initiated before administering MMR vaccine to people with untreated tuberculosis infection or disease. Tuberculin skin testing, if otherwise indicated, can be performed any time before or on the day of immunization. Otherwise, testing should be postponed for 4 to 6 weeks, because measles immunization temporarily may suppress tuberculin skin test reactivity. The effects of measles vaccination on interferon gamma release assay (IGRA) characteristics have not been determined; the same precautions as for tuberculin skin testing should be followed.

**Altered Immunity.** Immunocompromised patients with disorders associated with increased severity of viral infections should not receive live-virus measles vaccine (the exception is people with HIV infection, unless they have evidence of severe immunosuppression; see Immunization and Other Considerations in Immunocompromised Children, p 72, and HIV Infection, below). The risk of exposure to measles for immunocompromised patients can be decreased by immunizing their close susceptible contacts.

Immunized people do not shed or transmit infectious measles vaccine virus. Management of immunodeficient and immunosuppressed patients exposed to measles can be facilitated by previous knowledge of their immune status. If possible, children should receive measles vaccine before initiating treatment with biological response modifiers, such as tumor necrosis factor antagonists, and before transplantation, ideally with 2 doses. Susceptible patients who are immunocompromised should receive IG after measles exposure (see Care of Exposed People, p 541).

**Corticosteroids.** For patients who have received high doses of corticosteroids ( $\geq 2$  mg/kg of body weight or  $\geq 20$  mg/day of prednisone or its equivalent for people who weigh  $\geq 10$  kg) for 14 days or more and who otherwise are not immunocompromised, the recommended interval between stopping the corticosteroids and immunization is at least 4 weeks (see Immunization and Other Considerations in Immunocompromised Children, p 72). In general, inhaled steroids do not cause immunosuppression and are not a contraindication to measles immunization.

**HIV Infection.**<sup>1</sup> Measles immunization (administered as MMR vaccine) is recommended for all people  $\geq 12$  months of age with HIV infection who do not have evidence of measles immunity and who do not have evidence of severe immunosuppression, because measles can be severe and often is fatal in patients with HIV infection (see Human Immunodeficiency Virus Infection, p 459). For vaccination purposes, severe immunosuppression is defined in children 1 through 13 years of age as a CD4+ T-lymphocyte percentage  $< 15\%$  and in adolescents  $\geq 14$  years as a CD4+ T-lymphocyte count  $< 200$  lymphocytes/mm<sup>3</sup>. Severely immunocompromised HIV-infected infants, children, adolescents, and young adults should not receive measles virus-containing vaccine, because vaccine-related pneumonia has been reported (see Human Immunodeficiency Virus Infection, p 459). The quadrivalent measles-mumps-rubella-varicella (MMRV) vaccine should not be administered to any HIV-infected infant, regardless of degree of immunosuppression, because of lack of safety data in this population. The first dose of MMR vaccine should be administered at age 12 through 15 months and the second dose at age 4 through 6 years, or as early as 28 days after the first dose. Children, adolescents, and adults with newly diagnosed HIV infections and without evidence of measles immunity should complete a 2-dose schedule with MMR vaccine as soon as possible after diagnosis, unless they have evidence of severe immunosuppression. People with perinatally acquired HIV infection who were vaccinated against measles before initiation of cART should be considered unvaccinated and should be revaccinated with 2 doses of MMR vaccine once effective cART has been administered, unless they have other acceptable current evidence of measles immunity. All members of the household of an HIV-infected person should receive 2 doses of MMR unless they are HIV infected and severely immunosuppressed, were born before 1957, have laboratory evidence of measles immunity, have had age-appropriate immunizations, or have a contraindication to measles vaccine. Because measles vaccine virus is not shed after immunization, HIV-infected people are not at risk of measles vaccine virus infection if household members are immunized.

**Personal or Family History of Seizures.** Children with a personal or family history of seizures should be immunized after parents or guardians are advised that the risk of seizures after measles immunization is increased slightly. Risk of febrile seizures following receipt of

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<sup>1</sup>Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis*. 2014;58(3):309–318

MMR and MMRV vaccine at 12 through 23 months of age is discussed earlier in the chapter (see Use of MMRV Vaccine, p 544). Children receiving anticonvulsants should continue such therapy after measles immunization.

**Pregnancy.** A measles-containing vaccine should not be administered to women known to be pregnant. Women who receive MMR vaccine should not become pregnant for at least 28 days. This precaution is based on the theoretical risk of fetal infection, which applies to administration of any live-virus vaccine to women who might be pregnant or who might become pregnant shortly after immunization. No data from women who were inadvertently vaccinated while pregnant substantiate this theoretical risk. When immunizing adolescents and young adults against measles, recommended precautions include asking women if they are pregnant, excluding women who are, and explaining the theoretical risks to others.

**Outbreak Control.** Every suspected measles case should be reported immediately to the local health department, and every effort must be made to obtain laboratory evidence that would confirm that the illness is measles (including obtaining specimens for virus detection), especially if the illness may be the first case in the community. Subsequent prevention of spread of measles depends on prompt immunization of people at risk of exposure or people already exposed who cannot readily provide documentation of measles immunity, including the date of immunization. People who have not been immunized, including those who have been exempted from measles immunization for medical reasons, should be excluded from school, child care, and health care settings until at least 21 days after the onset of rash in the last case of measles. Extra doses of measles vaccine administered to previously immunized people are not associated with an increased risk of reactions.

**Schools and Child Care Facilities.** During measles outbreaks in child care facilities, schools, and colleges and other institutions of higher education, all students, their siblings, and personnel born in 1957 or after who cannot provide documentation that they received 2 doses of measles-containing vaccine on or after their first birthday or other evidence of measles immunity should be immunized. People receiving their second dose, as well as unimmunized people receiving their first dose as part of the outbreak-control program, may be readmitted immediately to the school or child care facility.

**Health Care Facilities.** If an outbreak occurs in an area served by a hospital or within a hospital, all employees and volunteers who cannot provide documentation that they have received 2 doses of measles vaccine, with the first dose administered on or after their first birthday, or laboratory evidence of immunity to measles should receive 2 doses of MMR vaccine. Because some health care personnel born before 1957 have acquired measles in health care facilities, immunization with 2 doses of MMR vaccine is recommended for health care personnel without serologic evidence of immunity in this age category during outbreaks. Serologic testing before immunization is not recommended during an outbreak, because rapid immunization is required to halt disease transmission. Health care personnel without evidence of immunity who have been exposed should be relieved of direct patient contact from the fifth to the 21<sup>st</sup> day after exposure, regardless of whether they received vaccine or IG after the exposure. Health care personnel who become ill should be relieved of patient contact until 4 days after rash develops.