

Measles

2 contact hours - \$18.00

Course Expires: March 1, 2011

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Course Objectives

When you finish this course, you will be able to:

- Describe the clinical features and medical management of measles.
- Outline the epidemiological features of measles including occurrence, transmission, and communicability.
- Describe current trends in the classification and prevention of measles.
- Discuss the characteristics and efficacy of the measles vaccine.
- Outline the scheduling and use of the measles vaccine in children and adults.
- Discuss adverse reactions associated with measles vaccination.
- Describe contraindications and precautions to measles vaccination.

Introduction

Measles is an acute, highly contagious 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 dreaded than smallpox.”

In 1846, Peter Panum described the incubation period of measles and lifelong immunity after recovery from the disease. Enders and Peebles isolated the virus in human and monkey kidney tissue culture in 1954. The first live attenuated vaccine was licensed for use in the United States in 1963 (Edmonston B strain).

Before a vaccine was available, infection with measles virus was nearly universal during childhood, and more than 90% of persons were immune by age 15 years. Measles is still a common and often fatal disease in developing countries. The World Health Organization estimates there were more than 30 million cases and 454,000 deaths from measles in 2004.

Measles Virus

The measles virus is a paramyxovirus, genus Morbillivirus. It is 100 to 200 nm in diameter, with a core of single-stranded 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 adsorption of virus to cells.

There is only one **antigenic** (antibody stimulating) type of measles virus. Although studies have documented changes in the H glycoprotein, these changes do not appear to be epidemiologically important (that is, no change in vaccine efficacy has been observed). Measles virus is rapidly inactivated by heat, light, acidic pH, ether, and trypsin. It has a short survival time (less than 2 hours) in the air or on objects and surfaces.

Pathogenesis

Measles is a systemic infection. The primary site of infection is the respiratory epithelium of the nasopharynx. Two to three days after invasion and replication in the respiratory epithelium and regional lymph nodes, a primary viremia occurs with subsequent infection of the reticuloendothelial system (microphages that are widely distributed in the body, for example, in the spleen, lymph nodes, and reticular connective tissue as part of the body's defenses).

Following further viral replication in regional and distal reticuloendothelial sites, a second viremia occurs 5 to 7 days after initial infection. During this viremia, there may be infection of the respiratory tract and other organs. Measles virus is shed from the nasopharynx beginning with the prodrome until 3 to 4 days after rash onset.

Measles Pathogenesis

- Respiratory transmission of virus
- Replication in nasopharynx and regional lymph nodes
- Primary viremia 2 to 3 days after exposure
- Secondary viremia 5 to 7 days after exposure with spread to tissues

Clinical Features

The **incubation** period of measles, from exposure to prodrome averages 10 to 12 days. From exposure to rash onset averages 14 days (range, 7 to 18 days). The **prodrome** lasts 2 to 4 days (range 1 to 7 days). It is characterized by fever, which increases in stepwise fashion, often peaking as high as 103°F to 105°F. This is followed by the onset of cough, coryza (runny nose), or conjunctivitis.

Koplik spots, a rash (enanthem) present on mucous membranes, is considered to be **pathognomonic** (a sign or symptom that is so characteristic of a disease that it makes the diagnosis) for measles. It occurs 1 to 2 days before the rash to 1 to 2 days after the rash, and appears as punctate blue-white spots on the bright red background of the **buccal mucosa** (mucous membrane of the inside of the cheek).



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CDC Public Health Image Library/Dr. Heinz F. Eichenwald

The measles rash is a maculopapular eruption that usually lasts 5 to 6 days. It begins at the hairline, and 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 discrete, but may become confluent, particularly on the upper body. Initially, lesions blanch with fingertip pressure.



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By 3 to 4 days, most do not blanch with pressure. Fine desquamation occurs over more severely involved areas. The rash fades in the same order that it appears, from head to extremities. Other symptoms of measles include anorexia, diarrhea, especially in infants, and generalized lymphadenopathy.

Complications

Approximately 30% of reported measles cases have one or more complications. Complications of measles are more common among children younger than 5 years of age and adults 20 years of age and older.

From 1985 through 1992, diarrhea was reported in 8% of measles cases, making this the most commonly reported complication of measles. Otitis media was reported in 7% of cases and occurs almost exclusively in children. Pneumonia (in 6% of reported cases) may be viral or superimposed bacterial, and is the most common cause of death.

Acute encephalitis occurs in approximately 0.1% of reported cases. Onset generally occurs 6 days after rash onset (range 1 to 15 days) and is characterized by fever, headache, vomiting, stiff neck, meningeal irritation, drowsiness, convulsions, and coma. Cerebrospinal fluid shows pleocytosis and elevated protein. The case-fatality rate is approximately 15%. Some form of

residual neurologic damage occurs in as many as 25% of cases. Seizures (with or without fever) are reported in 0.6% to 0.7% of cases.

Death from measles was reported in approximately 0.2% of the cases in the United States from 1985 through 1992. As with other complications of measles, the risk of death is higher among young children and adults. Pneumonia accounts for about 60% of deaths. The most common causes of death are pneumonia in children and acute encephalitis in adults.

Subacute sclerosing panencephalitis (SSPE) is a rare degenerative central nervous system disease believed to be due to persistent measles virus infection of the brain. Onset occurs an average of 7 years after measles (range 1 month to 27 years), and occurs in five to ten cases per million reported measles cases. The onset is insidious, with progressive deterioration of behavior and intellect, followed by ataxia (awkwardness), myoclonic seizures, and eventually death. SSPE has been extremely rare since the early 1980s.

Measles illness during pregnancy results in a higher risk of premature labor, spontaneous abortion, and low-birthweight infants. Birth defects (with no definable pattern of malformation) have been reported rarely, without confirmation that measles was the cause.

Atypical measles occurs only in persons who received inactivated ("killed") measles vaccine (KMV) and are subsequently exposed to wild-type measles virus. An estimated 600,000 to 900,000 persons received KMV in the United States from 1963 to 1967. KMV sensitizes the recipient to measles virus antigens without providing protection.

Subsequent infection with measles virus leads to signs of hypersensitivity polyserositis. The illness is characterized by fever, pneumonia, pleural effusions, and edema. The rash is usually maculopapular or petechial, but may have urticarial, purpuric, or vesicular components. It appears first on the wrists or ankles. Atypical measles may be prevented by revaccinating with live measles vaccine. Moderate to severe local reactions with or without fever may follow vaccination; these reactions are less severe than with infection with wild measles virus.

Modified measles occurs primarily in patients who received immune globulin (IG) as postexposure prophylaxis and in young infants who have some residual maternal antibody. It is usually characterized by a prolonged incubation period, mild prodrome, and sparse, discrete rash of short duration. Similar mild illness has been reported among previously vaccinated persons.

Rarely reported in the United States, hemorrhagic measles is characterized by high fever (105° to 106°F), seizures, delirium, respiratory distress, and hemorrhage into the skin and mucous membranes. Measles in an immunocompromised person may be severe with a prolonged course. It is reported almost exclusively in persons with T-cell deficiencies (certain leukemias, lymphomas, and AIDS). It may occur without the typical rash, and a patient may shed virus for several weeks after the acute illness.

Measles in developing countries has resulted in high attack rates among children younger than 12 months of age. Measles is more severe in malnourished children, particularly those with vitamin A deficiency. Complications include diarrhea, dehydration, stomatitis, inability to feed, and bacterial infections (skin and elsewhere). The case-fatality rate may be as high as 25%. Measles is also a leading cause of blindness in African children.

Laboratory Diagnosis

Isolation of measles virus is not recommended as a routine method to diagnose measles. However, virus isolates are extremely important for molecular epidemiologic surveillance to help determine the geographic origin of the virus and the viral strains circulating in the United States.

Measles virus can be isolated from urine, nasopharyngeal aspirates, heparinized blood, or throat swabs. Specimens for virus culture should be obtained from every person with a clinically suspected case of measles and should be shipped to the state public health laboratory or CDC, at the direction of the state health department. Clinical specimens for viral isolation should be collected at the same time as samples taken for serologic testing.

Because the virus is more likely to be isolated when the specimens are collected within 3 days of rash onset, collection of specimens for virus isolation should not be delayed until serologic confirmation is obtained. Clinical specimens should be obtained within 7 days, and not more than 10 days, after rash onset. A detailed protocol for collection of specimens for viral isolation is available on the CDC website at http://www.cdc.gov/ncidod/dvrd/revb/measles/viral_isolation.htm.

Serologic testing, most commonly by enzyme-linked immunoassay (ELISA or EIA), is widely available and may be diagnostic if done at the appropriate time. Generally, a previously susceptible person exposed to either vaccine or wild-type measles virus will first mount an IgM response and then an IgG response. The IgM response will be transient (1 to 2 months), and the IgG response should persist for many years. Uninfected persons should be IgM negative and will be either IgG negative or IgG positive, depending upon their previous infection history.

ELISA for IgM antibody requires only a single serum specimen and is diagnostic if positive. The preferred reference test is a capture IgM test developed by CDC. This test should be used to confirm every case of measles that is reported to have some other type of laboratory confirmation.

IgM capture tests for measles are often positive on the day of rash onset. However, in the first 72 hours after rash onset, up to 20% of tests for IgM may give false-negative results. Tests that are negative in the first 72 hours after rash onset should be repeated. IgM is detectable for at least 28 days after rash onset and frequently longer.

A variety of tests for IgG antibodies to measles are available and include ELISA, hemagglutination inhibition (HI), indirect fluorescent antibody tests, microneutralization, and plaque reduction neutralization. Complement fixation, while widely used in the past, is no longer recommended.

IgG testing for acute measles requires demonstration of a rise in titer of antibody against measles virus, so two serum specimens are always required. The first specimen should be drawn as soon after rash onset as possible. The second specimen should be drawn 10 to 30 days later. The tests for IgG antibody should be conducted on both specimens at the same time. The same type of test should be used on both specimens. The specific criteria for documenting an increase in titer depend on the test.

Tests for IgG antibody require two serum specimens, and a confirmed diagnosis cannot be made until the second specimen is obtained. As a result, IgM tests are generally preferred to confirm the diagnosis of measles.

Epidemiology

Measles occurs throughout the world. However, interruption of indigenous transmission of measles has been achieved in the United States and other parts of the Western Hemisphere.

The number of reported measles cases in the United States has declined from 763,094 in 1958 to fewer than 150 cases reported per year since 1997. From January 1 to April 25, 2008, a total of 64 confirmed measles cases were preliminarily reported to CDC, the most reported by this date for any year since 2001. Of the 64 cases, 54 were associated with importation of measles from other countries into the United States, and 63 of the 64 patients were unvaccinated or had unknown or undocumented vaccination status. Because these cases resulted from importations and occurred almost exclusively in unvaccinated persons, the findings underscore the ongoing risk for measles among unvaccinated persons and the importance of maintaining high levels of vaccination (MMWR, 2008).

Reservoir

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

Transmission

Measles transmission is primarily person to person via large respiratory droplets. Airborne transmission via aerosolized droplet nuclei has been documented in closed areas (e.g., office examination room) for up to 2 hours after a person with measles occupied the area.

Temporal Pattern

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

Communicability

Measles is highly communicable, with greater than 90% secondary attack rates among susceptible persons. Measles may be transmitted from 4 days before to 4 days after rash onset. Maximum communicability occurs from onset of prodrome through the first 3 to 4 days of rash.

Trends in the United States

Before 1963, approximately 500,000 cases and 500 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, and more than 90% had measles by age 15. The highest incidence was among 5 to 9-year-olds, who generally accounted for more than 50% of reported cases.

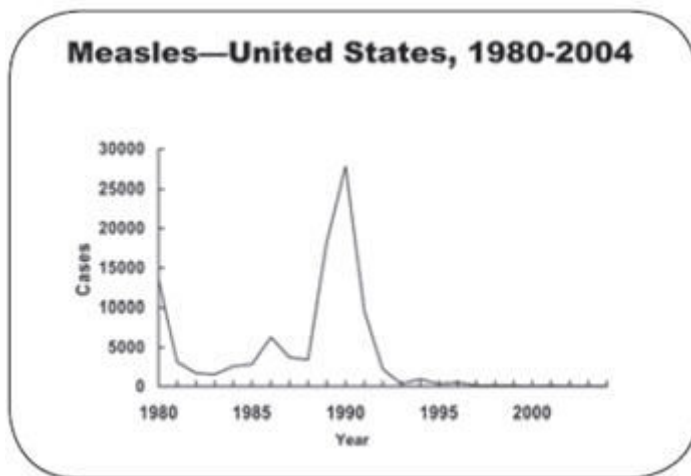


Image from CDC Pink Book

Following licensure of vaccine in 1963, the incidence of measles decreased by more than 98%, and 2 to 3-year epidemic cycles no longer occurred. Because of this success, a 1978 Measles Elimination Program set a goal to eliminate indigenous measles by October 1, 1982 (26,871 cases were reported in 1978). The 1982 elimination goal was not met, but in 1983, only 1,497 cases were reported (0.6 cases per 100,000 population), the lowest annual total ever reported up to that time.

During 1980 to 1988, a median of 57% of reported cases were among school-aged persons (5 to 19 years of age), and a median of 29% were among children younger than 5 years of age. A median of 8% of cases were among infants younger than 1 year of age.

From 1985 through 1988, 42% of cases occurred in persons who were vaccinated on or after their first birthday. During these years, 68% of cases in school-aged children (5 to 19 years) occurred among those who had been appropriately vaccinated. The occurrence of measles among previously vaccinated children (i.e., vaccine failure) led to the recommendation for a second dose in this age group.

Measles Resurgence from 1989 to 1991

From 1989 through 1991, a dramatic increase in cases occurred. During these 3 years a total of 55,622 cases were reported (18,193 in 1989; 27,786 in 1990; 9,643 in 1991). In addition to the increased number of cases, a change occurred in their age distribution. Prior to the resurgence, school-aged children had accounted for the largest proportion of reported cases. During the resurgence, 45% of all reported cases were in children younger than 5 years of age. In 1990, 48% of patients were in this age group, the first time that the proportion of cases in children younger than 5 years of age exceeded the proportion of cases in 5 to 19-year-olds (35%).

Overall incidence rates were highest for Hispanics and blacks and lowest for non-Hispanic whites. Among children younger than 5 years of age, the incidence of measles among blacks and Hispanics was four to seven times higher than among non-Hispanic whites. A total of 123 measles-associated deaths were reported (death-to-case ratio of 2.2 per 1,000 cases). Forty-nine percent of deaths were among children younger than 5 years of age. Ninety percent of fatal cases occurred among persons with no history of vaccination. Sixty-four deaths were reported in 1990, the largest annual number of deaths from measles since 1971.

The most important cause of the measles resurgence of 1989 to 1991 was low vaccination coverage. Measles vaccine coverage was low in many cities, including some that experienced large outbreaks among preschool-aged children throughout the early to mid-1980s. Surveys in areas experiencing outbreaks among preschool-aged children indicated that as few as 50% of children had been vaccinated against measles by their second birthday, and that black and Hispanic children were less likely to be age-appropriately vaccinated than were white children.

In addition, measles susceptibility of infants younger than 1 year of age may have increased. During the 1989 to 1991 measles resurgence, incidence rates for infants were more than twice as high as those in any other age group. The mothers of many infants who developed measles were young, and their measles immunity was most often due to vaccination rather than infection with wild virus. As a result, a smaller amount of antibody was transferred across the placenta to the fetus, compared with antibody transfer from mothers who had higher antibody titers resulting from wild-virus infection. The lower quantity of antibody resulted in immunity that waned more rapidly, making infants susceptible at a younger age than in the past.

The increase in measles in 1989 to 1991 was not limited to the United States. Large outbreaks of measles were reported by many other countries of North and Central America, including Canada, El Salvador, Guatemala, Honduras, Jamaica, Mexico, and Nicaragua.

Measles Since 1993

Reported cases of measles declined rapidly after the 1989 to 1991 resurgence. This decline was due primarily to intensive efforts to vaccinate preschool-aged children. Measles vaccination levels among 2-year-old children increased from 70% in 1990 to 91% in 1997. Since 1993, fewer than 500 cases have been reported annually, and fewer than 200 cases per year have been reported since 1997. A record low annual total of 37 cases was reported in 2004.

Available epidemiologic and virologic data indicate that measles transmission in the United States has been interrupted. The majority of cases are now imported from other countries or linked to imported cases. Most imported cases originate in Asia and Europe and occur both among U.S. citizens traveling abroad and persons visiting the United States from other countries. An aggressive measles vaccination program by the Pan American Health Organization has resulted in measles incidence now being very low in Latin America and the Caribbean. Measles elimination from the Americas appears to be an achievable goal.

Since the mid-1990s, no age group has predominated among reported cases of measles. Relative to earlier decades, an increased proportion of cases now occur among adults. In 1973, persons 20 years of age and older accounted for only about 3% of cases. In 1994, adults accounted for 24% of cases, and in 2001, for 48% of all reported cases.

The size and makeup of measles outbreaks has changed since the 1980s. Prior to 1989, the majority of outbreaks occurred among middle, high school and college student populations. As many as 95% of persons infected during these outbreaks had received one prior dose of measles vaccine. A second dose of measles vaccine was recommended for school-aged children in 1989, and 49 states now require two doses of measles vaccine for school-aged children. As a result, measles outbreaks in school settings are now uncommon.

During the measles resurgence of 1989 to 1991, outbreaks among preschool-aged children became more prominent. More than 200 outbreaks were reported during each of these years, several of which included more than 1,000 cases. The largest outbreak involving predominantly unvaccinated preschool-aged children was in metropolitan Los Angeles, California. More than 12,000 measles cases were reported during this outbreak, which continued for almost 5 years (1987 to 1992).

The last large outbreak involving preschool-aged children was reported in 1992. Since 1993, the largest outbreaks of measles have occurred in populations that refuse vaccination for religious or personal belief reasons, including communities in Utah and Nevada and Christian Scientist schools in Missouri and Illinois. Most outbreaks have involved limited spread from measles imported from outside the United States. The largest outbreak in 2000 involved nine persons in New York.

In 2003, a large measles outbreak occurred in the Republic of the Marshall Islands. Between July 13 and November 7, a total of 826 cases had been reported, with 100 measles-related hospitalizations and 3 deaths. The outbreak affected predominantly preschool-aged children (41% of cases); adults 20 years and older accounted for 24% of cases. The measles virus isolated in this outbreak (H1 genotype) has been documented to circulate in East Asia, particularly Japan, China, and Korea. Factors contributing to this outbreak were low population immunity due to inadequate vaccine coverage, absence of recent transmission of measles virus, and high susceptibility among infants. The outbreak was controlled with aggressive case finding and a large vaccination campaign targeting persons 6 months to 40 years of age.

From During January 1 to April 25, 2008, in the 64 preliminary confirmed measles cases patients ranged in age from 5 months to 71 years; 14 patients were aged <12 months, 18 were aged 1 to 4 years, 11 were aged 5 to 19 years, 18 were aged 20 to 49 years, and three were aged >50 years (MMWR, 2008).

Classification of Measles Cases

A suspect case is defined as a febrile illness accompanied by a generalized maculopapular rash. A probable case meets the measles case definition of generalized maculopapular rash lasting 3 days or longer, with fever (101° F [38.3° C] or higher), which is accompanied by cough, coryza, or conjunctivitis and has no or noncontributory serologic or virologic testing and is not epidemiologically linked to a confirmed case.

Measles Clinical Case Definition

- Generalized rash lasting 3 days or longer, **and**
- Temperature 101° F (38.3° C) or higher, **and**
- Cough or coryza or conjunctivitis

A confirmed case meets the case definition and is epidemiologically linked to another confirmed or probable case or is laboratory confirmed. A laboratory-confirmed case does not need to meet the clinical case definition. Only confirmed cases should be reported to CDC, but both confirmed and probable cases should be reported as soon as possible to the local or state health department.

Epidemiologic Classification

An international imported case has its source outside the country, rash onset occurs within 21 days after entering the country, and illness cannot be linked to local transmission. An indigenous case is any case that cannot be proved to be imported. Subclasses of indigenous cases exist; for more information, see CDC Manual for Surveillance of Vaccine-Preventable Diseases (available on the CDC website at: <http://www.cdc.gov/pubs/surv-manual/default.htm>).

Measles Vaccine

Measles virus was first isolated by John Enders in 1954. The first measles vaccines were licensed in 1963. In that year, both a live attenuated vaccine (Edmonston B strain) and an inactivated (“killed”) vaccine were licensed for use in the United States. The inactivated vaccine was withdrawn in 1967 because it did not protect against measles virus infection.

An additional problem with the inactivated measles vaccine was that recipients frequently developed a unique syndrome, atypical measles, if they were infected with wild-type measles virus. 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 vaccine (Schwarz strain) was first introduced in 1965 but also is no longer used in the United States. Another live, further attenuated strain vaccine (Edmonston-Enders strain) was licensed in 1968. These further attenuated vaccines caused fewer reactions than the original Edmonston B vaccine.

Characteristics

The only measles virus vaccine now available in the United States is a live, more attenuated Edmonston-Enders strain (formerly called “Moraten”). The vaccine is available as a single-antigen preparation, combined with rubella vaccine, combined with mumps and rubella vaccines (MMR), or combined with mumps, rubella, and varicella vaccine as MMRV (Proquad). The Advisory Committee on Immunization Practices (ACIP) recommends that MMR be used when any of the individual components is indicated. Use of single-antigen measles vaccine is not recommended.

Measles vaccine is prepared in chick embryo fibroblast tissue culture. MMR and MMRV are supplied as a lyophilized (freeze-dried) powder and are reconstituted with sterile, preservative-free water. The vaccines contain a small amount of human albumin, neomycin, sorbitol, and gelatin.

Immunogenicity and Vaccine Efficacy

Measles vaccine produces an inapparent or mild, non-communicable infection. Measles antibodies develop in approximately 95% of children vaccinated at 12 months of age and 98% of children vaccinated at 15 months of age. Seroconversion rates are similar for single-antigen measles vaccine, MMR, and MMRV.

Approximately 2% to 5% of children who receive only one dose of MMR vaccine fail to respond to it (i.e., primary vaccine failure). MMR vaccine failure may occur because of passive antibody in the vaccine recipient, damaged vaccine, incorrect records, or possibly 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 two 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 secondary vaccine failure (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.

Vaccination Schedule and Use

Two doses of measles vaccine, as combination MMR, separated by at least 4 weeks, are routinely recommended for all children. All persons born during or after 1957 should have documentation of at least one dose of MMR or other evidence of measles immunity. Certain adolescents and adults should receive two doses of MMR.



CDC Image

Courtesy: Marko Kokic, Canadian Red Cross

The first dose of MMR should be given on or after the first birthday. Any dose of measles-containing vaccine given before 12 months of age should not be counted as part of the series. Children vaccinated with measles-containing vaccine before 12 months of age should be revaccinated with two doses of MMR vaccine, the first of which should be administered when the child is at least 12 months of age.

A second dose of MMR is recommended to produce immunity in those who failed to respond to the first dose. The second dose of MMR vaccine should routinely be given at age 4 to 6 years, before a child enters kindergarten or first grade. The recommended visit at age 11 to 12 years can serve as a catch-up opportunity to verify vaccination status and administer MMR vaccine to those children who have not yet received two doses of MMR.

The second dose of MMR may be administered as soon as 1 month (i.e., minimum of 28 days) after the first dose. Children who have already received two doses of MMR vaccine at least 4 weeks apart, with the first dose administered no earlier than the first birthday, do not need an additional dose when they enter school. Children without documentation of adequate vaccination against measles, rubella, and mumps or other acceptable evidence of immunity to these diseases when they enter school should be admitted after receipt of the first dose of MMR. A second dose should be administered as soon as possible, but no less than 4 weeks after the first dose.

Only doses of vaccine with written documentation of the date of receipt should be accepted as valid. Self-reported doses or a parental report of vaccination is not considered adequate documentation. A healthcare worker should not provide an immunization record for a patient unless that healthcare worker has administered the vaccine or has seen a record that documents vaccination. Persons who lack adequate documentation of vaccination or other acceptable evidence of immunity should be vaccinated. Vaccination status and receipt of all vaccinations should be documented in the patient's permanent medical record and in a vaccination record held by the individual.

MMRV is approved by the Food and Drug Administration for children 12 months through 12 years of age (that is, until the 13th birthday). However, ACIP has previously stated a preference for use of combination vaccines when one or more component of the combination is indicated and none of the other components are contraindicated. MMRV should not be administered to persons 13 years of age or older.

Vaccination of Adults

Adults born in 1957 or later who do not have a medical contraindication should receive at least one dose of MMR vaccine unless they have documentation of vaccination with at least one dose of measles-, rubella-, and mumps-containing vaccine or other acceptable evidence of immunity to these three diseases. With the exception of women who might become pregnant and persons who work in medical facilities, birth before 1957 generally can be considered acceptable evidence of immunity to measles, rubella, and mumps.

Certain groups of adults may be at increased risk for exposure to measles and should receive special consideration for vaccination. These include persons attending colleges and other post-high school educational institutions, persons working in medical facilities, and international travelers.

Colleges and other post-high school educational institutions are potential high-risk areas for measles, rubella, and mumps transmission because of large concentrations of susceptible persons. Pre-matriculation vaccination requirements for measles immunity have been shown to significantly decrease the risk of measles outbreaks on college campuses where they are implemented and enforced. Colleges, universities, technical and vocational schools, and other institutions for post-high school education should require documentation of two doses of MMR vaccine or other acceptable evidence of measles, rubella, and mumps immunity before entry.

Students who have no documentation of live measles, rubella, or mumps vaccination or other acceptable evidence of measles, rubella, and mumps immunity at the time of enrollment should be admitted to classes only after receiving the first dose of MMR. A second dose of MMR should be administered no less than 4 weeks (i.e., minimum of 28 days) later. Students with evidence of prior receipt of only one dose of MMR or other measles-containing vaccine on or after their first birthday should receive a second dose of MMR, provided at least 4 weeks have elapsed since their previous dose.

Persons who work in medical facilities are at higher risk for exposure to measles than the general population. Between 1985 and 1991, at least 795 measles cases occurred in adult healthcare workers, including nurses, physicians, laboratory and radiology technicians, clerks, assistants and students.

An overall decline in measles incidence occurred after the 1989 to 1991 measles resurgence, with a total of 36 cases during 1993 to 1996 occurring among persons working in medical facilities. However, in 15 of the 75 measles outbreaks reported during 1993 to 1996, transmission occurred in a medical facility. All persons who work within medical facilities should have evidence of immunity to measles, mumps, and rubella.

Because any healthcare worker who is susceptible to measles or rubella can contract and transmit these diseases, all medical facilities should ensure measles and rubella immunity among those who work within their facilities. A possible exception might be a facility that treats only elderly patients considered at low risk for measles and rubella and their complications.

Adequate vaccination for measles, mumps, and rubella for healthcare workers born during or after 1957 consists of two doses of a live measles-containing vaccine and at least one dose of a live rubella-containing vaccine. Healthcare workers needing a second dose of measles-containing vaccine should be revaccinated at least 4 weeks after their first dose.

Although birth before 1957 is generally considered acceptable evidence of measles, mumps, and rubella immunity, medical facilities should consider recommending a dose of MMR vaccine to unvaccinated workers born before 1957 who do not have a history of prior measles disease or laboratory evidence of measles immunity, and to those without laboratory evidence of rubella immunity.

Serologic screening need not be done before vaccinating for measles and rubella unless the medical facility considers it cost-effective. Serologic testing is appropriate only if tracking systems are used to ensure that tested persons who are identified as susceptible are subsequently vaccinated in a timely manner. Serologic testing for immunity to measles and rubella is not necessary for persons documented to be appropriately vaccinated or who have other acceptable evidence of immunity. If the return and timely vaccination of those screened cannot be assured, serologic testing before vaccination should not be done.

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 two doses of MMR.

Revaccination

Revaccination is recommended for certain persons. The following groups should be considered unvaccinated and should receive at least one dose of measles vaccine:

People who were vaccinated

- Before the first birthday
- With killed measles vaccine (KMV)
- With KMV followed by live vaccine less than 4 months after the last dose of KMV
- Before 1968 with an unknown type of vaccine (the vaccine may have been KMV), **or**
- With IG in addition to a further attenuated strain or vaccine of unknown type.
(Revaccination is not necessary if IG was given with Edmonston B vaccine.)

Postexposure Prophylaxis

Live measles vaccine provides permanent protection and may prevent disease if given within 72 hours of exposure. Immune globulin (IG) may prevent or modify disease and provide temporary protection if given within 6 days of exposure. The dose is 0.25 mL/kg body weight, with a maximum of 15 mL intramuscularly. The recommended dose of IG for immunocompromised persons is 0.5mL/kg of body weight (maximum 15 mL) intramuscularly. IG may be especially indicated for susceptible household contacts of measles patients, particularly contacts younger than 1 year of age (for whom the risk of complications is highest).

If the child is 12 months of age or older, live measles vaccine should be given about 5 months later when the passive measles antibodies have waned. IG should not be used to control measles outbreaks.

Adverse Reactions Following Vaccination

Adverse reactions following measles vaccine (except allergic reactions) represent replication of measles vaccine virus with subsequent mild illness. These events occur 5 to 12 days postvaccination and only in persons who are susceptible to infection. There is no evidence of increased risk of adverse reactions following MMR vaccination in persons who are already immune to the diseases.

Fever is the most common adverse reaction following MMR vaccination. Although measles, rubella, and mumps vaccines may cause fever after vaccination, the measles component of MMR vaccine is most often associated with this adverse reaction. After MMR vaccination, 5% to 15% of susceptible persons develop a temperature of 103oF (39.4oC) or higher, usually occurring 7 to 12 days after vaccination and generally lasting 1 to 2 days. Most persons with fever are otherwise asymptomatic.

Measles- and rubella-containing vaccines, including MMR, may cause a transient rash. Rashes, usually appearing 7 to 10 days after MMR or measles vaccination, have been reported in approximately 5% of vaccinees.

Rarely, MMR vaccine may cause thrombocytopenia (low platelet count) within 2 months after vaccination. Estimates of the frequency of clinically apparent thrombocytopenia from Europe are one case per 30,000 to 40,000 vaccinated susceptible persons, with a temporal clustering of cases occurring 2 to 3 weeks after vaccination. The clinical course of these cases was usually transient and benign, although hemorrhage occurred rarely.

The risk for thrombocytopenia during rubella or measles infection is much greater than the risk after vaccination. Based on case reports, the risk for MMR-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.

Transient lymphadenopathy sometimes occurs following receipt of MMR or other rubella-containing vaccine, and parotitis has been reported rarely following receipt of MMR or other mumps-containing vaccine. Arthralgias and other joint symptoms are reported in up to 25% of susceptible adult women given MMR vaccine. This adverse reaction is associated with the rubella component. Allergic reactions following the administration of MMR or any of its component vaccines are rare. Most of these reactions are minor and consist of a wheal and flare or urticaria at the injection site.

Immediate, anaphylactic reactions to MMR or its component vaccines are extremely rare. Allergic reactions including rash, pruritus, and purpura have been temporally associated with mumps vaccination, but these are uncommon and usually mild and of brief duration. To date there is no convincing evidence that any vaccine causes autism or autism spectrum disorder. Concern has been raised about a possible relation between MMR vaccine and autism by some parents of children with autism. Symptoms of autism are often noticed by parents during the second year of life, and may follow administration of MMR by weeks or months.

Two independent nongovernmental groups, the Institute of Medicine (IOM) and the American Academy of Pediatrics (AAP), have reviewed the evidence regarding a potential link between autism and MMR vaccine. Both groups independently concluded that available evidence does not support an association, and that the United States should continue its current MMR vaccination policy. Additional research on the cause of autism is needed.

Contraindications and Precautions to Vaccination

Persons who have experienced a severe allergic reaction such as hives, swelling of the mouth or throat, difficulty breathing, hypotension, or shock following a prior dose of measles vaccine or to a vaccine component (e.g., gelatin, neomycin), should generally not be vaccinated with MMR.

In the past, persons with a history of anaphylactic reactions following egg ingestion were considered to be at increased risk for serious reactions after receipt of measles- or mumps-containing vaccines, which are produced in chick embryo fibroblasts. However, data suggest that anaphylactic reactions to measles- and mumps-containing vaccines are not associated with hypersensitivity to egg antigens but to other components of the vaccines (such as gelatin).

The risk for serious allergic reactions following receipt of these vaccines by egg-allergic persons is extremely low, and skin-testing with vaccine is not predictive of allergic reaction to vaccination. Therefore, MMR may be administered to egg-allergic children without prior routine skin testing or the use of special protocols.

MMR vaccine does not contain penicillin. A history of penicillin allergy is not a contraindication to vaccination with MMR or any other U.S. vaccine.

Women known to be pregnant should not receive measles vaccine. Pregnancy should be avoided for 4 weeks following MMR vaccine. Close contact with a pregnant woman is not a contraindication to MMR vaccination of the contact. Breastfeeding is not a contraindication to vaccination of either the woman or the breastfeeding child.

Replication of vaccine viruses can be prolonged in persons who are immunosuppressed or immunodeficient. Severe immunosuppression can be due to a variety of conditions, including congenital immunodeficiency, HIV infection, leukemia, lymphoma, generalized malignancy, or therapy with alkylating agents, antimetabolites, radiation, or large doses of corticosteroids. Evidence based on case reports has linked measles vaccine virus infection to subsequent death in at least six severely immunocompromised persons. For this reason, patients who are severely immunocompromised for any reason should not be given MMR vaccine. Healthy susceptible close contacts of severely immunocompromised persons should be vaccinated.

In general, persons receiving large daily doses of corticosteroids (2 mg/kg or more per day, or 20 mg or more per day of prednisone) for 14 days or more should not receive MMR vaccine because of concern about vaccine safety. MMR and its component vaccines should be avoided for at least 1 month after cessation of high-dose therapy.

Persons receiving low-dose or short-course (less than 14 days) therapy, alternate-day treatment, maintenance physiologic doses, or topical, aerosol, intra-articular, bursal, or tendon injections may be vaccinated. Although persons receiving high doses of systemic corticosteroids daily or on alternate days during an interval of less than 14 days generally can receive MMR or its component vaccines immediately after cessation of treatment, some experts prefer waiting until 2 weeks after completion of therapy. Patients with leukemia in remission who have not received chemotherapy for at least 3 months may receive MMR or its component vaccines.

Measles disease may be severe in persons with HIV infection. Available data indicate that vaccination with MMR has not been associated with severe or unusual adverse reactions in HIV-infected persons without evidence of severe immunosuppression, although antibody responses have been variable. MMR vaccine is recommended for all asymptomatic HIV-infected persons and should be considered for symptomatic persons who are not severely immunosuppressed.

Asymptomatic children do not need to be evaluated and tested for HIV infection before MMR or other measles-containing vaccines are administered. A theoretical risk of an increase (probably transient) in HIV viral load following MMR vaccination exists because such an effect has been observed with other vaccines. The clinical significance of such an increase is not known.

MMR and other measles-containing vaccines are 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.

People with moderate or severe acute illness should not be vaccinated until the illness has improved. This precaution is intended to prevent complicating the management of an ill patient with a potential vaccine adverse reaction, such as fever. Minor illnesses (such as otitis media or mild upper respiratory infections), concurrent antibiotic therapy, and exposure to or recovery from other illnesses are not contraindications to measles vaccination.

Receipt of antibody-containing blood products (such as immune globulin, whole blood or packed red blood cells, intravenous immune globulin) may interfere with seroconversion after measles vaccine. The length of time that such passively acquired antibody persists depends on the concentration and quantity of blood product received. For instance, it is recommended that vaccination be delayed for 3 months following receipt of immune globulin for prophylaxis of hepatitis A; a 7 to 11 month delay is recommended following administration of intravenous immune globulin, depending on the dose.

Persons who have a history of thrombocytopenic purpura or thrombocytopenia may be at increased risk for developing clinically significant thrombocytopenia after MMR vaccination. No deaths have been reported as a direct consequence of vaccine-induced thrombocytopenia. The decision to vaccinate with MMR depends on the benefits of immunity to measles, mumps, and rubella and the risks for recurrence or exacerbation of thrombocytopenia after vaccination or during natural infection with measles or rubella.

The benefits of immunization are usually greater than the potential risks, and administration of MMR vaccine is justified because of the even greater risk for thrombocytopenia after measles or rubella disease. However, deferring a subsequent dose of MMR vaccine may be prudent if the previous episode of thrombocytopenia occurred within 6 weeks after the previous dose of the vaccine. Serologic evidence of measles immunity in such persons may be sought in lieu of MMR vaccination.

Tuberculin skin testing (TST) is not a prerequisite for vaccination with MMR or other measles-containing vaccine. TST has no effect on the response to MMR vaccination. However, measles vaccine (and possibly mumps, rubella, and varicella vaccines) may transiently suppress the response to TST in a person infected with *Mycobacterium tuberculosis*.

If tuberculin skin testing is needed at the same time as administration of measles-containing vaccine, TST and vaccine can be administered at the same visit. 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 at least 4 weeks after vaccination. A delay in administering TST will remove the concern of any theoretical suppression of TST reactivity from the vaccine. TST screening can be performed and read before administering the measles-containing vaccine. This option is the least favored because it will delay receipt of the vaccine.

Vaccine Storage and Handling

Measles vaccine and MMR must be shipped with refrigerant to maintain a temperature of 50° F (10°C) or less at all times. Vaccine must be refrigerated immediately on arrival and protected from light at all times. The vaccine must be stored at refrigerator temperature (35° to 46°F [2° to 8°C]), but may be frozen. Diluent may be stored at refrigerator temperature or at room temperature. MMRV must be shipped to maintain a temperature of -4°F (-20°C) or less at all times. MMRV must be stored at an average temperature of 5°F (-15°C) or less at all times.

After reconstitution, measles and MMR vaccines must be stored at refrigerator temperature and protected from light. Reconstituted vaccine should be used immediately. If reconstituted vaccine is not used within 8 hours, it must be discarded. MMRV must be administered within 30 minutes of reconstitution.

References

Centers for Disease Control and Prevention. *Epidemiology and Prevention of Vaccine-Preventable Diseases*. Atkinson W, Hamborsky J, McIntyre L, Wolfe S, eds. 10th ed. 2nd printing, Washington DC: Public Health Foundation, 2008.

Morbidity and Mortality Weekly Report. (2008). Measles—United States, January 1 to April 25, 2008. May 9, 2008/57(18); 494-498. Accessed 9-20-08 from: <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5718a5.htm>.

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Post Test

Circle one answer per question. (Passing grade is 70% or greater.)

1. Infection with measles:
 - a) Is no longer considered a threat to the public health.
 - b) Was nearly universal during childhood before a vaccine was available.
 - c) Rarely results in serious illness or death.
 - d) Does not confer immunity to future infection.
2. The measles virus:
 - a) As not inactivated by heat or light and can live outside the body for several days.
 - b) Has many antigenic types.
 - c) Develops a primary and secondary viremia and infects the respiratory tract and other organs.
 - d) Is no longer preventable with the measles vaccine.
3. Clinical features of measles:
 - a) Include fever up to 105 degrees F., cough, coryza and maculopapular rash.
 - b) A hives-like rash that usually comes and goes for the first 2 days of infection.
 - c) Include Koplik spots that are present on the extremities.
 - d) May include a high fever, cough and coryza that are usually treated with penicillin.
4. Complications of measles infection:
 - a) Are rare and mild, usually involving upper respiratory infection.
 - b) Include acute encephalitis which occurs in 25% of cases.
 - c) Occur most often in the teen years.
 - d) Include pneumonia which is the most common cause of death.
5. Subacute sclerosing panencephalitis:
 - a) Is a rare degenerative central nervous system disease caused by persistent measles infection of the brain.
 - b) Usually occurs within 2 weeks of vaccination with the measles vaccine.
 - c) Rarely causes serious or long-lasting central nervous system symptoms.
 - d) Has an acute onset, usually within a month of measles infection.
6. Measles illness during pregnancy results in a higher risk of premature labor, spontaneous abortion, and low-birthweight infants.
 - a) True
 - b) False
7. Hypersensitivity polyserositis:
 - a) Occurs only in patients who received immune globulin as postexposure prophylaxis and in young infants who have some residual maternal antibody.
 - b) May occur in patients who received live measles vaccine.
 - c) Occurs only in persons who received inactivated measles vaccine and are later exposed to wild-type measles virus.
 - d) May be prevented by revaccinating with inactivated vaccine.

8. Hemorrhagic measles is:
 - a) Becoming epidemic in the United States.
 - b) Characterized by high fever, seizures, respiratory distress and hemorrhage into the skin and mucous membranes.
 - c) Also called modified measles.
 - d) Characterized by a prolonged incubation period, mild prodrome, and sparse, discrete rash of short duration.
9. Measles in developing countries:
 - a) Is rarely seen in children less than 1 year of age.
 - b) May occur without the typical rash.
 - c) Is rarely fatal.
 - d) Is a leading cause of blindness and death in children.
10. Testing for the measles virus:
 - a) Is recommended to diagnose measles.
 - b) Requires only one test for a positive diagnosis.
 - c) Requires 2 serum specimens that demonstrate a rising titer of antibody.
 - d) Should be done within 2 weeks of onset of rash.
11. Measles:
 - a) Is occasionally transmitted through animal carriers.
 - b) May be transmitted through asymptomatic human carriers.
 - c) Is primarily transmitted person to person via large respiratory droplets.
 - d) Can be transmitted up to 1 month after the onset of rash to unimmunized persons.
12. Measles cases in the United States:
 - a) Prior to 1963, occurred in epidemic cycles every 2 to 3 years with approximately 500,000 cases resulting in 500 deaths.
 - b) Decreased by 50% following licensure of vaccine in 1963.
 - c) Were completely eliminated by 1982.
 - d) Have increased to pre 1963 levels due to vaccine failure.
13. The measles resurgence of 1989 to 1991:
 - a) Was seen mostly among 6 to 19 year old children who had previously been vaccinated.
 - b) Saw an increased infection rate in infants younger than 1 year due to lack of antibody transferal from mothers who had never been vaccinated.
 - c) Occurred mostly in non-Hispanic white teens.
 - d) Was caused mostly by low vaccination coverage among black and Hispanic children.
14. Measles in the United States is:
 - a) Now seen primarily in the 60 to 80 year age group due to waning of immunity.
 - b) Seen primarily in school settings.
 - c) Now mostly seen as cases imported from Asia and Europe.
 - d) Mainly imported from South America and Mexico

15. Measles outbreaks since the 1980's:
- Have rarely occurred in the adult population.
 - Have increased in all age groups due to mutation of the virus.
 - Have occurred mostly in those who received one vaccination and those who have refused vaccination.
 - Have not occurred in the United States due to the aggressive campaign to vaccinate all children.
16. All suspected cases of measles should be reported as soon as possible to the local or state health department.
- True
 - False
17. The measles vaccine used today:
- Is the inactivated ("killed") vaccine that has been used since 1963.
 - Has sometimes caused atypical measles when a vaccinated person is exposed to wild-type measles virus.
 - Is a live, more attenuated Edmonston-Enders strain combined with mumps and rubella or mumps, rubella and varicella.
 - Is often used as a single-antigen vaccine.
18. Measles immunity:
- Occurs in more than 99% of persons who receive two doses of measles vaccine and appears to be lifelong.
 - Usually wanes in adults and requires revaccination.
 - Decreases as people age and is a major cause of measles transmission and outbreaks.
 - Generally is not as strong when single-antigen vaccine is used instead of measles, mumps and rubella combined vaccine.
19. Measles vaccination of children:
- Must occur at one month of age and again at 4 to 6 years of age.
 - Must be done at 4 to 6 years of age and again at 12 years of age
 - Cannot be given more than twice even if the vaccination has not been adequately documented.
 - Should be given at 12 months of age and again at 4 to 6 years of age.
20. Adults should be vaccinated if they:
- Were born before 1957.
 - Are entering college, even if they previously received 2 doses of MMR vaccine
 - Travel outside the United States and have not received two doses of MMR vaccine.
 - Are working in a healthcare setting, even if they previously received 2 doses of MMR vaccine.
21. Revaccination is recommended:
- For persons over the age of 50.
 - If there is planned travel outside of the United States.
 - For those vaccinated with the killed measles vaccine (KMV).
 - For children given the MMR vaccine at 1 year and again at 4 to 6 years of age.

22. Adverse reactions to the MMR vaccine:

- a) Frequently include a fever up to 105 degrees that occurs the day following vaccination.
- b) Include autism that is caused by the mumps component of the vaccine.
- c) May include transient thrombocytopenia that is usually benign.
- d) Include arthralgias that are reported in about 50% of adult women who receive the vaccine.

23. Administration of the MMR vaccine is contraindicated:

- a) In a person who is allergic to eggs because the vaccine is produced in chick embryo fibroblasts.
- b) In anyone receiving antibiotic therapy.
- c) If a tuberculin skin test has been given within the last week.
- d) In HIV infected persons with evidence of severe immunosuppression.

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Course Evaluation

Please answer each of the following questions. Questions with an asterisk (*) are required.

* 1. This course met the goals and learning objectives.

Yes No

* 2. The author was well prepared to write about the content in a way that facilitated my learning.

Yes No

* 3. This course was free from commercial bias.

Yes No

* 4. The learning activity met my continuing education needs.

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(If you answer "No", please enter the total time it took to finish the course, test, and evaluation.)

Yes

No. How long did it take to finish the course, test, and evaluation? _____

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