In Brief

Measles

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Author Disclosure

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Measles is a highly contagious disease characterized by cough, coryza, conjunctivitis, fever, a pathognomonic enanthem (Koplik spots), and a generalized maculopapular rash that starts at the hairline and spreads caudally to the feet. The causative agent is a virus of the genus Morbillivirus, family Paramyxoviridae. An ancient disease, described as long ago as the 7th century AD, measles is endemic worldwide. Even today, although totally preventable by vaccination, hundreds of thousands of deaths from measles occur each year. Prior to the introduction of vaccine in 1963, 3 to 4 million cases occurred annually in the United States, with an average of 450 deaths, most from pneumonia. Epidemic cycles occurred every 2 to 3 years, usually from late winter through early spring. By 15 years of age, 90% of children had contracted the disease. Humans are the only natural host, and the virus is transmitted by direct droplet contact or airborne spread. The incubation period from exposure to development of symptoms is usually between 8 and 12 days. Individuals are contagious 1 to 2 days before any symptoms appear and remain contagious until 4 days after the rash appears.

Measles vaccine was licensed in the United States in 1963. Initially, both live-attenuated and killed vaccines were used. However, the killed vaccine provided only partial immunity and was discontinued after 1968. The live-attenuated vaccines used in most countries are descendants from the prototype Edmonston strain. The attenuated virus is grown in cultures of chick embryo fibroblasts stabilized with human albumin, sorbitol, hydrolyzed gelatin, and a small amount of neomycin. The measles component usually is combined with mumps and rubella as MMR, administered as a 0.5-mL subcutaneous injection. Recently, varicella vaccine has been added to the combination. The vaccine is lyophilized and must be stored in a refrigerator or freezer, protected from light. Once reconstituted with sterile diluent, the vaccine remains active for 8 hours, provided it is kept cold and protected from light. The reconstituted solution is yellow and clear.

Fever develops 6 to 12 days after vaccination with MMR in 5% to 15% of recipients, usually lasting a day or so. A transient measleslike rash occurs in about 5% of recipients 7 to 10 days postvaccination. Such reactions occur much less frequently after administration of the second dose. Transient thrombocytopenia is a less common reaction. Autism, encephalitis, and encephalopathy have been related to measles vaccination, but causation has not been established for encephalitis and encephalopathy and has been refuted in autism after extensive study.

Seroconversion rates are between 95% and 98%, with an antibody response first detectable 12 to 15 days after vaccination and peak titers at 21 to 28 days. The antibody response includes immunoglobulin (Ig) M, IgG, IgA, and secretory IgA. Antibody concentrations may decrease and become undetectable with time, but there is a rapid anamnestic response upon reexposure to vaccine. Loss of immunity after initial seroconversion (secondary vaccine failure) is believed to occur in fewer than 0.2% of recipients.

Administration of measles vaccine to children who are allergic to eggs has been a concern. However, a study of children who had a history of severe egg allergies, including anaphylaxis, and received a dose of MMR documented no allergic reaction in any of the children. The risk of anaphylaxis is

very low, and skin testing is not predictive. Rarely, a hypersensitivity reaction occurs, typically consisting of a wheal and flare or urticarial reaction at the injection site. Other components of the vaccine usually are responsible, specifically neomycin or gelatin. Anyone who has a significant hypersensitivity reaction after a dose of measles vaccine should be tested for measles immunity; if found to be immune, that person should not be given a second dose. Another option is to skin test before administering a second dose. The rare patient who has an immediate anaphylactic reaction should not receive a second dose; testing should be performed to document immune status. Patients who have a history of anaphylactic reaction to gelatin or neomycin should not be immunized unless in an appropriate setting after consultation with an allergist/immunologist.

Pregnancy is a contraindication to vaccination with MMR because of the theoretical risk of harm to a fetus from inoculation with a live virus. Adolescent girls should be advised to wait 1 month after vaccination before becoming pregnant.

Children who are immunocompromised may be candidates for measles vaccine. In general, severely immunocompromised children should not receive live viral vaccines. Because natural infection can be fatal, children afflicted with human immunodeficiency virus (HIV) infection may receive measles vaccine based on their CD4 T-lymphocyte status. Their response to vaccination is not uniform, with some children having lower antibody titers, shortened duration of detectable antibodies, or failure to seroconvert. Children severely immunocompromised by HIV should not be immunized against measles because of the risk of vaccine-related pneumonia.

Other considerations before immunization include a prior history of thrombocytopenia, recent administration of immune globulin or blood products, and the recent use of high-dose steroids. Patients who have a history of thrombocytopenia, particularly if it occurred with a previous dose of MMR, are at increased risk for thrombocytopenia from the vaccine. Unless the risk of exposure is imminent, recipients of immune globulin or blood products that may interfere with vaccine should have administration of MMR deferred for an appropriate interval (see the *2006 Red Book*). Patients who have received 2 weeks or more of high-dose steroids (the equivalent of 2 mg/kg per day or 20 mg/day of prednisone, either on a daily or alternate-day schedule) should wait 1 month before receiving MMR vaccine. Those receiving shorter courses of steroids can be immunized after completing treatment.

Fever is a precaution, but not a contraindication to vaccination. Children who have minor illnesses with or without fever (otitis media, upper respiratory tract infections) should be vaccinated. Symptoms indicating moderate or serious illness are a reason for deferral to avoid confusing a manifestation of illness with an adverse reaction to the vaccine.

The implementation of measles vaccination programs in 1966 greatly reduced the number of reported cases. In 1983, 1,500 cases of measles were reported, down from 3 to 4 million cases 1 year prior to the widespread use of vaccine. The recommended age for vaccination was 15 months. However, beginning in 1984, the number of measles cases began to increase again, peaking in 1990 at approximately 28,000 cases, primarily because of unimmunized inner city children younger than age 2 years and susceptible adolescents who had primary vaccine failure. The increase in disease led to recommendations to implement a two-dose schedule and to change the recommended age of immunization.

The current recommendation is to administer the first dose earlier, between 12 and 15 months of age, despite slightly reduced efficacy from the presence of circulating maternal antibodies, and the second dose between 4 and 6 years of age. Any child who has not received two doses of measles vaccine after his or her first birthday should receive a second dose by age 11 to 12 years, but the second dose can be administered at any time, as long as it is 4 weeks after the first dose. The first dose can be administered as early as 12 months of age, which is the recommended age for children in high-risk areas, defined as an inner city area, an area where recent measles outbreaks has occurred in unvaccinated preschoolers, or where there have been more than five cases of measles among preschoolers during each of the last 5 years. The second dose at school entry is designed to capture the 5% of children who experience primary vaccine failure in the hopes of achieving immunity in that group. Almost all vaccine recipients who do not respond to the first dose mount an immune response to the second dose.

Measles no longer is endemic in the United States. In 2000, 86 cases of confirmed measles and in 2004 only 37 cases were reported to the Centers for Disease Control and Prevention, most imported from Southeast Asia by United States residents traveling abroad or by foreign nationals infected before coming to the United States. Very limited local spread occurred despite the exposure of hundreds of people on airline flights. Two United States outbreaks (defined as three or more cases) occurred in 2004 – one among 12- to 18-month-old children adopted from China and the other from an American student infected in India who subsequently infected two contacts. A much larger outbreak occurred in Indiana in 2005. An unvaccinated teenager traveling to perform missionary work contracted measles during a local

outbreak in Romania. She flew back to the United States and attended a church function the next day, exposing approximately 500 people. Subsequently, 34 cases of measles were reported: 32 in individuals who were not vaccinated and 2 in people who did not mount an immune response to vaccination.

Control measures in the event of an outbreak include immunization of susceptible individuals and the use of immune globulin. Isolation alone is insufficient because infected individuals are contagious during the prodromal phase, before disease is apparent. Susceptible individuals are those who lack evidence of immunity to measles. Acceptable evidence of immunity includes: documentation of two doses of MMR after the first birthday, serologic evidence of immunity, documentation of measles diagnosed by a physician, or birth before 1957. MMR given within 72 hours of exposure to measles may provide some protection and is preferred to immune globulin. Monovalent measles vaccine can be given to infants between 6 and 12 months of age and is preferable to MMR, which can be given if monovalent measles vaccine is not available. However, such infants require an additional two doses of measles vaccine at the recommended ages after their first birthdays because of the reduced efficacy of the vaccine when administered before 12 months of age. At least 1 month must elapse between subsequent doses.

Immune globulin, which may modify or prevent measles, is recommended for susceptible household contacts not vaccinated within 72 hours of initial exposure, provided it is given within 6 days of exposure. The usual dose is 0.25 mL/kg, with a maximum of 15 mL. Immunocompromised patients should receive 0.5 mL/kg to a maximum of 15 mL. Infants younger than 6 months of age usually are protected by maternal antibody. However, if the mother has measles, all children in the household not vaccinated after their first birthdays should receive immune globulin if they did not receive measles vaccine within 72 hours of initial exposure. The administration of any subsequent doses of MMR then must be deferred at least 5 to 6 months.

The elimination of endemic measles in the United States is a public health success. Measles now has been eliminated from the Americas through aggressive vaccination and surveillance programs started by the Pan American Sanitary Conference in 1994. However, measles remains endemic in developing countries throughout the rest of the world. The situation is improving, with the number of deaths from measles falling to 454,000 in 2004 from 871,000 in 1999 due to improved immunization efforts and better treatment for those suffering from the illness. Half of the deaths from measles occur in Africa. The United Nations International Children's Emergency Fund and the World Health Organization partnering with other organizations continue to work at eliminating measles. It is hoped that one day, measles will be relegated to the history books.

Comment: Even those of us old enough to have suffered through measles are not necessarily aware of how serious a disease it can be. Worldwide, as many as 1 million children die acutely from measles each year. With natural disease, 1 to 2 per 100,000 children have persistent measles infection that results in subacute sclerosing panencephalitis (SSPE), a degenerative brain disorder marked by insidious cognitive and behavioral deterioration and ending with dementia, blindness, and decortication. Although live measles vaccination carries a risk for SSPE, it is far less than the risk from natural infection – on the order of 1 per million. It would be a great achievement to relegate measles to the history books.

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Editor, In Brief