

## INFORMATION PAPER

DHA-IHB

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SUBJECT: Measles, Mumps, and Rubella (MMR) Infections and the MMR Vaccine

1. Purpose. To describe measles, mumps, and rubella and the vaccines to prevent these infections.

2. Facts.

a. Microbiology.

(1) The measles virus is a paramyxovirus, genus Morbillivirus. It is 100–200 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. Viral replication occurs in the epithelium of the nasopharynx within about 24 hours. There is only one antigenic type of measles virus. 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.

(2) Mumps virus is a paramyxovirus in the same group as parainfluenza and Newcastle disease virus. The virus has a single-stranded RNA genome. The virus can be isolated or propagated in cultures of various human and monkey tissues and in embryonated eggs. It has been recovered from the saliva, cerebrospinal fluid, urine, blood, milk, and infected tissues of patients with mumps. It replicates in the nasopharynx and regional lymph nodes. After 12-15 days, a viremia occurs which lasts from 3 to 5 days. During viremia, the virus spreads to multiple tissues, including the meninges, and glands such as the salivary, pancreas, testes, and ovaries. Mumps virus is rapidly inactivated by formalin, ether, chloroform, heat, and ultraviolet light.

(3) The name rubella is derived from Latin, meaning “little red.” Rubella virus is classified as a togavirus, genus Rubivirus. It is closely related to group A arboviruses, such as those that cause equine encephalitis virus. It is an enveloped RNA virus, with a single antigenic type that does not cross-react with other members of the togavirus group. Replication of the virus occurs in the nasopharynx and regional lymph nodes. A viremia occurs 5 to 7 days after exposure with spread of the virus throughout the body. Transplacental infection of the fetus occurs during viremia. Fetal damage occurs through destruction of cells as well as mitotic arrest. Rubella a relatively unstable virus that is inactivated by lipid solvent, formalin, ultraviolet light, acidic pH, and heat.

b. Disease.

(1) Measles is transmitted person to person via large respiratory droplets and by direct contact with nasal or throat secretions. The average incubation period is 10-12 days, with a rash occurring at about 14 days after initial exposure. The prodrome is marked by high fever followed by the onset of cough, runny nose, and red, watery eyes (conjunctivitis). Koplik spots may be seen on mucous membranes in the mouth; these lesions present as blue and white spots on bright red background and appear a few days before and after the measles rash. The characteristic measles rash appears as maculopapular lesions that start on the head and gradually proceed down the body over 5-6 days. Approximately 30% of measles cases will develop complications, which are most common in children younger than 5 years and adults 20 years and older. Complications include ear infections, diarrhea, pneumonia, or encephalitis (brain inflammation) and rarely death. Pneumonia occurs in up to 6% of cases and accounts for 60% of deaths attributed to measles.

(2) Mumps virus is transmitted via respiratory droplets from an infected person. Inflammation in infected tissues leads to characteristic symptoms of parotitis and aseptic meningitis. The incubation period for mumps is 14 to 18 days. The prodromal symptoms are nonspecific, and include myalgia, anorexia, malaise, headache, and low-grade fever. Parotitis (inflammation of salivary glands) is the most common manifestation and may be unilateral or bilateral, with single or multiple salivary glands affected. Parotitis occurs within the first 2 days and may first be noted as earache and tenderness on palpation of the angle of the jaw. Symptoms tend to decrease after 1 week and usually resolve after 10 days. Complications include meningitis, inflammation of the testicles (orchitis) or ovaries, and deafness (which is usually permanent).

(3) Rubella virus is spread through respiratory droplets. The incubation period for rubella is 14 days. Symptoms are often mild, and up to 50% of infections may be inapparent. In young children, rash is usually the first manifestation and a prodrome is rare. In older children and adults, there is often a 1 to 5 day prodrome with low-grade fever, malaise, lymphadenopathy, and upper respiratory symptoms preceding the rash. The rash of rubella is maculopapular and occurs 14 to 17 days after exposure. The rash usually occurs initially on the face and then progresses from head to foot. It lasts about 3 days and is occasionally pruritic. The rash is fainter than measles rash and does not coalesce. Other symptoms of rubella include conjunctivitis or orchitis. When a woman is infected in pregnancy, her fetus can develop Congenital Rubella Syndrome, with resultant deafness, developmental delays, and/or congenital malformations.

c. Epidemiology.

(1) Measles occurs throughout the world and humans are the only known reservoir of the virus. In temperate areas, measles disease occurs primarily in late winter and spring. The disease is highly communicable and may be transmitted from 4 days before to 4 days after rash onset. Before a vaccine was available in the United States, approximately 500,000 cases and 500 deaths were reported annually; infection with measles virus was nearly universal during childhood, and more than 90% of persons were immune by age 15 years. Following licensure of vaccine in 1963, the incidence of measles decreased by more than 98%, and 2-3 year epidemic cycles no longer occurred. Although measles elimination (i.e., interruption of year-round endemic transmission) was declared in the U.S. in 2000, importations of measles cases from endemic areas of the world continue to occur, leading to secondary measles cases and outbreaks in the U.S., primarily among unvaccinated persons. Measles is still a common and often fatal disease in developing countries and recent decreases in vaccination rates in Europe have also resulted in resurgence of measles outbreaks.

(2) Mumps is a human disease that occurs globally. Mumps incidence peaks predominately in late winter and spring, but the disease has been reported throughout the year. Contagiousness is similar to that of influenza and rubella, but is less than that for measles or varicella. The number of reported mumps cases in the United States has decreased more than 99% since licensure of the mumps vaccine in 1967. Before vaccine availability, most reported cases occurred in children 5 to 9 years old. In recent U.S. mumps outbreaks, the risks of being infected were highest among people aged 18-24 years. Data suggest being unvaccinated or only having received one lifetime dose of MMR vaccine was a risk factor in the outbreaks.

(3) Rubella is a human disease that occurs worldwide; there is no known animal reservoir. In temperate area, incidence is usually highest in late winter and early spring. Rubella is only moderately contagious. Reported rubella cases (57,686) peaked in the United States in 1969; following vaccine licensure in 1969, rubella incidence declined rapidly. Due to vaccination, the Centers for Disease Control and Prevention no longer considers rubella a major public health threat in the United States. Prevention of Congenital Rubella Syndrome (CRS) is the main objective of rubella vaccination programs. Congenital infection with rubella virus can affect virtually all organ systems, with deafness being the most common outcome. Up to 85% of infants are affected if infection occurs during the first trimester of pregnancy.

d. Vaccine.

(1) M-M-R®II produced by Merck, is a live virus vaccine which includes antigens for measles, mumps, and rubella. M-M-R®II is licensed for persons 12 months and older. The vaccine is propagated in chick embryo cells and human diploid cells and

contains sorbitol, gelatin, MSG, and neomycin. The product is packaged as a single-dose vial of lyophilized vaccine and a vial diluent. Before reconstitution, the lyophilized vaccine is a light yellow and once reconstituted is clear yellow. After reconstitution, vaccine should be used immediately or discarded if not used within 8 hours. Protect the vaccine from light at all times.

(2) ProQuad® (MMRV) produced by Merck is a live virus combination vaccine which includes antigens for measles, mumps, rubella, and varicella. ProQuad® is licensed for children 12 months through 12 years of age. The vaccine is propagated in chick embryo cells and human diploid cells and contains gelatin, MSG, and neomycin. The vaccine is reconstituted with sterile water. Unless the parent or caregiver expresses a preference for MMRV vaccine, separate MMR and varicella vaccines should be administered at different anatomical sites for the first dose for children 12 through 47 months of age.

e. Immunization.

(1) Pediatric schedule: Two doses of vaccine separated by at least 4 weeks will provide protection. Each 0.5-mL dose is administered subcutaneously. The first dose of MMR-containing vaccine should be administered at 12-15 months of age. The second dose should generally be administered at 4 to 6 years of age, before school entry. If MMRV vaccine is used, at least 3 months should elapse between doses of varicella-containing vaccine. For children who will travel internationally, MMR-containing vaccine may be administered between 6 and 12 months of age; however, any dose of MMR-containing vaccine administered before 12 months should not be counted as part of series.

(2) Adult schedule: All persons born during or after 1957 should have documentation of at least one dose of MMR-containing vaccine or other evidence of immunity to measles, mumps, and rubella. Adults born before 1957 are assumed to be immune by natural infection. Ensure at least one lifetime dose of MMR-containing vaccine has been provided to all adults born in 1957 or later. Ensure at least two lifetime doses (separated by at least 4 weeks) of MMR-containing vaccine have been administered to adults who are healthcare workers, those who travel overseas, or those who attend post-secondary educational institutions. When vaccination records are unavailable or uncertain, laboratory testing for immunity can prevent unnecessary revaccination.

f. Precautions. MMR-containing vaccines should not be administered to people who have had a severe allergic reaction to a previous dose of MMR-containing vaccine or a vaccine component. Those who are moderately or severely ill should wait until recovery before receiving vaccine. MMR-containing vaccination should generally be delayed until after delivery in women who are pregnant or plan to become pregnant

within 4 weeks. MMR-containing vaccination should be delayed at least 4 weeks after receipt of another live-virus injectable vaccine or live attenuated influenza vaccine. MMR-containing vaccination should also be delayed after receipt of blood products or completion of a course of immune-suppressing medication; see specific guidance in references for appropriate intervals before administration of MMR-containing vaccine. MMR-containing vaccination is contraindicated in people with severe immune-suppression; however, HIV-infected patients without severe immunosuppression should be vaccinated (with MMR, but not MMRV) to protect from measles infection. MMR-containing vaccination may reduce platelet counts in patients with a history of thrombocytopenia; the relative risks and benefits of vaccination should be evaluated in such patients. Tuberculin skin testing (TST) should be delayed if MMR vaccine has been administered in the previous 4 weeks in order to prevent suppression of TST reactivity.

g. Adverse Events. The most commonly reported adverse reactions following an MMR-containing vaccination are fever, mild rash, swelling of glands in cheeks or neck, temporary pain and stiffness in the joints (mostly in teenage or adult women), and temporary low platelet counts. Febrile seizures are possible, and more commonly associated with younger age and MMRV vaccination; patients with a personal or family history of seizures should receive MMR and varicella vaccines in separate anatomic sites and not receive MMRV vaccine.

h. DoD Policy. Military personnel require protection against measles, mumps, and rubella. New accessions must have adequate documentation of 2 lifetime doses of MMR-containing vaccines, or serologic evidence of immunity to at least measles and rubella. In the absence of such evidence, 1 dose of MMR-containing vaccine should be administered within the first 2 weeks of initial training, with a 2<sup>nd</sup> dose administered at least 4 weeks later.

i. Special Consideration. All persons aged  $\geq 6$  months who will be traveling outside the United States and are eligible to receive MMR-containing vaccine should be vaccinated before travel. Travelers aged  $\geq 12$  months should receive 2 doses of MMR-containing vaccine separated by at least 28 days, before travel.

3. References.

a. Centers for Disease Control and Prevention. Measles – United States, January 1- May 23, 2014. MMWR 2014;63(22):496-9.

b. 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 2013;62(No. RR-4).

c. 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 2010;59 (RR-3):1-12.

d. Multiple resources (e.g., product insert, Vaccine Information Statements) assembled by Immunization Healthcare Branch: [www.health.mil/MMR](http://www.health.mil/MMR)

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