

Good Afternoon Chair Monnes Anderson and members of the committee. My name is Stacy Cayce. I'm a resident of Hillsboro, in Senate District 12. I'm also the executive director for Oregonians For Medical Freedom.

I am here in favor of Senate Bill 869.

This bill will provide true informed consent for a medical procedure, using a pharmaceutical product. If you think about informed consent in terms of other medical procedures or pharmaceutical products this bill brings vaccinations into alignment with those.

I have two examples I want to share with you, where in my day to day life I've had examples of informed consent.

I have with me here today three boxes from prescription medication that has been prescribed to family members (don't worry, I've removed names to avoid any privacy concerns).

Inside these boxes contain the insert for these products. As you can see, they are long and contain a lot of information. These are provided when someone orders a prescription. Are there potentially scary side effects listed in there? Of course, the manufactures of the product are giving you all the data they have, good and bad. Could this change your mind if you want to take this medication? Possibly, but my guess is that you've already had a discussion with your medical provider and you are offered a consult with the pharmacist when you pick up your medication, at this point you understand the use of this medication despite any side effects, is necessary for your health and the good outweighs the bad. You've been able to make an informed choice.

My daughter needed a series of dental procedures recently. In her treatment plan, I was offered three different paths. I sat with a patient care expert in her dental office and we went over each procedure line by line, from the most invasive to the least invasive and the pros and cons of each. I was given full information regarding the pharmaceutical products to be used and the office information to contact other doctors that could be potentially involved in her procedures so that I could speak with them and schedule a consult to be informed of their role in her procedures. I needed to sign off on each one, understanding what was involved. Did each procedure pose a risk? Yes, of course. But through this process I could make the informed choice of what path I wanted to pursue. She still got her needed treatment, but I was informed, and consented.

I've outlined two examples that show how informed consent applies to other aspects of our lives. But what about vaccines? When a vaccine is given the medical provider is supposed to provide a document called the Vaccine Information Sheet or VIS. In a non-scientific poll of my friends who have children I asked them if they were provided this sheet when their child received a vaccination. 50% of them told me NO. Considering this is a law, that is concerning to see a 50% compliance. Is that providing true informed consent for a medical procedure?

This bill would be bringing vaccination into alignment with my two examples. If your pharmacist gives you the insert in your prescription, provides a consult and you have to accept or decline, that is informed consent. If a dentist office has to provide all options of a treatment plan, the risks and potential side effects of pharmaceuticals they are using, and you have to sign off on each one, that is informed consent.

In 2001, I was given an MMR vaccine, I was applying to volunteer as a doula at OHSU for a pilot program. I had also received the MMR as a child, again in 1991, 1995, and 1996. Why so many times? I test as "non immune" to rubella. In two of those dates I was pregnant, tested non immune and was given the vaccine immediately after birth. However, those were all given on a military base and when 2001 came around I didn't have quick access to those records to prove I had a vaccine within the last 10 years. The only thing I was told, and this was verbal, was asking if I was currently pregnant, and at the time I was not, if I was they could not give me the vaccine. I got pregnant about 3 months later. My third child, my son, was born healthy. When he was just a day old, I was sitting on my living room floor in the wee hours of the morning trying to nurse him. He was wailing, arching his back, and not acting at all like my first two children did in their first few days of life. I knew something was wrong. I took him to an urgent care pediatrician the next day, I explained how he wasn't eating well, he was always crying and I was concerned. My concerns were ignored. He also became very jaundiced and we never got him to nurse properly. I sought answers from many different doctors but got nothing. Then it was clear he wasn't meeting the most basic milestones, rolling over, sitting up, crawling, walking, babbling. Again, no answers. We pushed and pushed. Finally, a referral to a geneticist to see if there was something genetic. He found nothing. When he turned 2, his pediatrician gave me a diagnosis. PDD-NOS. Persuasive developmental disorder, not otherwise specified. Later he was diagnosed with autism.

In October 2001, the ACIP changed their recommendations on when MMR is given to women of childbearing age, from a recommendation that a woman should not get pregnant within 3 months of the vaccination to 28 days. They based this on a study of 680 women. That's all, just 680. They determined there was a theoretical risk of a small percent, and felt it was small enough to make this change in recommendation.

<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5049a5.htm>

The reason that MMR is not given during this time and also in the few months after a woman is pregnant is because the MMR vaccine is a live virus and there is a risk that the fetus can contract congenital rubella syndrome or CRS. This generally occurs when a pregnant woman is exposed to someone who has rubella, but since this is a live vaccine it can also be due to the vaccination and when it is given.

However, the insert, for the MMR vaccine, the very insert we would like to be shared with patients says, and I quote: "Women of childbearing age should be advised not to become pregnant for 3 months after vaccination and should be informed of the reasons for this precaution"

I was NOT informed of this. I was not provided an insert. I did not know about this precaution until my son was THREE years old, and only because I dug into the matter and not because any medical provider told me this.

The CDC provides what they call a Case Definition for case classification on congenital rubella syndrome.

For a classification called "suspected", this is for an infant who does not meet the criteria for a probable or confirmed diagnosis, but they have one or more of the list of findings (I've included this list in my testimony). On this list includes both jaundice and developmental delays.

I feel that my son was vaccine injured due to an MMR vaccine given to me within 3 months of conception. The vaccine insert for MMR clearly gives this precaution, but it was never explained to me, and the current recommendations that women are given is 28 days.

It is imperative that parents have ALL the information when a vaccine is given. With every medical procedure or product there is risk.

I respectfully request that you support Senate Bill 869.

Thank you for your time.

Case definition for case classification

The following case definition for congenital rubella syndrome was approved by the Council of State and Territorial Epidemiologists (CSTE) and published in 2009.^[10]

Suspected: An infant who does not meet the criteria for a probable or confirmed case but who has one or more of the following findings:

- cataracts,
- congenital glaucoma,
- congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis),
- hearing impairment,
- pigmentary retinopathy,
- purpura,
- hepatosplenomegaly,
- jaundice,
- microcephaly,
- developmental delay,
- meningoencephalitis, or
- radiolucent bone disease

(<https://www.cdc.gov/vaccines/pubs/surv-manual/chpt15-crs.html>)

Chapter 15: Congenital Rubella Syndrome

On this Page

- Disease Description
- Background
- Maintenance of Elimination
- Vaccination
- Case Definition
- Laboratory Testing
- Reporting
- Case Investigation
- Prevent Transmission from Infants with CRS

Manual for the Surveillance of Vaccine-Preventable Diseases

[Printer friendly version](#) [7 pages]

Authors: Huong McLean, PhD, MPH; Susan Redd; Emily Abernathy, MS; Joseph Icenogle, PhD, Gregory Wallace, MD, MS, MPH

Disease Description

Congenital rubella syndrome (CRS) is an illness resulting from rubella virus infection during pregnancy. When rubella infection occurs during early pregnancy, serious consequences—such as miscarriages, stillbirths, and a constellation of severe birth defects in infants can result. The risk of congenital infection and defects is highest during the first 12 weeks of gestation and decreases after the 12th week of gestation with defects rare after the 20th week of gestation.^[1-3] Common congenital defects of CRS include cataracts, congenital heart disease, hearing impairment, and developmental delay. Infants with CRS usually present with more than one sign or symptom consistent with congenital rubella infection. However, infants may present with a single defect. Hearing impairment is the most common single defect. See [Chapter 14, "Rubella,"](#) for more information on rubella infection.

[^Top of Page](#)

Background

The link between congenital cataracts and maternal rubella infection was first made in 1941 by Australian ophthalmologist, Norman Gregg, who had noticed an unusual number of infants with cataracts following a rubella epidemic in 1940. In the absence of vaccination, rubella is an endemic disease with epidemics every 6 to 9 years. If rubella infections occurred among nonimmune pregnant women, CRS cases can occur. During the 1962-1965 global rubella pandemic, an estimated 12.5 million rubella cases occurred in the United States, resulting in 2,000 cases of encephalitis, 11,250 therapeutic or spontaneous abortions, 2,100 neonatal deaths, and 20,000 infants born with CRS.^[4]

In 1969, live attenuated rubella vaccines were licensed in the United States. The goal of the rubella vaccination program was and continues to be to prevent congenital rubella infections, including CRS.^[5] Following vaccine licensure, the number of reported cases of CRS in the United States declined dramatically to <1 case per year or 4 cases total during 2005-2011 (CDC, unpublished data). In 28 (85%) of the 33 cases occurring during 1998-2011, the mother was born outside the United States. Of the 33 CRS cases occurring during this time, 16 (48%) were known importations (CDC, unpublished data). In 2004, an independent panel of internationally recognized experts in public health, infectious diseases, and immunizations reviewed the available data on rubella epidemiology and unanimously agreed that rubella elimination (i.e., the absence of year round endemic transmission) was achieved in the United States.^[5]

Although rubella has been eliminated in the United States, it continues to be endemic in many parts of the world. It is estimated that more than 100,000 infants are born with CRS annually worldwide.^[6] According to a survey of the member countries in the World Health Organization (WHO), the number of countries that have incorporated rubella-containing vaccines into their routine national immunization programs increased from 83 (13% of the birth cohort) in 1996 to 130 countries (40% of the birth cohort) in 2010. As of October 2010, the WHO Region of the Americas and European Region have established rubella elimination goals for the year 2010 and 2015, respectively; the Western Pacific Region has established targets for accelerated rubella control and CRS prevention goal (<1 case per 100,000) by 2015; and the Eastern Mediterranean Region has established a goal of CRS prevention without a target date for countries that have introduced national rubella vaccination programs.^[7] In addition, in 2011, WHO recommended for all countries that are providing two doses of measles vaccine and have not introduced rubella vaccine, to consider including rubella-containing vaccine in their immunization program.^[8] In 2010, the Pan American Health Organization (PAHO) announced that the Region of the Americas had achieved the rubella and CRS elimination goals set in 2003 based on surveillance data. Although regional documentation of elimination is ongoing, an expert panel unanimously agreed in December 2011 that CRS elimination has been maintained in the United States.^[7, 9]

[^Top of Page](#)

Maintenance of Elimination

The United States has established and achieved the goal of eliminating indigenous rubella transmission and CRS. Elimination of endemic rubella was documented and verified in the United States in 2004.^[5] However, because of international travel and countries without routine rubella vaccination, imported cases of rubella and CRS cases are likely. To maintain elimination, the United States should continue to maintain high vaccination rates among children, ensure that women of childbearing age, particularly women born outside of the United States, are vaccinated, and maintain good surveillance for both rubella and CRS.

Vaccination

See [Chapter 14, "Rubella,"](#) for information on vaccination with rubella-containing vaccines.

[^Top of Page](#)

Case Definition

Case definition for case classification

The following case definition for congenital rubella syndrome was approved by the Council of State and Territorial Epidemiologists (CSTE) and published in 2009.^[10]

Suspected: An infant who does not meet the criteria for a probable or confirmed case but who has one or more of the following findings:

- cataracts,
- congenital glaucoma,
- congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis),
- hearing impairment,
- pigmentary retinopathy,
- purpura,
- hepatosplenomegaly,
- jaundice,
- microcephaly,
- developmental delay,
- meningoencephalitis, or
- radiolucent bone disease.

Probable: An infant who does not have laboratory confirmation of rubella infection but has at least two of the following, without a more plausible etiology:

- cataracts or congenital glaucoma,
- congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis),
- hearing impairment, or
- pigmentary retinopathy;

OR

An infant who does not have laboratory confirmation of rubella infection but has at least one or more of the following, without a more plausible etiology:

- cataracts or congenital glaucoma,
- congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis),
- hearing impairment, or
- pigmentary retinopathy;

AND one or more of the following:

- purpura,
- hepatosplenomegaly,
- microcephaly,
- developmental delay,
- meningoencephalitis, or
- radiolucent bone disease.

Confirmed: An infant with at least one of the symptoms clinically consistent with congenital rubella syndrome listed above; and laboratory evidence of congenital rubella infection demonstrated by:

- isolation of rubella virus, or
- detection of rubella-specific immunoglobulin M (IgM) antibody, or
- infant rubella antibody level that persists at a higher level and for a longer period of time than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a two-fold decline per month), or
- a specimen that is PCR-positive for rubella virus.

Infection only: An infant without any clinical symptoms or signs of rubella but with laboratory evidence of infection demonstrated by:

- isolation of rubella virus, or
- detection of rubella-specific immunoglobulin M (IgM) antibody, or

- infant rubella antibody level that persists at a higher level and for a longer period of time than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a two-fold decline per month), or
- a specimen that is PCR-positive for rubella virus.

Comment: In probable cases, either or both of the eye-related findings (cataracts and congenital glaucoma) count as a single complication. In cases classified as infection only, if any compatible signs or symptoms (e.g., hearing impairment) are identified later, the case is reclassified as confirmed.

Epidemiologic classification of internationally-imported and U.S.-acquired

Congenital rubella syndrome cases will be classified epidemiologically as internationally imported or U.S.-acquired, according to the source of infection in the mother, using the definitions below, which parallel the classifications for rubella cases.

Internationally imported case: To be classified as an internationally imported CRS case, the mother must have acquired rubella infection outside the United States or in the absence of documented rubella infection, the mother was outside the United States during at least some of the period when she may have had exposure to rubella that affected her pregnancy (from 21 days before conception and through the first 24 weeks of pregnancy).

U.S.-acquired case: A U.S.-acquired case is one in which the mother acquired rubella from an exposure in the United States. U.S.-acquired cases are subclassified into four groups as described in the rubella case classification section in [Chapter 14](#), "Rubella."

Note: Internationally imported, import-linked, and imported-virus cases are considered collectively to be import-associated cases.

States may also choose to classify cases as "out-of-state-imported" when imported from another state in the United States. For national reporting, however, cases will be classified as either internationally imported or U.S.-acquired.

[^Top of Page](#)

Laboratory Testing

Diagnostic tests used to confirm CRS include serologic assays and detection of rubella virus.

For additional information on laboratory testing for rubella virus, see [Chapter 14](#), "Rubella." For additional information on use of laboratory testing in surveillance of vaccine-preventable diseases, see [Chapter 22](#), "Laboratory Support for the Surveillance of Vaccine-Preventable Diseases."

Virus detection (real-time RT-PCR, RT-PCR)

Rubella virus can be detected from nasal, throat, urine, and blood specimens from infants with CRS. Efforts should be made to obtain clinical specimens for virus isolation from infants at the time of the initial investigation (see [Appendix 15](#) (2 pages)). However, because infants with CRS may shed virus from the throat and urine for a prolonged period (a year or longer), specimens obtained later may also yield rubella virus.

As with rubella infection, molecular typing is recommended because it provides important epidemiologic information to track the epidemiology of rubella in the United States now that rubella virus no longer continuously circulates in this country. By comparing virus sequences from new case-patients with virus sequences from other cases, the origin of particular virus types in this country can be tracked.^[11] Furthermore, this information may help in documenting the maintenance of the elimination of endemic rubella virus transmission. Specimens for molecular typing should be obtained from patients with CRS as soon as possible after diagnosis. Appropriate specimens include throat swabs, urine, and cataracts from surgery. Specimens for virus detection and molecular typing should be sent to CDC as directed by the state health department.

Serologic testing

The serologic tests available for laboratory confirmation of CRS infections vary among laboratories. Enzyme immunoassays (EIA) are the most commonly used and widely available diagnostic test for rubella IgG and IgM antibodies. EIAs are sensitive and relatively easy to perform. EIA is the preferred testing method for IgM, using the capture technique, although indirect assays are also acceptable. In infants with CRS, IgM antibody can be detected in the infant's cord blood or serum and persists for about 6-12 months.

[^Top of Page](#)

Reporting

Each state and territory has regulations or laws governing the reporting of diseases and conditions of public health importance.^[12] These regulations and laws list the diseases to be reported and describe those persons or groups responsible for reporting, such as healthcare providers, hospitals, laboratories, schools, daycare and childcare facilities, and other institutions. Persons reporting should contact the state health department for state-specific reporting requirements.

Provisional reports of CRS cases should be sent by the state health department to CDC/NCIRD/DVD/Epidemiology Branch (404-639-8253) and to the National Notifiable Diseases Surveillance System (NNDSS). Reporting should not be delayed because of incomplete information or lack of confirmation; following completion of case investigations, data previously submitted to NNDSS should be updated with the available new information.

The *Congenital Rubella Syndrome Case Report* form ([Appendix 17](#) (2 pages)) is used to collect clinical and laboratory information on cases of CRS that are reported by state and local health departments. CRS cases are classified by year of patient's birth.

The following data are epidemiologically important and should be collected in the course of case investigation. Additional information may also be collected at the direction of the state health department.

- Demographic information
 - Name

- Address
- Age
- Sex
- Ethnicity
- Race
- Country of birth (mother)
- Length of time in United States (mother)
- Reporting source
 - County
 - Earliest date reported
- Clinical
 - Symptoms or syndromes
 - Cataracts
 - Hearing impairment
 - Developmental delay
 - Type of congenital heart defect
 - Pigmentary retinopathy
 - Purpura
 - Radiolucent bone disease
 - Hepatosplenomegaly
 - Meningoencephalitis
 - Microcephaly
 - Other
- Outcome (infant survived or died)
 - Date of death
 - Postmortem examination results
 - Death certificate diagnoses
- Laboratory (performed on both mother and infant)
 - Virus isolation
 - Genotype
 - PCR results
- Maternal history
 - Dates of rubella vaccinations
 - Number of doses of vaccine given
 - If not vaccinated, reason
 - History of documentation of rubella infection or disease during pregnancy
 - Rubella laboratory results
 - History of pregnancies within and outside the United States (including country and years of pregnancies)
- Travel outside the U.S. during pregnancy (countries visited with dates)
- Contact with foreign travelers during pregnancy
- Epidemiologic
 - Transmission setting
 - Source of transmission (e.g., age, vaccination status, relationship to decedent)
 - Source of exposure
 - Travel history

[^Top of Page](#)

Case Investigation

Cases of U.S.-acquired CRS are sentinel events indicating the presence of rubella infections in a community that may have been previously unrecognized. The diagnosis of a single case of U.S.-acquired CRS in a community should result in intensified rubella and CRS surveillance and an investigation to determine where the mother was exposed to rubella. If the mother was exposed in a different state, state health officials should contact the other state to alert public health officials to possible rubella circulation.

Infants with CRS may present with various manifestations of the syndrome, depending on timing of the infection in pregnancy. Infants born to women infected with rubella during pregnancy should be evaluated for infection and CRS; however, depending on the gestational age of the infant at the time of the mother's infection, symptoms may not be apparent. After 20 weeks' gestation, the only defect may be hearing impairment. Furthermore, some children are infected in utero but have no congenital defects.

Laboratory confirmation should be sought in all suspected CRS cases, regardless of signs or symptoms.

Conducting active surveillance

Surveillance for CRS should be implemented when confirmed or probable rubella cases are documented in a setting where pregnant women might have been exposed. [13] Women who contract rubella while pregnant should be monitored for birth outcome, and appropriate testing should be performed on the infant after birth. Healthcare providers should be advised to evaluate infants born with conditions consistent with CRS and to collect specimens for virus detection and to perform a rubella-specific IgM antibody test on infants suspected of having CRS.

Prevent Transmission from Infants with CRS

Cases of U.S.-acquired rubella have occurred among susceptible persons providing care for infants with CRS. [14] Because infants can shed the virus for prolonged periods, (up to 1 year of age or longer) infants with CRS should be considered infectious until they are at least 1 year old or until two cultures of clinical specimens obtained one month apart after the infant is older than three months of age are negative for rubella virus. Infants with CRS should be placed in contact isolation during any hospital admission before age one year or until the infant is no longer considered infectious. In addition, health officials should consider excluding infants with CRS from child care facilities until he or she is no longer considered infectious. Persons having contact with infants with CRS should have documented evidence of immunity to rubella (see [Chapter 14](#), "Rubella") and caregivers of infants with CRS should be aware of the potential hazard of the infants to susceptible pregnant contacts.

[^ Top of Page](#)

References

1. Peckham CS. Clinical and laboratory study of children exposed in utero to maternal rubella. *Arch Dis Child* 1972;47(254):571-77.
2. South MA and Sever JL. Teratogen update: the congenital rubella syndrome. *Teratology* 1985;31(2):297-307.
3. Miller E, Craddock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet* 1982;2(8302):781-84.
4. National Communicable Disease Center. Rubella surveillance. Bethesda, MD: U.S. Department of Health, Education, and Welfare 1969.
5. CDC. Elimination of rubella and congenital rubella syndrome—United States, 1969-2004. *MMWR* 2005;54(11):279-82.
6. Robertson SE, Featherstone DA, Gacic-Dobo M, Hersh BS. Rubella and congenital rubella syndrome: global update. *Revista panamericana de salud publica/Pan American journal of public health* 2003;14(5):306-15.
7. CDC. Progress toward control of rubella and prevention of congenital rubella syndrome— worldwide, 2009. *MMWR* 2010;59(40):1307-10.
8. Rubella vaccines: WHO position paper. *Wkly Epidemiol Rec* 2011;86(29):301-16.
9. CDC. Documentation and verification of measles, rubella and congenital rubella syndrome elimination in the Region of the Americas. *United States National Report* 2012.
10. Council of State and Territorial Epidemiologists. Public health reporting and national notification for congenital rubella syndrome. Position statement 09-ID-61. Atlanta, GA: The Council; 2009.
11. Icenogle JP, Frey TK, Abernathy E, Reef SE, Schnurr D, Stewart JA. Genetic analysis of rubella viruses found in the United States between 1966 and 2004: evidence that indigenous rubella viruses have been eliminated. *Clin Infect Dis* 2006;43(Suppl 3): S133-40.
12. Roush S, Birkhead G, Koo D, Cobb A, Fleming D. Mandatory reporting of diseases and conditions by health care professionals and laboratories. *JAMA* 1999;282(2):164-70.
13. CDC. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *MMWR* 2001;50(RR-12):1-23.
14. Greaves WL, Orenstein WA, Stetler HC, Preblud SR, Hinman AR, Bart KJ. Prevention of rubella transmission in medical facilities. *JAMA* 1982;248(7):861-4.

[^ Top of Page](#)

Related Pages

[Webcast related to this manual](#)

[Rubella vaccination](#)

Get Email Updates

To receive email updates about this page, enter your email address:

What's this? (<https://www.cdc.gov/emailupdates/>)

Submit

Related Links

[Vaccines & Immunizations](#)

File Formats Help:

How do I view different file formats (PDF, DOC, PPT, MPEG) on this site? (<https://www.cdc.gov/Other/plugins/>)



M-M-R® II (MEASLES, MUMPS, and RUBELLA VIRUS VACCINE LIVE)

DESCRIPTION

M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live) is a live virus vaccine for vaccination against measles (rubeola), mumps, and rubella (German measles).

M-M-R II is a sterile lyophilized preparation of (1) ATTENUVAX® (Measles Virus Vaccine Live), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; (2) MUMPSVAX® (Mumps Virus Vaccine Live), the Jeryl Lynn™ (B level) strain of mumps virus propagated in chick embryo cell culture; and (3) MERUVAX® II (Rubella Virus Vaccine Live), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.{1,2}

The growth medium for measles and mumps is Medium 199 (a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum) containing SPGA (sucrose, phosphate, glutamate, and recombinant human albumin) as stabilizer and neomycin.

The growth medium for rubella is Minimum Essential Medium (MEM) [a buffered salt solution containing vitamins and amino acids and supplemented with fetal bovine serum] containing recombinant human albumin and neomycin. Sorbitol and hydrolyzed gelatin stabilizer are added to the individual virus harvests.

The cells, virus pools, and fetal bovine serum are all screened for the absence of adventitious agents.

The reconstituted vaccine is for subcutaneous administration. Each 0.5 mL dose contains not less than 1,000 TCID₅₀ (tissue culture infectious doses) of measles virus; 12,500 TCID₅₀ of mumps virus; and 1,000 TCID₅₀ of rubella virus. Each dose of the vaccine is calculated to contain sorbitol (14.5 mg), sodium phosphate, sucrose (1.9 mg), sodium chloride, hydrolyzed gelatin (14.5 mg), recombinant human albumin (≤0.3 mg), fetal bovine serum (<1 ppm), other buffer and media ingredients and approximately 25 mcg of neomycin. The product contains no preservative.

Before reconstitution, the lyophilized vaccine is a light yellow compact crystalline plug. M-M-R II, when reconstituted as directed, is clear yellow.

CLINICAL PHARMACOLOGY

Measles, mumps, and rubella are three common childhood diseases, caused by measles virus, mumps virus (paramyxoviruses), and rubella virus (togavirus), respectively, that may be associated with serious complications and/or death. For example, pneumonia and encephalitis are caused by measles. Mumps is associated with aseptic meningitis, deafness and orchitis; and rubella during pregnancy may cause congenital rubella syndrome in the infants of infected mothers.

The impact of measles, mumps, and rubella vaccination on the natural history of each disease in the United States can be quantified by comparing the maximum number of measles, mumps, and rubella cases reported in a given year prior to vaccine use to the number of cases of each disease reported in 1995. For measles, 894,134 cases reported in 1941 compared to 288 cases reported in 1995 resulted in a 99.97% decrease in reported cases; for mumps, 152,209 cases reported in 1968 compared to 840 cases reported in 1995 resulted in a 99.45% decrease in reported cases; and for rubella, 57,686 cases reported in 1969 compared to 200 cases reported in 1995 resulted in a 99.65% decrease.{3}

Clinical studies of 284 triple seronegative children, 11 months to 7 years of age, demonstrated that M-M-R II is highly immunogenic and generally well tolerated. In these studies, a single injection of the vaccine induced measles hemagglutination-inhibition (HI) antibodies in 95%, mumps neutralizing antibodies in 96%, and rubella HI antibodies in 99% of susceptible persons. However, a small percentage (1-5%) of vaccinees may fail to seroconvert after the primary dose (see also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*).

A study{4} of 6-month-old and 15-month-old infants born to vaccine-immunized mothers demonstrated that, following vaccination with ATTENUVAX, 74% of the 6-month-old infants developed detectable neutralizing antibody (NT) titers while 100% of the 15-month-old infants developed NT. This rate of seroconversion is higher than that previously reported for 6-month-old infants born to naturally immune mothers tested by HI assay. When the 6-month-old infants of immunized mothers were revaccinated at 15

months, they developed antibody titers equivalent to the 15-month-old vaccinees. The lower seroconversion rate in 6-month-olds has two possible explanations: 1) Due to the limit of the detection level of the assays (NT and enzyme immunoassay [EIA]), the presence of trace amounts of undetectable maternal antibody might interfere with the seroconversion of infants; or 2) The immune system of 6-month-olds is not always capable of mounting a response to measles vaccine as measured by the two antibody assays.

There is some evidence to suggest that infants who are born to mothers who had wild-type measles and who are vaccinated at less than one year of age may not develop sustained antibody levels when later revaccinated. The advantage of early protection must be weighed against the chance for failure to respond adequately on reimmunization.{5,6}

Efficacy of measles, mumps, and rubella vaccines was established in a series of double-blind controlled field trials which demonstrated a high degree of protective efficacy afforded by the individual vaccine components.{7-12} These studies also established that seroconversion in response to vaccination against measles, mumps, and rubella paralleled protection from these diseases.{13-15}

Following vaccination, antibodies associated with protection can be measured by neutralization assays, HI, or ELISA (enzyme linked immunosorbent assay) tests. Neutralizing and ELISA antibodies to measles, mumps, and rubella viruses are still detectable in most individuals 11 to 13 years after primary vaccination.{16-18} See INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females*, for Rubella Susceptibility Testing.

The RA 27/3 rubella strain in M-M-R II elicits higher immediate post-vaccination HI, complement-fixing and neutralizing antibody levels than other strains of rubella vaccine{19-25} and has been shown to induce a broader profile of circulating antibodies including anti-theta and anti-iota precipitating antibodies.{26,27} The RA 27/3 rubella strain immunologically simulates natural infection more closely than other rubella vaccine viruses.{27-29} The increased levels and broader profile of antibodies produced by RA 27/3 strain rubella virus vaccine appear to correlate with greater resistance to subclinical reinfection with the wild virus,{27,29-31} and provide greater confidence for lasting immunity.

INDICATIONS AND USAGE

Recommended Vaccination Schedule

M-M-R II is indicated for simultaneous vaccination against measles, mumps, and rubella in individuals 12 months of age or older.

Individuals first vaccinated at 12 months of age or older should be revaccinated prior to elementary school entry. Revaccination is intended to seroconvert those who do not respond to the first dose. The Advisory Committee on Immunization Practices (ACIP) recommends administration of the first dose of M-M-R II at 12 to 15 months of age and administration of the second dose of M-M-R II at 4 to 6 years of age.{32} In addition, some public health jurisdictions mandate the age for revaccination. Consult the complete text of applicable guidelines regarding routine revaccination including that of high-risk adult populations.

Measles Outbreak Schedule

Infants Between 6 to 12 Months of Age

Local health authorities may recommend measles vaccination of infants between 6 to 12 months of age in outbreak situations. This population may fail to respond to the components of the vaccine. Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established. The younger the infant, the lower the likelihood of seroconversion (see CLINICAL PHARMACOLOGY). Such infants should receive a second dose of M-M-R II between 12 to 15 months of age followed by revaccination at elementary school entry.{32}

Unnecessary doses of a vaccine are best avoided by ensuring that written documentation of vaccination is preserved and a copy given to each vaccinee's parent or guardian.

Other Vaccination Considerations

Non-Pregnant Adolescent and Adult Females

Immunization of susceptible non-pregnant adolescent and adult females of childbearing age with live attenuated rubella virus vaccine is indicated if certain precautions are observed (see below and PRECAUTIONS). Vaccinating susceptible postpubertal females confers individual protection against subsequently acquiring rubella infection during pregnancy, which in turn prevents infection of the fetus and consequent congenital rubella injury.{33}

Women of childbearing age should be advised not to become pregnant for 3 months after vaccination and should be informed of the reasons for this precaution.

The ACIP has stated "If it is practical and if reliable laboratory services are available, women of childbearing age who are potential candidates for vaccination can have serologic tests to determine susceptibility to rubella. However, with the exception of premarital and prenatal screening, routinely performing serologic tests for all women of childbearing age to determine susceptibility (so that vaccine is given only to proven susceptible women) can be effective but is expensive. Also, 2 visits to the health-care provider would be necessary — one for screening and one for vaccination. Accordingly, rubella vaccination of a woman who is not known to be pregnant and has no history of vaccination is justifiable without serologic testing — and may be preferable, particularly when costs of serology are high and follow-up of identified susceptible women for vaccination is not assured."{33}

Postpubertal females should be informed of the frequent occurrence of generally self-limited arthralgia and/or arthritis beginning 2 to 4 weeks after vaccination (see ADVERSE REACTIONS).

Postpartum Women

It has been found convenient in many instances to vaccinate rubella-susceptible women in the immediate postpartum period (see PRECAUTIONS, *Nursing Mothers*).

Other Populations

Previously unvaccinated children older than 12 months who are in contact with susceptible pregnant women should receive live attenuated rubella vaccine (such as that contained in monovalent rubella vaccine or in M-M-R II) to reduce the risk of exposure of the pregnant woman.

Individuals planning travel outside the United States, if not immune, can acquire measles, mumps, or rubella and import these diseases into the United States. Therefore, prior to international travel, individuals known to be susceptible to one or more of these diseases can either receive the indicated monovalent vaccine (measles, mumps, or rubella), or a combination vaccine as appropriate. However, M-M-R II is preferred for persons likely to be susceptible to mumps and rubella; and if monovalent measles vaccine is not readily available, travelers should receive M-M-R II regardless of their immune status to mumps or rubella.{34-36}

Vaccination is recommended for susceptible individuals in high-risk groups such as college students, health-care workers, and military personnel.{33,34,37}

According to ACIP recommendations, most persons born in 1956 or earlier are likely to have been infected with measles naturally and generally need not be considered susceptible. All children, adolescents, and adults born after 1956 are considered susceptible and should be vaccinated, if there are no contraindications. This includes persons who may be immune to measles but who lack adequate documentation of immunity such as: (1) physician-diagnosed measles, (2) laboratory evidence of measles immunity, or (3) adequate immunization with live measles vaccine on or after the first birthday.{34}

The ACIP recommends that "Persons vaccinated with inactivated vaccine followed within 3 months by live vaccine should be revaccinated with two doses of live vaccine. Revaccination is particularly important when the risk of exposure to wild-type measles virus is increased, as may occur during international travel."{34}

Post-Exposure Vaccination

Vaccination of individuals exposed to wild-type measles may provide some protection if the vaccine can be administered within 72 hours of exposure. If, however, vaccine is given a few days before exposure, substantial protection may be afforded.{34,38,39} There is no conclusive evidence that vaccination of individuals recently exposed to wild-type mumps or wild-type rubella will provide protection.{33,37}

Use With Other Vaccines

See DOSAGE AND ADMINISTRATION, *Use With Other Vaccines*.

CONTRAINDICATIONS

Hypersensitivity to any component of the vaccine, including gelatin.{40}

Do not give M-M-R II to pregnant females; the possible effects of the vaccine on fetal development are unknown at this time. If vaccination of postpubertal females is undertaken, pregnancy should be avoided for three months following vaccination (see INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females* and PRECAUTIONS, *Pregnancy*).

Anaphylactic or anaphylactoid reactions to neomycin (each dose of reconstituted vaccine contains approximately 25 mcg of neomycin).

Febrile respiratory illness or other active febrile infection. However, the ACIP has recommended that all vaccines can be administered to persons with minor illnesses such as diarrhea, mild upper respiratory infection with or without low-grade fever, or other low-grade febrile illness.{41}

Patients receiving immunosuppressive therapy. This contraindication does not apply to patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Individuals with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems.

Primary and acquired immunodeficiency states, including patients who are immunosuppressed in association with AIDS or other clinical manifestations of infection with human immunodeficiency viruses;{41-43} cellular immune deficiencies; and hypogammaglobulinemic and dysgammaglobulinemic states. Measles inclusion body encephalitis{44} (MIBE), pneumonitis{45} and death as a direct consequence of disseminated measles vaccine virus infection have been reported in immunocompromised individuals inadvertently vaccinated with measles-containing vaccine.

Individuals with a family history of congenital or hereditary immunodeficiency, until the immune competence of the potential vaccine recipient is demonstrated.

WARNINGS

Due caution should be employed in administration of M-M-R II to persons with a history of cerebral injury, individual or family histories of convulsions, or any other condition in which stress due to fever should be avoided. The physician should be alert to the temperature elevation which may occur following vaccination (see ADVERSE REACTIONS).

Hypersensitivity to Eggs

Live measles vaccine and live mumps vaccine are produced in chick embryo cell culture. Persons with a history of anaphylactic, anaphylactoid, or other immediate reactions (e.g., hives, swelling of the mouth and throat, difficulty breathing, hypotension, or shock) subsequent to egg ingestion may be at an enhanced risk of immediate-type hypersensitivity reactions after receiving vaccines containing traces of chick embryo antigen. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases. Such individuals may be vaccinated with extreme caution, having adequate treatment on hand should a reaction occur (see PRECAUTIONS).{46}

However, the AAP has stated, "Most children with a history of anaphylactic reactions to eggs have no untoward reactions to measles or MMR vaccine. Persons are not at increased risk if they have egg allergies that are not anaphylactic, and they should be vaccinated in the usual manner. In addition, skin testing of egg-allergic children with vaccine has not been predictive of which children will have an immediate hypersensitivity reaction...Persons with allergies to chickens or chicken feathers are not at increased risk of reaction to the vaccine."{47}

Hypersensitivity to Neomycin

The AAP states, "Persons who have experienced anaphylactic reactions to topically or systemically administered neomycin should not receive measles vaccine. Most often, however, neomycin allergy manifests as a contact dermatitis, which is a delayed-type (cell-mediated) immune response rather than anaphylaxis. In such persons, an adverse reaction to neomycin in the vaccine would be an erythematous, pruritic nodule or papule, 48 to 96 hours after vaccination. A history of contact dermatitis to neomycin is not a contraindication to receiving measles vaccine."{47}

Thrombocytopenia

Individuals with current thrombocytopenia may develop more severe thrombocytopenia following vaccination. In addition, individuals who experienced thrombocytopenia with the first dose of M-M-R II (or its component vaccines) may develop thrombocytopenia with repeat doses. Serologic status may be evaluated to determine whether or not additional doses of vaccine are needed. The potential risk to benefit ratio should be carefully evaluated before considering vaccination in such cases (see ADVERSE REACTIONS).

PRECAUTIONS

General

Adequate treatment provisions, including epinephrine injection (1:1000), should be available for immediate use should an anaphylactic or anaphylactoid reaction occur.

Special care should be taken to ensure that the injection does not enter a blood vessel.

Children and young adults who are known to be infected with human immunodeficiency viruses and are not immunosuppressed may be vaccinated. However, vaccinees who are infected with HIV should be monitored closely for vaccine-preventable diseases because immunization may be less effective than for uninfected persons (see CONTRAINDICATIONS).{42,43}

Vaccination should be deferred for 3 months or longer following blood or plasma transfusions, or administration of immune globulin (human).{47}

Excretion of small amounts of the live attenuated rubella virus from the nose or throat has occurred in the majority of susceptible individuals 7 to 28 days after vaccination. There is no confirmed evidence to indicate that such virus is transmitted to susceptible persons who are in contact with the vaccinated individuals. Consequently, transmission through close personal contact, while accepted as a theoretical possibility, is not regarded as a significant risk.{33} However, transmission of the rubella vaccine virus to infants via breast milk has been documented (see *Nursing Mothers*).

There are no reports of transmission of live attenuated measles or mumps viruses from vaccinees to susceptible contacts.

It has been reported that live attenuated measles, mumps and rubella virus vaccines given individually may result in a temporary depression of tuberculin skin sensitivity. Therefore, if a tuberculin test is to be done, it should be administered either before or simultaneously with M-M-R II.

Children under treatment for tuberculosis have not experienced exacerbation of the disease when immunized with live measles virus vaccine;{48} no studies have been reported to date of the effect of measles virus vaccines on untreated tuberculous children. However, individuals with active untreated tuberculosis should not be vaccinated.

As for any vaccine, vaccination with M-M-R II may not result in protection in 100% of vaccinees.

The health-care provider should determine the current health status and previous vaccination history of the vaccinee.

The health-care provider should question the patient, parent, or guardian about reactions to a previous dose of M-M-R II or other measles-, mumps-, or rubella-containing vaccines.

Information for Patients

The health-care provider should provide the vaccine information required to be given with each vaccination to the patient, parent, or guardian.

The health-care provider should inform the patient, parent, or guardian of the benefits and risks associated with vaccination. For risks associated with vaccination see WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS.

Patients, parents, or guardians should be instructed to report any serious adverse reactions to their health-care provider who in turn should report such events to the U.S. Department of Health and Human Services through the Vaccine Adverse Event Reporting System (VAERS), 1-800-822-7967.{49}

Pregnancy should be avoided for 3 months following vaccination, and patients should be informed of the reasons for this precaution (see INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females*, CONTRAINDICATIONS, and PRECAUTIONS, *Pregnancy*).

Laboratory Tests

See INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females*, for Rubella Susceptibility Testing, and CLINICAL PHARMACOLOGY.

Drug Interactions

See DOSAGE AND ADMINISTRATION, *Use With Other Vaccines*.

Immunosuppressive Therapy

The immune status of patients about to undergo immunosuppressive therapy should be evaluated so that the physician can consider whether vaccination prior to the initiation of treatment is indicated (see CONTRAINDICATIONS and PRECAUTIONS).

The ACIP has stated that "patients with leukemia in remission who have not received chemotherapy for at least 3 months may receive live virus vaccines. Short-term (<2 weeks), low- to moderate-dose systemic corticosteroid therapy, topical steroid therapy (e.g. nasal, skin), long-term alternate-day treatment with low to moderate doses of short-acting systemic steroid, and intra-articular, bursal, or tendon injection of corticosteroids are not immunosuppressive in their usual doses and do not contraindicate the administration of [measles, mumps, or rubella vaccine]."{33,34,37}

Immune Globulin

Administration of immune globulins concurrently with M-M-R II may interfere with the expected immune response.{33,34,47}

See also PRECAUTIONS, *General*.

Carcinogenesis, Mutagenesis, Impairment of Fertility

M-M-R II has not been evaluated for carcinogenic or mutagenic potential, or potential to impair fertility.

Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with M-M-R II. It is also not known whether M-M-R II can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, the vaccine should not be administered to pregnant females; furthermore, pregnancy should be avoided for 3 months following vaccination (see INDICATIONS AND USAGE, *Non-Pregnant Adolescent and Adult Females* and CONTRAINDICATIONS).

In counseling women who are inadvertently vaccinated when pregnant or who become pregnant within 3 months of vaccination, the physician should be aware of the following: (1) In a 10-year survey involving over 700 pregnant women who received rubella vaccine within 3 months before or after conception (of whom 189 received the Wistar RA 27/3 strain), none of the newborns had abnormalities compatible with congenital rubella syndrome;{50} (2) Mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion. Although mumps vaccine virus has been shown to infect the placenta and fetus, there is no evidence that it causes congenital malformations in humans;{37} and (3) Reports have indicated that contracting wild-type measles during pregnancy enhances fetal risk. Increased rates of spontaneous abortion, stillbirth, congenital defects and prematurity have been observed subsequent to infection with wild-type measles during pregnancy.{51,52} There are no adequate studies of the attenuated (vaccine) strain of measles virus in pregnancy. However, it would be prudent to assume that the vaccine strain of virus is also capable of inducing adverse fetal effects.

Nursing Mothers

It is not known whether measles or mumps vaccine virus is secreted in human milk. Recent studies have shown that lactating postpartum women immunized with live attenuated rubella vaccine may secrete the virus in breast milk and transmit it to breast-fed infants.{53} In the infants with serological evidence of rubella infection, none exhibited severe disease; however, one exhibited mild clinical illness typical of acquired rubella.{54,55} Caution should be exercised when M-M-R II is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of measles vaccine in infants below the age of 6 months have not been established (see also CLINICAL PHARMACOLOGY). Safety and effectiveness of mumps and rubella vaccine in infants less than 12 months of age have not been established.

Geriatric Use

Clinical studies of M-M-R II did not include sufficient numbers of seronegative subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger subjects.

ADVERSE REACTIONS

The following adverse reactions are listed in decreasing order of severity, without regard to causality, within each body system category and have been reported during clinical trials, with use of the marketed vaccine, or with use of monovalent or bivalent vaccine containing measles, mumps, or rubella:

Body as a Whole

Panniculitis; atypical measles; fever; syncope; headache; dizziness; malaise; irritability.

Cardiovascular System

Vasculitis.

Digestive System

Pancreatitis; diarrhea; vomiting; parotitis; nausea.

Endocrine System

Diabetes mellitus.

Hemic and Lymphatic System

Thrombocytopenia (see WARNINGS, *Thrombocytopenia*); purpura; regional lymphadenopathy; leukocytosis.

Immune System

Anaphylaxis and anaphylactoid reactions have been reported as well as related phenomena such as angioneurotic edema (including peripheral or facial edema) and bronchial spasm in individuals with or without an allergic history.

Musculoskeletal System

Arthritis; arthralgia; myalgia.

Arthralgia and/or arthritis (usually transient and rarely chronic), and polyneuritis are features of infection with wild-type rubella and vary in frequency and severity with age and sex, being greatest in adult females and least in prepubertal children. This type of involvement as well as myalgia and paresthesia, have also been reported following administration of MERUVAX II.

Chronic arthritis has been associated with wild-type rubella infection and has been related to persistent virus and/or viral antigen isolated from body tissues. Only rarely have vaccine recipients developed chronic joint symptoms.

Following vaccination in children, reactions in joints are uncommon and generally of brief duration. In women, incidence rates for arthritis and arthralgia are generally higher than those seen in children (children: 0-3%; women: 12-26%),{17,56,57} and the reactions tend to be more marked and of longer duration. Symptoms may persist for a matter of months or on rare occasions for years. In adolescent girls, the reactions appear to be intermediate in incidence between those seen in children and in adult women. Even in women older than 35 years, these reactions are generally well tolerated and rarely interfere with normal activities.

Nervous System

Encephalitis; encephalopathy; measles inclusion body encephalitis (MIBE) (see CONTRAINDICATIONS); subacute sclerosing panencephalitis (SSPE); Guillain-Barré Syndrome (GBS); acute disseminated encephalomyelitis (ADEM); transverse myelitis; febrile convulsions; afebrile convulsions or seizures; ataxia; polyneuritis; polyneuropathy; ocular palsies; paresthesia.

Encephalitis and encephalopathy have been reported approximately once for every 3 million doses of M-M-R II or measles-, mumps-, and rubella-containing vaccine administered since licensure of these vaccines.

The risk of serious neurological disorders following live measles virus vaccine administration remains less than the risk of encephalitis and encephalopathy following infection with wild-type measles (1 per 1000 reported cases).{58,59}

In severely immunocompromised individuals who have been inadvertently vaccinated with measles-containing vaccine; measles inclusion body encephalitis, pneumonitis, and fatal outcome as a direct consequence of disseminated measles vaccine virus infection have been reported (see CONTRAINDICATIONS). In this population, disseminated mumps and rubella vaccine virus infection have also been reported.

There have been reports of subacute sclerosing panencephalitis (SSPE) in children who did not have a history of infection with wild-type measles but did receive measles vaccine. Some of these cases may have resulted from unrecognized measles in the first year of life or possibly from the measles vaccination. Based on estimated nationwide measles vaccine distribution, the association of SSPE cases to measles vaccination is about one case per million vaccine doses distributed. This is far less than the association with infection with wild-type measles, 6-22 cases of SSPE per million cases of measles. The results of a retrospective case-controlled study conducted by the Centers for Disease Control and Prevention suggest that the overall effect of measles vaccine has been to protect against SSPE by preventing measles with its inherent higher risk of SSPE.{60}

Cases of aseptic meningitis have been reported to VAERS following measles, mumps, and rubella vaccination. Although a causal relationship between the Urabe strain of mumps vaccine and aseptic meningitis has been shown, there is no evidence to link Jeryl Lynn™ mumps vaccine to aseptic meningitis.

Respiratory System

Pneumonia; pneumonitis (see CONTRAINDICATIONS); sore throat; cough; rhinitis.

Skin

Stevens-Johnson syndrome; erythema multiforme; urticaria; rash; measles-like rash; pruritis.

Local reactions including burning/stinging at injection site; wheal and flare; redness (erythema); swelling; induration; tenderness; vesiculation at injection site; Henoch-Schönlein purpura; acute hemorrhagic edema of infancy.

Special Senses — Ear

Nerve deafness; otitis media.

Special Senses — Eye

Retinitis; optic neuritis; papillitis; retrobulbar neuritis; conjunctivitis.

Urogenital System

Epididymitis; orchitis.

Other

Death from various, and in some cases unknown, causes has been reported rarely following vaccination with measles, mumps, and rubella vaccines; however, a causal relationship has not been established in healthy individuals (see CONTRAINDICATIONS). No deaths or permanent sequelae were reported in a published post-marketing surveillance study in Finland involving 1.5 million children and adults who were vaccinated with M-M-R II during 1982 to 1993.{61}

Under the National Childhood Vaccine Injury Act of 1986, health-care providers and manufacturers are required to record and report certain suspected adverse events occurring within specific time periods after vaccination. However, the U.S. Department of Health and Human Services (DHHS) has established a Vaccine Adverse Event Reporting System (VAERS) which will accept all reports of suspected events.{49} A VAERS report form as well as information regarding reporting requirements can be obtained by calling VAERS 1-800-822-7967.

DOSAGE AND ADMINISTRATION

FOR SUBCUTANEOUS ADMINISTRATION

Do not inject intravascularly.

The dose for any age is 0.5 mL administered subcutaneously, preferably into the outer aspect of the upper arm.

The recommended age for primary vaccination is 12 to 15 months.

Revaccination with M-M-R II is recommended prior to elementary school entry. See also INDICATIONS AND USAGE, *Recommended Vaccination Schedule*.

Children first vaccinated when younger than 12 months of age should receive another dose between 12 to 15 months of age followed by revaccination prior to elementary school entry.{32} See also INDICATIONS AND USAGE, *Measles Outbreak Schedule*.

Immune Globulin (IG) is not to be given concurrently with M-M-R II (see PRECAUTIONS, *General* and PRECAUTIONS, *Drug Interactions*).

CAUTION: A sterile syringe free of preservatives, antiseptics, and detergents should be used for each injection and/or reconstitution of the vaccine because these substances may inactivate the live virus vaccine. A 25 gauge, 5/8" needle is recommended.

To reconstitute, use only the diluent supplied, since it is free of preservatives or other antiviral substances which might inactivate the vaccine.

Single Dose Vial— First withdraw the entire volume of diluent into the syringe to be used for reconstitution. Inject all the diluent in the syringe into the vial of lyophilized vaccine, and agitate to mix thoroughly. If the lyophilized vaccine cannot be dissolved, discard. Withdraw the entire contents into a syringe and inject the total volume of restored vaccine subcutaneously.

It is important to use a separate sterile syringe and needle for each individual patient to prevent transmission of hepatitis B and other infectious agents from one person to another.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. M-M-R II, when reconstituted, is clear yellow.

Use With Other Vaccines

M-M-R II should be given one month before or after administration of other live viral vaccines.

M-M-R II has been administered concurrently with VARIVAX® [Varicella Virus Vaccine Live (Oka/Merck)], and PedvaxHIB® [*Haemophilus b* Conjugate Vaccine (Meningococcal Protein Conjugate)] using separate injection sites and syringes. No impairment of immune response to individually tested vaccine antigens was demonstrated. The type, frequency, and severity of adverse experiences observed with M-M-R II were similar to those seen when each vaccine was given alone.

Routine administration of DTP (diphtheria, tetanus, pertussis) and/or OPV (oral poliovirus vaccine) concurrently with measles, mumps and rubella vaccines is not recommended because there are limited data relating to the simultaneous administration of these antigens.

However, other schedules have been used. The ACIP has stated "Although data are limited concerning the simultaneous administration of the entire recommended vaccine series (i.e., DTaP [or DTwP], IPV [or OPV], Hib with or without Hepatitis B vaccine, and varicella vaccine), data from numerous studies have indicated no interference between routinely recommended childhood vaccines (either live, attenuated, or killed). These findings support the simultaneous use of all vaccines as recommended."{62}

HOW SUPPLIED

No. 4681 — M-M-R II is supplied as follows: (1) a box of 10 single-dose vials of lyophilized vaccine (package A), NDC 0006-4681-00; and (2) a box of 10 vials of diluent (package B). To conserve refrigerator space, the diluent may be stored separately at room temperature.

Storage

To maintain potency, M-M-R II must be stored between -58°F and +46°F (-50°C to +8°C). Use of dry ice may subject M-M-R II to temperatures colder than -58°F (-50°C).

Protect the vaccine from light at all times, since such exposure may inactivate the viruses.

Before reconstitution, store the lyophilized vaccine at 36°F to 46°F (2°C to 8°C). The diluent may be stored in the refrigerator with the lyophilized vaccine or separately at room temperature. **Do not freeze the diluent.**

It is recommended that the vaccine be used as soon as possible after reconstitution. Store reconstituted vaccine in the vaccine vial in a dark place at 36°F to 46°F (2°C to 8°C) and discard if not used within 8 hours.


For information regarding stability under conditions other than those recommended, call 1-800-MERCK-90.

REFERENCES

1. Plotkin, S.A.; Cornfeld, D.; Ingalls, T.H.: Studies of immunization with living rubella virus: Trials in children with a strain cultured from an aborted fetus, *Am. J. Dis. Child.* 110: 381-389, 1965.
2. Plotkin, S.A.; Farquhar, J.; Katz, M.; Ingalls, T.H.: A new attenuated rubella virus grown in human fibroblasts: Evidence for reduced nasopharyngeal excretion, *Am. J. Epidemiol.* 86: 468-477, 1967.
3. Monthly Immunization Table, *MMWR* 45(1): 24-25, January 12, 1996.
4. Johnson, C.E.; et al: Measles Vaccine Immunogenicity in 6- Versus 15-Month-Old Infants Born to Mothers in the Measles Vaccine Era, *Pediatrics*, 93(6): 939-943, 1994.
5. Linneman, C.C.; et al: Measles Immunity After Vaccination: Results in Children Vaccinated Before 10 Months of Age, *Pediatrics*, 69(3): 332-335, March 1982.
6. Stetler, H.C.; et al: Impact of Revaccinating Children Who Initially Received Measles Vaccine Before 10 Months of Age, *Pediatrics* 77(4): 471-476, April 1986.
7. Hilleman, M.R.; Buynak, E.B.; Weibel, R.E.; et al: Development and Evaluation of the Moraten Measles Virus Vaccine, *JAMA* 206(3): 587-590, 1968.
8. Weibel, R.E.; Stokes, J.; Buynak, E.B.; et al: Live, Attenuated Mumps Virus Vaccine 3. Clinical and Serologic Aspects in a Field Evaluation, *N. Engl. J. Med.* 276: 245-251, 1967.
9. Hilleman, M.R.; Weibel, R.E.; Buynak, E.B.; et al: Live, Attenuated Mumps Virus Vaccine 4. Protective Efficacy as Measured in a Field Evaluation, *N. Engl. J. Med.* 276: 252-258, 1967.
10. Cutts, F.T.; Henderson, R.H.; Clements, C.J.; et al: Principles of measles control, *Bull WHO* 69(1): 1-7, 1991.
11. Weibel, R.E.; Buynak, E.B.; Stokes, J.; et al: Evaluation Of Live Attenuated Mumps Virus Vaccine, Strain Jeryl Lynn, First International Conference on Vaccines Against Viral and Rickettsial Diseases of Man, World Health Organization, No. 147, May 1967.
12. Leibhaber, H.; Ingalls, T.H.; LeBouvier, G.L.; et al: Vaccination With RA 27/3 Rubella Vaccine, *Am. J. Dis. Child.* 123: 133-136, February 1972.
13. Rosen, L.: Hemagglutination and Hemagglutination-Inhibition with Measles Virus, *Virology* 13: 139-141, January 1961.
14. Brown, G.C.; et al: Fluorescent-Antibody Marker for Vaccine-Induced Rubella Antibodies, *Infection and Immunity* 2(4): 360-363, 1970.
15. Buynak, E.B.; et al: Live Attenuated Mumps Virus Vaccine 1. Vaccine Development, *Proceedings of the Society for Experimental Biology and Medicine*, 123: 768-775, 1966.

16. Weibel, R.E.; Carlson, A.J.; Villarejos, V.M.; Buynak, E.B.; McLean, A.A.; Hilleman, M.R.: Clinical and Laboratory Studies of Combined Live Measles, Mumps, and Rubella Vaccines Using the RA 27/3 Rubella Virus, *Proc. Soc. Exp. Biol. Med.* **165**: 323-326, 1980.
17. Unpublished data from the files of Merck Research Laboratories.
18. Watson, J.C.; Pearson, J.S.; Erdman, D.D.; et al: An Evaluation of Measles Revaccination Among School-Entry Age Children, 31st Interscience Conference on Antimicrobial Agents and Chemotherapy, Abstract #268, 143, 1991.
19. Fogel, A.; Moshkowitz, A.; Rannon, L.; Gerichter, Ch.B.: Comparative trials of RA 27/3 and Cendehill rubella vaccines in adult and adolescent females, *Am. J. Epidemiol.* **93**: 392-393, 1971.
20. Andzhaparidze, O.G.; Desyatskova, R.G.; Chervonski, G.I.; Pryanichnikova, L.V.: Immunogenicity and reactogenicity of live attenuated rubella virus vaccines, *Am. J. Epidemiol.* **91**: 527-530, 1970.
21. Freestone, D.S.; Reynolds, G.M.; McKinnon, J.A.; Prydie, J.: Vaccination of schoolgirls against rubella. Assessment of serological status and a comparative trial of Wistar RA 27/3 and Cendehill strain live attenuated rubella vaccines in 13-year-old schoolgirls in Dudley, *Br. J. Prev. Soc. Med.* **29**: 258-261, 1975.
22. Grillner, L.; Hedstrom, C.E.; Bergstrom, H.; Forssman, L.; Rigner, A.; Lycke, E.: Vaccination against rubella of newly delivered women, *Scand. J. Infect. Dis.* **5**: 237-241, 1973.
23. Grillner, L.: Neutralizing antibodies after rubella vaccination of newly delivered women: a comparison between three vaccines, *Scand. J. Infect. Dis.* **7**: 169-172, 1975.
24. Wallace, R.B.; Isacson, P.: Comparative trial of HPV-77, DE-5 and RA 27/3 live-attenuated rubella vaccines, *Am. J. Dis. Child.* **124**: 536-538, 1972.
25. Lalla, M.; Vesikari, T.; Virolainen, M.: Lymphoblast proliferation and humoral antibody response after rubella vaccination, *Clin. Exp. Immunol.* **15**: 193-202, 1973.
26. LeBouvier, G.L.; Plotkin, S.A.: Precipitin responses to rubella vaccine RA 27/3, *J. Infect. Dis.* **123**: 220-223, 1971.
27. Horstmann, D.M.: Rubella: The challenge of its control, *J. Infect. Dis.* **123**: 640-654, 1971.
28. Ogra, P.L.; Kerr-Grant, D.; Umana, G.; Dzierba, J.; Weintraub, D.: Antibody response in serum and nasopharynx after naturally acquired and vaccine-induced infection with rubella virus, *N. Engl. J. Med.* **285**: 1333-1339, 1971.
29. Plotkin, S.A.; Farquhar, J.D.; Ogra, P.L.: Immunologic properties of RA 27/3 rubella virus vaccine, *J. Am. Med. Assoc.* **225**: 585-590, 1973.
30. Liebhaver, H.; Ingalls, T.H.; LeBouvier, G.L.; Horstmann, D.M.: Vaccination with RA 27/3 rubella vaccine. Persistence of immunity and resistance to challenge after two years, *Am. J. Dis. Child.* **123**: 133-136, 1972.
31. Farquhar, J.D.: Follow-up on rubella vaccinations and experience with subclinical reinfection, *J. Pediatr.* **81**: 460-465, 1972.
32. Measles, Mumps, and Rubella — Vaccine Use and Strategies for Elimination of Measles, Rubella, and Congenital Rubella Syndrome and Control of Mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP), *MMWR* **47**(RR-8): May 22, 1998.
33. Rubella Prevention: Recommendation of the Immunization Practices Advisory Committee (ACIP), *MMWR* **39**(RR-15): 1-18, November 23, 1990.
34. Measles Prevention: Recommendations of the Immunization Practices Advisory Committee (ACIP), *MMWR* **38**(S-9): 5-22, December 29, 1989.
35. Jong, E.C., *The Travel and Tropical Medicine Manual*, W.B. Saunders Company, p. 12-16, 1987.
36. Committee on Immunization Council of Medical Societies, American College of Physicians, Phila., PA, *Guide for Adult Immunization*, First Edition, 1985.
37. Recommendations of the Immunization Practices Advisory Committee (ACIP), Mumps Prevention, *MMWR* **38**(22): 388-400, June 9, 1989.
38. King, G.E.; Markowitz, L.E.; Patriarca, P.A.; et al: Clinical Efficacy of Measles Vaccine During the 1990 Measles Epidemic, *Pediatr. Infect. Dis. J.* **10**(12): 883-888, December 1991.
39. Krasinski, K.; Borkowsky, W.: Measles and Measles Immunity in Children Infected With Human Immunodeficiency Virus, *JAMA* **261**(17): 2512-2516, 1989.
40. Kelso, J.M.; Jones, R.T.; Yunginger, J.W.: Anaphylaxis to measles, mumps, and rubella vaccine mediated by IgE to gelatin, *J. Allergy Clin. Immunol.* **91**: 867-872, 1993.
41. General Recommendations on Immunization, Recommendations of the Advisory Committee on Immunization Practices, *MMWR* **43**(RR-1): 1-38, January 28, 1994.
42. Center for Disease Control: Immunization of Children Infected with Human T-Lymphotropic Virus Type III/Lymphadenopathy-Associated Virus, *Annals of Internal Medicine*, **106**: 75-78, 1987.

43. Krasinski, K.; Borkowsky, W.; Krugman, S.: Antibody following measles immunization in children infected with human T-cell lymphotropic virus-type III/lymphadenopathy associated virus (HTLV-III/LAV) [Abstract]. In: Program and abstracts of the International Conference on Acquired Immunodeficiency Syndrome, Paris, France, June 23-25, 1986.
44. Bitnum, A.; et al: Measles Inclusion Body Encephalitis Caused by the Vaccine Strain of Measles Virus. *Clin. Infect. Dis.* 29: 855-861, 1999.
45. Angel, J.B.; et al: Vaccine Associated Measles Pneumonitis in an Adult with AIDS. *Annals of Internal Medicine*, 129: 104-106, 1998.
46. Isaacs, D.; Menser, M.: Modern Vaccines, Measles, Mumps, Rubella, and Varicella, *Lancet* 335: 1384-1387, June 9, 1990.
47. Peter, G.; et al (eds): Report of the Committee on Infectious Diseases, Twenty-fourth Edition, American Academy of Pediatrics, 344-357, 1997.
48. Starr, S.; Berkovich, S.: The effect of measles, gamma globulin modified measles, and attenuated measles vaccine on the course of treated tuberculosis in children, *Pediatrics* 35: 97-102, January 1965.
49. Vaccine Adverse Event Reporting System — United States, *MMWR* 39(41): 730-733, October 19, 1990.
50. Rubella vaccination during pregnancy — United States, 1971-1981. *MMWR* 31(35): 477-481, September 10, 1982.
51. Eberhart-Phillips, J.E.; et al: Measles in pregnancy: a descriptive study of 58 cases. *Obstetrics and Gynecology*, 82(5): 797-801, November 1993.
52. Jespersen, C.S.; et al: Measles as a cause of fetal defects: A retrospective study of ten measles epidemics in Greenland. *Acta Paediatr Scand.* 66: 367-372, May 1977.
53. Losonsky, G.A.; Fishaut, J.M.; Strussenber, J.; Ogra, P.L.: Effect of immunization against rubella on lactation products. II. Maternal-neonatal interactions, *J. Infect. Dis.* 145: 661-666, 1982.
54. Landes, R.D.; Bass, J.W.; Millunchick, E.W.; Oetgen, W.J.: Neonatal rubella following postpartum maternal immunization, *J. Pediatr.* 97: 465-467, 1980.
55. Lerman, S.J.: Neonatal rubella following postpartum maternal immunization, *J. Pediatr.* 98: 668, 1981. (Letter)
56. Gershon, A.; et al: Live attenuated rubella virus vaccine: comparison of responses to HPV-77-DE5 and RA 27/3 strains, *Am. J. Med. Sci.* 279(2): 95-97, 1980.
57. Weibel, R.E.; et al: Clinical and laboratory studies of live attenuated RA 27/3 and HPV-77-DE rubella virus vaccines, *Proc. Soc. Exp. Biol. Med.* 165: 44-49, 1980.
58. Bennetto, L; Scolding, N. Inflammatory/post-infectious encephalomyelitis. *J Neurol Neurosurg Psychiatry* 2004;75(Suppl 1):i22-8.
59. Fenichel, GM. Neurological complications of immunization. *AnnNeurol* 1982;12(2):119-28.
60. CDC, Measles Surveillance, Report No. 11, p. 14, September 1982.
61. Peltola, H.; et al: The elimination of indigenous measles, mumps, and rubella from Finland by a 12-year, two dose vaccination program. *N. Engl. J. Med.* 331: 1397-1402, 1994.
62. Centers for Disease Control and Prevention. Recommended childhood immunization schedule — United States, January-June 1996, *MMWR* 44(51 & 52): 940-943, January 5, 1996.

Dist. by: Merck Sharp & Dohme Corp., a subsidiary of
 **MERCK & CO., INC.**, Whitehouse Station, NJ 08889, USA

For patent information: www.merck.com/product/patent/home.html

Copyright © 2016 Merck Sharp & Dohme Corp., a subsidiary of **Merck & Co., Inc.**
 All rights reserved.

Revised: 11/2016

uspi-v205c-i-1611r006



MMWR

Weekly

December 14, 2001 / 50(49);1117

Persons using assistive technology might not be able to fully access information in this file. For assistance, please send e-mail to: mmwrq@cdc.gov. Type 508 Accommodation and the title of the report in the subject line of e-mail.

Notice to Readers: Revised ACIP Recommendation for Avoiding Pregnancy After Receiving a Rubella-Containing Vaccine

On October 18, 2001, the Advisory Committee on Immunization Practices (ACIP) reviewed data from several sources indicating that no cases of congenital rubella syndrome (CRS) had been identified among infants born to women who were vaccinated inadvertently against rubella within 3 months or early in pregnancy. On the basis of these data, ACIP shortened its recommended period to avoid pregnancy after receipt of rubella-containing vaccine from 3 months to 28 days.

Data were available from the U.S. Rubella Vaccine in Pregnancy Registry (1), the U.K. National Congenital Rubella Surveillance Programme (National Congenital Registry Surveillance Programme, unpublished data, 2001; P. Tookey, Ph.D., Center of Paediatric Epidemiology and Biostatistics, Institute of Child Health, London, personal communication, April 2001), and Sweden and Germany (G. Enders, M.D., Laboratory of Enders and Partners, and Institute for Virology, Infectology, and Epidemiology, personnel communication, September 2001) on 680 live births to susceptible women who were inadvertently vaccinated 3 months before or during pregnancy with one of three rubella vaccines (HPV-77, Cendehill, or RA 27/3). None of the infants was born with CRS. However, a small theoretical risk of 0.5% (upper bound of 95% confidence limit=0.05%) cannot be ruled out. Limiting the analysis to the 293 infants born to susceptible mothers vaccinated 1--2 weeks before to 4--6 weeks after conception, the maximum theoretical risk is 1.3%. This risk is substantially less than the $\geq 20\%$ risk for CRS associated with maternal infection during the first 20 weeks of pregnancy.

Measles-mumps-rubella (MMR) vaccine and its component vaccines should not be administered to women known to be pregnant. Because a risk to the fetus from administration of these live virus vaccines cannot be excluded for theoretical reasons, women should be counseled to avoid becoming pregnant for 28 days after vaccination with measles or mumps vaccines or MMR or other rubella-containing vaccines.

The goal of the U.S. rubella vaccination program is to prevent congenital rubella infection. ACIP recommended that MMR vaccine should be offered to all women of childbearing age (i.e., adolescent girls and premenopausal women) who do not have acceptable evidence of rubella immunity.

Most rubella cases in the United States occur among young Hispanic adults born outside the United States (2), and most infants with CRS are born to foreign-born mothers. Ensuring immunity in women of childbearing age, especially those at highest risk for exposure, will help to prevent CRS.

References

1. CDC. Measles, mumps, and rubella---vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1998;47(no. RR-8).
2. Reef SE, Frey TK, Abernathy E, et al. The changing epidemiology of rubella in the 1990s: on the verge of elimination and new challenges for control and prevention. JAMA(in press).

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of pages found at these sites.

Disclaimer All *MMWR* HTML versions of articles are electronic conversions from ASCII text into HTML. This conversion may have resulted in character translation or format errors in the HTML version. Users should not rely on this HTML document, but are referred to the electronic PDF version and/or the original *MMWR* paper copy for the official text, figures, and tables. An original paper copy of this issue can be obtained from the Superintendent of Documents, U.S. Government Printing Office (GPO), Washington, DC 20402-9371; telephone: (202) 512-1800. Contact GPO for current prices.

**Questions or messages regarding errors in formatting should be addressed to mmwrq@cdc.gov.

Page converted: 12/13/2001

[HOME](#) | [ABOUT MMWR](#) | [MMWR SEARCH](#) | [DOWNLOADS](#) | [RSS](#) | [CONTACT](#)
[POLICY](#) | [DISCLAIMER](#) | [ACCESSIBILITY](#)

SAFER • HEALTHIER • PEOPLE™

Morbidity and Mortality Weekly Report
Centers for Disease Control and Prevention
1600 Clifton Rd, MailStop E-90, Atlanta, GA 30333,
U.S.A



[Department of Health
and Human Services](#)

This page last reviewed 12/13/2001