Official websites use .gov A .gov website belongs to an official government organization in the United States. Secure .gov websites use HTTPS A lock ( ) or https:// means you've safely connected to the .gov website. Share sensitive information only on official, secure websites. Tatiana Lanzieri, MD; Penina Haber, MPH; Joseph P. Icenogle, PhD, MS; and Manisha Patel, MD, MS The 14th edition of the “Pink Book” was published August 2021. Vaccine-specific recommendations may be outdated. Refer to the Advisory Committee on Immunization Practices Vaccine Recommendations and Guidelines for the most updated vaccine-specific recommendations. Printer friendly version [14 pages] The name rubella is derived from Latin, meaning “little red.” Rubella was initially considered to be a variant of measles or scarlet fever. It was not until 1814 that it was first described as a separate disease in the German medical literature, hence the common name “German measles.” In 1914, Alfred F. Hess postulated a viral etiology based on his work with monkeys. Following a widespread epidemic of rubella infection in 1940, Norman Gregg, an Australian ophthalmologist, reported in 1941 the occurrence of congenital cataracts among infants born following maternal rubella. This was the first published recognition of congenital rubella syndrome (CRS). Rubella virus was first isolated in 1962 by two independent groups, Paul D. Parkman and colleagues and Thomas H. Weller and Franklin A. Neva. The first rubella vaccines were licensed in 1969. In 1971, a combined measles, mumps, and rubella (MMR) vaccine was licensed for use in the United States. In 2005, a combination measles, mumps, rubella, and varicella (MMRV) vaccine was licensed. Rubella virus is the sole member of the genus Rubivirus, in the family Matonaviridae. It is an enveloped virus with a single-stranded RNA of positive polarity and has a single antigenic type. Following respiratory transmission, the virus replicates in the nasopharynx and regional lymph nodes. In a pregnant woman, placental infection occurs during viremia and may lead to transplacental fetal infection. Fetal damage occurs through destruction of cells, as well as disruption of cell division. Fetal infection often results in a persistent infection

typically leading to hearing impairment and ocular and cardiovascular abnormalities. The average incubation period of rubella is 14 days, with a range of 12 to 23 days. Symptoms are often mild, and up to 50% of infections may be subclinical or inapparent. In young children, rash is usually the first symptom. In older children and adults, there may be a 1- to 5-day prodrome with low-grade fever, malaise, lymphadenopathy, and upper respiratory symptoms preceding the rash. Lymphadenopathy may begin a week before the rash and last several weeks. The rubella rash 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 a measles rash, does not coalesce, and is often more prominent after a hot shower or bath. Postauricular, posterior cervical, and suboccipital nodes may be involved. Arthralgia (joint pain) and arthritis are rare in children and adult males but occur frequently in adult women. Joint symptoms tend to occur at about the same time or shortly after the rash appears and may last for up to 1 month. Fingers, wrists, and knees are often affected. Chronic arthritis is rare. Other symptoms of rubella include conjunctivitis, testalgia, or orchitis. Small, red (Forschheimer) spots may be noted on the soft palate but are not diagnostic for rubella. Complications of rubella are rare. Hemorrhagic manifestations occur in approximately 1 per 3,000 cases. These manifestations may be secondary to low platelets and vascular damage, with thrombocytopenic purpura being the most common. Gastrointestinal, cerebral, or intrarenal hemorrhage may also occur. Effects may last from days to months, and most patients recover. Encephalitis occurs in 1 in 6,000 cases and may be fatal. Additional rare complications include granulomas in persons with primary immune deficiencies, orchitis, neuritis, and a late syndrome of progressive panencephalitis. Prevention of congenital rubella syndrome (CRS) is the main objective of rubella vaccination programs. Infection with rubella virus is most consequential in early gestation and can lead to miscarriages, stillbirths, and severe birth defects in infants. The risk of CRS is

highest when a woman acquires rubella during the first 12 weeks of gestation. Congenital infection with rubella virus can affect many organ systems. Congenital rubella syndrome includes a constellation of birth defects, such as deafness, eye abnormalities (cataracts, glaucoma, retinopathy, microphthalmia), and congenital heart disease. Many rash illnesses can mimic rubella infection, so clinical diagnosis is unreliable. Acute or recent rubella infection can be confirmed by detection of rubella virus by polymerase chain reaction (PCR), a significant rise in rubella specific immune globulin (Ig)G antibody from paired acute- and convalescent-phase sera, or the presence of rubella-specific IgM antibody. The optimal time for serum collection for IgM detection is 5 days after onset of symptoms (fever and rash). If serum is collected less than 5 days after onset and is IgM negative, a second sample is necessary to confirm or rule out rubella using IgM detection. In persons with rubella infection, the virus may be detected in nasal, throat, urine, blood, and cerebrospinal fluid specimens up to 10 days after rash onset (most successful within 3 days). In infants with suspected CRS, nasopharyngeal swabs and/or urine should be collected as close to birth as possible. If CRS is confirmed, infants should be screened for viral shedding monthly after the age of 3 months until two consecutive negative tests are obtained. Viral shedding may be detected for up to one year. Rubella used to be a worldwide infection. Endemic rubella and CRS were eliminated in the United States in 2004, and in the region of the Americas in 2009. Rubella is a human disease. There is no known animal reservoir and no evidence of insect transmission. Infants with CRS may shed rubella virus for an extended period. Rubella is spread from person-to-person via direct contact or droplets shed from the respiratory secretions of infected persons. Rubella may be transmitted by persons with subclinical or asymptomatic cases (up to 50% of all rubella virus infections). Since rubella elimination in the United States, sporadic cases of rubella have been imported or linked to an imported case, with no temporal pattern. Rubella is most contagious when the rash first appears, but virus may be shed from 7 days before

to 7 days after rash onset. Infants with CRS shed large quantities of virus from body secretions for up to 1 year and can therefore transmit rubella to persons caring for them who are susceptible to the disease. Rubella and congenital rubella syndrome became nationally notifiable diseases in 1966. Following vaccine introduction in 1969, rubella incidence declined dramatically. Rubella outbreaks continued to occur among adolescents and young adults and in settings where unvaccinated adults gathered. National recommendations to vaccinate susceptible postpubertal females, adolescents, persons in military service, college students, and persons in certain work settings, as well as increased rubella vaccination efforts in the Region of the Americas, led to further declines in rubella and CRS cases. In 2004, endemic rubella was declared eliminated in the United States, with fewer than 10 cases reported annually and less than one CRS case per year. Since 2012, all rubella cases reported in the United States had evidence the patients were infected outside the United States. In most CRS cases reported since 1998, the mother was born outside the United States. Among nine CRS cases reported in the United States between 2004 and 2014, all were import-associated or from unknown sources. Among children born during 2016–2017, 90.7% received measles, mumps, and rubella-containing vaccine by age 24 months; this was not statistically significantly different from the coverage of 90.3% for children born during 2014–2015. In 1971, a combined measles, mumps, and rubella (MMR) vaccine was licensed for use in the United States, and the current rubella vaccine component (RA27/3) was licensed in 1979. In 2005, a combination measles, mumps, rubella, and varicella (MMRV) vaccine was licensed. Rubella vaccine is available as measles, mumps, and rubella vaccine (MMR [MMR-II]) and measles, mumps, rubella, and varicella vaccine (MMRV [ProQuad]). Both MMR and MMRV vaccine contain live, attenuated viruses. Single-antigen rubella vaccine is not available in the United States. The Advisory Committee on Immunization Practices (ACIP) recommends that MMR or MMRV vaccine be used when any of the individual components is indicated. MMR vaccine is a

lyophilized preparation of measles virus vaccine live, an attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture; mumps virus vaccine live, the Jeryl Lynn strain of mumps virus propagated in chick embryo cell culture; and rubella virus vaccine live, the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts. MMRV vaccine contains measles, mumps, and rubella virus of equal titer and identical to those in the MMR vaccine. The titer of Oka varicella zoster virus is higher in MMRV vaccine than in single-antigen varicella vaccine, a minimum of 9,772 plaque-forming units (PFU) versus 1,350 PFU, respectively. MMR and MMRV vaccines are supplied as a lyophilized (freeze-dried) powder and are reconstituted with sterile, preservative-free water and vaccine contains gelatin. MMR and MMRV vaccines are administered by the subcutaneous route. Each dose of MMR and MMRV vaccine contains neomycin as an antibiotic. It contains no adjuvant or preservative. MMR vaccine or MMRV vaccine can be used to implement the vaccination recommendations for prevention of measles, mumps, and rubella. MMR vaccine is licensed for use in persons age 12 months or older. MMRV vaccine is licensed for use in persons age 12 months through 12 years; MMRV vaccine should not be administered to persons age 13 years or older. Two doses of MMR vaccine, separated by at least 4 weeks, are routinely recommended for children age 12 months or older. Dose 1 of MMR vaccine should be given at age 12 through 15 months. A second dose of MMR vaccine is recommended based on previous observations of the failure of some to generate an immune response to measles following dose 1. Dose 2 is routinely given at age 4 through 6 years, before a child enters kindergarten or first grade. All students entering school should receive 2 doses of MMR vaccine (with the first dose administered at age 12 months or older) before enrollment. Dose 2 of MMR vaccine may be administered as soon as 4 weeks after dose 1. The minimum interval between doses of MMRV vaccine is 3 months, although when dose 2 is administered 4 weeks following dose 1, it can be considered

valid. For the first dose of measles, mumps, rubella, and varicella vaccines at age 12 through 47 months, either separate MMR and varicella (VAR) vaccines, or MMRV vaccine, may be used. However, the risk of febrile seizures is about twice as high for children receiving MMRV vaccine versus separate MMR and VAR vaccines. Providers who are considering administering MMRV should discuss the benefits and risks of both vaccination options with the parents. Unless the parent or caregiver expresses a preference for MMRV, separate MMR vaccine and VAR vaccine should be administered for the first dose in this age group. For the second dose of measles, mumps, rubella, and varicella vaccines at any age and for the first dose at age 48 months or older, the use of MMRV generally is preferred over separate injections of its equivalent component vaccines (i.e., MMR vaccine and VAR vaccine). Adults born in 1957 or later should receive at least 1 dose of MMR vaccine unless they have documentation of vaccination with at least 1 dose of measles, mumps, and rubella-containing vaccine or other acceptable presumptive evidence of immunity to these three diseases. Except for health care personnel, who should have documented immunity, birth before 1957 generally can be considered acceptable evidence of immunity to measles, mumps, and rubella. Colleges and other post-high-school educational institutions are potential high-risk areas for measles, mumps, and rubella transmission because of large concentrations of persons. Prematriculation vaccination requirements for measles immunity have been shown to significantly decrease the risk of measles outbreaks on college campuses where such requirements are implemented and enforced. All students entering colleges, universities, technical and vocational schools, and other institutions for post-high-school education should receive 2 doses of MMR vaccine or have other acceptable evidence of measles, mumps, and rubella immunity before entry. For unvaccinated health care personnel born before 1957 who lack laboratory evidence of measles, mumps, or rubella immunity or laboratory confirmation of disease, health care facilities should have policies that offer 2 doses of MMR vaccine at the

appropriate interval for measles and mumps and 1 dose of MMR vaccine for rubella, respectively. Health care facilities should also have policies for such personnel that recommend 2 doses of MMR vaccine during an outbreak of measles or mumps and 1 dose during an outbreak of rubella. This recommendation is based on serologic studies indicating that among hospital personnel born before 1957, 5% to 10% had no detectable measles, mumps, or rubella antibody. Adequate vaccination for health care personnel born during or after 1957 consists of at least 1 dose of MMR for rubella, and 2 appropriately spaced MMR doses for measles and mumps. Elimination of indigenous rubella and CRS can be maintained by continuing efforts to vaccinate susceptible adolescents and women of childbearing age, particularly those born outside the United States. These efforts should include vaccinating in family planning clinics and sexually transmitted disease (STD) clinics, and as part of routine gynecologic care. Efforts should also be made to maximize use of premarital serology results when such tests assess rubella immunity; emphasize vaccination for college students; vaccinate women postpartum and postabortion; immunize female prison staff and, when possible, female prison inmates; offer vaccination to at-risk women through the special supplemental program for Women, Infants, and Children (WIC); and implement vaccination programs in certain workplaces, particularly those employing persons born outside the United States. Measles-, mumps-, or rubella- virus-containing vaccine administered prior to age 12 months (e.g., for international travel) should not be counted as part of the 2-dose series. Children vaccinated before age 12 months should be revaccinated with 2 doses of appropriately spaced MMR or MMRV vaccine, the first dose administered when the child is age 12 through 15 months (12 months if the child remains in an area where disease risk is high) and the second dose at least 4 weeks later. Persons who experienced perinatal HIV-infection who may have received MMR vaccine prior to the establishment of effective combined antiretroviral therapy (cART), should be revaccinated with 2 appropriately spaced doses of MMR (i.e., the dose does not count)

unless they have other acceptable current evidence of immunity. MMR series should be administered once effective cART has been established for at least 6 months and there is no evidence of severe immunosuppression. Generally, persons can be considered immune to rubella if they were born before 1957, have serologic evidence of rubella immunity (equivocal test results should be considered negative), or laboratory confirmation of disease, or have documentation of adequate vaccination for rubella. Birth before 1957 provides only presumptive evidence of rubella immunity; it does not guarantee that a person is immune to rubella. Birth before 1957 is not acceptable evidence of rubella immunity for women who could become pregnant. Clinical diagnosis of rubella is unreliable and should not be considered in assessing immune status. Because many rash illnesses may mimic rubella infection and many rubella infections are unrecognized, the only reliable evidence of previous rubella infection is the presence of serum rubella IgG antibody. Laboratories that regularly perform antibody testing are generally the most reliable. At least 95% of vaccinated persons age 12 months or older develop serologic evidence of rubella immunity after a single dose, and more than 90% have protection against clinical rubella for at least 15 years. Follow-up studies indicate that 1 dose of vaccine confers long-term, probably lifelong, protection. Seroconversion rates are similar for MMR and MMRV vaccines. Although titers to rubella wane in the years after vaccination, there is no evidence that this leads to significant susceptibility to clinical rubella or CRS. Clinical rubella and CRS-affected pregnancies are extremely rare in vaccinated persons the United States. *MMRV only As with other vaccines, a history of a severe allergic reaction (anaphylaxis) to a vaccine component or following a prior dose is a contraindication to further doses. Moderate or severe acute illness (with or without fever) in a patient is considered a precaution to vaccination, although persons with minor illness may be vaccinated. MMR and MMRV vaccines both contain minute amounts of neomycin and gelatin. Persons with alpha-gal allergy may wish to consult their physician before receiving a vaccine that contains

gelatin. Severe immunocompromise (e.g., from hematologic and solid tumors, receipt of chemotherapy, congenital immunodeficiency, long-term immunosuppressive therapy or patients with HIV infection who are severely immunocompromised) is a contraindication for MMR and MMRV vaccination. If the person's level of immunocompetence is uncertain, the decision to vaccinate should be made by the health care provider that prescribed the immunosuppressive medication for those patients whom immunocompromise is due to medication. Patients who have not received chemotherapy for at least 3 months, whose disease remains in remission, and who have restored immunocompetence, may receive MMR or MMRV vaccine. Healthy, susceptible close contacts of severely immunocompromised persons should be vaccinated. Persons receiving systemic high-dose corticosteroid therapy (2 milligrams per kilogram of body weight or more per day or 20 milligrams or more per day of prednisone) for 14 days or more should not receive MMR or MMRV vaccine because of concern about vaccine safety. MMR or MMRV should not be administered for at least 1 month after cessation of systemic high-dose corticosteroid therapy. Although persons receiving high doses of systemic corticosteroids daily or on alternate days for less than 14 days generally can receive MMR or MMRV immediately after cessation of treatment, some experts prefer waiting until 2 weeks after completion of therapy Available data indicate that vaccination with MMR has not been associated with severe or unusual adverse reactions in HIV-infected persons who are not severely immunosuppressed, although antibody responses have been variable. MMR vaccine is recommended for susceptible HIV-infected persons age 12 months or older with no evidence of current severe immunosuppression ("no evidence of current severe immunosuppression" is defined as CD4 percentages greater than or equal to 15% for 6 months or longer for persons age 5 years or younger; and CD4 percentages greater than or equal to 15% and CD4 count greater than or equal to 200 cells/mm3 for 6 months or longer for persons older than age 5 years). MMR vaccine is not recommended for HIV-infected

persons with evidence of severe immunosuppression. MMRV is not approved for and should not be administered to a person known to be infected with HIV. A family history of congenital or hereditary immunodeficiency in first-degree relatives (e.g., parents and siblings) is a contraindication for MMR or MMRV vaccine, unless the immune competence of the potential vaccine recipient has been substantiated clinically or verified by a laboratory. *MMRV only A history of thrombocytopenic purpura or thrombocytopenia is a precaution for MMR and MMRV vaccine. Such persons may be at increased risk for developing clinically significant thrombocytopenia after MMR or MMRV vaccination. Receipt of specific antiviral drugs (e.g., acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination is a precaution for MMRV vaccine due to the varicella component. These drugs should be avoided for 14 days after vaccination. Simultaneous use of aspirin or aspirin-containing products is a precaution for MMRV vaccine due to the varicella component. The manufacturer recommends that vaccine recipients avoid the use of salicylates for 6 weeks after receiving MMRV vaccine because of the association between aspirin use and Reye syndrome following chickenpox. A personal or family (i.e., sibling or parent) history of seizures of any etiology is a precaution for MMRV vaccine but not MMR. Children with a personal or family history of seizures of any etiology should ideally be vaccinated with separate MMR and VAR vaccines because the risks for using MMRV vaccine in this group of children generally outweigh the benefits. MMR vaccine may be administered to egg-allergic persons without prior routine skin testing or the use of special protocols. The effect of the administration of antibody-containing blood products (e.g., immune globulin, whole blood or packed red blood cells, or intravenous immune globulin) on the response to MMR or MMRV vaccine is unknown. Because of the potential inhibition of the response to vaccination by passively transferred antibodies, neither MMR vaccine nor MMRV vaccine (nor VAR vaccine) should be administered for 3 to 11 months after receipt of antibody-containing blood products. The interval between the

antibody-containing blood product and receipt of MMR or MMRV vaccine is determined by the type of product administered. Antibody-containing products should not be given for 2 weeks following vaccination unless the benefits exceed those of the vaccine. In such cases, vaccine recipients should either be revaccinated later at the appropriate intervals (ranging 3 to 11 months) or tested for immunity and revaccinated if seronegative. Need for tuberculin skin testing or interferon-gamma release assay (IGRA) testing is a precaution for MMR and MMRV vaccine. Measles vaccine (and possibly mumps, rubella, and varicella vaccines) may transiently suppress the response to tuberculin skin test (TST) in a person infected with Mycobacterium tuberculosis. TST and measles-containing vaccine may be administered at the same visit if necessary. Simultaneously administering TST and measles-containing vaccine does not interfere with reading the TST result at 48 to 72 hours and ensures that the person has received measles vaccine. If the measles-containing vaccine has been administered recently, TST screening should be delayed for at least 4 weeks after vaccination. Receipt of specific antiviral drugs (e.g., acyclovir, famciclovir, or valacyclovir) 24 hours before vaccination is a precaution for MMRV vaccine due to the varicella component. These drugs should be avoided for 14 days after vaccination. Pregnancy is a contraindication for MMR or MMRV vaccine. Pregnancy should be avoided for 4 weeks following MMR or MMRV vaccine. Close contact with a pregnant woman is not a contraindication to MMR or MMRV vaccination of the contact. If a pregnant woman inadvertently receives MMR or MMRV vaccine, termination of pregnancy is not recommended because the risk to the fetus appears to be extremely low. Instead, individual counseling for these women is recommended. Data from 321 susceptible women who received rubella vaccine showed no evidence of CRS in offspring. Studies conducted in six Latin American countries showed a negligible or absent risk for CRS after administration of rubella vaccine shortly before or during pregnancy. Of the 1,980 susceptible pregnant women followed, 70 (3.6%) of the infants had congenital rubella infection, but none had

congenital defects associated with CRS. MMR MMRV Studies have shown MMR and MMRV vaccines are safe and well-tolerated. The National Academy of Medicine, formerly called the Institute of Medicine, reviewed the evidence between MMR vaccination and certain adverse events. The experts determined that evidence supports a causal relation between MMR vaccination and anaphylaxis, febrile seizures, thrombocytopenic purpura, transient arthralgia, and measles inclusion body encephalitis in persons with demonstrated immunodeficiencies. Most adverse events reported following MMR vaccination (such as fever and rash) are attributable to the measles component. After MMR vaccination, 5% to 15% of susceptible persons develop a temperature of 103°F (39.4°C) or higher, usually occurring 7 to 12 days after vaccination and generally lasting 1 or 2 days. Most persons with fever do not have other symptoms. MMR vaccine is associated with a very small risk of febrile seizures; approximately one case for every 3,000 to 4,000 doses of MMR vaccine administered. The febrile seizures typically occur 6 to 14 days after vaccination and do not appear to be associated with any long-term sequelae. Children with a personal or family history of febrile seizures or family history of epilepsy might be at increased risk for febrile seizures after MMR vaccination. Allergic reactions following the administration of MMR vaccine are rare. Most of these are minor and consist of a wheal and flare or urticaria at the injection site. Immediate, anaphylactic reactions to MMR vaccine occur in 1.8 to 14.4 cases per million doses. Arthralgias and other joint symptoms are reported in up to 25% of adult women following MMR vaccine and are associated with the rubella component. Transient lymphadenopathy sometimes occurs following receipt of MMR or other rubella-containing vaccine, and parotitis has been reported rarely (less than 1%) following receipt of MMR or other mumps-containing vaccine. Rarely, MMR vaccine may cause thrombocytopenia within two months after vaccination. The clinical course of these cases is usually transient and benign, although hemorrhage occurs rarely. Based on case reports, the risk for MMR vaccine-associated thrombocytopenia may be higher

for persons who have previously had immune thrombocytopenic purpura, particularly for those who had thrombocytopenic purpura after an earlier dose of MMR vaccine. Measles inclusion body encephalitis has been documented after measles vaccination in persons with immune deficiencies. The illness is also known to occur within 1 year after initial infection with wild-type measles virus and has a high death rate. In the cases after MMR vaccination, the time from vaccination to development of measles inclusion body encephalitis was 4–9 months, consistent with development of measles inclusion body encephalitis after infection with wild-type measles virus. In MMRV vaccine prelicensure studies conducted among children age 12 to 23 months, fever (reported as abnormal or elevated greater than or equal to 102°F oral equivalent) was observed 5 to 12 days after vaccination in 21.5% of MMRV vaccine recipients compared with 14.9% of MMR vaccine and VAR vaccine recipients. Two postlicensure studies indicated that one additional febrile seizure per 2,300 to 2,600 children age 12 through 23 months occurred 5 to 12 days after the first dose of MMRV vaccine, compared with children who had received the first dose of MMR vaccine and VAR vaccine administered as separate injections at the same visit. Data from postlicensure studies do not suggest that this increased risk exists for children age 4 to 6 years receiving the second dose of MMRV vaccine. Multiple studies, as well as a National Academy of Medicine Vaccine Safety Review, refute a causal relationship between autism and MMR vaccine or between inflammatory bowel disease and MMR vaccine. For MMR-II and Proquad storage and handling specifics, refer to the manufacturer. For complete information on storage and handling best practices and recommendations, please refer to CDC’s Vaccine Storage and Handling Toolkit [3 MB, 65 pages]. Rubella and congenital rubella syndrome became nationally notifiable diseases in 1966. For information on guidance for state and local health department staff who are involved in surveillance activities for vaccine-preventable diseases, please consult the Manual for the Surveillance of Vaccine-Preventable Diseases. The editors would like to acknowledge Zaney Leroy,

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