Rubella (German Measles)

Summary

Rubella is an infectious viral disease characterized by two distinct illnesses: postnatal rubella, which is generally self-limited and mild; and congenital rubella syndrome (CRS), which has potentially deadly or debilitating effects on the developing fetus during maternal infection, especially if infected early in pregnancy. Postnatal rubella cases are often subclinical; symptomatic individuals may present with lymphadenopathy, malaise, and low-grade fever, followed by an erythematous maculopapular rash. Rubella virus has effectively been eradicated from the Americas region thanks to vaccination; epidemic rubella in the U.S. last occurred in 1964, and rubella was declared eliminated from the United States in 2004. However, it remains endemic in other parts of the world and can be imported by international travelers. It is most prevalent in winter and spring, but can be imported any time of year.

Agent

Rubella virus is a single-stranded RNA virus and the sole member of the genus *Rubivirus*, in the family Matonaviridae. There is only one antigenic type.

Transmission

Reservoir**:**

Humans.

Mode of transmission:

- Postnatal rubella: direct or droplet contact with nasopharyngeal secretions of infected persons; can also be transmitted from mother to fetus during pregnancy.
- CRS: Infants with CRS can shed virus in nasopharyngeal secretions and urine.

Period of communicability:

- Postnatal rubella: from 7 days before through 7 days after the onset of rash.
- CRS: Infants with CRS shed large quantities of virus in nasopharyngeal secretions and urine for up to a year, and can transmit infection to susceptible contacts.

Clinical Disease

Incubation period:

For postnatally acquired rubella, average of 14 days, with a range of 12-23 days.

Illness:

- Postnatal rubella:
  - Usually a mild disease; up to 50% of infections are subclinical or inapparent
  - Diffuse erythematous maculopapular rash often the first sign in children; may be preceded by 1-5 day prodrome of low-grade fever, malaise, lymphadenopathy (commonly sub-occipital, postauricular and cervical), and upper respiratory symptoms in older children and adults

        - Rash usually starts on face and progresses downward, lasts about 3 days, and is sometimes itchy. Rubella rash is fainter than measles rash, does not coalesce, and may be more prominent after a hot shower or bath
    - Arthralgias and arthritis commonly occur in adult female cases, occurring at the same time or shortly after the rash appears, lasting up to a month
    - Small red Forschheimer spots may appear on soft palate, but are not diagnostic for rubella. Conjunctivitis, orchitis, or testalgia may also occur.
    - Leukopenia and thrombocytopenia can occur, but hemorrhagic complications are rare (1 in 3000 cases). Encephalitis occurs in 1 in 6000 cases, more often in adults, and can be fatal.
- Congenital Rubella Syndrome (CRS):
    - CRS can lead to miscarriage, stillbirth, and/or severe birth defects in infants, including:
        - Ophthalmologic (cataracts, retinopathy, glaucoma, microphthalmia)
        - Congenital heart disease (e.g., patent ductus arteriosus, peripheral pulmonary artery stenosis)
        - Deafness or hearing impairment
        - Neurologic (behavioral disorders, developmental delay, meningoencephalitis)
        - Hepatosplenomegaly, jaundice, purpuric skin lesions (blueberry muffin syndrome), radiolucent bone disease
    - Occurrence of congenital defects is:
        - 50% or greater if infection occurs during the first month of gestation
        - 20-30% if during the second month of gestation
        - 5% if during the 3rd or 4th month of gestation
    - Approximately one third of infants with congenital rubella syndrome die before one year of age

Laboratory Diagnosis

Laboratory diagnosis can be made using serology (detection of rubella-specific IgM, a significant rise between acute and convalescent IgG, or persistence of unexpectedly high IgG in an infant), PCR, or viral isolation. Serology testing is most commonly used. (Note that depending on epidemiological circumstances, additional testing to rule out measles may also be needed.)

Postnatal Rubella

- Sera should be collected as early as possible, but within 7-10 days of illness onset and then 2-3 weeks later for convalescent titers
    - 50% of cases are IgM-positive on the day of rash onset; >90% are positive five days after rash onset. Therefore, if serum collected <5 days after rash onset is

negative, a second sample is needed to confirm or rule out rubella. IgM is typically detectable up to 30 days after rash onset in acute postnatal rubella infection.

- Serum rubella IgM test results can be falsely positive in persons with other viral infections (e.g., acute infection with Epstein-Barr virus [infectious mononucleosis], recent cytomegalovirus infection, and parvovirus infection) or in the presence of rheumatoid factor. A person may also be rubella IgM positive after recent vaccination.
  - IgG screening for rubella is recommended as part of prenatal care. IgM testing of asymptomatic, unexposed pregnant people is **not recommended** due to the high likelihood for false positives; however, it is not uncommon, usually due to ordering error or labs automatically running IgM and IgG tests together.
- IgG avidity testing is available at CDC, which can help distinguish distant exposure from infection or vaccination (high avidity) from more recent infection occurring within the last 4 months (low avidity).

- For postnatal rubella cases, PCR on a nasopharyngeal swab, throat swab, and/or urine may be useful (in addition to serology) if collected from two days before rash onset to four days after rash onset; however, PCR is more commonly done for suspected CRS cases.

Congenital Rubella Syndrome (CRS)

- Sera for IgM for suspected CRS cases should be collected as close to birth as possible, and again at 1 month of age if the initial IgM test is negative. If paired sera are collected, the second sample should be collected 14-21 days after the acute specimen.
  - At 3 months of age, approximately 50% of cases still have detectable IgM in serum; IgM may remain detectable up to 6 months after birth in CRS cases.
  - The presence of rubella IgG in an infant after 9 months of age (when maternal antibodies should have diminished) and the absence of vaccination or (new) exposure to rubella would confirm CRS.
- In addition to serology, clinical samples for suspected CRS cases should include nasopharyngeal swabs, throat swabs, and urine for PCR and/or viral isolation, collected as close to birth as possible.
  - To screen for continued shedding of virus in confirmed CRS cases, nasopharyngeal, throat, and/or urine samples should be collected monthly, beginning after the age of 3 months, and continuing until there have been two consecutive negative tests collected a month apart.

Treatment

Supportive.

Surveillance

Rubella Case Definition (2013):

Laboratory criteria: Rubella infection confirmed by one or more of the following laboratory tests:

- Isolation of rubella virus
- Detection of rubella-virus specific nucleic acid by polymerase chain reaction (PCR)
- IgG seroconversion (not explained by MMR vaccination during the previous 6-45 days) or a significant rise between acute- and convalescent-phase titers in serum rubella IgG antibody level by any standard serologic assay
- Positive serologic test for rubella IgM antibody (not explained by MMR vaccination during the previous 6-45 days and not otherwise ruled out by more specific testing in a public health laboratory).

Serum rubella IgM test results that are false positives have been reported in persons with other viral infections (e.g., acute infection with Epstein-Barr virus (infectious mononucleosis), recent cytomegalovirus infection, and parvovirus infection) or in the presence of rheumatoid factor.

Confirmed:

- A person with or without symptoms who has laboratory evidence of rubella confirmed by one of the above laboratory tests in the laboratory criteria, **or**
- An illness characterized by all of the following:
    - Acute onset of generalized maculopapular rash **and**
    - Temperature greater than 99.0°F or 37.2°C **and**
    - Arthralgia, arthritis, lymphadenopathy, or conjunctivitis **and**
    - Epidemiologic linkage to a laboratory-confirmed case of rubella

Probable:

In the absence of a more likely diagnosis, an illness characterized by all of the following:

- Acute onset of generalized maculopapular rash; **and**
- Temperature greater than 99.0° F or 37.2° C, if measured; **and**
- Arthralgia, arthritis, lymphadenopathy, or conjunctivitis; **and**
- Lack of epidemiologic linkage to a laboratory confirmed case of rubella; **and**
- Noncontributory or no serologic or virologic testing.

Suspect: Any generalized rash illness of acute onset that does not meet the criteria for probable or confirmed rubella or any other illness.

Epidemiologic Classification

Internationally imported case: An internationally imported case is defined as a case in which rubella results from exposure to rubella virus outside the U.S. This is evidenced by at least some of the exposure period (12–23 days before rash onset) occurring outside the U.S. and the onset of rash within 23 days of entering the United States (U.S.) and no known exposure to rubella in the U.S. during that time. All other cases are considered U.S.-acquired cases.

U.S.-acquired case: A U.S.-acquired case is defined as a case in which the patient had not been outside the United States during the 23 days before rash onset or was known to have

been exposed to rubella within the U.S. These cases are subclassified into four mutually exclusive groups:

- Import-linked case: Any case in a chain of transmission that is epidemiologically linked to an internationally imported case.
- Imported-virus case: Any case for which an epidemiologic link to an internationally imported case was not identified but for which viral genetic evidence indicates an imported rubella genotype (i.e., a genotype that is not occurring within the U.S. in a pattern indicative of endemic transmission). An endemic genotype is the genotype of any rubella virus that occurs in an endemic chain of transmission (i.e., lasting ≥12 months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.
- Endemic case: A case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of rubella virus transmission continuous for ≥12 months within the U.S.
- Unknown source case: A case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.-acquired chain of transmission or an endemic chain of transmission within the U.S.

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 U.S. For national reporting, however, cases will be classified as either internationally imported or U.S.-acquired.

Congenital Rubella Syndrome Case Definition (2010):

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

- Cataracts or 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
- Radiolucent bone disease

Probable: An infant without an alternative etiology that does not have laboratory confirmation of rubella infection, but does have at least 2 of the following:

- Cataracts or congenital glaucoma*
- Congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis)
- Hearing impairment
- Pigmentary retinopathy

AND one or more of the following:

- Purpura
- Hepatosplenomegaly
- Jaundice
- Microcephaly
- Developmental delay
- Meningoencephalitis
- Radiolucent bone disease

* In probable cases, either or both of the eye-related findings (cataracts and congenital glaucoma) count as a single complication.

Confirmed:

An infant with at least one symptom (listed above) that is clinically consistent with congenital rubella syndrome; and laboratory evidence of congenital rubella infection as demonstrated by:

- Isolation of rubella virus
- Detection of rubella-specific immunoglobulin M (IgM) antibody
- Infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (i.e., rubella titer that does not drop at the expected rate of a twofold dilution per month)
- A specimen that is PCR-positive for rubella virus

Infection Only:

An infant without any clinical symptoms or signs but with laboratory evidence of infection as demonstrated by one of the laboratory criteria listed above.

Note: If any compatible signs or symptoms (e.g., hearing loss) 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 U.S. or in the absence of documented rubella infection, if the mother was outside the U.S. during 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 U.S. U.S.-acquired cases are subclassified into four mutually exclusive groups:

- Import-linked case**:** Any case in a chain of transmission that is epidemiologically linked to an internationally imported case.
- Import-virus case**:** A case for which an epidemiologic link to an internationally imported case was not identified but for which viral genetic evidence indicates an imported rubella genotype (i.e., a genotype that is not occurring within the U.S. in a pattern indicative of endemic transmission). An endemic genotype is the genotype of any rubella virus that occurs in an endemic chain of transmission (i.e., lasting ≥12 months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.
- Endemic case**:** A case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of rubella virus transmission continuous for ≥12 months within the U.S.
- Unknown source case**:** A case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.-acquired chain of transmission or an endemic chain of transmission within the U.S.

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

Reporting:

Report all suspected, probable, or confirmed cases of rubella or CRS to the Epidemiology and Response Division (ERD) at 505-827-0006. Information needed includes: patient's name, age, sex, race, ethnicity, home address, home phone number, occupation, and health care provider.

Case Investigation:

Complete the CDC Rubella Surveillance Worksheet (or Congenital Rubella Syndrome Surveillance Worksheet, as applicable) and mail to the Epidemiology and Response Division, P.O. Box 26110, Santa Fe, New Mexico 87502-6110, or fax to 505-827-0013. Investigation information should also be entered in NMEDSS per established procedures.

Control Measures

The goal of controlling rubella infections is to prevent birth defects in the fetuses of susceptible mothers.

1. Case management

1.1. Isolation: Standard and droplet precautions and isolation are recommended for seven days following the onset of rash in postnatal rubella cases. Contact precautions are required for up to one year for children with CRS, until two consecutive sets of nasopharyngeal and urine cultures, taken after three months of age and at least one month apart, are negative.

1.1.a Infants with CRS should not attend daycare or interact with anyone without evidence of immunity to rubella until determined to be no longer infectious.

2. Contact management

2.1. All contacts should be traced, with particular attention to contacts that are pregnant or potentially pregnant.

2.2. Evidence of immunity to rubella includes at least one of the following:

2.2.a Written documentation of vaccination with one dose of live rubella virus-containing vaccine administered on or after the first birthday (e.g., MMR, MMRV)

2.2.b Laboratory evidence of immunity (e.g., IgG+ titer)

2.2.c Laboratory confirmation of rubella disease

2.2.d Birth before 1957

2.3. Quarantine: People exposed to an infectious case of rubella or CRS who do not have evidence of immunity should be vaccinated with a dose of MMR (or MMRV) vaccine as soon as possible, if not contraindicated. (This is <u>not</u> effective as post-exposure prophylaxis, but can help protect against future exposures, limiting the duration and spread of an outbreak.)

2.3.a Contraindications to MMR or MMRV vaccine include, but are not limited to: pregnancy, immunocompromise, and age younger than 1 year. Pregnant women who do not have evidence of immunity should be vaccinated immediately after giving birth.

2.3.b People who have no evidence of immunity and do not receive an MMR or MMRV vaccine should be excluded until 23 days after the onset of rash in the last case of rubella.

2.3.c Unvaccinated people who receive MMR or MMRV vaccine as part of rubella outbreak control may immediately return to school or work, *provided* all people without documentation of rubella immunity have been excluded.

2.4. Immune globulin (IG) has been attempted as post-exposure prophylaxis in early pregnancy for exposed susceptible women; however, the available evidence indicates these attempts have failed to prevent CRS in the fetus, and therefore routine use in exposed pregnant patients is not recommended.

3. Prevention

3.1. Routine immunization is the primary mechanism to control rubella infection. Rubella vaccine is a live attenuated virus vaccine. Typically, it is combined with measles and mumps into the MMR vaccine (or additionally with varicella into the MMRV vaccine). The

immunization is recommended for children aged 12-15 months, followed by a second immunization preferably at 4-6 years of age. Over 95% of those vaccinated aged 12 months and older develop serologic evidence of rubella immunity after a single dose, and >90% have protection against clinical rubella for at least 15 years. Protection is likely lifelong.

3.2. Emphasis should be placed on the immunization of at-risk persons, including health care workers, childcare workers, other persons who have contact with young children, pregnant women, or congregate institutions (e.g., colleges, military sites), and foreign-born persons (especially women of reproductive age). Those persons who have not received at least one dose of vaccine or who have no serologic evidence of immunity are considered susceptible and should be immunized with MMR or MMRV vaccine if not contraindicated.

Managing Rubella in Child Care Centers and Schools

Adults or children with postnatal rubella should be excluded from work, school, or childcare for seven days following the onset of rash, and especially avoid contact with pregnant or potentially pregnant family members or friends who do not have evidence of immunity.

All persons having contact with a child with CRS should first have evidence of their immunity to rubella verified. Children with CRS should not attend childcare, unless in a setting where they would exclusively have contact with people with documented immunity to rubella (e.g., no other infants under 1 year of age). Children with CRS should be considered contagious until they are at least one year old, or until two consecutive sets of nasopharyngeal and urine samples taken a month apart are negative for rubella virus.

References

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See Rubella Fact Sheets (English) (Spanish).