Rubella Outbreak Control Guidelines

Infectious agent

Virus: Togavirus, genus *Rubivirus*; closely related to group A arboviruses.

Clinical manifestations

Symptoms

- Often mild and can include:
  - Fever, rash, arthritis/arthralgia, conjunctivitis, lymphadenopathy.
  - 30 – 50% of cases may be asymptomatic.
- Prodrome
  - Usually seen only in older children and adults, lasts 1 – 5 days and precedes the rash.
    - Consist of low grade fever, malaise, headache, swollen glands, and upper respiratory tract symptoms.
  - Postauricular, suboccipital and posterior cervical lymphadenopathy precedes rash by 5 – 10 days.
- Rash
  - Generalized, maculopapular usually begins on face and spreads downward.
  - The rash usually appears 14 – 17 days after exposure and lasts 1 – 3 days.
  - In children, rash is commonly the first symptom.
  - The rash is usually fainter than measles rash and does not coalesce.

Complications

- Uncommon in children, but occur more often in adults.
- Arthritis and/or arthralgia occur in 70% of women.
- Encephalitis (1/6,000 cases) and thrombocytopenia (1/3,000 cases) are rare complications.

Congenital Rubella Syndrome (CRS)

Maternal infection in early gestation may lead to fetal death, anomalies, spontaneous abortion or premature delivery. There is no infant rash presentation in CRS.

Commonly described anomalies are:

- Ophthalmologic (cataracts, retinopathy, microphthalmos, and congenital glaucoma),
- Cardiac (patent ductus arteriosus and pulmonary artery stenosis),
- Neurologic (mental retardation, meningoencephalitis, and behavioral disorders),
- Auditory (sensorineural hearing impairment),
- Enlargement of the spleen and liver, AND
- Growth retardation, radiolucent bone disease, purpura, and thrombocytopenia.
- Manifestation of CRS symptoms may be delayed for up to two years.

The occurrence of CRS related manifestations is:

- 85% if maternal infection occurs during the first 12 weeks of pregnancy,
- 54% during the first 13 to 16 weeks of gestation, AND

- 25% during the end of the second trimester.
- Defects are rare when infection occurs after the 20th week of gestation.

Incubation period

- 12 – 23 days with most symptoms appearing within 16 – 18 days after infection.

Period of communicability

- Infectious period is considered to be 7 days before to 7 days after the onset of rash.
- Children born with CRS may shed rubella virus for up to one year and should be considered infectious unless nasopharyngeal and urine cultures are repeatedly negative.

Transmission

- Person to person transmission occurs via airborne or droplets shed from respiratory secretions.
- May be transmitted by persons with subclinical or asymptomatic cases (up to 50% of all rubella virus infections).

Basic epidemiology

- Rubella occurs worldwide. In temperate areas, incidence is usually higher in winter and early spring.
- In October 2004, CDC declared that rubella was no longer endemic in the U.S.

Case definition for rubella

Approved by CSTE 2013
Case classification

Suspect case

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

Probable case

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.

Confirmed case

- A case with or without symptoms who has laboratory evidence of rubella infection confirmed by one or more of the following laboratory tests:
- Isolation of rubella virus OR
- Detection of rubella-virus specific nucleic acid by polymerase chain reaction; OR
- IgG seroconversion† or a significant rise between acute and convalescent-phase titers in serum rubella IgG antibody level by any standard serologic assay; OR
- Positive serologic test for rubella IgM antibody† * 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, if measured; AND
- Arthralgia, arthritis, lymphadenopathy, or conjunctivitis; AND
- Epidemiologic linkage to a laboratory-confirmed case of rubella.

†Not explained by MMR vaccination during the previous 6 – 45 days

* For NYS, test must be completed by Wadsworth Center.

Note: False-positive serum IgM results have been reported in the presence of other viral infections (e.g., acute infection with Epstein-Barr virus, recent cytomegalovirus infection and parvovirus infection) or in the presence of rheumatoid factor. *Patients with laboratory evidence of recent measles infection are excluded from a rubella diagnosis due to cross reactivity of test results*.

Epidemiologic classification

Internationally imported case

- Rubella results from exposure to rubella virus outside of the U.S. as evidenced by at least some of the exposure period (12 – 23 days before rash onset) occurring outside the U.S., AND
- Onset of rash occurs within 23 days of entering the 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

- Any case in which the patient has not been outside the U.S. during the 23 days before rash onset, OR
- Was known to have been exposed to rubella within the U.S.
- U.S. acquired sub classifications:
  - Import-linked case: epi-linked in a chain of transmission to an internationally imported case.
  - Imported-virus case: an epi-link to an internationally imported case was not identified but evidence indicates imported genotype, i.e. a genotype that is not occurring within the U.S.
  - 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. can not be established after a thorough investigation.

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

Case definition for Congenital Rubella Syndrome (CRS)

Approved by CSTE 2007/2010

Clinical case definition

- An illness, usually manifesting in infancy, resulting from rubella infection in utero and characterized by signs or symptoms from the following categories:
  - Cataracts/congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis), hearing impairment, pigmentary retinopathy,
  - Purpura, jaundice, hepatosplenomegaly, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease.

Laboratory criteria for diagnosis

- Isolation of rubella virus, OR
- Demonstration of rubella-specific immunoglobulin M (IgM) antibody, OR
- 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), OR
- PCR positive rubella virus.

Case classification

Suspect case

- An infant that does not meet the criteria for a probable or confirmed case but who has one of more of the following clinical findings:
  - cataracts or congenital glaucoma
  - congenital heart disease
  - hearing impairment
  - pigmentary retinopathy
  - purpura
  - hepatosplenomegaly
  - jaundice
  - microcephaly
  - developmental delay
  - meningoencephalitis or
  - radiolucent bone disease

Probable case*

- An infant without an alternative etiology that does not have laboratory confirmation of rubella infection but has at least two of the following:
  - cataracts or congenital glaucoma*
  - congenital heart disease
  - hearing impairment
  - pigmentary retinopathy
- An infant without an alternative etiology that does not have laboratory confirmation of rubella infection but has at least one or more of the following:
  - cataracts or congenital glaucoma*

- congenital heart disease
- hearing impairment
- pigmentary retinopathy AND
- one or more of the following:
  - purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, or radiolucent bone disease.

*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 loss) are identified later, the case is reclassified as confirmed.

Confirmed case

- An infant with at least one symptom that is clinically consistent with congenital rubella syndrome; and laboratory evidence of congenital rubella infection as 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 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), OR
  - 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 laboratory criteria discussed above.

Note: Due to the rarity of CRS, additional CSTE information will not be included here. *Please s*ee http://www.cdc.gov/ncphi/disss/nndss/casedef/rubellasc_current.htm for epidemiological classifications.

Testing and diagnosis

- Diagnostic tests used to confirm acute or recent rubella infection or CRS include serologic testing and virus detection.
- Because many rash illnesses may mimic rubella infection and 20% – 50% of rubella infections may be subclinical, laboratory testing is the only way to confirm the diagnosis.
- Isolation of wild-type virus is considered the gold standard.
- All suspect and probable cases and should have both serologies for IgM and IgG and viral testing.
- The acute specimen should be drawn at the first contact with the suspected rubella case and should be collected as early as possible (within 7 – 10 days) after onset of illness.
- Any negative IgM drawn before day 5 of rash onset should be drawn and repeated on or after day 5.
- The convalescent serum specimen (IgG) should be collected about 7 – 21 days after the first specimen. In most rubella cases, rubella IgG is detectable by 8 days after rash onset.
  - For comparison of acute and convalescent samples (“paired-sera”), assays must be run together in one laboratory at the same time and with the same test (“run in parallel”).

- Rubella virus can be isolated from nasal, blood, throat, urine and cerebrospinal fluid specimens from persons with rubella and CRS. The best results come from throat swabs.
    - Virus may be isolated from 1 week before to 2 weeks after rash onset. However, maximum viral shedding occurs up to day 4 after rash onset.

Specimen collection

Collection for IgM and IgG or culture

- Contact commercial laboratory regarding instructions and notification for specimen shipment.
- Use a separate kit for each specimen.
- Carefully complete the history form, including the clinical information, test results, provider name and phone number, patient name, DOB and county of residence.
- Specimen kits are not routinely available from Wadsworth Center. For questions or special requests, please contact the NYSDOH Bureau of Immunization (518) 473 – 4437 or Diagnostic Immunology at (518) 474 – 4177.

Specimen source

- For rubella IgM and IgG: serum.
- For PCR/culture: Clinical specimen from the nasopharynx or throat is preferred. Other sites include blood, urine and cerebrospinal fluid.

Procedure

- Rubella IgG and IgM serology
    - Acute serum specimen: collect serum within 7 – 10 days of onset of symptoms.
    - Convalescent serum specimen: collect serum 14 – 21 days after the acute specimen.
    - Separate acute and convalescent serum specimens need to be collected using serum separator tube.
    - Carefully complete the history form as described above.
    - Label specimen tube with patient's name and collection date.
    - When possible, centrifuge serum separator tube 20 – 30 minutes after collection.
- Rubella viral testing
    - Collect specimen ideally within 3 – 5 days of onset of symptoms.
    - Use separate specimen containers for each sample.
    - Nasopharyngeal or throat swab: Rub the two dry sterile swabs on the nasopharynx and /or throat.
    - Immerse swab tips in 5 ml of stabilizing buffer in the screw cap specimen tube.
    - Break the swabs to fit in the specimen tube and seal tightly.
    - Urine: Add specimen to a sterile centrifuge tube or screw-cap cup.
    - Insert specimen cup into plastic zip-lock bag or package specimen tube as for other samples.
    - Carefully complete the history form as described above.
    - Label specimen containers with patient's name and collection date.

Please note: Viral PCR testing is available at Wadsworth Center.

Transport

- Serum
  - Do NOT freeze.
  - Refrigerate at 4°C until shipping.
  - Ship with cold packs.
  - Samples must have an outer packaging to prevent freezing.
  - Viral specimen:
  - If unable to ship within 24 hours, preserve at -70°C.
  - Avoid freeze-thaw cycles.
  - Can ship with dry or wet ice or cold packs.

Mailing instructions for Wadsworth Center

- Please consult with the NYSDOH Bureau of Immunization prior to specimen shipment at (518) 473 – 4437.
- Rubella IgG and IgM serology submission by overnight mail
  - Put specimen kit into Styrofoam mailing box.
  - Include 1 – 2 cold packs to keep specimen refrigerated.
  - If specimen will be delivered on a weekend or holiday, call Diagnostic Immunology in advance: (518) 474 – 4177.

    Overnight delivery should be mailed to:
    Diagnostic Immunology
    David Axelrod Institute
    Wadsworth Center, NYSDOH
    120 New Scotland Avenue
    Albany, NY 12208

- Rubella viral specimen submission by overnight mail
  - Specimens must be delivered Monday – Friday (no weekends, no holidays).
  - Put specimen kit into Styrofoam mailing box.
  - Include 1 – 2 cold packs to keep specimen refrigerated.

    Overnight delivery should be mailed to:
    Virus Isolation Laboratory
    David Axelrod Institute
    Wadsworth Center, NYSDOH
    120 New Scotland Avenue
    Albany, NY 12208

Case investigation

<u>Demographics</u>

- Name
- Address
- DOB/age
- Occupation/Setting
- Race
- Ethnicity
- Gender

- Country of birth
- Length of time in the U.S.

Reporting Source

- Date reported
- Source
- Provider
- County

Clinical information

- Date of rash onset and duration
- Symptoms
- Hospitalizations and duration of stay
- Complications

Pregnancy history if patient is female

- Number of weeks gestation at onset of illness
- Date of serological immunity
- Prior diagnosis of rubella and dates
- Number and dates of previous pregnancies and location
- Pregnancy outcome (termination, CRS, normal infant)

Laboratory

- Laboratory name
- Date of acute serology specimen
- Date of convalescent serology specimen
- Results
- Other tests

Vaccine history

- Type
- Manufacturer
- Number of doses
- Vaccination dates
- Reason if not vaccinated

Epidemiology

- Date of investigation
- Transmission setting
- Associated with outbreak
- Source of Exposure
- Travel history

Create line listing

- If three or more probable or confirmed cases

Control measures

- Should be implemented as soon as at least one case of rubella is confirmed in a community. The goal of rubella case investigation is to prevent exposure of susceptible pregnant women and thereby prevent CRS.

Control measures for adults and children

- Exclude case from work or school until seven days after the onset of rash.
- The main strategies are to define at-risk populations, to ensure that susceptible persons are rapidly vaccinated (or excluded if a contraindication to vaccination exists), and to maintain active surveillance to permit modification of control measures if the situation changes.
- In settings where pregnant women may be exposed, control measures should begin as soon as rubella is suspected and should not be postponed until laboratory confirmation.
- Review immunization and clinical status of all contacts.
- Rubella immunity is defined as any of the following:
  - Documentation of at least 1 dose of rubella-containing vaccine administered on or after the age of 1 year, OR
  - Serologic evidence of immunity, OR
  - Born before 1957, except for women of child-bearing age or for health care personnel who must have serologic confirmation or vaccine documentation.

  Note: Clinical diagnosis of rubella is unreliable and should not be considered in assessing immune status.

- All persons at risk who cannot readily provide laboratory evidence of immunity or a documented history of vaccination on or after their first birthday should be considered susceptible. Vaccinate if no contraindications exist.
- Recommend immunization of susceptible contacts that are not pregnant.
  - Vaccine theoretically could prevent rubella if administered within 72 hours of exposure.
  - Contacts who are vaccinated may return to work or school immediately.
  - Exclude contacts who are not vaccinated until 3 weeks after the rash onset of the last reported case or until proof of immunity against rubella disease is demonstrated.

Pregnant contacts

- Exclude pregnant women that do not provide documented proof of rubella immunity until 3 weeks after the rash onset of the last reported case in the school or workplace.
- Obtain blood for rubella IgM AND IgG testing for immunity. Test but also save a sample for repeated testing at a later time.
  - If the rubella IgG is negative on the first sample, then obtain a second specimen three to four weeks after the initial specimen.
  - Repeat the rubella IgM and IgG on both the second sample AND the first sample in parallel.
  - If the rubella IgG is negative on the second sample, then obtain a third specimen six weeks after exposure. Repeat the rubella IgM and IgG on both the third sample AND the first sample in parallel.

Medical settings

- Mandatory exclusion and vaccination of susceptibles should be practiced in rubella outbreaks in medical settings because women and others may be exposed.

Extracurricular activities and events

- For 3 weeks after the last exposure of a school to the case, the school with the rubella case should contact any school to which students are traveling or from which students are coming and inform them that:
  - There is a confirmed rubella case at the school,
  - Non-immune students are excluded from school and activities, AND
  - All students from the non-infected school must have proof of immunity to rubella before the students can travel to the infected school.

Reporting

- A Confidential Case Report Form (DOH-389) must be submitted.
- The LHD must be notified immediately by telephone of any suspected case of rubella disease. The report should not wait for laboratory confirmation of the case.
- LHDs must notify the New York State Department of Health Bureau of Immunization within 24 hours of their notification, but preferably by telephone, as soon as the case is reported to them.