

Investigative Guidelines

March 2021

1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

- 1. To prevent congenital rubella syndrome (CRS).
- 2. To identify exposed pregnant women in a timely manner, determine their susceptibility and infection status, and provide or assure appropriate counseling about the risk of fetal infection.
- 3. To assure that children with suspected CRS are tested to confirm or rule out the diagnosis.
- 4. To evaluate the effectiveness of disease prevention efforts.

1.2 Laboratory and Physician Reporting Requirements

Physicians are required to report all cases of acute disease (including suspected cases) immediately. Labs are required to report rubella-specific positive tests (e.g., IgM, virus isolation, PCR) immediately, day or night.

1.3 Local Health Department Reporting and Follow-Up Responsibilities

- 1. Report all confirmed and presumptive cases (see definitions below) to the Acute and Communicable Disease Prevention (ACDP) program immediately, day or night. Call 971-673-1111 to reach the state epidemiologist on call.
- Begin follow-up investigation within 24 hours. Submit all case data electronically within 7 days of initial report. If rubella is suspected, facilitate collection and transport of specimens immediately to Oregon State Public Health Laboratory (OSPHL). Collect data that must accompany all specimens sent to OSPHL (see §3.4).
- 3. Initiate special control measures within 24 hours and complete them within 72 hours of initial report (see §5, Controlling Further Spread).
 - Identify persons who were exposed to the case during the period of communicability particularly women known to be or possibly pregnant.
 - Alert physicians, hospital emergency rooms, and other sites visited by the case during the period of communicability.
 - Alert physicians, hospital emergency rooms, student infirmaries, and local officials of the potential for additional cases; encourage them to consider rubella in patients presenting with a rash illness. Make special arrangements for patient flow to minimize transmission between potential cases and

susceptibles. Advise healthcare workers to immediately report any suspected case.

- Set up special clinics as needed to immunize susceptible persons.
- If indicated, prepare and distribute a press release in conjunction with the Immunization Program staff. Do not notify the press without consultation with the Oregon Health Authority (OHA).
- Identify and exclude susceptibles (i.e., unimmunized children and staff) when rubella has been identified in a school or daycare facility (see §§5 and 6).

1.4 State Public Heath Reporting Responsibilities

ACDP on-call epidemiologist should notify CDC Emergency Operations, immediately, day or night.

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

Rubella virus, an RNA-coded virus in the Togaviridae family.

2.2 Description of Illness

Acute Infection in Children and Adults

Rubella (German measles) is a mild febrile, rash illness. Young children usually experience little or no prodrome, while adolescents and adults often report 1–5 days of headache, fever, malaise, anorexia, mild conjunctivitis, rhinorrhea, or sore throat. Lymphadenopathy (usually suboccipital, postauricular, and posterior cervical) may precede the rash by 5–10 days. Prodromal signs and symptoms (if any) typically subside rapidly after rash onset. Fever rarely exceeds 39°C (102°F) and rarely persists beyond the first day of rash.

The maculopapular rash appears first on the face and spreads down the neck, arms, trunk, and legs. Lesions are pink and may become confluent on the face, but typically are pinpoint by the second day. The rash of rubella — typically lasting about 3 days—appears, spreads, and fades more quickly than that of measles.

CRS

The importance of rubella derives not from acute disease, which is usually quite mild, but the potentially devastating effects of in utero infections. A fetus infected early in pregnancy (especially first trimester) has a high probability of developing congenital rubella syndrome—a constellation of problems that includes low birth weight, eye defects (cataracts, microphthalmia, glaucoma, chorioretinitis), sensorineural deafness, cardiac defects (patent ductus arteriosus, peripheral pulmonary artery stenosis, atrial or ventricular septal defects), CNS defects (microcephaly, meningoencephalitis, mental retardation), hepatitis, hepatomegaly, thrombocytopenic purpura, splenomegaly, and bone lesions.

2.3 Reservoirs

Other acutely infected humans.

2.4 Modes of Transmission

Person-to-person via contact with infectious nasopharyngeal secretions and droplets and indirectly by objects contaminated with nasopharyngeal secretions of an infected patient, or the urine of an infant with CRS. As noted, vertical transmission from mother to fetus is also common.

2.5 Incubation Period

Ranges between 12–23 days; typically, 16–18 days.

2.6 Period of Communicability

- 1. Virus is typically secreted in nasopharyngeal secretions from about 7 days before until 7 days after rash onset. Some cases may shed as long as 14 days after the onset of the rash. Cases are most contagious just before and for a few days after rash onset.
- 2. Infants with CRS shed the virus in the nasopharyngeal secretions and urine for a highly variable period of time. Virus can be isolated from the nasopharynx of some 10–20% of these infants at 6 months of age, and shedding can persist for more than a year for a few.

2.7 Treatment

No specific treatment.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Confirmed Case Definitions (Reportable to OHA)

Acute Disease

Absent rubella immunization or receipt of antibody-containing blood products within the previous 45 days¹:

- confirmatory lab tests (rubella virus isolation, detection of virus by PCR, or ≥4-fold rise in antibody titer); or
- suggestive lab tests (positive IgM) with compatible illness (acute onset generalized maculopapular rash + temperature >99°F (37.2°C) + arthralgia, arthritis, lymphadenopathy or conjunctivitis).

CRS

Demonstration in the fetus or neonate of:

- rubella virus in body fluids or tissue, or
- a specimen that is PCR-positive for rubella virus, or

¹ Note that up to 10% of vaccinated individuals may remain IgM-positive even 10 weeks post vaccination.

• IgM antibodies or IgG antibodies that remain elevated during and after the first 6 months of life. (Maternal IgG antibody obtained by the fetus transplacentally would decline during this period of time.)

3.2 Presumptive Case Definitions (Reportable to OHA)

Acute Disease

A person who is epi-linked to a confirmed case and who has acute onset of generalized maculopapular rash, fever >37.2°C (99°F), and one or more of the following: arthralgias, arthritis, lymphadenopathy, or conjunctivitis. These individuals should not have had an MMR immunization within the 45 days before onset.

CRS

A child born with any two of the following complications: cataracts/congenital glaucoma, congenital heart disease, deafness, or pigmentary retinopathy; or, any one of the above and purpura, hepatosplenomegaly, jaundice, microcephaly, mental retardation, meningoencephalitis, or radiolucent bone disease.

3.3 Suspect Case Definitions (Not reportable to OHA)

Acute Disease

Anyone with an undiagnosed illness with rash and fever.

CRS

A child born with any of the complications listed above but not meeting the presumptive case definition.

3.4 Services Available at the Oregon State Public Health Laboratory (OSPHL)

The OSPHL does **not** currently test specimens for suspect cases of rubella.

Washington State Public Health Laboratory (WSPHL) performs testing for rubella-specific IgM and IgG antibodies (see testing algorithm on page 11). Viral cultures and PCR for rubella virus can be performed at CDC.

All suspect rubella cases and specimens submitted for testing must be coordinated with and approved by ACDP. Specimens for rubella testing for suspect cases should be sent to the OSPHL. Specimens will be forwarded to the WSPHL for serology testing or to CDC for virus isolation and PCR testing.

If rubella is considered a real possibility:

- Contact ACDP epidemiologists for approval to test specimens.
- After the request has been approved, please refer to the OSPHL Lab Test Menu for all specific instructions to properly collect, store, and transport specimens, available at: www.healthoregon.org/labtests.
- Collect the following required information: submitter, method of transport, expected specimen arrival date, tracking number, patient initials, DOB, rash

onset date, specimen collection date, specimen type(s), and test(s) requested.

- Persons suspected to have rubella should have serum drawn and specimens collected for viral testing (throat swab preferred) at the time of the first healthcare visit. Urine samples may also contain virus; collection of both respiratory and urine samples can increase the likelihood of detecting virus.
- Ensure that all forms noted as required on the Lab Test Menu page are completed.

IgM antibodies may not be detectable before 5 days after rash onset. If the IgM is negative in specimens taken before day 5, serologic testing should be repeated. If testing is for documentation of seroconversion (IgG), a second serum sample should be collected about 7–21 days after the first specimen. False-positive serum rubella IgM tests have occurred in persons with parvovirus B19 infections or infectious mononucleosis or with a positive rheumatoid factor.

Clinical specimens for virus isolation should be collected at the same time as samples taken for serologic testing, ideally within 4 days of rash onset. However, rubella virus has been isolated from 1 week before to 2 weeks after rash onset.

When a pregnant woman is known to have been exposed, collect specimens as you would for other suspect cases. Serum should be collected immediately for rubella antibody titer determination. If the pregnant woman is suspected to have acute rubella infection too late to draw an acute serum specimen, a single convalescent specimen that demonstrates rubella IgG antibody may also be tested for IgM rubella antibody to confirm the diagnosis.

Although this is not recommended, many pregnant women with no known exposure to rubella are tested for rubella IgM as part of their prenatal care. If rubella test results are IgM-positive for persons who have no or low risk of exposure to rubella, additional laboratory evaluation should be conducted. Consult with ACDP.

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. 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. In infants with CRS, IgM antibody can be detected in the infant's cord blood or serum and persists for about 6–12 months. Consult with ACDP.

4. ROUTINE CASE INVESTIGATION

4.1 Identify the Source of Infection

Ask about possible exposures during the period between 12–23 days before onset, including:

• Name, diagnosis, phone number, and address of any household member, playmate, or other contact with a rash illness. (Anyone meeting the

presumptive case definition should be reported and investigated in the same manner as a confirmed case.)

- Name of any indoor group activity attended (e.g., church, parties, family gatherings)
- Out-of-area travel history, including: places visited, routes, flight numbers, motels, tours, and tourist attractions visited
- Work or attendance at any school or daycare facility
- Work in or visits to any healthcare facility
- Visits to any health care provider

4.2 Identify Potentially Exposed Persons (Contacts)

Identify persons who have been in contact with the patient during the period from 7 days before to 7 days after onset of rash, including household members, school or daycare classmates, playmates, home visitors, etc.

Identify (among close contacts of the case) women who are pregnant or who are sexually active and not using reliable contraception. Determine their immune status (by documented history of immunization or previously positive serological test). If they are susceptible, refer to $\S6$, Managing Special Situations.

4.3 Determine Rubella Immune Status of Exposed Contacts

Nothing is foolproof, but any of the following are considered acceptable evidence of immunity:

- Birth before 1957 (but see §6.3)
- Laboratory-confirmed disease
- Laboratory evidence of immunity (protective antibody titers); or
- Documentation of vaccination with 1 dose of live rubella-virus-containing vaccine

4.4 Environmental Evaluation

None.

5. CONTROLLING FURTHER SPREAD

5.1 Education

Advise the patient or parents of the case to avoid potentially susceptible women who are, or may be, pregnant for 7 days after rash onset. Susceptible contacts who may have been infected may shed virus up to 7 days prior to onset; advise these individuals of precautions that should be taken to minimize exposure of susceptible pregnant women.

5.2 Isolation and School or Daycare Restrictions

1. Hospitalized rubella patients (including infants) should be placed on droplet precautions for the period of communicability.

- Restrict children with confirmed, presumptive, or suspected rubella from attendance at school or daycare centers while they could be contagious. Children with CRS may be contagious until they are one year of age, unless repeated culture results are negative. This restriction may be removed by written certification by a medical doctor, public health nurse, or school nurse stating that the infection is no longer communicable. (OAR 333-019-0010 and 333-019-0014)
- 3. Restrict infected employees of schools, daycare facilities, and healthcare facilities from working during the period of communicability. The local health officer may waive restrictions if adequate measures are taken to prevent transmission. (OAR 333-019-0010)
- 4. In the event of an outbreak, exclude susceptible children and staff from schools and daycare facilities as deemed necessary by the local health officer. Susceptible individuals should be excluded for at least 23 days from the last date of attendance of any communicable case (student or staff).

5.3 Follow-up of Case

All presumptive and suspected CRS cases should be evaluated with appropriate lab tests to confirm or rule out rubella infection.

5.4 **Protection of Contacts**

Passive Immunization

Immune globulin (IG) given after exposure may suppress symptoms without preventing infection or viremia. Administering IG to a susceptible, exposed pregnant woman has not been shown to prevent CRS. It is not generally recommended and should only be considered when abortion is not an option. Pregnant women should be advised that the effectiveness of IG administration has not been demonstrated (and is doubtful).

Active Immunization

There is no good evidence that giving rubella vaccine after exposure prevents illness, but there is likewise no evidence that vaccinating an already infected person is harmful. Therefore, since a single exposure to rubella may not lead to infection and since immunization would at least provide protection for future exposures, vaccination is recommended, unless specifically contraindicated. Contraindications to MMR vaccine include: pregnancy, anaphylactic reaction to eggs or egg products, anaphylactic reaction to neomycin, and compromised immunity. To be effective, vaccine should be administered at least two weeks before or deferred for at least 3 months after receipt of IG or other antibody-containing products, because passively acquired antibodies might interfere with the response to the vaccine.

Prior administration of anti-Rho(D) human immune globulin or blood products is not a contraindication to postpartum vaccination. Seroconversion should be evaluated serologically in 6 to 8 weeks. If seroconversion cannot be established, revaccination is indicated.

Vaccination Protocols

- Give the first dose of MMR at 12–15 months of age and a second dose at school entry, 4 to 6 years of age.
- Offer vaccine to susceptible females who are not pregnant or who are not at risk of becoming pregnant within 1 month, as well as all susceptible males born on or after January 1, 1957—preferable within 48 hours of exposure. (Persons born before 1957 are generally immune due to naturally acquired rubella infection.)
- Do not vaccinate pregnant women. While CRS resulting from rubella vaccination during pregnancy has not been observed, it is a theoretical concern. Although congenital defects have not been seen in babies born to mothers immunized during pregnancy, vaccine virus has been isolated from spontaneously aborted fetuses from such women. Since available data suggest that the risk of CRS resulting from prenatal immunization is very low, receipt of rubella vaccine in pregnancy is not ordinarily an indication for termination of pregnancy. Advise such women to receive rubella vaccine as soon as possible after delivery.
- Since protecting and possibly vaccinating women of child-bearing age is vitally important, take the following steps to protect exposed, susceptible sexually active women:
 - Determine pregnancy status. Exclude pregnant women from the outbreak setting for at least 23 days from the last day on which a case was present in the facility while communicable.
 - Recommend immunization for those who indicate they are not pregnant and who will not be at risk of pregnancy for at least 1 month.
 - Explain the theoretical risks to those who are pregnant or who are not sure of their pregnancy status. Assess their immune and pregnancy status as quickly as possible. If timely serologic confirmation is not possible, the decision to be vaccinated is ultimately made by the patient and her physician after discussing risks with local public health officials.

5.5 Environmental Measures

None.

6. MANAGING SPECIAL SITUATIONS 4

6.1 Exposure of a Pregnant Woman

Determine the woman's immune status immediately by

- testing serum for rubella antibodies, or
- a previously positive serological test.

Susceptible women should be monitored for occurrence of a rash illness for 23 days after last exposure. A repeat serological test should be done approximately

35 days after last exposure (23 days maximum incubation plus 12 days for development of antibody), regardless of the development of any illness.

6.2 Infection of a Pregnant Woman

Counsel infected pregnant women regarding the risk of CRS. The effects of rubella infection on the fetus depend on gestational age. CRS occurs in a minimum of 20–25% of infants born to women with first trimester infections. The actual risk may be considerably higher; if infected infants are followed for at least 2 years, up to 80% of these infants have some evidence of CRS. By the 16th week of gestation, the risk of CRS falls to approximately 10–20%. Defects rarely occur following infection beyond 20 weeks of gestation.

After initial counseling, pregnant women should be offered the opportunity to receive additional counseling.

6.3 Outbreak Control — Healthcare, School or Daycare Facilities

An outbreak is defined as three or more cases linked by time and place. Consider the following strategies:

<u>Active Surveillance</u>. Search for all potential cases of rubella (but remember that 30–50% of infections may not be apparent). Daily surveys of staff, students, parents, etc., may be indicated.

<u>**Case Management**</u>. Minimize exposure of hospitalized susceptibles placing infected persons under droplet precautions. Evaluate patient flow patterns to minimize transmission. Restrict cases to home for 7 days after rash onset. Travel should be postponed or conducted in such a way as to minimize transmission.

Exclusion of Susceptibles. Exclude susceptible individuals, especially pregnant women, from any facility while transmission is likely for at least 23 days from the last day on which a case was present and communicable.

<u>Vaccination of Susceptibles</u>. Immunize all non-pregnant individuals without documented immunity or history of rubella vaccination who are at risk of infection with MMR. Unexposed susceptibles who are vaccinated may be readmitted, excluded until 23 days have elapsed since the last date of exposure. During an outbreak of rubella, healthcare facilities should recommend 1 dose of MMR vaccine for unvaccinated personnel born before 1957 who lack laboratory evidence of rubella immunity or laboratory confirmation of disease.

UPDATE LOG

March 2021, Reporting period updated for LHDs. It's now immediately reportable. (Juventila Liko) <u>https://secure.sos.state.or.us/oard/viewSingleRule.action;JSESSIONID_OARD=0Fu</u> <u>2JSSGgBnydkcVHysg6pRnTJNubDoX42LIYX9TFLuFSYf2G1P-!-</u> 1212097070?ruleVrsnRsn=268992

November 2018. Algorithm revised. (Juventila Liko)

- August 2018. Updated recommendations regarding options for testing in Oregon. (Sarah Humphrey, Juventila Liko)
- March 2017. Lab section revised for clarity and to transport specimens to the OSPHL. (Juventila Liko)
- March 2015. Updated case definition (3.1) to match CDC definition and added flowchart for testing criteria. (Juventila Liko)
- February 2015. The lab section was updated to reflect the most recent OSPHL guidelines. (Juventila Liko)
- August 2013. Outbreak definition revised to be more in line with the national definition. (Juventila Liko)
- March 2013. Updated acceptable evidence of immunity. (Juventila Liko)
- December 2012. Clarified LHD responsibilities regarding rubella testing at WSPHL. (Juventila Liko)
- December 2008. Revised 3.D to reflect the latest CDC recommendation on laboratory testing. (Juventila Liko)
- October 2007. Case definitions revised to require symptoms. This is more in line with the national definition, and acknowledges the fact that with our incidence of disease being so low, IgM has a poor positive predictive value. (Juventila Liko)

November 2006. Case definition was modified to require epilinkage. (Juventila Liko)

August 2006. The language about when to draw blood for serologic testing (Section 3D) was revised to clarify the distinction between IgG testing (which requires acute and convalescent) and IgM testing (which requires a single specimen collected a little later than an acute). (Juventila Liko)

Testing criteria for rubella

