Rubella, Acquired

Signs and Symptoms	• Prodrome 1-5 days before rash, with low grade fever, malaise, and anorexia. • **Maculopapular rash** – first in the face, spreads down the body, typically lasts 3 days, and can be pruritic. Spreads and fades more quickly than measles rash. • Mild coryza, conjunctivitis, lymphadenopathy may occur. • Arthralgia, arthritis (more frequent in adults). • Up to 50% of cases have asymptomatic infections.		
Incubation	Varies from 14-21 days, usually 16-18 days		
Case classification	**Clinical definition:** Illness characterized by acute onset of generalized maculopapular rash; **AND** temperature greater than 99.0 F; **AND** arthralgia/arthritis or lymphadenopathy or conjunctivitis.		
	Confirmed case: Laboratory confirmed **OR** meets clinical definition **AND** epi linked to a confirmed case	**Probable case:** meets clinical definition, has no serologic or virologic testing, **AND** not linked to a confirmed case	**Suspected case:** Any generalized rash illness of acute onset
Differential diagnosis	Measles, Parvovirus, Cytomegalovirus, Epstein Barr virus - mononucleosis, Scarlet fever, Contact dermatitis, Erythema multiforme, Syphilis - cutaneous manifestations.		
Treatment	Supportive.		
Laboratory	Clinical diagnosis is unreliable, therefore cases must be laboratory confirmed. **IgM serum antibody:** Detection of rubella-specific IgM in conjunction with clinical compatible symptoms can confirm the diagnosis. If collected less than 5 days after rash onset and negative, another specimen is required. False positives and false negatives can occur. PHL performs this test. **IgG serum antibody:** Significant rise in rubella-specific IgG antibody between acute and convalescent specimens can confirm the diagnosis. First specimen should be collected as early in the illness as possible (no longer than 10 days). The minimum interval between the first and second specimen should be at least 7 days (14-21 days is ideal). PHL performs this test. **RT- PCR:** Specimens should be collected as early as possible after the onset of illness, ideally within 5 days of rash onset. On days 0-5 collect an NP/throat swab. On days 6-9 collect and NP/throat swab and urine. Virus may be detectable from 1 week before to 2 weeks after rash onset. PHL does not perform this test but will send samples to a reference lab as needed.		
Public Health investigation	• Assess the likelihood of rubella: confirm compatible clinical symptoms, verify vaccination and travel history, and assess exposure risk such as contact with a person with rubella/rash illness or recent visit(s) to a health care facility. • Recommend immediate isolation of case until rubella is ruled out or 7 days after rash onset. • Medical consultation is required immediately if a pregnant woman is suspected to be infected with rubella. • Consult with DOH Office of Communicable Disease Epidemiology regarding confirmatory testing and appropriate specimen collection. • Recommend appropriate infection control precautions to prevent additional exposures in healthcare facilities, schools, and other public settings. • Coordinate identification of close contacts and determination of their immune status. • Identify potentially exposed pregnant women and determine their rubella immunity. • Refer exposed susceptible pregnant women to their prenatal care provider for consultation. • Recommend rubella cases and susceptible contacts to avoid contact with pregnant women • Recommend vaccination for susceptible contacts (does not change isolation recommendations).		

Congenital Rubella Syndrome (CRS)

Signs and Symptoms	Severity of symptoms and signs depends on the period of gestation at which the infection occurs and are grouped in two categories for clinical case definition purposes:		
	a) • Eye defects: cataracts, microphthalmia, glaucoma, retinopathy • Cardiac defects: patent ductus arteriosus, peripheral pulmonary artery stenosis • Sensorial deafness	**b)** • Central nervous system defects: microcephaly, developmental delay • Hepatosplenomegaly, thrombocytopenic purpura, jaundice, meningoencephalitis • Radiolucent bone disease	
Incubation	Infection occurs in utero. Infection rate highest during first trimester of pregnancy. Defects can be evident at birth, or not be apparent until later in life, especially deafness and developmental delay.		
Case classification	**Clinical definition:** An illness, usually manifesting in infancy and characterized by signs or symptoms described previously in categories a and b.		
	Confirmed case: A clinically consistent case that is laboratory confirmed **Infection only:** Laboratory evidence of infection without any clinical symptoms or signs	**Probable case:** A case that is not laboratory confirmed, and that has any **two** complications listed in category **a** OR **one** complication listed in category **a** <u>and</u> **one** complication listed in category **b**	**Suspected case:** Some compatible clinical findings, does not meet criteria for probable case
Differential diagnosis	Other causes of congenital defects: cytomegalovirus, toxoplasmosis, herpes simplex, varicella zoster, syphilis, parvovirus, human immunodeficiency virus, enteroviruses. Non-infectious neonatal conditions: neonatal hyperthyroidism, tuberous sclerosis, incontinentia pigmenti, Aicardi syndrome, hereditary congenital cataract with hypertrophic cardiomyopathy. (See Appendix C.)		
Treatment	Supportive.		
Laboratory	Clinical diagnosis is unreliable, therefore cases <u>must</u> be laboratory confirmed. **IgM antibody:** Detection of rubella-specific IgM can confirm the diagnosis. If collected at less than 1 month of age and negative, another specimen is required. False positives and false negatives can occur. PHL performs this test. **IgG antibody:** Congenital rubella can be diagnosed by rubella-specific IgG antibody levels that persist at a high level and for a longer period than expected from passive transfer of maternal antibody. PHL performs this test. **RT- PCR/Virus isolation:** Virus can be detected from nasal and throat secretions, blood, urine, and cerebrospinal fluid for a year or longer. Viral isolation should always be attempted. PHL does not perform this test but will send samples to a reference lab as needed.		
Public Health investigation	• Assess the likelihood of CRS: confirm compatible clinical signs and symptoms in infant; determine maternal exposure and/or disease, and review maternal immunization history. • Consult with DOH Office of Communicable Disease Epidemiology to obtain confirmatory testing. • Coordinate appropriate laboratory specimen collection, transportation, and testing. • Infants confirmed or suspected to have CRS should be cared for using contact precautions until one year of age or until 2 consecutive clinical specimens collected after the age of 3 months and one month apart are negative. Children should meet same criteria before attending child care centers. Addition of droplet precautions may be prudent (Section 6.A.1. of guideline.) • Coordinate identification of close contacts and determine their immune status.		

Rubella (Acquired and Congenital)

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To prevent congenital rubella syndrome (CRS).
2. To assure that children with suspected CRS are tested to confirm or rule out the diagnosis in a timely manner in order to assure prompt treatment and prevent spread of the disease.
3. To assure that acquired rubella probable cases are tested to confirm or rule out the diagnosis. Healthy People 2020 objectives include maintaining elimination* of cases of U.S.-acquired rubella and CRS among children <1 year of age in the United States.
4. To identify exposed pregnant women in a timely manner, determine their susceptibility and infection status, and provide appropriate counseling about the risk of fetal infection.
5. To evaluate the effectiveness of disease prevention efforts such as immunization.

*The Healthy People 2020 goal to demonstrate maintenance of elimination is no CRS cases and 10 cases or less of acquired rubella annually in the United States.

B. Legal Reporting Requirements

1. Health care providers: **immediately notifiable to local health jurisdiction**
2. Health care facilities: **immediately notifiable to local health jurisdiction**
3. Laboratories: no reporting requirements
4. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (OCDE) within 7 days of case investigation completion or summary information required within 21 days

C. Local Health Jurisdiction Investigation Responsibilities

1. Begin an investigation on the day of notification.
2. Facilitate transport of specimens to Washington State Public Health Laboratories (PHL) to confirm the diagnosis.
3. Isolate the case until 7 days after the rash onset (unless the diagnosis is ruled out).
4. Identify contacts of the case and sites of potential transmission during the period of communicability.
5. Make appropriate recommendations to susceptible contacts, particularly pregnant women (see Section 6).
6. Enhance surveillance for additional cases.
7. Contact OCDE immediately regarding all reports of suspected acquired rubella or CRS for assistance with confirmation of diagnosis. Complete the rubella investigation form (http://www.doh.wa.gov/Portals/1/Documents/5100/210-074-ReportForm-Rubella.pdf) and enter the data into the Public Health Issues Management System (PHIMS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Rubella virus, an RNA-coded Rubivirus in the Togaviridae family. (Rubella has sometimes been called “German measles” or “three-day measles” but is unrelated to measles.)

B. Description of Illness

1. Acquired Rubella in Children and Adults

Up to 50% of persons with rubella have either subclinical infections or mild symptoms without a rash. Those with symptoms usually experience a mild febrile rash illness. Young children generally have little or no prodrome, while adolescents and adults often report 1–5 days of low grade fever, malaise, and anorexia. Mild coryza and conjunctivitis may also occur. Lymphadenopathy (usually suboccipital, postauricular, and posterior cervical) is a major clinical manifestation and may last several weeks. Fever rarely persists beyond the first day of rash.

The maculopapular rash appears first on the face and spreads down the body. Lesions are pink and rarely coalesce. The rash of acquired rubella typically lasts 3 days and is occasionally pruritic, spreading and fading more quickly than the rash caused by measles.

Arthralgia and arthritis occur frequently in adults. Up to 70% of adult females with infections experience rubella joint symptoms which appear about the same time as the rash and may persist for up to one month. Fingers, wrists, and knees are most commonly affected.

Complications are rare, occurring more often in adults. They can include encephalitis, neuritis, orchitis, and thrombocytopenia. Hemorrhagic manifestations can occur and are usually secondary to low platelets and vascular damage. Thrombocytopenic purpura is the most common of these, and this manifestation is seen more often in children than adults.

Differential diagnoses for acquired rubella include, but are not limited to, measles, parvovirus, cytomegalovirus, Epstein Barr virus - mononucleosis, scarlet fever, contact dermatitis, erythema multiforme, and cutaneous manifestations of syphilis.

2. Congenital Rubella Syndrome (CRS)

The importance of rubella derives not from acquired disease, which is usually mild, but from the potentially devastating effects on the fetus that can occur when a pregnant woman is infected with rubella, especially if the infection occurs early in pregnancy.

Rubella virus can be transmitted vertically from mother to fetus, causing the spectrum of congenital anomalies that define CRS. The main objective of vaccination programs is to prevent congenital rubella.

CRS is a constellation of problems in the newborn that can include any of the following: low birth weight, eye defects (cataracts, microphthalmia, glaucoma, retinopathy), sensorineural deafness, cardiac defects (patent ductus arteriosus, peripheral pulmonary artery stenosis), central nervous system defects (microcephaly, mental retardation), thrombocytopenic purpura, hepatosplenomegaly, and bone lesions.

Deafness is the most common birth defect associated with CRS, and is sometimes the only manifestation. In mild forms of CRS, there may be no apparent clinical manifestations at birth, but the onset of CRS-related symptoms can be delayed until 2–4 years of age.

Fetal infection can occur at any time during pregnancy, but not every infant born to a woman that has acquired rubella during pregnancy will become infected. The likelihood of fetal infection is highest during the first trimester. Studies of women with clinical rubella during the first trimester that had abortions have found 40-90% of fetuses to be infected**. When the fetus is infected the severity of effects on fetal development depends on the period of gestation at which the infection occurs. A fetus infected early in pregnancy has a high probability of developing CRS. In fetuses infected with rubella during the first 12 weeks (first trimester) of pregnancy, CRS-associated congenital defects can occur in up to 85%. The likelihood of congenital defects decreases when fetal infection occurs later in the gestational period, dropping to 35% after fetal infection has occurred during weeks 13-16 of gestation. Another study found no observable defects in 2 year-old children where maternal infection with rubella had occurred during pregnancy, but after 20 weeks of gestation**.

Differential diagnoses for CRS include, but are not limited to, other infections causing congenital defects (e.g. cytomegalovirus, toxoplasmosis, herpes simplex, varicella zoster) and non-infectious neonatal conditions (e.g. tuberous sclerosis, incontinentia pigmenti, Aicardi syndrome.) See Appendix C. for an in depth list.

**Reef SE, Plotkin SA. Chapter 29: Rubella. In: Wilson CB, Nizet V, Maldonado YA, Remington JS, and Klein JO, eds. *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant*. 8th ed. Philadelphia, PA: Elsevier/Saunders, 2016:894-932.

C. Rubella in Washington

Six cases of acquired rubella have been reported to the Department of Health during the last 10 years. All of those cases were import-associated, the most recent reported in 2013. In 2000, an infant with CRS was born in WA to a mother who acquired rubella outside the United States.

Table 1. Confirmed Rubella cases in Washington State 2005-2015

Year	County	Age/Sex	Where exposed	Genotype
2005	King	Adult male	Jordan	Not available
2008	Foreign National	Female exchange student	China	1E
2010	King	Adult male	Vietnam	Not available
2011	King	Adult female	India	2B
2011	King	Adult male	House guest with rubella	2B
2013	King	Infant male	Travel to India without ACIP-recommended vaccination	Not available

D. Reservoir

Humans. The peak incidence in endemic countries occurs during late winter and early spring.

E. Modes of Transmission

Acquired rubella is transmitted person-to-person by direct or droplet contact with infectious nasopharyngeal secretions. CRS is transmitted vertically from an infected pregnant woman to her fetus.

F. Incubation Period

The incubation period for acquired rubella ranges from 12–23 days (typically 16–18 days).

G. Period of Communicability

1. Virus is typically secreted in nasopharyngeal secretions of persons with acquired rubella from about 7 days before until 7 days after rash onset. Cases are most contagious when the rash is erupting. Persons who are asymptomatic are communicable but the period of communicability is difficult to define.
2. Infants with CRS can shed the virus in the nasopharyngeal secretions and urine for a year or longer. Rubella virus has been recovered from the lenses of children with CRS and congenital cataracts for several years after birth.

H. Treatment

Treatment is supportive.

3. CASE DEFINITIONS

A. Acquired Rubella

1. **Clinical Case Definition**: An illness that has all the following characteristics:
   - Acute onset of generalized maculopapular rash
   - Temperature greater than 99.0° F (greater than 37.2° C), if measured
   - Arthralgia/arthritis, lymphadenopathy, or conjunctivitis
2. **Laboratory Criteria for Diagnosis**
   - Isolation of rubella virus from a clinical specimen, or
   - Detection of rubella virus-specific nucleic acid by polymerase chain reaction, or
   - IgG Seroconversion: Significant rise in serum rubella immunoglobulin G antibody level between acute- and convalescent-phase specimens, by any standard serologic assay (not explained by MMR vaccination in the previous 6-45 days), or
   - Positive serologic test for rubella immunoglobulin M (IgM) antibody
3. **Case Definition (2013)**

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

   Probable: a case that meets the clinical case definition, has no or noncontributory serologic/virologic testing, and is not epidemiologically linked to a laboratory-confirmed case.

   Confirmed: a case that is laboratory confirmed (with or without symptoms) or that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case
4. **Comments:**
   - Only confirmed cases are reported to CDC.
   - False positive serum rubella IgM test results 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.

B. Congenital Rubella

1. **Clinical Description:** Presence of any defect(s) or laboratory data consistent with congenital rubella infection. Infants with congenital rubella syndrome usually present with more than one sign or symptom consistent with congenital rubella infection. However, infants may present with a single defect. Hearing impairment is the most common single defect.

2. **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
   - Detection of rubella virus by polymerase chain reaction (PCR).

3. **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:

   a. Cataracts/congenital glaucoma, congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis), hearing impairment, pigmentary retinopathy.

   b. Purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis, radiolucent bone disease.

4. **Case Definition (2010)**

   Suspected: A case with some compatible clinical findings but does not meet the criteria for a probable or confirmed case.

   Probable†: A case that is not laboratory confirmed and that has any two complications listed in paragraph "a" of the clinical case definition or one complication from paragraph "a" and one from paragraph "b", and lacks evidence of any other etiology.

   Confirmed: A clinically consistent case that is laboratory confirmed.

   Infection only: A case that demonstrates laboratory evidence of infection, but without any clinical symptoms or signs.

   †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.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Diagnostic tests used to confirm either acquired or congenital rubella include serology, viral cultures, and polymerase chain reaction (PCR). Since many rash illnesses may mimic acquired rubella, laboratory testing is the *only* way to confirm the diagnosis.

Detection of rubella-specific immunoglobulin M (IgM) antibody can confirm the diagnosis of both acquired and congenital rubella. However, these tests need to be interpreted with caution

since false positive and false negative results can occur. Serum should generally be collected as early as possible after the onset of illness, usually at the first clinical encounter. However, IgM antibodies may not be detectable before day 5 after rash onset or during the first month of life for babies with possible CRS. If a negative result is obtained from a specimen drawn less than 5 days after rash onset for acquired rubella or at less than one month of age for a neonate suspected to have CRS, another specimen will be required.

Demonstration of a significant rise in rubella-specific immunoglobulin G (IgG) antibody between acute and convalescent specimens can also confirm the diagnosis of acquired rubella. The first specimen should be collected as early in the illness as possible (within 7 days after rash onset if possible and no longer than 10 days.) The minimum interval between the first and second specimen should be no less than 7 days and an interval of 14-21 days is ideal.

Either isolation of rubella virus or detection of rubella RNA in nasal or throat secretions, blood, urine, or cerebral spinal fluid is diagnostic for rubella infection, but is performed by very few laboratories. Please consult with an OCDE epidemiologist regarding collection of specimens for rubella virus isolation or PCR testing. If rubella is strongly suspected, specimens can be sent to a regional reference laboratory for testing. Specimens for viral isolation should be collected as soon as possible after rash onset, ideally within 4 days of rash onset. However, rubella virus has been isolated from one week before to 2 weeks after rash onset.

Congenital rubella can be diagnosed by high rubella IgG antibody levels that persist for a longer period than would be expected from passive transfer of maternal antibody. Consult with an OCDE epidemiologist for assistance.

B. Services Available at the Washington State Public Health Laboratories (PHL)

PHL performs an enzyme-linked immunosorbent assay (ELISA) for rubella-specific IgM and IgG antibodies. Viral cultures and PCR for rubella virus are not performed at PHL, but specimens can be forwarded to CDC for testing. In addition, PHL can forward serum to CDC for avidity testing (to distinguish between recent and past rubella infection) when appropriate. Please consult with an OCDE epidemiologist prior to submitting samples for testing.

C. Specimen Collection

Serologic testing: Please see Section 4A for information regarding the timing of serum collection for serologic tests. Information on specimen collection and submission instructions can be found at PHL Microbiology testing menu:

IgM: http://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-RubellaIgM-EIA-V1.pdf
IgG: http://www.doh.wa.gov/Portals/1/Documents/5240/SCSI-RubellaIgG-EIA-V1.pdf

Viral isolation and PCR testing: A nasopharyngeal swab, throat swab or nasal wash in viral transport media, as well as urine are all acceptable specimens for viral isolation. Specimens should be maintained at refrigeration temperature and transported immediately to PHL. If the specimen will not reach PHL within 72 hours it should be frozen at -70 °C and transported in dry ice. Testing will be done at CDC or at our regional reference laboratory, Minnesota Department of Health (MDH). For additional information regarding collection, storage and shipping of specimens for **viral isolation and PCR**, see:

CDC guidelines: http://www.cdc.gov/vaccines/pubs/surv-manual/chpt22-lab-support.pdf.
MDH guidelines: http://www.health.state.mn.us/divs/idepc/diseases/rubella/hcp/labtesting.pdf.

All specimens sent to PHL, including specimens for testing at other reference laboratories must be accompanied by a completed PHL virology form http://www.doh.wa.gov/Portals/1/Documents/5230/302-017-SerVirHIV.pdf.

Along with the patient and submitter names, be sure to include the date of collection, date of rash onset, specimen source, and immunization history (if known) on the form.
Please note: PHL requires that all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified.

5. ROUTINE CASE INVESTIGATION

The goal of a rubella case investigation is to prevent transmission of rubella virus and avoid exposure of susceptible pregnant women, thereby preventing cases of CRS.

Because the incidence of rubella is low in the United States, CDC recommends that health agencies should consider even one case of rubella as a potential outbreak.

A. Evaluate the Diagnosis

1. Review the clinical presentation and physical exam findings. Assess risks for exposure including history of maternal rash illness during gestation (CRS) or travel during the likely exposure period (acquired rubella), and immunization status of the patient to determine the likelihood of the diagnosis. Sources of immunization data might include medical records (including records of prenatal rubella screening for women who have been pregnant), immunization cards kept by parents, school/child care certificate of immunization (CIS) forms, and Washington State Immunization Information System (WIIS)
2. Laboratory confirmation is critical for rubella since the clinical diagnosis alone is unreliable. Collect serum and specimens for viral isolation.

   Note: When evaluating the possibility of CRS in an infant, an important consideration is that infants born to an immune mother are ordinarily protected for 6-9 months following birth. The duration of protection, as evidenced by the presence of rubella-specific IgG antibody in serum, depends on the amount of maternal antibodies acquired transplacentally.

B. Identify Potential Sources of Infection

Evaluate the activities of the case during the likely exposure period (12–23 days prior to the onset of rash). Identify situations where the case might have been at increased risk of exposure to rubella. Collect the following information:

1. Contact information for any household member, playmate, or other contact who had a rash illness during the likely exposure period
2. Any travel outside of the United States or to an area of the United States where rubella has recently occurred
3. Any contact with visitors from outside the United States or an area of the United States where rubella has recently occurred
4. Any visit to a doctor's office, clinic, or hospital (find out exact time[s], date[s], name of the clinic[s], duration of visit[s], and areas of the facility visited)
5. Any indoor group activities attended (e.g., church, theaters, tourist locations, public or

commercial travel, parties, athletic events, family gatherings) and contact information of the person who organized the group or event

6. Any work or volunteer activities in a health care setting, or attendance or work at a school, child care, college, prison, refugee center, etc.

   Note: Since many persons with acquired rubella (20–50%) are asymptomatic, identifying the source patient is not always possible.

C. Identify Exposed Contacts and Potential Sites of Transmission

1. Identify persons who have been in contact with the patient during the period from 7 days before to 7 days after onset of rash. These should include household members, school or child care classmates, playmates, and home visitors.
2. Determine public gatherings attended where identification of the individuals present may not be possible.
3. **Identify (among close contacts of the case) women who are pregnant or who are sexually active and could possibly be pregnant.** Determine their pregnancy status (if not known).
4. Determine the rubella immunity status of exposed contacts. Persons are considered immune to rubella‡ if they:

   a. Were born before January 1, 1957 (unless there is reason to believe the woman may be or could become pregnant). Heath care workers born before January 1, 1957 should consider receiving a dose of measles, mumps and rubella (MMR) vaccine if there is no laboratory evidence of immunity.

   b. Have laboratory evidence of immunity to rubella.

   c. Have laboratory confirmation of disease

   d. Have written documentation of vaccination with at least one dose of rubella-containing vaccine (usually in the form of MMR vaccine administered on or after the first birthday).
5. Alert all health care facilities visited by the case during the contagious period and make recommendations regarding management of susceptible contacts (see Section 6).
6. On rare occasions, a press release may be indicated to inform persons who may have had close contact with the case but who cannot be identified. The press release should include information about the symptoms of acquired rubella and instructions for what possibly-exposed susceptible persons are being asked to do.

   ‡ Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine Preventable Diseases. Hamborsky J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation, 2015

D. Enhance Surveillance for Additional Cases

Alert health care providers, hospital emergency rooms, and student infirmaries of the potential for additional cases; encourage health care providers to consider acquired rubella in any person(s) presenting with a rash illness, take appropriate infection control precautions, and report suspected cases to public health. See Appendix A for a sample health alert.

Since up to 50% of acquired rubella infections may be asymptomatic, all susceptible pregnant women exposed to rubella virus must be tested for rubella infection regardless of whether or not a rash develops (see Section 6). In addition, other susceptible persons directly exposed to

respiratory secretions of a person with rubella infection can be tested for asymptomatic infection. Asymptomatic rubella infection can be diagnosed by a positive rubella-specific IgM antibody test or a significant rise in IgG antibody level between acute- and convalescent-phase tests.

E. Environmental Evaluation

None.

6. CONTROLLING FURTHER SPREAD

Control measures should be implemented as soon as a single case of acquired or congenital rubella is suspected, particularly if the setting is one where pregnant women might be exposed.

A. Infection Control Recommendations/Case Management

1. Hospitalized patients confirmed or suspected to have acquired rubella should be place on droplet precautions until 7 days after the onset of the rash. Infants confirmed or suspected to have CRS should be cared for using contact precautions until one year of age or until 2 consecutive clinical specimens collected one month apart and after the age of 3 months are negative.

   Recent reports of rubella exposure in hospital settings have suggested that adding droplet precautions is prudent for infants with CRS until one year of age[I].

   [I] Congenital rubella syndrome exposure in a pediatric hospital: experience from developing world. D Sureshkumar, R Gopalakrishnan, L Jessani. From 3rd International Conference on Prevention and Infection Control (ICPIC 2015). Geneva, Switzerland. 16-19 June 2015

2. Persons suspected to have acquired rubella should be advised to do the following while contagious (from one week before, if applicable, and until 7 days after the onset of the rash):
   - Stay home and not attend child care, school, work, social activities or other public places.
   - Avoid all women who are, or may be, pregnant (especially those known to be potentially susceptible).
3. Children suspected to have CRS should not attend child care centers while they could be contagious. Children with CRS may be contagious until they are one year of age or more, and rubella virus has been recovered from the lens of children with congenital cataracts for up to several years. 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 only after appropriate testing has been completed (i.e., when 2 consecutive urine and nasopharyngeal cultures collected one month apart after 3 months of age have yielded negative results).

B. Management of Non-Pregnant Contacts

1. Education

- All contacts regardless of immune status should be educated about the symptoms of acquired rubella.
- All contacts regardless of immune status who develop a rash illness within 23 days of the date of last exposure should call their health department and be evaluated for rubella infection. Symptomatic contacts should avoid pregnant women and public settings until testing for rubella has been done.

- All contacts regardless of immune status should be informed that rubella virus can be shed up to 7 days prior to onset of symptoms and that up to 50% of persons with rubella infection may remain asymptomatic, but may nevertheless shed rubella virus. Therefore, contacts should be advised to minimize exposure of susceptible pregnant women until 23 days has passed since the date of last exposure to rubella, regardless of whether symptoms develop.

2. Vaccination and Exclusion

There is no evidence that giving rubella vaccine after exposure has already occurred will prevent infection, 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 provide protection in the event of future exposures, vaccination of susceptible persons is recommended, unless specifically contraindicated (see Section 8).

- Contacts with documented immunity to rubella do not need to be revaccinated or excluded from public settings.
- Contacts with unknown immune status (i.e., those born on or after January 1, 1957 who cannot provide laboratory evidence of immunity or a documented history of vaccination on or after their first birthday) should be vaccinated. If these persons work or spend time in a setting with pregnant women, serum should be drawn to determine rubella immune status before vaccination.
- Contact known to be susceptible (i.e., children under one year old, persons with documented negative rubella-specific IgG antibody, person who have been exempted from vaccination for medical, religious or philosophical reasons) should be vaccinated if no contraindications exist.
- Contacts that are vaccinated and then develop a rash illness within 23 days of the last exposure to rubella should be isolated and investigated as a suspect rubella case. Consult with an Office of Communicable Disease Epidemiology epidemiologist to discuss diagnostic testing. Specimens for virus isolation may be necessary to determine whether the rash is due to vaccine or wild rubella virus.
- Susceptible contacts who chose to be vaccinated do not need to be excluded from public settings after vaccination but must avoid all settings where close contact with pregnant women might be possible until 23 days after the date of last exposure to rubella has passed.
- Susceptible contacts who chose not to (or cannot) be vaccinated should be excluded from all public settings until 23 days after the date of last exposure to rubella has passed.

  Susceptible healthcare workers exposed to rubella should be excluded from work beginning 7 days after the first exposure to rubella and continuing until 23 days after the date of last exposure to rubella has passed **regardless of whether or not they were vaccinated after the exposure**. If a rash appears during this time and rubella is confirmed, the healthcare worker may return to work after 7 full days after the date of rash onset have passed.

C. Management of Pregnant Women Exposed to Rubella

1. Determine if the pregnant woman had a positive rubella-specific serologic test documented prior to her exposure (routinely done as part of prenatal screening). A pregnant woman with a positive serologic result prior to her exposure can discuss the need to rule out reinfection with

her health care provider.

Reinfection with rubella in previously immune persons is rare and more likely to occur following vaccine-induced immunity than when immunity follows natural disease. In addition, the risk of fetal infection in such situations is extremely rare. The lack of demonstrated intrauterine transmission of virus associated with maternal reinfections likely indicates that viremia was absent or greatly reduced because the primary infection had induced some maternal immunity**.

**Reef SE, Plotkin SA. Chapter 29: Rubella. In: Wilson CB, Nizet V, Maldonado YA, Remington JS, and Klein JO, eds. Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant. 8th ed. Philadelphia, PA: Elsevier/Saunders, 2016:894-932.

2. If the pregnant woman does not have a positive rubella-specific serologic test documented prior to her exposure, collect serum for IgM and IgG testing and follow Algorithm 1 below for collection of follow-up specimens.
3. Exclude all pregnant women of unknown immune status from any site(s) where the potential for exposure to rubella exists until each woman's immune status has been determined. If she is found to be susceptible, she should be excluded from any site where she faces the risk of transmission until 46 days (2 incubation periods) after the onset of rubella symptoms in the last known case at that site[§].

   §Centers for Disease Control and Prevention (CDC). Control and Prevention of Rubella: Evaluation and Management of Suspected Outbreaks, Rubella in Pregnant Women, and Surveillance for Congenital Rubella Syndrome. MMWR Morb Mortal Wkly Rep. 2001;50[No.RR-12]:19

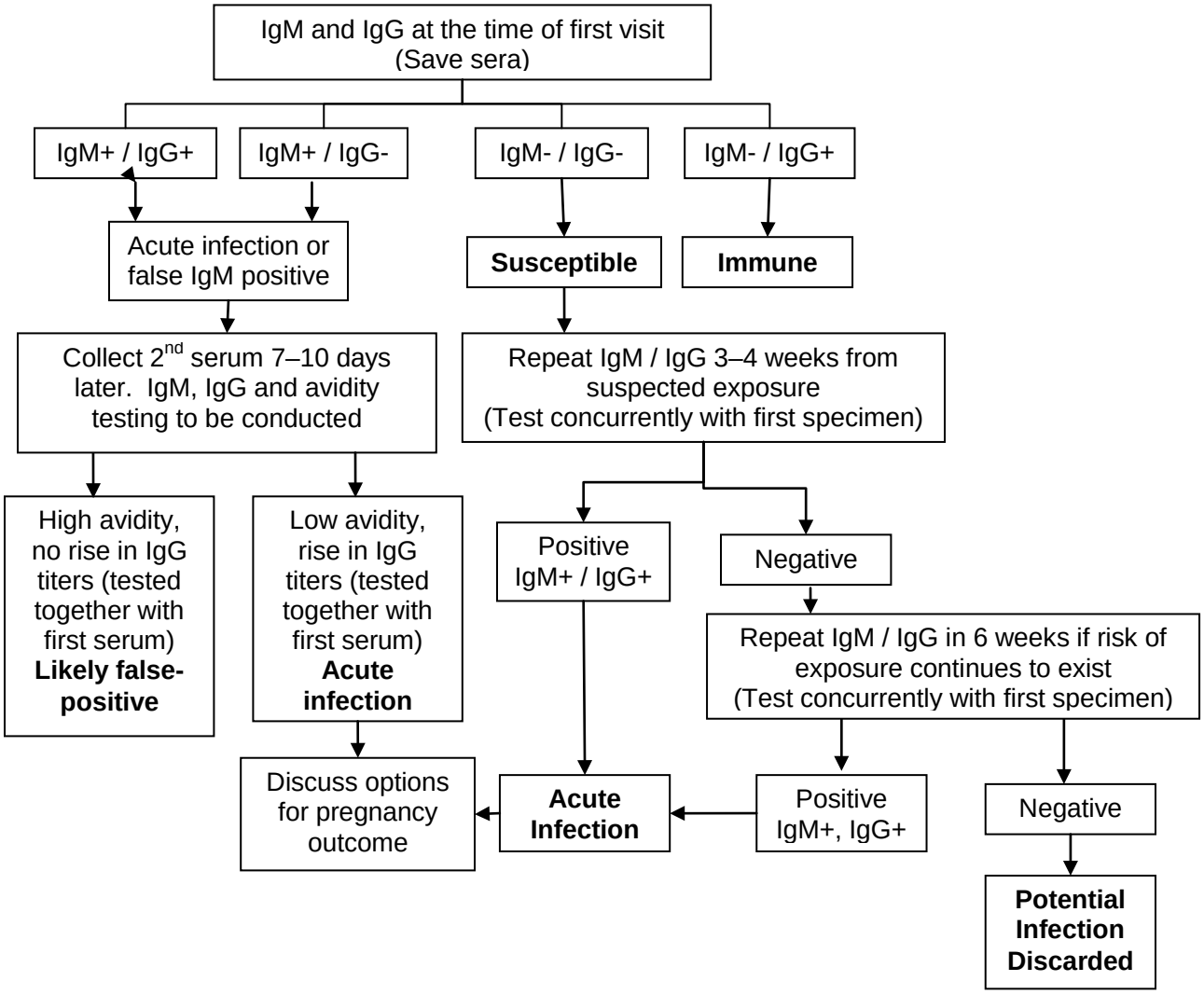
4. Consider administering immune globulin (IG) to a susceptible, pregnant woman if she is exposed to a person with confirmed rubella early in pregnancy and abortion is not an option. Though IG may reduce the likelihood of rubella symptoms in the woman, the absence of symptoms consistent with acquired rubella in a woman who has received IG does not necessarily mean that fetal infection has been prevented. Infants with CRS have been born to exposed woman who received IG and remained asymptomatic. IgM antibody can be used to detect maternal infections, even after IG has been administered and testing for rubella infection should still be done.
5. If the pregnant woman develops a rubella infection, see Section 7.

D. Management of Other Exposed Persons

Persons potentially exposed to the same source as the case or present in the same high-risk setting during the likely exposure period should have their rubella immunity status assessed. They should be told to watch for symptoms of acquired rubella during the 12 to 23 days following their exposure regardless of immunization status.

For additional information regarding case and contact management, see: Manual for the surveillance of vaccine-preventable diseases. Centers for Disease Control and Prevention, Atlanta, GA, 2012. Available at: http://www.cdc.gov/vaccines/pubs/surv-manual/chpt14-rubella.html

Algorithm for serologic evaluation of pregnant women



Source: Adapted from Manual for the surveillance of vaccine-preventable diseases. Centers for Disease Control and Prevention, Atlanta, GA, 2012. http://www.cdc.gov/vaccines/pubs/surv-manual/chpt14-rubella.html

7. MANAGING SPECIAL SITUATIONS

A. Infection of a Pregnant Woman

When rubella infection has been confirmed in a pregnant woman, she should be counseled regarding the risk of congenital rubella syndrome (CRS). The rate of fetal infection and the effects of the infection on the fetus, should it occur, depend on gestational age.

- The likelihood of fetal rubella infection is highest when the mother's infection occurs in the first 12 weeks (first trimester) of pregnancy (up to 90%).
- Among fetuses infected with rubella during the first 12 weeks of pregnancy, CRS-associated congenital defects occur in up to 85%.
- The likelihood of congenital defects decreases if the fetal rubella infection occurs later in the

gestational period, dropping to 35% if infection occurs during weeks 13 to 16 of gestation**. Two different studies found no defects among children evaluated at 2 years of age following fetal infections that occurred after 16 weeks or after 20 weeks of gestation, respectively**.

After initial assessment and counseling, and if the gestational age of the fetus is such that abortion remains an option, pregnant women with confirmed rubella infection should be offered the opportunity to receive additional counseling in order to decide whether to have an abortion.

When a pregnant woman is confirmed to have rubella, pregnancy outcomes (e.g. abortion, stillbirth, congenital rubella-associated defects) should be recorded and reported, and laboratory evaluation of infants should be documented.

**Reef SE, Plotkin SA. Chapter 29: Rubella. In: Wilson CB, Nizet V, Maldonado YA, Remington JS, and Klein JO, eds. Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant. 8th ed. Philadelphia, PA: Elsevier/Saunders, 2016:894-932.

B. Outbreak Control—Healthcare, School or Child Care Facilities

Measures implemented for the purpose of rubella outbreak control may interrupt disease transmission and will increase vaccination coverage among persons who might not otherwise be protected from the disease. Outbreak control strategies should include defining at-risk populations, ensuring prompt vaccination of susceptible persons or if a contraindication to vaccination exists, excluding them from settings where exposure could occur, and maintaining active surveillance.

Control measures may need to be modified if additional cases are identified.

During an outbreak the following response measures should be considered:

- **Active Surveillance:** Search for all potential cases of rubella. Daily health surveys of staff, students, parents, etc., may be indicated.
- **Case Management:** Minimize exposure of susceptible contacts in health care facilities by placing all persons with suspected or confirmed rubella under droplet precautions. Evaluate patient flow patterns to minimize transmission. Restrict confirmed cases to home until 7 days have passed since the date of rash onset. Travel should be postponed until the person is no longer contagious or, if absolutely necessary, conducted in such a way as to prevent or minimize transmission.
- **Vaccination and Exclusion of Susceptible Contacts:** In an outbreak setting, it is important to identify the at-risk population and immunize all non-pregnant individuals without documented evidence of immunity (See Section 5.C.4.) within that population as quickly as possible. Ideally, exposed susceptible contacts should be excluded until 23 days have elapsed since the last date of exposure regardless of whether or not they were vaccinated after their exposure. Such individuals **must** be excluded from any setting where their readmission creates a potential for exposure of a pregnant woman to rubella.

  Note: Persons with unknown immunity can choose to have a serum specimen collected prior to vaccination to be tested for rubella-specific IgG antibody. If test results provide evidence of immunity (see Section 5.C.4.) no further exclusion is needed.

  Exclude any pregnant woman of unknown immune status from sites with the potential for rubella transmission until her immune status has been determined. If she is found to be susceptible, she should be excluded from any site where she faces the risk of transmission until 46 days (2 incubation periods) after the onset of rubella symptoms in the last known case at that site. (See Section 6C)

8. ROUTINE PREVENTION

A. Immunization Recommendations

Routine immunization with at least one dose of rubella-containing vaccine during childhood is recommended. At least 95% of susceptible persons develop rubella antibodies after a single dose of vaccine. However, rubella vaccination is almost universally given in the United States as part of the measles, mumps, rubella (MMR) vaccine, and two doses of the measles and mumps antigens are now recommended for disease prevention and are required for school attendance. The first dose of MMR should be given at 12–15 months of age and the second dose should be administered when the child is 4–6 years of age. Persons born in 1957 or later should receive at least one dose of MMR if they do not have evidence of immunity to all three of these diseases.

Contraindications to MMR vaccine include:

- A history of a severe allergic reaction (i.e., hives, swelling of the mouth or throat, difficulty breathing, low blood pressure, shock) following a previous dose or vaccine components (e.g., neomycin, gelatin) (MMR can be given to egg-allergic persons);
- Pregnancy (women should avoid getting pregnant for 4 weeks after vaccination with MMR);
- Significant immunosuppression; and
- Recent receipt of antibody-containing blood products.

An acute illness that is moderate to severe is a precaution, but not a contraindication, and vaccination can be considered during an outbreak.

For more information about MMR vaccine schedules, adverse reactions and contraindications, please see the most recent ACIP recommendations.

B. Prevention Recommendations

Routine childhood immunization and vaccination of adults without documented immunity is the best way to prevent rubella.

ACKNOWLEDGMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

January 2011:
The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision.

February 2016:
Language used to describe the disease and the management of exposed contacts was modified for clarity.
A table showing incidence of rubella in WA in the last decade and data regarding fetal infection and congenital defects risk were added.
Case definitions for acquired rubella and CRS were updated to reflect CSTE 2013 (acquired) and 2010 (CRS) case definitions.
Differential diagnoses for acquired rubella and CRS were added along with Appendix C. which contains in depth information regarding differential diagnosis for CRS.

APPENDIX A: SAMPLE PROVIDER ALERT

Health Advisory: Rubella in a [city or county] [infant/child/adolescent/adult]
[date] (e.g. May 7, 2004)

Action requested:

- **Increase your index of suspicion for rubella.**
- **Take measures to prevent exposure of pregnant women to rubella should a person with a rash illness present to your office. Ideally, persons with a rash illness should bypass patient waiting areas.**
- **Report all suspected cases of rubella to [LHJ] by calling XXX-XXX-XXXX immediately. Do not send specimens to a commercial lab. Do not wait until serologic confirmation is available to notify [LHJ].**

Background: A confirmed case of rubella has occurred in [an adolescent] who lives in [city] and attends/works at/frequents [school name/work place/other community site]. The person had recently [traveled out of the country/other exposure description] where he was likely exposed. Rash onset was 05/01/04. He could have been contagious from 04/24/04 through 05/08/04. [School mates and their families/coworkers/attendees] have been notified by letter of possible exposure. Unimmunized persons or persons with unknown immunity status from this setting should be vaccinated and stay home away from others during the incubation period (23 days after most recent exposure) or until documentation of immunity is available.

Rubella Immunity

- Documentation of one dose of rubella-containing vaccine on or after the 1st birthday
- Serologic evidence of immunity
- Birth before 1957 (not acceptable evidence of rubella immunity for women who might become pregnant)
- Only serology or documented vaccination should be accepted

Symptoms: Rubella is a mild viral illness consisting of low-grade fever, upper respiratory symptoms, lymphadenopathy (often post-auricular), body aches and maculopapular rash. The red rash usually begins on the face and spreads to the rest of the body. Unfortunately, up to 50% of rubella case can be asymptomatic.

Incubation period: 12–23 days. If susceptible persons were exposed to this individual in the community, we expected to see resultant cases become ill 05/06/04 through 05/31/04.

Diagnostic testing: Rubella can be confirmed by serologic/virologic tests. [LHJ] can assist you with collection of specimens and rapid testing at a public health laboratory.

Treatment: Largely supportive

APPENDIX B: SAMPLE LETTER TO SCHOOL

[date] May 7, 2004

Dear Parent, Guardian, or Staff Member:

A student who attends [name of school] has had **rubella.** The student was present at school and would have been contagious on all school days from [date] 4/24/04 through [date] 05/08/04. Rubella is a mild viral illness also known by the names of German measles and 3-day measles. Rubella is characterized by swollen glands, low-grade fever, and a rash that lasts from 1 to 3 days. It is possible to have the infection but not have any symptoms at all. Rubella is of particular concern for pregnant women exposed during their first 12 weeks of pregnancy since this disease can damage the developing fetus in the mother's womb. The time between being exposed and developing symptoms is 12 to 23 days (typically 14 to 18 days).

We urge you to check your child's (or your own, if a staff member) immunity against rubella. Immunization with rubella vaccine (MMR) or having had the disease provides immunity. By the time a student enters kindergarten he/she should have had two MMRs since the first birthday. If your child has had two MMR immunizations, you do not need to do anything at this time. If your child has had only one MMR immunization, please consider obtaining a second MMR dose at this time. This immunization can be obtained through your health care provider or most pharmacies. If you need help finding a health care provider or if you don't have health insurance, call the Family Health Hotline at 1-800-322-2588 or visit ParentHelp123 website.

ESPECIALLY IMPORTANT FOR FEMALES WHO ARE OR MAY BE PREGNANT: Most women are immune to rubella because they have been immunized or have had the disease. Damage to a developing fetus from rubella can occur when a pregnant woman gets the disease. Pregnant women who have not been immunized against rubella should consult a physician for advice.

In an effort to avoid spread of rubella in the community, we have asked the school to review immunization records. If your child has no school record of immunization (MMR) you are asked to keep her/him at home between [date] 05/06/16 and [date] 05/31/16. If another case of rubella occurs, this time may be extended. If you signed an exemption but you know that your child was immunized, your child may return to school when you provide a copy of a medical record showing proof of MMR prior to [date] 04/24/16 or a copy of a blood test showing immunity to rubella.

If your child (or you, if a staff member) develops a rash illness between [date] 5/06/16 and [date] 5/31/16, please consult a physician and do not attend school. Let the clinic know by phone before going to the waiting room that your child may have rubella. Also please notify [LHJ] at XXX-XXXX if your child develops a rash during this time and avoid exposing other people.

If you have further questions about this disease or your possible exposure, please call [LHJ] at (XXX) XXX-XXXX.

Sincerely,

[] Ruby Ola, MD
Epidemiologist

APPENDIX C: DIFFERENTIAL DIAGNOSIS FOR CONGENITAL RUBELLA SYNDROME (CRS)

Infectious conditions that present with congenital defects common to CRS include:

Toxoplasmosis[1]	**Cytomegalovirus[1]**	**Syphilis[1]**	**Herpes Simplex[1]**
Chorioretinitis Hydrocephalus Jaundice Hepatosplenomegaly Myocarditis Respiratory distress Rash Microcephaly Seizures Lymphadenopathy Hearing loss Developmental delay Prematurity	Chorioretinitis Jaundice Hepatosplenomegaly Low birth weight Petechial rash Purpura Microcephaly Seizures Hearing loss Developmental delay Seizures Pneumonitis Enamel defect	Low birth weight Hearing loss Lymphadenopathy Hepatosplenomegaly Meningitis Choroiditis Hydrocephalus Seizures Developmental delay Jaundice Osteochondritis Hydrops fetalis Hutchinson teeth	Meningitis Encephalitis Microcephaly Eye defects: chorioretinitis, keratoconjuntivitis, microphtalmia Hepatitis Jaundice Pneumonitis Disseminated intravascular coagulation Seizures Apnea Vesicular skin lesions
Varicella Zoster[1]	**Parvovirus[2]**	**HIV[1]**	**Enterovirus (coxsackie, parechovirus)[1]**
Chorioretinitis Cataracts Limb atrophy Cerebral cortical atrophy-microcephaly Developmental delay Skin lesions Low birth weight	Most commonly: Intrauterine fetal death Other manifestations: Fetal anemia Hydrops fetalis Rash Eye defects Bone marrow abnormalities	Low birth weight Hepatosplenomegaly Developmental delay Progressive encephalopathy Recurrent bacterial infections	Sepsis Neurodevelopmental delay Myocarditis Cortical necrosis Respiratory failure Hydrops fetalis

The TORCH screen, which includes Toxoplasmosis, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus, and Herpes infection, is one of the most frequently ordered serologic tests for establishing etiology when congenital anomalies are seen.

Non-infectious conditions that present with congenital defects common to CRS include:

Tuberous sclerosis[3]	**Incontinentia pigmenti[4]**	**Aicardi Syndrome[5]**	**Neonatal Hyperthyroidism[6]**
Retinal lesions Heart rhabdomyoma Kidney tumors Developmental delay Brain tumors Lung disease	Erythematous vesicular rash Retinopathy Seizures Microcephaly Developmental delay Increased skin pigmentation Breast abnormalities Pulmonary hypertension	Microcephaly Seizures Eye defects: (microphtalmia, coloboma, corioretinal lacunae) Costovertebral defects Scoliosis Hand malformations Developmental delay	Exophthalmos Tachycardia- heart failure Respiratory distress Thrombocytopenia Fetal growth retardation Prematurity Hepatosplenomegaly Jaundice Pulmonary hypertension Hydrops fetalis

References

1. Wilson, Cristopher B. *Remington and Klein's Infectious Diseases of the Fetus and Newborn Infant*, Eight Edition. Philadelphia, PA: Elsevier, 2016.
2. Neu N, Duchon J, Zachariah P. TORCH Infections. Clin Perinatol 42 (2015) 77–103
3. Northrup H, Koenig MK, Pearson DA, et al. Tuberous Sclerosis Complex. 1999 Jul 13 [Updated 2015 Sep 3]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1220/
4. Scheuerle AE, Ursini MV. Incontinentia Pigmenti. 1999 Jun 8 [Updated 2015 Feb 12]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1472/
5. Sutton VR, Van den Veyver IB. Aicardi Syndrome. 2006 Jun 30 [Updated 2014 Nov 6]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1381/
6. Zimmerman D. Fetal and Neonatal Hyperthyroidism. Thyroid. January 2009, 9(7): 727-733. doi:10.1089/thy.1999.9.727.