TABLE 230e-1 COMMON TRANSIENT AND PERMANENT MANIFESTATIONS IN INFANTS WITH CONGENITAL RUBELLA SYNDROME

Transient Manifestations	Permanent Manifestations
Hepatosplenomegaly	Hearing impairment/deafness
Interstitial pneumonitis	Congenital heart defects (patent ductus arteriosus, pulmonary arterial stenosis)
Thrombocytopenia with purpura/petechiae (e.g., dermal erythropoiesis, or "blueberry muffin syndrome")	Eye defects (cataracts, cloudy cornea, microphthalmos, pigmentary retinopathy, congenital glaucoma)
Hemolytic anemia	Microcephaly
Bony radiolucencies	Central nervous system sequelae (mental and motor delay, autism)
Intrauterine growth retardation	
Adenopathy	
Meningoencephalitis	

clinical presentations, and the high rates of subclinical and mild disease. Illnesses that may be similar to rubella in presentation include scarlet fever, roseola, toxoplasmosis, fifth disease, measles, and illnesses with suboccipital and postauricular lymphadenopathy. Thus laboratory documentation of rubella virus infection is considered the only reliable way to confirm acute disease.

Laboratory assessment of rubella infection is conducted by serologic and virologic methods. For acquired rubella, serologic diagnosis is most common and depends on the demonstration of IgM antibodies in an acute-phase serum specimen or a fourfold rise in IgG antibody titer between acute- and convalescent-phase specimens. The enzyme-linked immunosorbent assay IgM capture technique is considered most accurate for serologic diagnosis, but the indirect IgM assay also is acceptable. After rubella virus infection, IgM antibody may be detectable for up to 6 weeks. In case of a negative result for IgM in specimens taken earlier than day 5 after rash onset, serologic testing should be repeated. Although uncommon, reinfection with rubella virus is possible, and IgM antibodies may be present. To detect a rise in IgG antibody titer indicative of acute disease, the acute-phase serum specimen should be collected within 7–10 days after onset of illness and the convalescent-phase specimen ~14–21 days after the first specimen.

IgG avidity testing is used in conjunction with IgG testing. Low-avidity antibodies indicate recent infection. Mature (high-avidity) IgG antibodies most likely indicate an infection occurring at least 2 months previously. This test helps distinguish primary infection from reinfection. Avidity testing may be particularly useful in diagnosing rubella in pregnant women and assessing the risk of CRS.

Rubella virus can be isolated from the blood and nasopharynx during the prodromal period and for as long as 2 weeks after rash onset. However, as the secretion of virus in individuals with acquired rubella is maximal just before or up to 4 days after rash onset, this is the optimal time frame for collecting specimens for viral cultures. Rubella can also be diagnosed by viral RNA detection in a reverse-transcriptase polymerase chain reaction (RT-PCR) assay.

Congenital Rubella Syndrome A clinical diagnosis of CRS is reasonable when an infant presents with a combination of cataracts, hearing impairment, and heart defects; this pattern is seen in ~10% of infants with CRS. Infants may present with different combinations of defects depending on when infection occurs during gestation. Hearing impairment is the most common single defect of CRS. However, as with acquired rubella, laboratory diagnosis of congenital infection is highly recommended, particularly because most features of the clinical presentation are nonspecific and may be associated with other intrauterine infections. Early diagnosis of CRS facilitates appropriate medical intervention for specific disabilities and prompts implementation of infection control measures.

Diagnostic tests used to confirm CRS include serologic assays and virus detection. In an infant with congenital infection, serum IgM antibodies are normally present for up to 6 months but may be detectable for up to 1 year after birth. In some instances, IgM may not be detectable until 1 month of age; thus infants who have symptoms consistent with CRS but who test negative shortly after birth should be retested at 1 month. A rubella serum IgG titer persisting beyond the time expected after passive transfer of maternal IgG antibody (i.e., a rubella titer that does not decline at the expected rate of a twofold dilution per month) is another serologic criterion used to confirm CRS.

In congenital infection, rubella virus is isolated most commonly from throat swabs and less commonly from urine and cerebrospinal fluid. Infants with congenital rubella may excrete virus for up to 1 year, but specimens for virus isolation are most likely to be positive if obtained within the first 6 months after birth. Rubella virus in infants with CRS can also be detected by RT-PCR.

Rubella Diagnosis in Pregnant Women In the United States, screening for rubella IgG antibodies is recommended as part of routine prenatal care. Pregnant women with a positive IgG antibody serologic test are considered immune. Susceptible pregnant women should be vaccinated postpartum.

A susceptible pregnant woman exposed to rubella virus should be tested for IgM antibodies and/or a fourfold rise in IgG antibody titer between acute- and convalescent-phase serum specimens to determine whether she was infected during pregnancy. Pregnant women with evidence of acute infection must be clinically monitored, and gestational age at the time of maternal infection must be determined to assess the possibility of risk to the fetus. Of women infected with rubella virus during the first 11 weeks of gestation, up to 90% deliver an infant with CRS; for maternal infection during the first 20 weeks of pregnancy, the CRS rate is 20%.

TREATMENT RUBELLA

No specific therapy is available for rubella virus infection. Symptom-based treatment for various manifestations, such as fever and arthralgia, is appropriate. Immunoglobulin does not prevent rubella virus infection after exposure and therefore is not recommended as routine postexposure prophylaxis. Although immunoglobulin may modify or suppress symptoms, it can create an unwarranted sense of security: infants with congenital rubella have been born to women who received immunoglobulin shortly after exposure. Administration of immunoglobulin should be considered only if a pregnant woman who has been exposed to rubella will not consider termination of the pregnancy under any circumstances. In such cases, IM administration of 20 mL of immunoglobulin within 72 h of rubella exposure may reduce—but does not eliminate—the risk of rubella.

PREVENTION

After the isolation of rubella virus in the early 1960s and the occurrence of a devastating pandemic, a vaccine for rubella was developed and licensed in 1969. Currently, the majority of rubella-containing vaccines (RCVs) used worldwide are combined measles and rubella (MR) or measles, mumps, and rubella (MMR) formulations. A tetravalent measles, mumps, rubella, and varicella (MMRV) vaccine is available but is not widely used.

The public health burden of rubella infection is measured primarily through the resulting CRS cases. The 1964–1965 rubella epidemic in the United States encompassed >30,000 infections during pregnancy. CRS occurred in ~20,000 infants born alive, including >11,000 infants who were deaf, >3500 infants who were blind, and almost 2000 infants who were mentally retarded. The cost of this epidemic exceeded $1.5 billion. In 1983, the cost per child with CRS was estimated at $200,000.

In most countries, there is little documented evidence to illuminate the epidemiology of CRS. Clusters of CRS cases have been reported in developing countries. Before the introduction of an immunization program, the incidence of CRS is 0.1–0.2 per 1000 live births during endemic periods and 1–4 per 1000 live births during epidemic periods. Where rubella virus is circulating and women of childbearing age are susceptible, CRS cases will continue to occur.

The most effective method of preventing acquired rubella and CRS is through vaccination with an RCV. One dose induces seroconversion in ≥95% of persons ≥1 year of age. Immunity is considered long-term and