230e Rubella (German Measles)

Laura A. Zimmerman, Susan E. Reef

Rubella was historically viewed as a variant of measles or scarlet fever. Not until 1962 was a separate viral agent for rubella isolated. After an epidemic of rubella in Australia in the early 1940s, the ophthalmologist Norman Gregg noticed the occurrence of congenital cataracts among infants whose mothers had reported rubella infection during early pregnancy, and congenital rubella syndrome (CRS; see "Clinical Manifestations," below) was first described.

ETIOLOGY

Rubella virus is a member of the Togaviridae family and the only member of the genus *Rubivirus*. This single-stranded RNA enveloped virus measures 50–70 nm in diameter. Its core protein is surrounded by a single-layer lipoprotein envelope with spike-like projections containing two glycoproteins, E1 and E2. There is only one antigenic type of rubella virus, and humans are its only known reservoir.

PATHOGENESIS AND PATHOLOGY

Although the pathogenesis of postnatal (acquired) rubella has been well documented, data on pathology are limited because of the mildness of the disease. Rubella virus is spread from person to person via respiratory droplets. Primary implantation and replication in the nasopharynx are followed by spread to the lymph nodes. Subsequent viremia occurs, which in pregnant women often results in infection of the placenta. Placental virus replication may lead to infection of fetal organs. The pathology of CRS in the infected fetus is well defined, with almost all organs found to be infected; however, the pathogenesis of CRS is only poorly delineated. In tissue, infections with rubella virus have diverse effects, ranging from no obvious impact to cell destruction. The hallmark of fetal infection is chronicity, with persistence throughout fetal development in utero and for up to 1 year after birth.

Individuals with acquired rubella may shed virus from 7 days before rash onset to ~5–7 days thereafter. Both clinical and subclinical infections are considered contagious. Infants with CRS may shed large quantities of virus from bodily secretions, particularly from the throat and in the urine, up to 1 year of age. Outbreaks of rubella, including some in nosocomial settings, have originated with index cases of CRS. Thus only individuals immune to rubella should have contact with infants who have CRS or who are congenitally infected with rubella virus but are not showing signs of CRS.

EPIDEMIOLOGY

The largest recent rubella epidemic in the United States took place in 1964–1965, when an estimated 12.5 million cases occurred, resulting in ~20,000 cases of CRS. Since the introduction of the routine rubella vaccination program in the United States in 1969, the number of rubella cases reported each year has dropped by >99%; the rate of vaccination coverage with rubella-containing vaccine has been >90% among children 19–35 months old since 1995 and >95% for kindergarten and first-grade entrants since 1980. In 1989 a goal for the elimination of rubella and CRS in the United States was set, and in 2004 a panel of experts agreed unanimously that rubella was no longer an endemic disease in this country. The criteria used to document lack of endemic transmission included low disease incidence, high nationwide rubella antibody seroprevalence, outbreaks that were few and contained (i.e., small numbers of cases), and lack of endemic virus transmission (as assessed by genetic sequencing). In the United States, interruption of endemic transmission of rubella virus has been sustained since 2001; in 2012, however, three cases of CRS were reported in infants whose mothers had acquired rubella infection abroad. Thus health care providers should remain vigilant, considering the possibility of rubella infection in patients emigrating or returning from countries without rubella control programs and the accompanying potential for CRS among their infants.

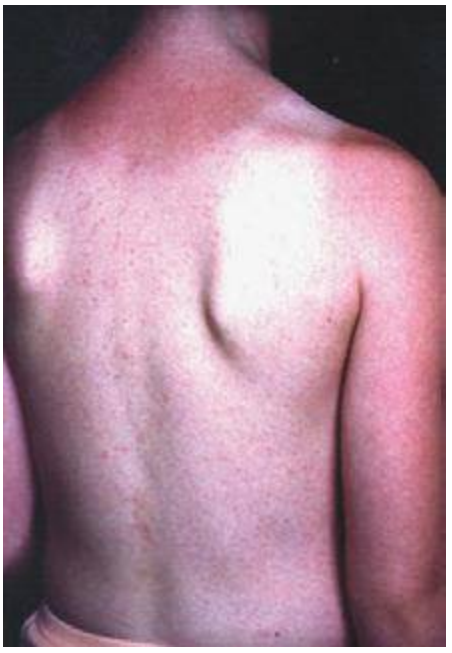

FIGURE 230e-1 Mild maculopapular rash of rubella in a child.

Although rubella and CRS are no longer endemic in the United States, they remain important public health problems globally. The number of rubella cases reported worldwide in 1999 was ~900,000; this figure declined steadily to 94,030 in 2012. However, numbers of rubella cases are substantially underestimated because cases in many countries are identified through measles surveillance systems that are not specific for rubella. In 2010, it was estimated that 103,000 cases of CRS occur globally.

CLINICAL FEATURES

Acquired Rubella Acquired rubella commonly presents with a generalized maculopapular rash that usually lasts for up to 3 days (Fig. 230e-1), although as many as 50% of cases may be subclinical or without rash. When it occurs, the rash is usually mild and may be difficult to detect in persons with darker skin. In children, rash is usually the first sign of illness. However, in older children and adults, a 1- to 5-day prodrome often precedes the rash and may include low-grade fever, malaise, and upper respiratory symptoms. The incubation period is 14 days (range, 12–23 days).

Lymphadenopathy, particularly occipital and postauricular, may be noted during the second week after exposure. Although acquired rubella is usually thought of as a benign disease, arthralgia and arthritis are common in infected adults, particularly women. Thrombocytopenia and encephalitis are less common complications.

Congenital Rubella Syndrome The most serious consequence of rubella virus infection can develop when a woman becomes infected during pregnancy, particularly during the first trimester. The resulting complications may include miscarriage, fetal death, premature delivery, or live birth with congenital defects. Infants infected with rubella virus in utero may have myriad physical defects (Table 230e-1), which most commonly relate to the eyes, ears, and heart. This constellation of severe birth defects is known as *congenital rubella syndrome*. In addition to permanent manifestations, there are a host of transient physical manifestations, including thrombocytopenia with purpura/petechiae (e.g., dermal erythropoiesis, "blueberry muffin syndrome"). Some infants may be born with congenital rubella virus infection but have no apparent signs or symptoms of CRS and are referred to as "infants with congenital rubella infection only."

DIAGNOSIS

Acquired Rubella Clinical diagnosis of acquired rubella is difficult because of the mimicry of many illnesses with rashes, the varied