121 Rubella

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Introduction

Initially, rubella was considered to be a variant of measles or scarlet fever; however, in 1814, rubella was recognized as a distinct clinical entity. In 1866, Veale introduced the name rubella for the clinical syndrome associated with a maculopapular rash of children and young adults. Rubella is frequently called "German measles" and is the third of six viral exanthems of childhood, with measles and scarlet fever being the first and second. In 1914, Hess suggested a viral etiology predicated on work performed in animal models; however, the etiology was never firmly established until 1938 when Hiro and Tosaka confirmed the viral origin by passing disease to children using filtered nasal washings (16 nonimmune children).

Rubella was considered a benign disease until the early 1940s when, following a widespread outbreak in Australia, an Australian ophthalmologist, Norman Gregg, first described congenital defects, as described below, of infants born to mothers who developed rubella early in pregnancy. With an increasing recognition of the congenital rubella syndrome and after pandemics between 1962 and 1965, a definitive need for the development of a vaccine became apparent. Parkman and Weller first isolated rubella in cell culture in 1962, which ultimately led to the development and licensure of a vaccine in 1969.

Etiology

Rubella is a single negative stranded RNA virus that is enveloped. It is classified as a togavirus, genus rubivirus of the togaviridae family. The other genus in the family of togaviridae is alphavirus. In contrast to the alphaviruses, which replicate in arthropods and invertebrates, rubella virus has no invertebrate host. The only known host of rubella is humans. This virus is relatively unstable and is inactivated by lipid solvents, formalin, ultraviolet light, low pH, and heat. There is only one immunologically distinct serotype of rubella virus. The spherical particles of rubella virus measure 50–70 nm in diameter.

Pathogenesis

Rubella virus is transmitted by the respiratory route. After exposure, replication of the virus is thought to occur in the upper respiratory tract including the nasopharnyx and regional lymph nodes. Viremia ensues approximately 5–7 days after exposure. During periods of viremia, transplacental infection can take place, resulting in fetal damage, particularly during the first trimester of gestation. In studies conducted with volunteers, virus can be detected 7 days prior to and approximately 14 days after the onset of rash. Rubella has a worldwide distribution, although clinically recognized disease occurs less frequently in tropical regions than in temperate zones. Humans are the only known host. As noted above, rubella is spread from person to person via airborne transmission. Rubella is highly contagious and the incidence of infection during an epidemic cycle approaches 100% for susceptible individuals.

In temperate climates such as North America and Europe, rubella is most prevalent from March through May. Persons with subclinical infection are contagious and can transmit infection to others.

Fetal infection can occur at any time during pregnancy; however, the risk is greatest during the first trimester and decreases thereafter. The risk of congenital anomalies in live-born children following fetal infection varies according to the month of pregnancy in which maternal infection occurred, being the highest during the first 8 weeks at 85%.

Clinical Manifestations

The incubation period for rubella is approximately two weeks with a range of 12–23 days. Symptoms are generally mild and many infections are totally asymptomatic. A maculopapular rash is characteristic of infection, as illustrated in *Fig. 121.1*. The rash begins on the face and progresses distally, persisting approximately 3 days. Arthralgia and arthritis are frequent complications in adults (occurring in as many as 70% of adult women).

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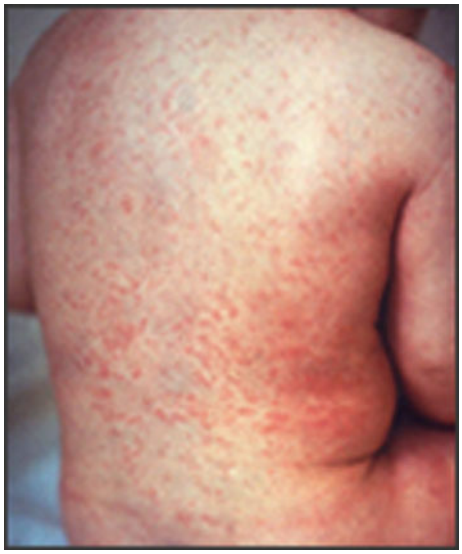

Figure 121.1

When arthritis occurs, it frequently involves the fingers, wrists, and knees. Encephalitis is a rare complication, occurring in approximately 1 in 6,000 cases. Additional complications include orchitis, neuritis, and a late-onset syndrome of progressive pan encephalitis. In addition, hemorrhagic manifestations may be present during the acute illness.

The most significant complication of rubella is the congenital rubella syndrome. Prevention of this syndrome has been the main objective of rubella vaccination programs worldwide. Fetal infection may lead to death, or premature delivery. The congenital rubella syndrome involves virtually all organ systems. Deafness is the most common finding of congenital infection. Other manifestations include ocular abnormalities of cataracts, glaucoma, retinopathy, and microphthalmia. Cardiac defects include peripheral pulmonic stenosis and coarctation of the aorta. Neurologic abnormalities include microcephaly and, ultimately mental retardation. A late-onset congenital rubella syndrome has been described that results in diabetes mellitus and a progressive encephalopathy.

Diagnosis

While clinical findings can suggest a diagnosis of rubella, maculopapular rashes can be attributed to a variety of other etiologies. Thus, laboratory confirmation is required. Definitive diagnosis is achieved by isolation of virus either in cell culture or by polymerase chain reaction. Rubella virus can be detected in blood, urine, cerebrospinal fluid, and nasal and throat swabs. It is present generally 1 week prior to the onset of illness and 2 weeks after rash onset.

Serology is a common method for confirmation of diagnosis. Acute and convalescent serospecimens can be tested by enzyme-linked immunosorbent assays for evidence of antibodies directed against rubella virus. The application of IgM antibodies for confirmation of diagnosis has been used; however, infection attributed to parvoviruses will cause false-positive IgM tests.

Treatment and Prevention

There is no definitive antiviral therapy for rubella infection. Administration of immunoglobulin to susceptible persons experimentally exposed to rubella can prevent clinical disease; however, there have been many reports of failure. As a consequence, it is not routinely recommended.

Since 1979, the RA27/3 rubella vaccine, a live attenuated virus, has been used for the prevention of rubella. The vaccine virus is not communicable except in the setting of breast feeding. It is combined with measles and mumps as an MMR vaccine, or, in addition, with varicella as MMRV. Over 90% of vaccinated individuals will derive significant protection from both clinical disease as well as blood-borne infection for a minimum of 15 years. The first dose of vaccine is recommended for administration between 12 and 15 months of age, with a subsequent dose at school entry (4–6 years of age).

The vaccine can be administered to individuals exposed to rubella within 3 days of exposure.

The vaccine is contraindicated for pregnant women and those who are immunodeficient or receiving immunosuppressive therapies, including individuals with leukemia, human immunodeficiency virus infection, lymphoma, or other malignancies.

Adverse reactions to the vaccine have included arthralgia and arthritis, attributed to the rubella component of MMR. The development of a rash is most likely attributed to the measles component of the vaccine. Additional common complaints include fever, lymphadenopathy, and arthralgia.

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