A Brief Review of Rubella, Measles & MMR Vaccine

Seema Hashmi , Quazi Saleem Sairy Abdulla

Dept of Microbiology & Zoology

Milliya Arts Science & Management Science College Beed

Abstract

The human population has long been aware of the disease or virus known as rubella. Also known as German measles, it is generally considered to be a simple childhood disease that runs its course within a few days . However, when women develop the disease during their first trimester of pregnancy, rubella may have serious consequences for the unborn child. As a result, rubella has been the subject of scientific study for many years. The rubella virus is of the rubivirus genus, which is the only known member of the Togaviridae family. Humans are apparently the only host that may contract this infection.The review article presents a review of rubella

Introduction

Structure

Rubella virus is a spherical 40- to 80-nm, single-stranded RNA virus consisting of an electron-dense 30- to 35-nm core surrounded by a lipoprotein envelope. The RNA has a molecular weight of about 3 × 10^{-6}. The virus particles are generally spherical with spiky hemagglutinin-containing surface projections. The rubella virus is a member of the genus *Rubivirus* in the family Togaviridae Hobman TC, Chantler J (2007)

Classification and Antigenic Types

Rubella virus is the single member of the genus *Rubivirus* in the family Togaviridae. It is serologically distinct from other members of the Togaviridae, and, unlike most other togaviruses, is not known to be transmitted by an arthropod. Only one genetically stable serotype of rubella virus has been identified. Phylogenetic tree analysis of nine virus strains indicate the existence of at least three distinct genetic lineages.

Rubella virus contains three major structural polypeptides: two membrane glycoproteins, E1 and E2 and a single nonglycosylated RNA-associated capsid protein, within the virion. One of the envelope proteins, E1, is responsible for viral hemagglutination and neutralization. E2 has been found in two forms, E2a and E2b due to differences in glycosylation. The differences among strains of rubella viruses have been correlated with differences in the antigenicity of E2.

Measles

Rubella (German measles) is a common mild disease caused by Rubella virus & Is characterized by a rash. It affects children and adolescents worldwide and can also affect young adults.

Clinical Manifestations

Postnatal Infection

Postnatal rubella is often asymptomatic but may result in a generally mild, self-limited illness characterized by rash, lymphadenopathy, and low-grade fever. As is the case for many viral diseases, adults often experience more severe symptoms than do children. In addition, adolescents and adults may experience a typical mild prodrome that is not seen in infected children; this occurs 1 to 5 days before the rash and characterized by headache, malaise, and fever. The typical picture of rubella includes a maculopapular rash that appears first on the face and neck and quickly spreads to the trunk and upper extremities and then to the legs. It often fades on the face while progressing downwards. The lesions tend to be discrete at first, but rapidly coalesce to produce a flushed appearance. The onset of rash is often accompanied by low-grade fever. Although the rash usually lasts 3 to 5 days (hence the term “3-day measles”), the associated fever rarely persists for more than 24 hours.

MULTIPLICATION

The earliest and perhaps the most prominent and characteristic symptom of rubella infection is lymphadenopathy of the postauricular, occipital, and posterior cervical lymph nodes; this is usually most severe during the rash but may occur even in the absence of rash.

Postnatal rubella usually resolves without complication. However, a number of studies report that as many as one-third of adult women with rubella experience self-limited arthritis of the extremities and/or polyarthralgia; such effects are rare in children or men. Other complications of rubella, reported with much less frequency than arthritis, include encephalitis and thrombocytopenic purpura.

Congenital Infection

Rubella infection acquired during pregnancy can result in stillbirth, spontaneous abortion, or several anomalies associated with the congenital rubella syndrome. The clinical features of congenital rubella vary and depend on the organ system(s) involved and the gestational age at the time of maternal infection . The classic triad of congenital rubella syndrome includes cataracts, heart defects, and deafness, although many other abnormalities, as noted in the Table, may be seen. Defects may occur alone or in combination and may be temporary or permanent. The risk of rubella-associated congenital defects is greatest during the first trimester of pregnancy. Some defects have been reported after maternal infections in the second trimester

Pathogenesis of rubella.

Rubella infection in the first 3 or 4 months of pregnancy provides opportunities during the period of maternal viremia for invasion of the placenta and subsequent fetal infection. Development of infection probably depends upon gestational age. It has been estimated that the fetus has a 40 to 60 percent chance of developing multiple rubella-associated defects if the mother is infected during the first 2 months of pregnancy, with the risk dropping to 30 to 35 percent during the third month of gestation and 10 percent during the fourth. This difference in both risk for and severity of fetal infection seen with gestational age may be associated with immature host defenses during the first trimester of pregnancy.

During fetal infection, the virus can multiply in and damage virtually any organ system. Pathogenesis of the congenital defects is not fully understood; however, a number of mechanisms have been proposed. Cell culture studies show that the virus produces chromosomal abnormalities, slows cellular growth rates, and causes cell lysis and death in some cell types; these effects appear capable of producing the characteristic abnormalities of cell structure and function. In addition, rubella infection induces angiopathy of early placental and embryonic tissues, causing interference with the fetal blood supply and subsequent compromised growth and/or malformation of the fetus. In the congenitally infected fetus and infant, virus persistence occurs in the presence of neutralizing antibodies; immunological tolerance does not develop.

Host Defenses

Postnatal infection rapidly induces a specific immune response which provides lifelong protection against the natural disease. Neutralizing and hemagglutination-inhibiting antibodies appear shortly

after the onset of rash and reach maximum levels in 1 to 4 weeks. Specific antibodies persist after infection. Cell-mediated immunity also develops in convalescence and can be detected for years following infection. When exposed to rubella virus, individuals with neutralizing or hemagglutination-inhibiting antibodies are most often protected. However, reinfection with rubella virus has been documented in individuals with demonstrated natural immunity and, more commonly, in vaccinees. The vast majority of such reinfections are asymptomatic, detectable only by a boost in antibody titer; however, a few cases of reinfection-associated rash and arthritis have been reported.

Epidemiology

Rubella occurs worldwide. There have been no major epidemics in the United States since the licensure of the live attenuated rubella vaccine in 1969. However, limited sporadic outbreaks of rubella continue to occur each year, particularly in settings (such as schools) where susceptible individuals come into close contact. The incidence of infection shows the same prominent seasonal pattern as for other respiratory diseases. The incidence increases in winter, peaks in spring, and then subsides to extremely low levels in summer and fall.

Epidemiologic data suggest that maximum infectivity occurs from 3 days before the onset of rash until 3 days afterward. However, throat swabs from children with rubella have been reported to contain virus from as early as 10 days before the onset of rash to as late as 28 days afterward. In addition, asymptomatic individuals have been reported to transmit rubella.

In the prevaccine era, the disease usually affected children 5 to 9 years old. However, because rubella is less contagious than diseases such as measles and varicella, a significant proportion of the population (10 to 15 percent) escaped rubella infection in childhood. Widespread vaccine use has reduced rubella incidence by more than 99 percent overall However, a greater percentage of cases that do occur are now reported in unvaccinated young adults. An average of 39 cases per year of congenital rubella were reported to the Centers for Disease Control between 1969 and 1979, falling rather dramatically to an average of only 7 cases per year between 1979 and 1988. A slight resurgence of rubella and congenital rubella was noted in 1989 to 1991. However, subsequently the reported numbers of cases have been the lowest ever recorded. In infants with congenital rubella, the virus commonly persists during the first year of life and occasionally even longer. Such infants thus can serve as reservoirs of infection for health care personnel and other contacts.

Diagnosis

The occurrence of the typical rash and lymphadenopathy may suggest the diagnosis of rubella. Laboratory diagnosis of rubella is typically made by using serologic studies (i.e., detection of IgM and/or fourfold antibody rises). The presence of specific IgM antibodies indicates recent rubella infection.

Specific IgG antibodies in healthy individuals demonstrate immunity to rubella. Antibodies are detectible by a variety of methods including the neutralization test (seldom used because of its complexity and expense), hemagglutination inhibition, ELISA, and indirect immunofluorescent immunoassay. Virus can be readily recovered in cell cultures from respiratory tract secretions and, in infants with congenital infection, from urine, cerebrospinal fluid, and blood. Presence of virus in inoculated cultures can be recognized by viral interference or immunoperoxidase staining assays. Because virus isolation procedures are costly and require a relatively sophisticated virologic laboratory, they are seldom used except for the diagnosis of congenital rubella. Watson JC, Hadler SC,(1998)

Congenital rubella in the neonate is diagnosed by virus isolation or serologic testing. The affected neonate has circulating antibodies, including transplacentally acquired maternal IgG antibody and actively produced fetal and neonatal IgM antibody. Maternal IgG antibody is detectable in the neonate and wanes during the first 6 months of life. Therefore, the persistence of IgG antibody beyond 6 months or the demonstration of IgM antibody is diagnostic for congenital rubella infection .

Control

Vaccines

Rubella is preventable with the rubella vaccine with a single dose being more than 95% effective.[1] in combination with the measles vaccine and mumps vaccine, known as the MMR vaccine**.A**hmed et al (2012)

Since 1969, several live attenuated rubella vaccines for the prevention of rubella have been licensed for use in the United States. The vaccine in current use is prepared from attenuated rubella virus (RA 27/3) and induces immunity by producing a modified rubella infection in susceptible recipients. It is administered subcutaneously. Two doses are recommended. The first may be given starting at 12

months. Most commonly, the initial dose is administered The second dose is given either at school entry or at entry to middle school or high school. Vaccine-induced infection is usually asymptomatic in children, but is associated more frequently with rubella-like symptoms in adults (most commonly in women over the age of 25). Vaccine-associated reactions include fever, lymphadenopathy, and arthritis and are usually mild and transient. Dominguez G, Wang CY, (2010)

Although the levels of vaccine-induced antibody are lower than those produced by the natural disease, approximately 95 percent of vaccines seroconvert between 14 and 28 days following vaccination. As with all attenuated vaccines, the duration of protection may be a matter of concern. In 1982, the Centers for Disease Control reported surveillance studies on individuals enrolled in a vaccine study in 1969. During the first 4 years after vaccination, there was approximately a 50 percent drop in the hemagglutination inhibition titer, with generally stable titers after that time. Nevertheless, measurable antibody levels persisted in 97 percent of vaccinees over the 10-year study period. The continued decline in reported cases of rubella in the indicates that immunity conferred by vaccination appears adequate to interrupt the transmission of disease. Katz SL, Kempe (2015)

The immunization strategy is aimed at minimizing the potential for exposure of pregnant women (and through them, their fetuses) to rubella by using vaccination programs designed primarily to provide widespread childhood immunity to rubella and to reduce the occurrence of disease in the community. A continued downward trend in cases of rubella has been reported by the Centers for Disease Control, with a record low of 225 cases in 1988. Still of concern, however, is the fact that approximately 6 to 11 percent of postpubertal women show no serologic evidence of immunity to rubella virus. Additional emphasis is therefore being placed on immunization of this population. Suggested additional strategies for rubella control include: (1) proof of rubella immunity as a prerequisite for college entry; (2) requiring vaccination of susceptible health care and military personnel; (3) rubella prevention and control programs in correctional institutions; (4) encouraging persons in religious groups who do not seek health care to accept vaccination; (5) vaccination of young adults visiting in or emigrating to the U.S. from countries in which rubella vaccine is not used routinely; and (6) vaccination of susceptible women after childbirth, miscarriage, or abortion.

Although the use of rubella vaccine is not recommended under any circumstances during pregnancy, data collected since 1971 indicate that vaccination within the first 3 months of conception poses little risk of congenital rubella syndrome and should not be an automatic reason for interruption of pregnancy. However, the theoretical risk for vaccine-induced congenital rubella infection remains, and women are advised not to become pregnant for 3 months following rubella immunization.

Immunoglobulin

No specific chemotherapeutic measures are available for the treatment of rubella. Immunoglobulin has been used in attempts to prevent rubella in pregnant women exposed to the virus. However, immunoglobulin does not appear to be highly effective. Congenital infection has been observed in the infants of women given appropriately timed large doses. The failure of antibody to prevent infection and spread to the fetus may be due to direct cell-to-cell spread of virus. Therefore, immunoglobulin is not routinely recommended for prophylaxis of rubella in early pregnancy.

REFERENCES

Ahmed R, Barouch DH, Butera ST, Crotty S, Godzik A, Kaufmann DE, McElrath MJ, Nussenzweig MC, Pulendran B, et al: A Blueprint for HIV Vaccine Discovery. Cell Host Microbe. 2012, 12: 396-407. 10.1016/j.chom.2012.09.008.PubMed CentralView ArticlePubMedGoogle Scholar

Dominguez G, Wang CY, (2010) Progress toward control of rubella and prevention of congenital rubella syndrome: Worldwide, 2009. MMWR Morb Mortal Wkly Rep 59(40):1307–1310.

Hobman TC, Chantler J (2007) Rubella virus. Fields Virology, eds Knipe DM, Howley PM (Lippincott Williams & Wilkins, Philadelphia), 5th Ed, Vol I, pp 1069–1100.

Katz SL, Kempe CH, Black FL, Lepow ML, Krugman S, Haggerty RJ, Enders JF: Studies on an attenuated measles-virus vaccine. VIII. General summary and evaluation of the results of vaccine. N Engl J Med. 1960, 263: 180-184. 10.1056/NEJM196007282630408.View ArticlePubMedGoogle Scholar

Watson JC, Hadler SC, Dykewicz CA, Reef S, Phillips L: Measles, mumps, and rubella–vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep. 1998, 47: 1-57.PubMedGoogle Scholar