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REVIEW ARTICLE

A Comprehensive Review on Rubella Virus

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Abstract: Rubella, colloquially known as German measles, is an exceptionally contagious viral illness that primarily affects children and non-immune young adults. While the infection is typically mild and self-limiting in most cases, rubella virus infection during early pregnancy can have devastating consequences, leading to a range of severe birth defects collectively termed congenital rubella syndrome (CRS). The etiological agent, Rubella virus (RV), is an enveloped, positive-sense single-stranded RNA virus and the sole member of the genus Rubivirus within the Matonaviridae family. Despite the availability of an effective and safe rubella vaccine, the disease continues to pose a significant global health threat, with an estimated 100,000 cases of CRS occurring annually worldwide, predominantly in regions with suboptimal vaccination coverage. This comprehensive review delves into the intricate details of rubella virus, encompassing its epidemiological patterns, modes of transmission, and the complex pathogenic mechanisms underlying congenital rubella syndrome

Keywords: Parkinson's disease, SINEMET, Levodopa, Carbidopa, Pramipexole, Trihexyphenidyl.

1. Introduction

Rubella, also referred to as German measles, is a highly contagious viral illness caused by the Rubella virus (RV). Although typically mild in most cases, RV infection during early pregnancy can have severe consequences for the developing fetus, leading to a range of birth defects known as congenital rubella syndrome (CRS). Despite the availability of an effective vaccine, rubella remains a significant global health concern, with an estimated 100,000 cases of CRS occurring annually worldwide. [1-3]

Rubella virus, the sole member of the genus Rubivirus in the Matonaviridae family, is an enveloped virus with a single-stranded, positive-sense RNA genome. [4,5] The virus is primarily transmitted through respiratory droplets and can spread rapidly in susceptible populations. While natural infections are exclusive to humans, the virus can cause a range of clinical manifestations, from asymptomatic or mild cases to more severe complications.[6] This review aims to provide a comprehensive overview of rubella virus, including its epidemiology, transmission, pathogenesis, clinical manifestations, diagnosis, prevention strategies, and current challenges in the quest for global eradication.

2. Rubella virus

2.1. Epidemiology

Rubella is a globally distributed disease, with outbreaks occurring cyclically in temperate regions, often peaking during the spring seasons. [7] Before the introduction of the rubella vaccine in 1969, widespread outbreaks occurred every 6–9 years in the United States and every 3–5 years in Europe, primarily affecting children aged 5–9 years. [8, 9] Since the implementation of vaccination programs, the incidence of rubella has significantly declined in countries with high vaccination coverage. However, rubella remains a significant public health concern in regions with low vaccination rates or limited access to healthcare resources. According to the World Health Organization (WHO), an estimated 17,865 rubella cases were reported globally in 2022 [10-11], with the majority occurring in countries with suboptimal vaccination coverage.

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2.2. Transmission

Rubella virus is primarily transmitted through direct contact with respiratory droplets from infected individuals or through contact with contaminated surfaces. The virus can spread rapidly in susceptible populations, particularly in settings with close, prolonged contact, such as schools, childcare facilities, and healthcare settings. Interestingly, asymptomatic or mild cases contribute significantly to the transmission of rubella, accounting for up to 50% of all infections. [12] The virus is most contagious during the late prodromal phase, approximately 7 days before the onset of the rash, and can remain transmissible for up to 7 days after the rash appears. Infants born with congenital rubella syndrome can also serve as reservoirs for the virus, shedding the virus for an extended period, up to 18–24 months of age. [13] The risk of transmission from these infants is highest during the first month of life and gradually decreases over time.

2.3. Pathogenesis

Rubella virus primarily targets the upper respiratory tract and nasopharyngeal lymphoid tissues, where it initially replicates. Subsequently, the virus spreads to regional lymph nodes and enters the bloodstream, leading to a transient viremia and systemic dissemination. The pathogenesis of rubella during pregnancy is particularly concerning, as the virus can cross the placental barrier and infect the developing fetus, leading to a range of severe birth defects collectively termed congenital rubella syndrome (CRS). The risk of CRS is highest during the first trimester of pregnancy, with up to 90% of fetuses [14, 15] affected if the mother is infected during this critical period. CRS can lead to various congenital abnormalities, including but not limited to:

- Growth delays and intrauterine growth restriction
- Congenital heart defects
- Cataracts and other eye defects
- Sensorineural hearing loss
- Developmental delays and intellectual disabilities
- Hepatosplenomegaly
- Thrombocytopenia and bleeding disorders

In addition to CRS, rubella virus infection can also cause long-term persistent infections, such as Fuchs' uveitis syndrome, where the virus is detected in the eye fluid of affected individuals, indicating prolonged viral persistence. [16]

2.4. Clinical manifestations

Rubella typically presents as a mild, self-limiting illness in most cases, with symptoms appearing approximately 2–3 weeks after exposure to the virus. Common symptoms include Low-grade fever (usually below 102°F or 38.9°C), Headache, Stuffy or runny nose, Red, itchy eyes, Swollen and tender lymph nodes, particularly at the base of the skull, back of the neck, and behind the ears, Maculopapular rash, typically beginning on the face and spreading downwards. [17] While rubella is usually mild in children, adult women may experience more severe symptoms, such as polyarthralgia or arthritis, particularly affecting the fingers, wrists, and knees. Rare complications of rubella include encephalitis, thrombocytopenia, and hepatitis.[18]

Table 1. Symptoms of Rubella vs. CRS

Rubella	Congenital Rubella Syndrome (CRS)
Low-grade fever	Growth delays/intrauterine growth restriction
Headache	Congenital heart defects
Stuffy/runny nose	Cataracts and other eye defects
Red, itchy eyes	Sensorineural hearing loss
Swollen, tender lymph nodes	Developmental delays/intellectual disabilities
Maculopapular rash	Hepatosplenomegaly
Polyarthralgia/arthritis (in adults)	Thrombocytopenia and bleeding disorders

2.5. Diagnosis

The diagnosis of rubella is primarily based on clinical symptoms and laboratory testing. [19] Laboratory tests commonly used for rubella diagnosis include:

2.5.1. Serological tests

Serological tests are widely used for the diagnosis of rubella, as well as for determining immunity status. The presence of rubella-specific IgM antibodies indicates acute or recent infection, while IgG antibodies suggest past exposure or immunity [20]

- Enzyme-linked immunosorbent assay (ELISA) for detecting rubella-specific IgM and IgG antibodies
- Hemagglutination inhibition (HAI) assay

2.5.2. Molecular tests

- Reverse transcription-polymerase chain reaction (RT-PCR) for detecting rubella virus RNA
- Viral culture (less commonly used)

It is crucial to differentiate rubella from other exanthematous febrile illnesses, such as measles, scarlet fever, dengue fever, and various viral infections, based on clinical presentation and laboratory findings. [21]

Table 2. Laboratory Tests for Rubella Diagnosis and Their Characteristics

Test	Characteristic
Enzyme-linked Immunosorbent Assay (ELISA)	Detects rubella-specific IgM and IgG antibodies
Hemagglutination Inhibition (HAI) Assay	Measures antibodies that inhibit rubella virus from agglutinating red blood cells
Reverse Transcription-Polymerase Chain Reaction (RT-PCR)	Detects rubella virus RNA, useful for acute infection
Viral Culture	Less commonly used, detects presence of live virus

2.6. Prevention and control

The most effective strategy for preventing rubella and congenital rubella syndrome is through widespread vaccination. The rubella vaccine, typically administered as part of the measles-mumps-rubella (MMR) or measles-mumps-rubella-varicella (MMRV) combination vaccines, provides long-lasting immunity against the virus. The WHO recommends the administration of two doses of the MMR or MMRV vaccine, with the first dose given at 12–15 months of age and the second dose at 4–6 years of age or according to national immunization schedules. [22-24] Catch-up vaccination campaigns are also essential for susceptible populations, including adolescents and adults, particularly women of childbearing age.

In addition to routine vaccination programs, other preventive measures include:

- Surveillance and outbreak response
- Isolation of infected individuals
- Maintaining high vaccination coverage rates
- Educating healthcare providers and the public about the importance of rubella vaccination

2.7. Treatment and Management

There is no specific antiviral treatment for rubella virus infection. Management of rubella primarily focuses on supportive care and symptom relief, such as rest, adequate hydration, and the use of over-the-counter medications for fever and body aches. In severe cases or complications, hospitalization and specific treatment may be required. [25] For pregnant women infected with rubella, close monitoring and frequent ultrasound examinations are crucial to assess fetal development and potential congenital abnormalities. In cases of confirmed or suspected CRS, a multidisciplinary team approach involving obstetricians, neonatologists, and other specialists is recommended for optimal management and care of the affected newborn.

2.8. Current challenges for Rubella treatment

Despite significant progress in rubella control and prevention, several challenges [26] remain in achieving global eradication of the disease:

2.8.1. Suboptimal vaccination coverage

Low vaccination rates, particularly in developing countries and hard-to-reach populations, contribute to the persistence of rubella transmission.

2.8.2. Waning immunity

While rubella immunity is generally believed to be lifelong after natural infection or vaccination, some studies have suggested the potential for waning immunity over time, especially in older age groups.

2.8.3. Importation and outbreaks

Rubella outbreaks can occur in previously rubella-free regions due to the importation of the virus by travelers from endemic areas, posing a risk to susceptible populations.

2.8.4. Vaccine hesitancy

Vaccine hesitancy and misinformation about vaccine safety continue to be barriers to achieving high vaccination coverage rates in some communities.

2.8.5. Limited surveillance and reporting

Inadequate surveillance and reporting systems in some regions can hinder accurate estimates of rubella burden and the effectiveness of control measures. To address these challenges, ongoing efforts are needed to strengthen immunization programs, enhance surveillance systems, and improve public awareness and education about the importance of rubella vaccination. Additionally, continued research into the development of novel rubella vaccines, improved diagnostic tools, and a deeper understanding of the virus's molecular mechanisms and pathogenesis is crucial for advancing rubella control and prevention strategies.

3. Conclusion

Rubella virus, although typically causing a mild illness, can have severe consequences during pregnancy, leading to congenital rubella syndrome and a range of birth defects. While the availability of an effective vaccine has significantly reduced the global burden of rubella, the disease remains a public health concern in regions with suboptimal vaccination coverage. Continued efforts are needed to strengthen immunization programs, enhance surveillance systems, and address barriers to achieving high vaccination rates. Additionally, ongoing research into the virus's pathogenesis, diagnostic tools, and novel prevention strategies is crucial for the ultimate goal of global rubella eradication.

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