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Newsletter

Rubella in pregnancy

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Introduction

Rubella virus is a single-stranded RNA virus that belongs to the *Togaviridae* family. It has been known to cause a mild measles-like illness (hence the original name "German measles") since the 19th century, and was not seen as a cause of significant disease. But in 1941 it was reported by an Australian ophthalmologist that rubella infection early in pregnancy was associated with congenital cataracts and other abnormalities in the infants, and this was called congenital rubella syndrome (CRS).

Epidemiology and transmission

Humans are the only known host for rubella virus, which is transmitted mainly by droplet spread. The incubation period is between 12 and 23 days. People are most infectious from around one week before the rash appears until about one week after.

Postnatal rubella

Between 25% and 50% of people who acquire rubella after the postnatal period are asymptomatic. Symptomatic infection is characterised by lymphadenopathy, a maculopapular rash (see Figure 1) and fever. The rash typically starts on the face and spreads to the rest of the body within 24 hours. It is not confluent, usually lasts 3 – 5 days, and may desquamate during convalescence. Up to 70% of women develop arthritis or arthralgia concurrent with or soon after the rash starts, and this may last for up to one month. Joint pain occurs less often in children and men. Other rare complications include encephalitis and thrombocytopaenia.

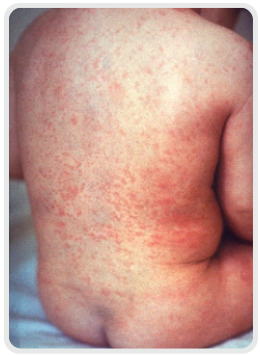

Figure 1. Typical rubella rash (CDC PHIL Photo ID 712)

Congenital rubella syndrome (CRS)

The effects of rubella virus on the foetus depends largely on the time of infection. In general, foetal illness and manifestations are more severe during the first few weeks of gestation as this is the main period of organogenesis. Transplacental transmission of rubella virus during the first few weeks of gestation can result in miscarriage or stillbirth. The risk for, and extent of, the clinical manifestations of CRS are summarised in Table 1. Whether maternal infection is primary or secondary (i.e. re-infection) also influences the overall risk to the foetus. In contrast to primary infection, the risk of foetal infection is less than 10% during the first 16 weeks of gestation following a secondary infection.

Table 1. Risk for and extent of clinical manifestations of CRS by time of maternal infection*

Gestational Period	Risk (%)	Malformations
First trimester	38 - 100	Ocular defects, cardiovascular defects, CNS defects, sensorineural hearing loss, intrauterine growth restriction
Second trimester	4 - 60	Sensorineural hearing loss, retinopathy, microcephaly, intellectual impairment
Third trimester	0 - 18	Intrauterine growth restriction

* From De Santis M, et al.

Ocular defects include cataracts (see Figure 2), microphthalmia and retinopathy. Reported cardiovascular defects include patent ductus arteriosus, ventricular septal defects and pulmonary artery hypoplasia. Intellectual impairment, behavioural disorders, and language and other developmental delays are the most common CNS defects reported. Transient manifestations include thrombocytopaenic purpura, low birth weight, haemolytic anaemia, hepatosplenomegaly and a large anterior fontanelle. There is also an association with an increased risk of diabetes mellitus and thyroid disorders late in childhood and adulthood.

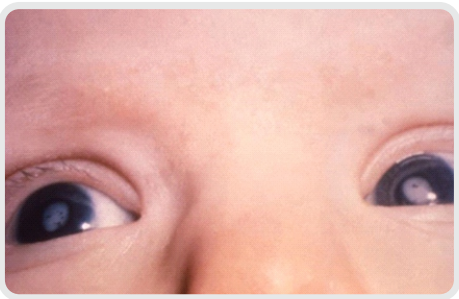

Figure 2. Cataracts due to congenital rubella syndrome (CDC PHIL Photo ID 4284)

Diagnosis

Postnatal rubella

The mainstay of the diagnosis of postnatally acquired rubella is serology. Rubella-specific IgM usually becomes detectable 3 – 6 days after the onset of the rash and remains positive for 8 weeks. Unfortunately, due in part to the increased sensitivity of modern IgM-specific serological assays, primary rubella infection is not the only reason for a positive result. Other causes for a positive rubella-specific IgM result include:

- Previous rubella vaccination (low levels of IgM antibody may persist for several years)
- Secondary infection (re-infection)
- Heterotypic antibodies due to recent infection with other viruses, e.g. EBV, CMV, parvovirus B19
- Auto-immune diseases, e.g. SLE, due to the presence of rheumatoid factor
- Non-specific polyclonal activation of memory B cells triggered by other viral infections

Rubella-specific IgG usually develops several days after IgM, and remains positive lifelong in most people. In an effort to differentiate between primary and secondary rubella infection, rubella IgG avidity testing should be performed on all samples taken from pregnant women that test positive for both IgG and IgM. After initial (primary) infection IgG antibodies are of low avidity, which slowly increases over weeks to months.

Congenital rubella syndrome

Prenatal diagnosis

Prenatal diagnosis of foetal infection is recommended in all cases of proven maternal infection, as maternal infection does not always result in vertical transmission to the foetus. Non-invasive ultrasonographic examination is not 100% sensitive as not all rubella-associated foetal abnormalities are distinguishable echographically. Foetal blood, amniotic fluid or chorionic villus samples obtained through invasive techniques should be submitted for testing. Foetal infection is confirmed with the detection of rubella RNA by RT-PCR in these samples, or by detection of rubella-specific IgM in foetal blood. It is important to keep in mind that false-negative results can occur if foetal sampling is not performed at least 6 – 8 weeks after maternal infection, and that IgM antibodies are only produced from around 22 weeks of gestation.

Postnatal diagnosis

Congenital rubella syndrome can be confirmed in an infant with suggestive clinical symptoms by detection of rubella RNA by RT-PCR in urine or a nasopharyngeal swab, or by the detection of rubella-specific IgM before 3 months of age.

Treatment

Unfortunately there is no specific treatment for rubella infection. Maternal administration of high-dose immunoglobulin is not recommended as it neither prevents viraemia nor foetal infection.

Maternal screening and immunity

Ideally, women should be tested for immunity against rubella virus by determining rubella-specific IgG levels before becoming pregnant. Rubella-specific IgG levels > 10 IU/mL are considered to denote protection. IgG levels after vaccination are usually lower than those seen after natural infection.

If IgG levels are found to be less than 10 IU/mL, the individual should be immunised against rubella with MMR. As this is a live-attenuated virus vaccine every woman of child-bearing potential should be advised to delay conception for at least 1 month after the vaccination. If, however, a woman is inadvertently vaccinated early in pregnancy, this should not be regarded as an indication for terminating the pregnancy. No cases of CRS have been reported in the more than 1 000 instances where women were unknowingly immunised early in pregnancy.

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