SCHOLASTIC:
Journal of Natural and Medical Education
*Volume 2 Issue 6, Year 2023 ISSN: 2835-303X*
*https://univerpubl.com/index.php/scholastic*

# Virus Infections during Pregnancy

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**Article Information**

**Received:** April 19, 2023
**Accepted:** May 20, 2023
**Published:** June 21, 2023

**Keywords:** *viremia, glaucoma, retinopathy, cataract, deafness, hearing loss.*

**ABSTRACT**

In the last decade, infections from the torch group have become widespread — various infectious diseases (rubella, toxoplasmosis, cytomegalovirus, herpes and other infections) of the embryo, fetus and newborn, infection of which occurs in uterus and during childbirth.

Thanks to the active fight against severe infectious diseases by immunization of the population, rubella has reduced the rate of its spread, however, it is still a common disease both in our country and around the world. The regions with the highest prevalence are Southeast Asia and Africa Although WHO statistics have positive dynamics, so far the number of countries that do not use the rubella vaccine is quite large (for 2019 — 26 countries) [4]. In Russia, the rubella infection has not yet been defeated. Based on studies of the incidence of rubella in the Russian Federation, there are 5 cases of rubella infection as of 2017 in the studied regional centers [5].

The reduction of morbidity worldwide is an important indicator of the success achieved by the scientific community in the fight against this pathology. According to WHO, in 2020, in 168 countries of the world, the rubella vaccine is included in the mandatory list reflected in the national calendar. A positive trend can be observed when evaluating data from 2000: since the beginning of the XXI century, the number of registered cases has decreased by 97% (from 670,894 cases in 2000 to 14621 cases in 2018) [4]. But this does not negate the fact that rubella is still a very dangerous disease. It is especially important in the "mother — fetus —child" system. It is on the study of the impact on this system that this study is based. Rubella is an acute anthroponotic viral infection, most common in childhood and young age. The source can be either an infected person or a carrier. It is transmitted by airborne droplets, contact and transplacental pathways. Among the manifestations of the disease can be noted the presence of a small spotted papular rash, fever and lymphadenopathy. The most dangerous infection of a

woman during pregnancy [5, 6]. In 1941, the role of rubella in the formation of congenital malformations in children was proved for the first time. This discovery belongs to the famous Australian ophthalmologist Norman Gregg. In 1940, there was a rubella epidemic in Sydney, and Gregg was the first to draw attention to the characteristic triad of symptoms in children (deafness, cataracts, heart defects) whose mothers had a rubella infection. It was from this time that a close study of the relationship between rubella and the appearance of congenital malformations in children began. Despite this, the virus was isolated in tissue culture only in 1962, and the vaccine was created in 1969 [7, 8]. According to the ICD classification, there are: rubella infection without complications, rubella infection with neurological complications and rubella infection with other complications [9]. It is also permissible to divide into congenital and acquired rubella. Acquired rubella is characterized by the fact that infection occurs by airborne droplets or contact and the appearance of characteristic symptoms. A diffuse enlargement of the lymph nodes, as well as intoxication, joins the fine-spotted rash and fever. Congenital rubella refers to a chronic infection that is transmitted by the transplacental route. It is this type of infection that is considered the most dangerous, as it can lead to disorders of the development of organs and systems, fetal death and the threat of miscarriage [10]. Rubella belongs to the genus Rubivirus, family Togaviridae. The virus has a spherical shape, a diameter of 60-65 nm and has an icosahedral nucleocapsid. Glycoprotein spicules containing hemagglutinins can be found on the surface. The nucleocapsid contains a genome consisting of a single-stranded RNA molecule and three proteins. Nucleocapsid proteins potentiate the induction of humoral and cellular response [11]. The virus has a pronounced hemolytic and hemagglutinating activity, and also has weak neuraminidase activity. It has a tropicity to the mucous membranes of the respiratory system, genitourinary tract, skin, lymphatic system, is strongly exposed to the external environment, is not resistant. The slightest changes in the acid-base balance, exposure to radiation or chemicals are detrimental to the virus [12]. The incubation period of the disease lasts up to three weeks. During the first 14 days after infection, viremia occurs and the virus spreads in the body. After the humoral and cellular immunity systems are turned on, this process stops. At this time, humoral antibodies appear in the serum and cellular mechanisms are activated. Patients are contagious a week before the onset of symptoms and for three days after. This is due to the fact that class A immunoglobulin begins to be produced on the 3rd-4th day after the manifestation of characteristic symptoms, that is, rash, fever and lymphadenopathy. Then immunoglobulins of class M and G appear, they remain in the body for up to two months [13, 14]. At the present stage, a live attenuated vaccine against rubella is used (vaccine rubella cultural live attenuated). This vaccine contains at least 1000 tissue cytopathogenic doses of rubella virus [15]. The calendar of preventive vaccinations in Russia prescribes the timing of vaccination against rubella: the first — at 12 months, revaccination — at 6 years. It is possible to vaccinate children under 18 years of age who have not been ill, have not been vaccinated, as well as girls aged 18 to 25 years [16].

Vaccination during pregnancy and lactation is contraindicated due to the risk of infection of the fetus. After the introduction of the vaccine, side effects may occur in the form of minor manifestations of the disease (the appearance of a small skin rash, fever, enlarged lymph nodes, nausea, vomiting). There are certain guidelines for vaccination of women of childbearing age: it is necessary to make sure that the woman is not pregnant and will take measures to avoid conception within 8 weeks after vaccination [17]. To understand the pathogenesis of rubella infection during pregnancy, the development of fetal protective devices during intrauterine development should be taken into account. That is why the period in which the mother was infected is important. Transmission of infection from the mother occurs during the spread of the virus in her body, it is during viremia that rubella poses the greatest danger to the fetus. If the infection entered the maternal body from the 1st to the 11th week of pregnancy, then most often it leads to a violation of the development of fetal organ systems and the appearance of a rubella

symptom complex. When the mother is infected before the 18th week, there is a violation of the development of the fetal sensory system, in particular the inner ear, which leads to the development of hearing loss in the fetus. When the mother's body is affected at a later date, the percentage of children with congenital rubella is significantly reduced. The main role in this is played by the developing immune mechanisms of the fetus. But even at this time, the risk of developing intrauterine malformations is extremely high. Pregnant women who become ill during this period require no less monitoring and supervision than those infected at an earlier time [18, 19]. The humoral link of immunity plays the most significant role in the immune response of the fetus. The appearance of the first antibodies begins already from the 10th week, and the activation of the cellular link begins from the 15th week of gestation. IgM antibodies are the first to be detected, which are unable to penetrate the placental barrier. This is important in the diagnosis of congenital rubella, as their detection indicates infection. Starting from the 16th week, IgG and IgA antibodies appear in the fetal body. It is due to the appearance of maternal IgG that there is a decrease in the development of intrauterine disorders, although the development of the fetal immune response also plays a role [19, 20]. The virus is able to penetrate the placenta and affect the developing systems of the fetus. It has a tropicity to the cells of the nervous system, which, due to their immaturity, are an excellent target. An important factor is that the effect is not only on the structure of the cell, but also on its ability to differentiate.

The viral agent is able to inhibit the stages of mitosis and have a destructive effect on the endoplasmic reticulum. It is also important to note that the cardiovascular system is also damaged. The damaging effect is directed at the vascular walls and lining of the heart, which can lead to severe ischemic damage to various organs. The virus is capable of altering cellular RNA, which is responsible for transmitting genetic information to the apparatus synthesizing cellular protein. This cellular disorder leads to a perversion of metabolism, which causes the destruction of cells. These processes potentiate further progression of intrauterine malformations. Complicating the situation is the possible addition of fetal hypoxia, which is often noted with the development of congenital rubella [21]. In the modern classification, the symptom complex described by Gregg (heart defects, damage to the visual analyzer and hearing) is commonly referred to as "small" rubella syndrome [22]. The peculiarity of this triad is that it is not combined with severe brain damage and mental retardation, unlike the "big" rubella syndrome, which is a more severe manifestation of congenital rubella. It includes deep lesions of the structures of the nervous system (anencephaly, hydrocephalus, microcephaly), the cardiovascular system (tetrad of Fallot, vascular transposition, septal defects, pulmonary artery stenosis), the sensory system (glaucoma, retinopathy, cataract, deafness, hearing loss), skeletal apparatus (divergence of sutures, non-infection of the hard palate, violation of the development of tubular bones) and organs of the genitourinary and digestive systems. Hepatitis, pneumonia and myocarditis may often be associated with these manifestations [19, 23]. Children suffering from congenital rubella syndrome are adynamic, sluggish. There is drowsiness, irritability, inability to learn.

Very often they lag behind their peers in both physical and mental development. The development of speech and motor skills is disrupted. It is difficult for such children to carry out purposeful actions and actions according to the established plan. Speech development may also be impaired. The danger is the development of epileptic seizures, which usually manifest themselves in the later stages of the disease. This disease can lead to the appearance of schizophrenia or the development of autism [22, 23]. A dangerous complication of congenital rubella infection is rubella encephalitis. This is an acute disease with a rapid onset. The first symptoms are headache and nausea, followed by subfebrile fever, vomiting, disorders of the muscular system, impaired consciousness. Children very often fall into a coma. It is during this

period that irreversible changes occur in the organs and systems of the child. It is possible to develop cerebral edema, cerebellar disorders, neuritis of cranial nerves.

Both the central and peripheral parts of the nervous system are covered. Epileptic status may develop [19]. It is also possible to develop a late congenital rubella syndrome. Most often it manifests itself in the first year of a child's life (4-6 months), is accompanied by growth retardation and the presence of exanthema, but diseases that join due to weakened immunity play a more important role. Due to reduced immune function, such children are susceptible to pneumonia, vasculitis and other diseases that increase the mortality rate in congenital rubella [23]. Diagnosis of rubella infection in a pregnant woman is not difficult. The attending physician should pay attention to the condition of the lymph nodes, their size and consistency. With typical rubella, lymphadenopathy is observed. It is worth considering the complaints of a woman in labor about the appearance of rashes or spots on various parts of the body. The typical localization of a rash with rubella is the occipital region, then it can spread to the face and limbs. The patient has itching, joint pain. It is mandatory to conduct clinical trials. In the blood test, you can detect leukopenia with a moderate shift to the left and the presence of atypical lymphocytes.

If rubella is suspected, the doctor should find out whether the pregnant woman has been vaccinated and find out about the presence of contact with other patients. It is necessary to study the discharge of the nasopharynx, urine, cerebrospinal fluid, since it is in them that the virus can be isolated [20]. To diagnose congenital rubella, special tests are carried out to determine the content of IgM and IgG antibodies. The condition of the eyes and ears is carefully monitored. But currently the most accurate diagnostic method is polymerase chain reaction (PCR). It is thanks to this method that at this stage of the development of medicine, the scientific community was able not only to clarify the etiology of the infectious process, but also to study in more detail the pathologies of the neonatal period as a whole [21]. It is early diagnosis that plays a crucial role in the tactics of pregnancy management. If the infection of the mother occurred before the 18th week of gestation, this is an indicator of an artificial termination of pregnancy. If the term is higher, then there should be confirmation that the infection of the fetus has occurred. In this case, termination of pregnancy can be performed up to the 28th week of pregnancy. At later terms, pregnancy is most often preserved, but children born require a thorough clinical examination, a virological examination should be carried out. It is recommended to use only breastfeeding. Based on the above statistical, research and clinical data, it can be concluded that the measures taken to combat rubella infection bring positive results. Early diagnosis, vaccination, information at the family planning stage — these methods of combating rubella bear fruit. Observing the recommendations of WHO and the clinical recommendations of the Russian Federation to combat this infection, it is possible to avoid the development of undesirable consequences. All control measures have proved their effectiveness on the example of countries in which the rubella virus has completely ceased to exist. Therefore, the main vector in the elimination of the rubella virus is the transfer of knowledge and the introduction of technologies acquired over many years to those countries and regions where rubella infection is still widespread. Only such measures have practical significance.

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