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## ОСОБЕННОСТИ ДИАГНОСТИКИ И ПРОЯВЛЕНИЙ ГЕРПЕС ВИРУСНОЙ ИНФЕКЦИИ В ПОЛОСТИ РТА У БЕРЕМЕННЫХ

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### РЕЗЮМЕ

Проблемам диагностики и лечения герпес вирусной инфекции посвящено большое количество публикаций, что позволяет считать ее достаточно изученной.

Таким образом, несмотря на определенные успехи в изучении этиологии и патогенеза герпетической инфекции в полости рта, сведения у беременных с герпетическим стоматитом малочисленны. В связи с этим проведение исследований по этой проблеме является актуальным.

Эффективность терапии простого герпеса зависит как от эффективности используемых специ-

фических противовирусных препаратов, так и от конечного иммунокорректирующего эффекта, что с одной стороны, вызвало необходимость исследования иммунного статуса пациентов, страдающих данным заболеванием, с другой - разработку различных схем комбинированного лечения с использованием различных специфических противовирусных препаратов и иммуномодуляторов, причем включение физиотерапевтических методов считается наиболее безопасным в данный период.

**Ключевые слова:** Вирус простого герпеса ВПГ-1, беременность, иммуноферментный анализ (ИФА), генитальный герпес (инфекция генитальной или анальной области), гингивостоматит.

## FEATURES OF DIAGNOSIS AND MANIFESTATIONS OF HERPES VIRUS INFECTION IN THE ORAL CAVITY IN PREGNANT WOMEN

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### ABSTRACT

A large number of publications are devoted to the problems of diagnosis and treatment of herpes viral infection, which makes it possible to consider it sufficiently studied.

Thus, despite certain advances in the study of the etiology and pathogenesis of herpes infection in the oral cavity, information in pregnant women with herpetic stomatitis is scarce. In this regard, research on this problem is relevant.

The effectiveness of herpes simplex therapy depends both on the effectiveness of the specific antiviral drugs used and on the final immune corrective effect, which, on the one hand, necessitated the study of the immune status of patients suffering from this disease, on the other hand, the development of various schemes of combined treatment using various specific antiviral drugs and immune modulators, and the inclusion of

physiotherapeutic methods is considered the safest in this period.

**Key words:** Herpes simplex virus HSV-1, pregnancy, enzyme-linked immune sorbent assay (ELISA), genital herpes (an infection in the genital or anal area), gingivostomatitis.

### RELEVANCE OF THE TOPIC

Currently, there is an increasing interest in the problem of herpes simplex (HS) on the part of clinicians of various specialties, which is associated with a number of objective points: there is an increase in the infection of the population and a significant increase in the frequency of clinical manifestations of viral infections; heterogeneity of the mechanisms of the formation of immune disorders, which underlie both relapses of the viral process and leading to the development of HSV-associated diseases [1];

extremely pronounced clinical polymorphism of PG, from limited lesions of the skin, mucous membranes and conjunctiva of the eyes to systemic, generalized forms involving vital internal organs in the viral process, as well as the development of malignant neoplasms against the background of chronic HSV persistence [2].

80 representatives of the Herpes virioli family were discovered, of which about eight are pathogenic for humans and are subdivided, in turn, into  $\alpha$ -,  $\beta$ -,  $\gamma$ -herpes viruses [3].

A large number of publications are devoted to the problems of diagnosis and treatment of herpes viral infection, which makes it possible to consider it sufficiently studied. At the same time, data on the state of secretory immunity of the oral mucosa and their influence on the clinical features of the disease are ambiguous [6]. Viral infections are characterized by a number of unique pathogenetic features. The cytopathic effect of viruses is due to strictly intracellular parasitism. Viruses start the cellular genetic program of cell death (apoptosis) [1]. The mechanism of the cytopathic action of viruses is due to the suppression of the synthesis of cellular DNA, RNA and proteins, the destruction of cellular lysosomes and the release of lysosomal enzymes, which have a detrimental effect on cellular structures [8]. The virus in saliva in the absence of signs of damage to the oral mucosa is detected in 10% of persons infected with HSV [10].

Recurrent herpes is characterized by the appearance of grouped vesicles on the mucous membrane, which, merging, form ulcers. In case of relapses, the localization of the vesicles does not change and corresponds to the innervation zone of the affected nerve [11]. When localized on the lip (recurrent labial herpes), the lesion is more pronounced than when localized in the oral cavity (recurrent herpetic stomatitis). Healing of ulcers with recurrent herpes also occurs without scarring. The spread of infection to adjacent areas of the skin around the mouth is observed quite often, especially when lubricating the lips with a fat ointment [3]. In persons without pronounced immunity disorders, recurrent herpetic stomatitis is manifested by the formation of small ulcers surrounded by a red corolla, in areas of the mucous membrane, where the epithelium has pronounced signs of keratinization (fixed part of the gums and palate). The defeat of the mucous membrane of the cheeks and tongue in recurrent herpes is observed rarely and usually in patients with immunodeficiency [9, 12].

In the pathogenesis of the disease, 4 periods are distinguished: prodromal, catarrhal, periods of rashes and extinction of the disease. By severity, there are mild, moderate and severe forms. Already in the catarrhal period of the disease, pronounced gingivitis often occurs, which in the future, especially in severe

form, acquires an erosive and ulcerative character [20]. There is marked bleeding of the gums and oral mucosa. In saliva, the pH shift is first determined to the acidic side, then to the alkaline, while interferon is usually absent in saliva, and the lysozyme content is markedly reduced. The manifestation of primary herpes infection in women during pregnancy is especially alarming, since the possible effect of herpes on the embryo or fetus is possible [19, 20].

The modern standards for the etiological diagnosis of herpes vims infections include a serological method using enzyme-linked immune sorbent assay (ELISA). Since herpes simplex viruses have a mechanism of "escape" from the immune system, allowing them to persist for a long time, non-sterile immunity is formed in the body [15]. Virus-neutralizing antibodies that persist throughout life, although they prevent the spread of the vims by inhibiting its replication, do not prevent the occurrence of relapses; therefore, the specific humoral response formed in BBVI reflects the infection of the organism with the pathogen, but does not protect it [20].

Detection of IgM antibodies indicates an active infectious process, the phase of convalescence is established when testing IgG antibodies, however, as a result of developing immunosuppression, which is often observed with prolonged persistence of the pathogen, IgM and IgG antibodies may be absent or detected in low titers [11]. This fact reduces the importance of serological diagnostics in BBVI: it does not allow differentiating the latent form of infection from the chronic one, predicting the course of the disease, and determining the tactics of therapy for sick children [13].

For the greatest information content, it is additionally recommended to use ELISA in the study of paired sera containing IgG antibodies, with an interval between sampling of 7-10 days, to establish the fact of an increase in IgG antibodies by 4 times, which may also serve as an indication of the course of primary infection [14]. To confirm the chronic form of infection, an enzyme-linked immune sorbent assay for determining the avidity of IgG antibodies can be used [5].

Pregnancy leads to a change in a woman's immunity. And when observing relapses of herpes lesions, treatment of the triggered process is necessary, but the action of herpes is not as pathogenic as the primary introduction of herpes cells [15]. Herpetic lesions of the oral mucosa have frequent and painful exacerbations in the form of chronic recurrent herpetic stomatitis, the treatment of which in women during pregnancy should be directed without harming the course of pregnancy [10].

During pregnancy, a suppressive restructuring of the immune system occurs, aimed at developing and maintaining immunological tolerance to fetal allo



antigens. An important condition is the switching of the immune response from type 1 T-helpers (Th1) to type 2 and 3 T-helpers (Th2, Th3), which leads to the predominance of the synthesis of anti-inflammatory cytokines - IL-4, IL-10 and others [5]. IL-10 plays a key role in the development of pregnancy, as it inhibits the production and implementation of the trophoblast-destructive activity of TNF- $\alpha$  [18]. In addition, TGF- $\beta$  (transforming growth factor B) secreted by the cells of the decidual membrane of the uterus blocks the development of Th1-mediated reactions and simultaneously stimulates differentiation of villi of the early placenta and cytotrophoblastic invasion [5,6].

The influence of herpes infection on the course of pregnancy and the condition of the fetus is due to two main mechanisms. Firstly, infection of the placenta, amniotic fluid and membranes, as well as the fetus itself, is possible. This can lead to damage to the placenta, membranes, teratogenic changes in the tissues of the embryo and fetus, to the development of local or generalized lesions, as well as to latent infection of the fetus, with subsequent clinical manifestations in the postnatal period [18]. Secondly, the influence of GI with the development of fever in pregnant women, dysfunctions of the fetoplacental system, homeostasis, and hormonal balance is possible. These reasons can lead to early and late miscarriages, delayed pregnancy, premature birth, antenatal malnutrition, hypoxia, fetal malformations and death, the development of congenital forms of infection in newborns [15, 17].

The variety of clinical manifestations is due to the duration and form of manifestation of infection in a pregnant woman, the properties and virulence of the virus, the state of the placental barrier and the protective forces of both the mother and the fetus [14]. The study of the influence of herpes infection on the course of pregnancy, the development of the fetus and the newborn showed that the most serious danger in any trimester of pregnancy are generalized forms of GI in women and primary infection during childbirth [20]. Herpetic infections in pregnant women are among the most common diseases that determine intrauterine infection, embryo and fetopathies, and obstetric pathology. In recent years, there has been a trend towards an increase in the infection of pregnant women with the herpes simplex virus and the ability of GI, under certain conditions, to endemic spread [14, 16].

Most often, primary herpes is manifested in the form of herpetic gingivostomatitis. Single or multiple vesicles appear on the mucous membrane of the oropharynx, which quickly open up with the formation of painful erosions, which are then covered with a whitish coating. The mucous membrane of the oral cavity, the gums become swollen, hyperemic, with a cyanotic shade and sharply painful. The pain syndrome is so pronounced that it makes it difficult

to eat and drink [1]. Gradually, acute inflammatory phenomena subside and erosion begins to epithelize from the periphery to the center. Complete regression of the rash occurs in 2-3 weeks. After the disappearance of the clinical manifestations of primary herpes or asymptomatic infection, the herpes viral infection becomes latent. During this period, HSV is in an inactive state in the nerve ganglia, and HSV-1 most often affects the trigeminal ganglia [8]. At the same time, the production of antibodies to HSV begins. However, with a decrease in immunity under the influence of a number of unfavorable factors, relapses of the disease may occur with varying frequency - from several days to several months or even years [19].

HSV-1 is a highly contagious infection, widespread and endemic throughout the world. Most HSV-1 infections occur during childhood, then the infection persists throughout life [6]. In the vast majority of cases, HSV-1 infection develops oral herpes (an infection in or around the mouth, sometimes called orolabial or orofacial herpes), but in some cases, the virus also causes genital herpes (an infection in the genital or anal area) [7].

The active stage in both asymptomatic and manifest forms of infection can be detected by laboratory methods. Laboratory markers of activation are antibodies to ultra-early proteins (anti CMV - IEA antibodies), IgM to structural proteins (L), low avidity IgG, an increase in IgG antibody titers, the appearance of sero conversion (i.e., the appearance of a positive antibody response in previously negative samples), an increase in the frequency of detection of viruses in various clinical material [18].

In the immune genesis of CGS of the oral mucosa in pregnant women, changes in T- and B-cell and humoral immunity dominate [7]. For pregnant women with recurrent herpetic stomatitis of the oral mucosa, an interferon deficiency state is characteristic, which is manifested by an increase in serum interferon and a pronounced decrease in the production of alpha and gamma interferon. With CGS in pregnant women, the regulation of the immune response at the level of the oral mucosa is impaired, which indicates a weakening of the antiviral defense [16].

Thus, despite certain advances in the study of the etiology and pathogenesis of herpes infection in the oral cavity, information in pregnant women with herpetic stomatitis is scarce. In this regard, research on this problem is relevant [12].

#### Conclusion

The effectiveness of herpes simplex therapy depends both on the effectiveness of the specific antiviral drugs used and on the final immune corrective effect, which, on the one hand, necessitated the study of the immune status of patients suffering from this disease, on the other hand, the development of various schemes of



combined treatment using various specific antiviral physiotherapeutic methods is considered the safest in drugs and immune modulators, and the inclusion of this period [11,13].

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