



# FEATURES OF THE COURSE OF HIV INFECTION IN INFANTS AND CHILDREN (LITERARY REVIEW)

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**Resume.** General information about the development and pathophysiology of HIV infection in children is similar to that in adults, but the method of infection, clinical picture and treatment features often differ. HIV-infected children also have unique problems of social integration.

Keywords: HIV-1 retrovirus, antiretroviral therapy

# **ОСОБЕННОСТИ ТЕЧЕНИЕ ВИЧ ИНФЕКЦИИ У МЛАДЕНЦЕВ И ДЕТЕЙ** (ЛИТЕРАТУРНЫЙ ОБЗОР)

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**Резюме.** Общие сведения о развитии и патофизиологии ВИЧ-инфекции у детей аналогичны таковым у взрослых, однако способ заражения, клиническая картина и особенности лечения часто различаются. ВИЧ-инфицированные дети также имеют уникальные <u>проблемы социальной интеграции</u>.

Ключевые слова: ретровирус ВИЧ-1, антиретровирусной терапия

Infection with the human immunodeficiency virus (HIV) causes HIV-1 retrovirus (less commonly related HIV-2 retrovirus). Infection leads to progressive damage to the immune defense and the frequent development of opportunistic infections and cancer. The terminal stage of HIV infection is acquired immunodeficiency syndrome (AIDS). Diagnosis is based on the detection of viral antibodies in the blood of children > 18 months and tests based on nucleic acid amplification (such as polymerase chain reaction (PCR) analysis in children < 18 months. A combination of antiretroviral drugs is used for treatment.

General information about the development and pathophysiology of HIV infection in children is similar to that in adults, but the method of infection, clinical picture and treatment features often differ. HIV-infected children also have unique problems of social integration.

#### Epidemiology of HIV infection in infants and children

In the USA, HIV was probably detected in children at almost the same time as in adults, but was not recognized clinically for several years. To date, about 10,000



cases of the disease have been registered among children and younger adolescents, which is only 1% of the total number of cases. In 2018, < 100 new cases of the disease were diagnosed in children < 13 years old (1).

More than 95% of HIV-infected children in the United States acquired the infection from their mother either before or during birth (vertical transmission). Most of the remaining children (including children with hemophilia or other blood clotting disorders) were given the disease by transfusion of contaminated blood or its products. Several cases were the result of sexual violence. Vertical transmission has decreased significantly in the US from 25% in 1991 (resulting in > 1,600 infected children per year). Vertical transmission has been reduced through the use of comprehensive serological examination and treatment of infected pregnant women both during pregnancy and during childbirth and by providing short-term antiretroviral prophylaxis for unprotected newborns.

However, the total number of HIV-infected adolescents and young adults (13-24 years old) in the United States continues to grow, despite tangible progress in reducing perinatal transmission of HIV infection. This paradoxical increase is the result of a higher survival rate among perinatally infected children, as well as new cases of HIV infection acquired through sexual transmission among other adolescents and young people (especially among young men who have sex with men). Reducing HIV transmission among young men who have sex with men continues to be an important goal of household HIV control measures, along with a continued decline in vertical transmission.

About 1.7 million children worldwide have HIV infection (4% of the total number of cases worldwide). Every year, about 160,000 more healthy children become infected (9% of all new infections) and about 100,000 children die. Although these figures represent a staggering number of patients, new programs created to provide antiretroviral therapy (ART) to pregnant women and children have reduced the annual number of new childhood infections and deaths by 33-50% in the last few years (1). However, infected children still receive almost no ART as often as adults, and interrupting vertical transmission and providing treatment to HIV-infected children remain the two most important goals of global pediatric HIV medicine.

#### Ways of HIV transmission

The risk of infection for a child born to an HIV-infected mother who did not receive antiretroviral therapy (ART) during pregnancy is estimated at 25% (varies from 13 to 39%).

Risk factors for vertical transmission of infection include:

• Seroconversion during pregnancy or lactation (the main risk)





- High concentration of viral RNA in blood plasma (the main risk)
- Progressive maternal disease

• Low indicators of the number of peripheral CD4+ T-lymphocytes in the mother

Premature rupture of the amniotic membranes is no longer considered an important risk factor.

Caesarean section before the start of active labor reduces the risk of transmission of the disease from mother to child. HIV is found in both cellular and non-cellular fractions of breast milk. The frequency of transmission during breastfeeding is about 6:100 infants per year. The overall risk of transmission of infection through breastfeeding is estimated at 12-14%, due to the different duration of breastfeeding. The risk of transmission of the virus during breastfeeding is highest in women with a high concentration of viral RNA in plasma (for example, in women infected during pregnancy or during breastfeeding).

Classification of HIV infection in infants and children

A wide range of diseases is associated with HIV infection, among which AIDS is the most severe.

Clinical categories among children < 13 years old (Clinical categories for children < 13 years old with HIV infection) are determined by the presence or absence of certain common opportunistic infections or cancer. The following categories are distinguished:

- $\bullet$  N Asymptomatic course
- A Mild symptoms
- B Moderate symptoms
- C Severe symptoms

Immunological categories (stages of HIV infection) in children < 13 years old (Immunological categories (stages of HIV infection) for children < 13 years old with HIV infection, depending on the age-specific number of CD4 + T cells or their percentage) reflect the degree of suppression of immunity based on the content of CD4+ T cells (absolute number and as a percentage of the total number of lymphocytes):

- 1 = no signs of immunosuppression
- 2 = moderate suppression
- 3 = severe suppression

Thus, a child who has been diagnosed with grade B3 will have moderate clinical symptoms and severe immunodeficiency. Clinical and immunological categories form a unidirectional hierarchy; after a diagnosis of a certain severity, a child cannot be transferred to a category with less severe manifestations of the disease, regardless of clinical or immunological improvement.



Immunological categories (stages of HIV infection) for children < 13 years old with HIV infection, depending on the age-specific number of CD4 + T cells or their percentage

### Symptoms and signs of HIV infection in infants and children

Infants infected in the perinatal period usually do not show symptoms during the first few months of life, even if combined ART has not been initiated. Although the average age of symptoms is about 3 years, in some children the infection proceeds without symptoms for > 5 years, and with the use of appropriate ART, such children can live to adulthood. In the era before the development of ART in 10-15% of children, the disease had a rapid progressive course with the appearance of symptoms in the first year of life and a fatal outcome at the age of 18-36 months; it is believed that the infection of such children with HIV occurred in utero. However, most children probably become infected during childbirth or shortly after birth, and they are characterized by a slower progression of the disease (the survival rate was more than 5 years even before the introduction of ART into routine practice).

The most common manifestations of HIV infection in children who do not receive ART include generalized lymphadenopathy, hepatomegaly, splenomegaly, lack of weight gain, oral candidiasis, diseases of the central nervous system (CNS) (including developmental delay, which can progress), lymphoid interstitial pneumonia, recurrent bacteremia, opportunistic infections, recurrent diarrhea, mumps, cardiomyopathy, hepatitis, nephropathy and cancer.

#### **Complications of HIV infection in children**

The resulting complications, as a rule, entail opportunistic infections (and, less often, cancer). Combined ART has made such infections quite rare, and currently they mostly occur in undiagnosed children who have not yet received ART, or in children who are not inclined to perform ART.

# Diagnosis of HIV infection in infants and children

• Serum antibody tests

• Virological analyses of nucleic acid (ANC; including polymerase chain reaction testing for HIV DNA detection or HIV RNA analysis)

# Prognosis for HIV infection in infants and children

Before the introduction of ART into routine practice, 10-15% of children in industrialized countries and possibly 50-80% of children in developing countries died before the age of 4; however, with the use of appropriate combined ART regimens, most perinatally infected children live to adulthood. The number of perinatally infected young people who have already given birth or become fathers of their own children is increasing.



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