EMJ MS
EUROPEAN MULTIDISCIPLINARY JOURNAL OF MODERN SCIENCE
https://emjms.academicjournal.io/index.php/ Volume: 4

# HIV Encephalopathy and its Pathogenetic Aspects

***Zokirov Muzaffar***
*Fergana Medical Institute of Public Health, Department of Internal Diseases №1*

**Abstract**: Today, HIV infection remains one of the most global problems of the modern world. Every year, new mechanisms of the pathogenesis of the virus in the body, as well as its complications, are discovered. This article summarizes the pathogenetic aspects of HIV-encephalopathy, for a more complete understanding of all the mechanisms of this complication of HIV infection.

**Keywords**: human immunodeficiency virus, HIV-Encephalopathy, pathogenetic aspect, neurotoxin effect, blood - brain barrier.

**Introduction.** The number of HIV-infected people in the world in 2021 amounted to 37.6 million people, of which 1.5 million were new cases. In the total number of HIV-infected 1.7 million children under 14 years of age [1]. As of November 1, 2020, there were 42,098 people living with HIV in Uzbekistan [2]. For 10 months since the beginning of the year, 3337 cases of HIV infection were registered in the country, including 1919 among men (57.5%) and 1418 among women (42.5%), however, the difficult epidemiological situation around the world makes it difficult to assess the actual situation on HIV infection [3]

The possibility of treating HIV-infected patients with the use of antiretroviral drugs has reduced the death rate from AIDS by several times. In this regard, new challenges are being put forward for healthcare to improve the quality of life of HIV-infected people. An important task that requires special attention is the correction of disorders of the central nervous system in HIV-infected patients. The use of antiviral therapy has increased the life expectancy of patients with HIV infection, however, to date, such drugs that could completely eradicate the virus from the body. In this regard, it is necessary to deal with the pathological effect of the virus on body tissues, including nervous tissue, throughout the life of an HIV-infected patient [4].

**Results .**This task is not only a medical, but also a social problem, since HIV is characterized by the defeat of young and working age, and lesions of the nervous system are often detected already in the early stages of the disease. Impairment of cognitive processes creates certain difficulties in study, work, daily activities and personal life of patients with HIV. About 1/3 of HIV-infected people are in the age range of 15-25 years. On average, this is about 3,000 new infections per day. [3,5]

The CNS has two unique barriers that protect it from the effects of chemical and biological pathological factors. The cells of the blood-brain barrier are "sewn" together by tight bonds through which many cells cannot pass. From the side of the brain, the barrier is covered with a thin basement membrane. Pericytes are located on the membrane from the side of the nervous tissue. They are located along the capillaries and have a long process structure. The processes braid the capillaries and form tight bonds with endotheliocytes [4].

There is evidence that pericytes can move, taking over the functions of macrophages. These cells are thought to be able to replicate and differentiate into osteoblasts, adiposities,

chondrocytes, smooth muscle cells, and others. The version that these cells may have the ability to differentiate into cells of the nervous tissue is not ruled out, which is currently being actively studied. In recent studies, data have been obtained indicating that a decrease in the number of pericytes in the CNS leads to impaired BBB permeability, and pathologies of neurocognitive processes associated with these disorders. The processes of atrocities, which tightly braid the vascular wall in the nervous tissue, also have the functions of indirect protection, creating a case for the capillaries of the brain [6].

The hematoliquor barrier is built from the cuboidal epithelium of the choroid sinus. It is also characterized by a close interweaving of cells with the formation of tight junctions, which prevents the transport of many pathogenic substances to the brain and spinal cord. However, this barrier is much weaker than the BBB, since the main function of this barrier is to maintain the required amount of cerebrospinal fluid [5].

The most popular theory is the penetration of the virus through the BBB with infected cells. Lymphocytes and monocytes become infected with the virus immediately before entering the CNS. After infection, they penetrate the BBB, where monocytes are transformed into per vascular macrophages, which have the ability to transmit the virus to other cells of the nervous tissue [1,3].

According to many scientific data, the endothelium of the vascular wall does not have CD4 receptors and co-receptors CCR5 and CXCR4. Most of the scientific evidence available to date indicates that there are no CD4 receptors in the cells of the walls of cerebral vessels, or they are present in a very small amount. At the same time, there are C-type lectins (MBL, mannose -binding lectin) on the surface of nerve cells , which have similar functions to DC-SIGN of dendritic cells. Their only difference is that their affinity for gp120 of the virus is weaker. An important feature of the virus is its ability to enhance the expression of DC-SIGN, which contributes to the fact that the virus actively moves and multiplies in the nervous tissue [6].

An interesting fact is that in the urogenital tract, due to the absence of CD4 receptors in its epithelium, the virus uses the same mechanism for penetration and reproduction. The gp120 virus protein reacts with the C-type lectin of the epithelial wall. The result of this process is the destruction of tight intercellular junctions, due to which the virus gains access to CD4 receptors located in the mucous membrane. The dense epithelial barrier is only permeable to particles up to 30 nm in size, and the virus is known to be 80-100 nm in diameter. However, HIV passes through this barrier in 120 minutes [5, 7].

The penetration of the virus into the CNS can also occur through the intercellular gaps of the endothelial wall. This mechanism is quite possible in the later stages of HIV infection, when under the action of toxins and other pathogenic agents the endothelial wall is destroyed, intercellular contacts are weakened and become easily accessible for the penetration of infectious particles. The virus can easily diffuse through such weakened contacts. The subsequent destruction of the nervous tissue occurs as a result of the direct effect of the virus on the brain cells. Accession of secondary diseases further worsens the state of the BBB, causing local inflammatory processes [7].

In the absence of adequate antiretroviral therapy, encephalopathy develops in 2/3 of HIV-infected patients. Signs of encephalopathy are detected in 25% of cases even at the stage of the absence of clinical manifestations of AIDS, and in 3-5% of cases they are the first manifestations of disease progression [11].

HIV encephalopathy is a special clinical syndrome of sub cortical-frontal dementia, which develops under the direct influence of the virus on the tissues of the nervous system and is

characterized by motor, cognitive and behavioral disorders. The question of at what stage of HIV infection neurological disorders begin to develop is still open [6].

Damage to the nervous tissue occurs as a result of direct (with the participation of viral proteins) and indirect (inflammation) mechanisms [7]. Each model of damage implies infection of macrophages and microglia with viral particles at the initial stage . The direct mechanism of damage implies the death of neurons under the direct influence of viral proteins [8]. The second model explains neuronal damage through the inflammatory process of brain tissue in response to HIV integration. Both of these mechanisms can be present simultaneously at any stage of HIV infection [9]. The virus is not detected in the neurons themselves; however, various immunopathological mechanisms triggered by the presence of HIV in the nervous tissue cause functional and structural changes in neurons [10].

Virus-infected brain cells produce viral particles and inflammatory mediators. Due to their cytotoxic properties, densely packed endotheliocytes are destroyed, which leads to a decrease in the total number of neurons and destruction of the myelin sheath of cells [51]. Viral replication also affects the functioning of oligodendrocytes and astrocytes. The neurotoxin effect of the viral protein gp120 has a detrimental effect on neurons, the effect of which is also due to the effect on neurotransmitter processes, which ultimately leads to the inevitable death of neurons [2, 10].

Damage to astrocytes occurs due to the action of low molecular weight peptides produced by infected microglial cells [3]. This leads to an excess of glutamate, which has an excitatory effect on nerve cells. As a result of its excess, a number of biochemical processes are triggered, resulting in the destruction of the neuron membrane and cell death [4,9].

**Conclusions:** In addition to those described above, other processes mediated by acute and subsequent chronic inflammation also have a damaging effect on the CNS. Cells are actively affected by inflammatory cytokines, chemokines and other substances that disrupt the electrolyte balance, integrity and biochemical processes of neurons. The cells of the nervous tissue are highly sensitive to any changes in the environment and are quickly destroyed.

Viral particles multiply in the CNS with the formation of certain quasi -species, while the activity of them is very isolated from the lymph and blood circulation. In this regard, the selection of adequate ARVT has certain difficulties, since many drugs do not penetrate through the BBB. It is also important to note that the activity and metabolism of CD4 cells is relatively less pronounced in the brain; therefore, virions accumulating in the CNS have some autonomy in relation to the viral load of all other body systems. The viral load in brain tissue in HIV encephalopathy is high; however, it does not correlate with the severity of the disease and is an indicator of the activity of the virus.

## Literature

1. UNAIDS. gap. Report. Geneva: UNAIDS, 2016. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gapreport_en.pdf
2. Federal Scientific for the Prevention and Combat of AIDS of the Public Office of the Central Scientific Research Institute Rospotrebnadzor . Reference on HIV infection in the Russian Federation as of June 30, 2016.
3. Pokrovsky, VV HIV/AIDS reduces the number of Russians and their life expectancy / VV Pokrovsky., N. Ladnaia , A . Pokrovskaya // Demographic Review. - 2017. - No. 1. - P. 65–82.
4. Human immunodeficiency virus - medicine: a guide for doctors / Ed. N. A. Belyakova, A. G. Rakhmanova. - St. Petersburg: Baltic Medical Education Center, 2010. - 752 p.

5. Fauci, AS The human immunodeficiency virus: infectivity and mechanisms of pathogenesis / AS Fauci // Science. - 1988. - Feb. — Vol. 239, no. 4840.—P. 617–622.
6. Onishchenko, G. G. HIV infection is a problem of humanity / G. G. Onishchenko // HIV infection and immunosuppressant. - 2009. - V. 1, No. 1. - S. 5-9.
7. Fidelity of two retroviral reverse transcriptases during DNA-dependent DNA synthesis in vitro / JD Roberts, BD Preston, LA Johnston et al. // Mol. cell . biol . - 1989. - Vol . 9, no . 2. - P. 469-176.
8. Dementieva, N. E. Features of HIV replication and compartmentalization in the CNS / N. E. Dementieva, A. S. Shelomov // HIV infection and immunosuppression . - 2012. - V.4, No. 4. - S. 132 - 133.
9. Bartlett J. Clinical aspects of HIV infection / J. Bartlett, J. Gallant , P. Fam. - 2012. - M.: R. Valent , 2012. - 528 p.
10. Analysis of mutations associated with drug resistance in untreated patients infected with various genetic forms of HIV type 1 common in the countries of the former Soviet Union / E. Vazquez de Parga , A. G. Rakhmanova, L. Perez-Alvarez et al. // HIV -infection and immunosuppression . - 2009. - V. 1, No. 2. - S. 50–56.
11. Ragin, AB Diffusion tensor imaging of subcortical brain injury in patients infected with human immunodeficiency virus / AB Ragin, Y. Wu, P. Storey , BA Cohen, RR Edelman, LG Epstein // J. Neurovirol . - 2005. - Vol. 11. – P. 292–298.