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THE EFFECT OF CMVI ON THE NERVOUS SYSTEM AND KIDNEYS IN NEWBORNS

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Resume

Intrauterine infections occupy one of the leading places in the structure of perinatal mortality. Cytomegalovirus infection ranks first among congenital infections, making a great contribution to the formation of various malformations. The literature review describes the pathogenetic mechanisms of the virus' effect on the fetus and newborn, kidney organs and the central nervous system. CMVI develops as a result of infection of the mother with the virus or its reactivation, causing the development of infection. When the fetus is infected in the early stages of pregnancy, various malformations of the central nervous system, cardiovascular, urinary systems, etc. are formed. When infected in late pregnancy, infectious lesions of various organs and systems are revealed in newborns. In 40-90% of newborns with manifest CMVI, there are long-term neurological consequences and kidney disease, hearing loss, as well as damage to the organs of vision.

Key words: newborns, clinic, diagnosis, congenital cytomegalovirus infection, kidney damage

Резюме. Внутриутробные инфекции занимают одно из ведущих мест в структуре перинатальной смертности. Цитомегаловирусная инфекция занимает первое место среди врожденных инфекций, внося большой вклад в формирование разнообразных пороков развития. В обзоре литературы описываются патогенетические механизмы воздействия вируса на организм плода и новорожденного, органы почек и ЦНС. ЦМВИ развивается вследствие заражения матери вирусом или его реактивации, обусловливая развитие инфекции. При инфицировании плода на ранних сроках беременности формируются разнообразные пороки развития ЦНС, сердечно-сосудистой, мочевыделительной систем и др. При заражении в поздние сроки беременности у новорожденных выявляют

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инфекционные поражения различных органов и систем. У 40—90% новорожденных при манифестной ЦМВИ имеют место отдаленные неврологические последствия и болезни почек снижение слуха, а также поражения органов зрения.

Ключевые слова: новорожденные, клиника, диагностика, врожденная цитомегаловирусная инфекция, поражения почек.

Резюме. Ҳомила ичи инфекциялари перинатал ўлим даражасининг етакчи ўринларидан бирини эгаллайди. Цитомегаловирус инфекцияси ҳомила ичи инфекциялари орасида биринчи ўринни эгаллаб, турли хил туғма нуқсонлар ривожланишига катта ҳисса қўшади. Ўрганилган манбалар таҳлил қилинганда, ҳомилага ва янги туғилган чақалоқлар организмида асаб тизими ва буйракларига таъсирининг патогенитик механизмлари тасвирланган. ЦМВИ онанинг вирус билан зарарланиши ёки она организмида қайта фаолланиши билан боғлиқ. Она ҳомиладорлигининг эрта даврида инфекцияланганида марказий асаб тизими, юрак-қон томир, сийдик ажратиш тизими ва бошқа органларининг турли нуқсонлари ҳосил бўлади. Ҳомиладорликнинг кечки даврида инфекцияланганда эса янги туғилган чақалоқларда турли органлар ва тизимларнинг инфекцияли зарарланиншлари аниқланади. Ўткир ЦМВИ билан касалланган янги туғилган чақалоқларнинг 40-90% да узоқ муддатли неврологик асоратлар, эшитишнинг бузилиши, буйрак касалликлари билан боғлиқ муаммолар ва кўриш органлари шикастланиши юзага келади.

Калит сўзлар: янги туғилган чақалоқлар, клиника, диагностика туғма цитомегаловирус инфекцияси, буйрак шикастланиши,

Intoduction

Cytomegalovirus infection (CMVI) is an urgent problem of perinatology, complicating the course of pregnancy, childbirth and the neonatal period, leading to serious intrauterine malformations with subsequent serious complications and death [52.]. Recently, great importance has been attached to the study of herpesvirus infections. One of the significant pathogens in the herpesvirus family is cytomegalovirus (CMV). According to the authors [44,49]

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in recent years, the infection rate of children with CMV has increased by 30.3%, and among newborns it has increased 2.1 times, the number of cases of intrauterine infection has increased 5 times. They not only result in a high mortality rate, especially in the perinatal period, but in some cases are also the cause of profound disability caused by congenital malformations and chronic diseases [44,49].

CMVI has the highest proportion among congenital infections [36]. An important factor in its spread is the asymptomatic course in most adults and low awareness of the danger that infection of the fetus and newborn child entails. CMVI is revealed, according to various data, in 0.18–2.5% of newborns [23]. CMVI is characterized by its wide distribution among both the adult population (40-95%) and children (20-60%). Congenital CMVI is the most common intrauterine infection (IUI) and occupies one of the leading places in the structure of perinatal morbidity and mortality. Every year in the world, congenital CMVI is revealed in 0.5-6.1% of living newborns. The variety of clinical manifestations of the disease is determined by the ability of CMV to affect the fetus at any stage of pregnancy [23,13,29]. CMVI is a widespread viral infection caused by cytomegalovirus (Human Cytomegalovirus), characterized by diverse manifestations from asymptomatic to severe generalized forms with damage to internal organs and the central nervous system (in persons with immunodeficiency and with intrauterine fetal damage).

Congenital cytomegalovirus infection is usually the result of transplacental transmission of the pathogen (with primary infection of a non–immune pregnant woman, reactivation of a previously acquired infection during pregnancy or infection of an immune pregnant woman with another strain of cytomegalovirus) from the mother to the fetus, less often - with infection of the fetus in the intranatal period (in the presence of cytomegalovirus lesions of the birth canal [9,14]. Cytomegalovirus infection has not yet been fully studied.[29]. Congenital CMVI is the leading cause of severe congenital pathology, a serious world-standards level medical and social problem that needs to be solved [49]. CMV has an immunosuppressive ability and, with intrauterine infection, creates prerequisites for the development of immunological tolerance to this pathogen, the formation of its long-term persistence and reaction in the postnatal period. Physiological immune insufficiency of young children in combination with the immunosuppressive effect of CMV causes delayed manifestation of CMV in 10-15% of cases. In 90%

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of cases, congenital CMVI occurs in a subclinical form, which is most often diagnosed after manifestation or when long-term consequences are revealed in the form of kidney abnormalities, delayed psychomotor development, deafness, cirrhosis of the liver, etc. CMV infection is the cause of early neonatal of the newborns mortality.

It is known that with CMVI of newborns, the entire body is affected with a continuous connection of individual links of the pathological process caused by lesions and hemodynamic disorders that have arisen in utero, which aggravates the course of some transient conditions, in particular, it concerns the adaptation period. Moreover, the frequency of CMVI complications from all organs and systems in newborns is quite high, which determines the relevance of the problem of studying the features of CMVI lesions, early diagnosis of complications and pathogenetically justified treatment correction. For the first time , the German pathologist H. . Ribbert described the cells of the kidneys and parotid salivary gland altered by cytomegaly in deceased newborns in 1881, mistakenly assuming defeat by protozoa. In 1955, Margaret Smith isolated CMV and cultivated it in the laboratory, which gave rise to its active study. Cytomegalovirus belongs to the Herpes viridae family, Beta-herpes viridae subfamily and has the species name Herpes human virus (HHV5) (official name) or Cytomegalovirus (common name) [49,8,30.] CMVI is one of the most frequently diagnosed intrauterine infections: prospective antibodies to CMVI virus are found in 80% of the population over 35 years old, which indicates that the latent (asymptomatic) form of this infection has been transferred by the overwhelming majority.

In the resent years in histological examination of infants who died from various causes, an unidentified CVMI during their lifetime is revealed more often [14]. Modern view on the problem of congenital cytomegalovirus infection: CMV is a large DNA genome (nucleocapsid diameteris 100-120 nm), the possibility of replication without cell damage, low cytopathogenicity in tissue culture, slow replication, relatively low virulence, significant suppression of cellular immunity. CMV has a relative insensitivity to the action of interferon, is not sensitive to the action of antibiotics, low sensitivity to acyclovir and its analogues. 3 strains of CMV have been registered in international catalogs — AD 169, Davis and Kerr. All strains have etiological significance for humans, several strains of the virus can be isolated from one person[48,8,34]. It is known that at least 10% of pregnancy pathologies have an infectious nature;

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about 10% of children with congenital CMVI develop a clinically marked disease with the formation, in most cases, of late complications, more often from the central nervous system. On average, 10% of children with antenatal CMV infection and asymptomatic course of the disease have neurological consequences of the infection. At the same time, only 10% of congenital pneumonias have an etiology [50] Congenital cytomegalovirus infection is a viral disease manifested by polymorphic clinical symptoms with damage to the salivary glands, visceral organs, central nervous system and the formation of giant cells with typical intracellular and cytoplasmic inclusions. Congenital cytomegaly is one of the most common forms of congenital infection, affecting from 0.2 to 2.5% of newborns. [24,33]. There are congenital and acquired CVMI (primary, secondary). Congenital infection occurs if during pregnancy there is a primary infection of the mother with CMV, or reactivation of an existing latent infection. Cytomegalovirus infection in the structure of perinatal mortality is 37.5% among deceased newborns [52]. Barycheva L.Yu. and co-authors (2015) found that in children with malformations with congenital cytomegalovirus infection, mortality rates are 61.4%. Congenital CMVI can occur both asymptomatically and in severe form, in which a fatal outcome is often noted. At the same time, almost 90% of children who have suffered a severe form of CMVI later have a variety of somatic and neurological developmental defects, and with an asymptomatic course, only 5-17% of children have various pathologies caused by different strains of CMVI [52]. The virus and antibodies to it are found in about 1-100% of newborns and children of the first 2-3 months of life. Its clinical manifestations are evident only against the background of immunodeficiency conditions. Among pregnant women, the frequency of identification of antibodies (AT) to CMVI, according to various studies, ranges from 40 to 90%. The frequency of primary CMVI in women during pregnancy does not exceed 1%. Intrauterine infection of CMV fetuses in women with primary CMVI during pregnancy reaches 30-50%, while only 5-18% of infected children have manifest congenital CMVI. In 80% of children, congenital CMVI remains asymptomatic, and is clinically manifested later, 5-18% develop a manifest form of the disease with a severe course[42,30,27]. The greatest risk to the fetus is a primary infection in the early stages of pregnancy. On average, 2% (0.7–4%) of women have primary infection during pregnancy, while in 35-40% (24%-75%) of cases, the infection is transmitted to the fetus [39]. In women who are seropositive for CMV before pregnancy, the probability

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of fetal infection is significantly lower due to the fact that highly active maternal antibodies protect most newborns from the development of congenital CMV. CMV is tropic to neurons and neuroglia (immature glial cells in the periventricular region are most susceptible to cytomegalovirus), epithelial cells of salivary and mammary glands, renal tubules, bladder, lungs, liver, intestines, genital tract, vascular endothelium, leukocytes (lymphocytes, macrophages, neutrophils), fibroblasts and megakaryocytes [48].

The infection rate of newborns with cytomegalovirus, according to WHO, is 0.2-2.3% in highly developed countries, while in developing countries this indicator reaches up to 6% [29,27].

According to some data, about 10% of all congenital infected children are born with symptoms of the infectious process. Of the remaining 90% of children who do not have symptoms at birth, 10-15% have long-term consequences of the infection [4]. In the absence of specific therapy, generalized CMVI in newborns can lead to death in 80% of cases, and with the survival of the latter, severe consequences can be revealed in 50% of infants [31,32]. At the same time, fetal infection and the development of severe forms of the disease are most often noted in cases when a woman suffers a primary infection during pregnancy [41]. In terms of teratogenic ability, cytomegalovirus (CMVI) ranks second after the causative agent of rubella. [40]

The decisive factor in the development of congenital CMVI is viremia in the mother due to primary or repeated infection with the virus, or its reactivation. The clinical picture of generalized ECMVI is characterized by CNS lesion (100%), anemia (79.0%), small anomalies (38.2%) and congenital heart defects (20.6%), colitis (8.8%) and the addition of various bacterial infections mainly of pulmonary localization (67.6%), as well as the development during the first year of life of a disabling pathologies: Cerebral spastic infantile paralysis (29.4%), sensorineural visual impairment (20.6%) and hearing impairment (2.9%) [11,18,21,48].

Congenital cytomegalovirus infection should be distinguished from acquired infection, which occurs as a result of postnatal infection of a child and manifests after 3 weeks of life. Postnatally acquired CVMI in children of the first year of life is more often asymptomatic, by the type of respiratory disease or with prolonged subfebrility in the form of a mononucleosis-like syndrome. Currently, it has been proven that acquired CVMI is not accompanied by

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disorders of the central nervous system and rarely has a generalized character with damage to the visceral organs[26].

An unusually wide range of clinical manifestations of CMVI is closely related to the variety of relationships between the virus and the macroorganism. CMVI can occur acutely (actively), chronically (latently with relapses), and manifests itself in congenital and acquired forms. Cytomegaloviruses are characterized by the ability to persist in the body with irregular production of viral particles and exacerbations of chronic infection, contributing to the formation of a variety of somatic pathology [53].

The incidence of CMVI fetus depends not so much on the presence of the virus in the mother's body as on the activity of the infectious process during pregnancy [30]. The presence of CMV in the blood leads to infection of the placenta, its demage, and further infection of the fetus [12]. A possible way of infection of the fetus is ascending, or transcervical. The cause of the ascending infection is the presence of a virus in the cervical canal of a pregnant woman. Reactivation of CMV in the endometrium and demage tothe embryo in an ascending way without the pathogen entering the blood may be one of the causes of spontaneous miscarriages in the early stages. CMV can also infect smooth muscle cells, bone marrow stroma cells, the retina of the eye [17] and the adrenal glands [2]. After the virus overcomes the entrance gate, the vascular endothelial cells are initially infected. The virus persists and multiplies in endotheliocytes [30]. Further spread of infection occurs due to direct cellular contact of infected endotheliocytes with polymorphonuclear leukocytes and their migration, including through the blood-brain barrier. CMV penetrates into the cell by pinocytosis or veropexis. When the DNA of the virus reaches the nucleus of the host cell, the replication process begins and the formation of daughter viral particles [39], which, leaving the infected cell, are "covered" with an outer shell. In this case, the outer shell of virions is formed with the participation of the cell membrane damaged by cytomegalovirus [30].

Daughter viral particles interact with the receptors of neighboring cells, repeating the process. The affected cells carry out not only the synthesis of viral particles, but also retain the ability to muco-protein secretion, which ensures their masking and prevents the "attack" of T-killers. Infected cells acquire the characteristic appearance of an "owl's eye", due to an increase in size by 3-4 times, the cytoplasm due to the large diameter of the nucleus is visualized only in the form of a thin strip. Intracellular basophilic inclusions appear in the cell,

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representing immature virions. [38] Pathogenesis of kidney damage: there are several mechanisms by which viral infections can lead to kidney damage: • infection of glomerular cells or tubules with the development of direct cytotoxic damage; • like any filtered substance, viral particles (with a diameter of 5-300nm) can enter the glomerulus with blood, which can lead to the formation of IR; • viruses can be an antigenic stimulus for the immune system, which leads to the production of autoantibodies against cross-reacting epitopes of glomerular cells[42].

In 40-90% of surviving newborns suffering from manifest CMVI, there are long-term neurological consequences, in the form of delayed psychomotor, mental development (55% of cases), sensory-neural deafness (58%) or bilateral hearing loss (37%), impaired speech perception while maintaining hearing (27%), one or more of the four signs (microcephaly, seizures, paresis / paralysis, chorioretinitis) with a frequency of about 50% of cases. Congenital CMVI is associated with sensorineural disability. In 25-40% of cases, children have mental disabilities that manifest themselves at an older age: cognitive impairment, low learning ability at school, inability to read, hyperactivity combined with inability to concentrate, behavioral problems [24,50].

Damage to the nervous system is revealed with a frequency of 10 to 100%: according to data [3] in 55% of cases, [1] — in 68% of cases, [10] — 10-89,3%, [38] — 80% and in 100% of cases with cerebral form [12,10,1]. The most common (in 68% of cases) is CNS depression [12], which manifests itself in the form of hypotension and ranges from 27% to 56.7% [1, 10], hyporeflexia 50.5% [10], including a weak sucking reflex 19% [1]. Malformations of the central nervous system are revealed in the form of occlusive hydrocephalus, agenesis of the corpus callosum, vascular malformation [27]. Microcephaly is observed in 10-18.5% of cases [12, 5.10,], in the study — in 28.2% of cases, according to other authors, in 42-56.5% of cases [17.1]. Hydrocephalus is diagnosed in 15.5— 23% of cases [12,], in the study [12], hypertension-hydrocephalus syndrome was revealed in 54.2% of children with cerebral ECMVI and 57% with generalized form, in the study [10], hydrocephalus syndrome was noted in 78.6% of the subjects, and an increase in intracranial pressure in 53.9%.

Convulsive syndrome was observed in 7-13% of children [1], in the study [12] in 21% of children with ECMVI with a cerebral form and in 26% with a generalized form. Meningo- and encephalitis is diagnosed in 7.85— 25% of cases with cerebral ECMVI [38, 12, 10] and in 3-32% in children with

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generalized form [38, 12]. During lumbar puncture, lymphocytic cytosis is revealed in the cerebrospinal fluid, according to [38], 16-20 cells in 1 μl and protein from 0.38—0.52 g / l [30] and up to >120 mg / dl, which corresponds to 1.2 g/ l in 46% of the studied [1]. Hypertension is also revealed in 17.4% [28] and tremor in 32.5% [32] and swelling of the brain in 37.8% [12]. Changes in NSG are detected in 37.7—87% of cases [5,] in the form of intracerebral hemorrhages [24] in 7.3% of cases [10], ventriculomegaly from 4.5% to 20% [24.5], in the study — 55%, and according the date [10] up to 78.6%, according to the results of the study [5] there were revealed the expansion of the occipital and temporal horns of the lateral ventricles in 16.0% and 4.3% of cases, respectively, as well as the expansion of the subarachnoid spaces 4.3%. Intracerebral calcifications are found in the range from 0.6 to 25.8% of cases [23, 10.5], and in the study up to 59%, according to observations [11] petrifications occur in 79% of newborns with cerebral CMVI. Hyperechogenicity of periventricular zones occurs in 10,1—17,9% [5, 10], periventricular leukomalacia develops in 5-20%. In newborn children with cerebral form of ECMVI, periventricular cysts are revealed in 37.5% of cases [11], subependimal cysts in 11.6% [5, 10].

Kidney damage is one of the most frequent in cytomegalovirus infection. It was first described by L. Jackson in 1922. Cytomegalic metamorphosis mainly affects the nephrothelium of convoluted tubules, although sometimes glomeruli are involved in the process, replication of the virus in the kidneys is possible, areas of lymphohistiocytic infiltration are detected [34]. Kidney damage by the type of nephrosonephritis is possible [35]. A number of kidney diseases that manifest at an early age have their origins in the ante- and perinatal periods. One of the causes of kidney damage existing at the time of birth is intrauterine infections, among which cytomegalovirus infection occupies one of the leading places [46].

When studying kidney pathology in children with congenital CMI, it was found that it is possible to form abnormalities of the urinary system. Anomalies of kidney development are represented by doubling, polycystic fibrosis, hypoplasia, horseshoe kidney, obstruction of the urinary tract. There is congenital CMI accompanied by clinical symptoms of interstitial nephritis, including the development of nephrotic syndrome, dysmetabolic nephropathy, concomitant urinary tract infection [30]. Kidney damage in cytomegalovirus infection can manifest itself in the form of interstitial nephritis, malformations,

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often complicated by severe recurrent secondary pyelonephritis, and very rarely in the form of nephrotic syndrome [48,29,27]. It was found that 1-2% of children at birth secrete the virus in the urine, and by the age of one year their number increases to 10-20%. The incidence of CMVI depends not so much on the presence of the virus in the mother's body as on the activity of the infectious process during pregnancy [22].

According to Suzdaltev L.V. 2013 population studies, the number of newborns with congenital malformations is increasing. In their structure, the proportion of congenital defects of the kidneys and organs of the urinary system is 26-30%. [45]. The genitourinary system is affected in 68,% [38]- 87% [42] newborns with cytomegaly: according to [7]-30%. Interstitial nephritis develops in 10% [25] -3.4%[11], and glomerulonephritis–in 6.4%% [38], nephrotic and urinary syndrome is diagnosed in 19.3% [38], children with CMVI, secondary urinary tract infection, including pyelonephritis 31.%, cystitis-in 25.7%[38],. Increased echogenicity of the renal parenchyma is revealed in 4.3% [5], cases stroma fibrosis and nephrosclerosis including glomerulosclerosis are also described in the literature [52], in 8.7% [38]. Risk factors for kidney damage in CMVI are the presence of chronic extragenital and genital pathology in mothers, as well as the pathological course of pregnancy. Kidney lesions in CMVI occur in the structure of a generalized form, are characterized by non-specificity, low symptoms and are "masked" by symptoms of the underlying disease. The presence of large kidney malformations indicates an early teratogenic effect of CMI with a disturbance of the formation of the urinary system under the action of cytomegaly virus [47]. Kidney damage in CMVI, more often causes acute glomerular lesion, with the development of glomerulopathy, membranoproliferative glomerulonephritis (GL), membranous nephropathy, mesangioproliferative GL, IgA nephropathy, TMA [43].

It can be assumed that newborn children with abnormalities of the pyelourethral segment should be examined for CMVI, which, in the presence of an infectious process, will make it possible to carry out specific therapy in a specialized department and prevention of the progression of congenital pyelectasia [28]. Cytomegalovirus infection is classified by the WHO European Regional Office as a group of diseases that determine the future of infectious pathology. It was found that 1-2% of children at birth secrete the virus in the urine, and by the age of one year their number increases to 10-20% [51]. Studies by J.D. Semidotskaya and co-authors (1999) showed that in patients

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with chronic forms of glomerulonephritis, the presence of IgG to cytomegalovirus was noted in 68% of cases, and IgM – in 54%. The clinical data of the form differed in a more severe course. Immunological indicators were characterized by a decrease in the level of T-helpers and an increase in the level of T-suppressors, as well as activation of the complement system and some indicators of phagocytic activity [34].

Laboratory diagnostics of CMVI is based on the detection of the virus itself or its DNA, its antigens, as well as specific antibodies to the virus in the studied samples. The main methods of laboratory diagnosis of CMVI are cytological and histological studies, virological and molecular biological methods, enzyme immunoassay, immunofluorescence reaction, immunofluorescence detection of cytomegalovirus antigens and determination of early proteins of its replication. [30,33] For the etiological verification of intrauterine infection, two groups of methods are used, conventionally designated as "direct" and "indirect". Direct laboratory tests include methods aimed at detecting the pathogen itself (classical, microbiological), its genome (polymerase chain reaction - PCR) or antigens (immunofluorescence). Discovery of CMV by direct laboratory methods in a child during the first 3 weeks of life indicates intrauterine transmission of the virus from mother to child [37].

Indirect or serological methods include methods that allow detecting specific antibodies to pathogen antigens in the patient's blood serum. In recent years, enzyme immunoassay (ELISA) has been most often used for this [19]. The gold standard of laboratory diagnosis of CMVI in newborns is considered to be a combination of direct and indirect diagnostic methods, which can significantly increase the diagnostic capabilities of laboratory verification of this disease. At the same time, PCR is most often used from direct methods (specificity and sensitivity - more than 90%), and from indirect methods - ELISA (specificity and sensitivity - more than 75%) [41].One of the first stages in the diagnosis of intrauterine infection, determining the scope of therapeutic and preventive measures in the early neonatal period is a histological examination of the afterbirth. Cytomegaly is characterized by the presence of placentitis with lymphocytic and plasmocytic infiltration, necrosis and sclerosis of the villi, blood clots in the vessels and edema of the stroma of the villi. [49]. Discovery of the CMV genome by DNA hybridization and polymerase chain reaction is currently the most recognized diagnostic method [52]. When conducting ELISA with parallel determination of avidity of antibodies, serological examination

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can significantly complement the results of virological and molecular methods of CMVI diagnosis. The avidity of antibodies gradually increases during the immune process. Determination of avidity of class G anticytomegalovirus antibodies increases the diagnostic value of the method.

According to the degree of avidity of class G immunoglobulins, the period and severity of the infectious process can be indirectly characterized. The discovery of low-grade anticytomegalovirus antibodies of class G indicates a current or recently transferred CMVI, and discovery of high-grade antibodies makes it possible to exclude the active phase of the disease [14]. Thus, laboratory diagnostics should be based on the use of a set of methods that include not only verification of the etiological agent and detection of serological markers of the immune response (specific antibodies), but also determination of the severity of the infectious process (study of viral replication activity and separate determination of M and G class anticytomegalovirus antibodies with their avidity) [33]. A detailed blood test (UAC) with differentiation and liver tests may be useful, but not mandatory. Cranial ultrasonography or CT and ophthalmological evaluation should also be performed. Periventricular calcifications are usually revealed during CT. [33,50].

Hearing acuity testing should be carried out routinely for all infected newborns at birth, and accompanied by long-term careful monitoring, because hearing loss can develop after the neonatal period and progress).

Thus, CMVI in newborns is the most common of all congenital infections, but so far there are many unresolved questions about the diagnosis, about the effect on the central nervous system and kidneys, the prevention of this infection, and therefore, the problem is urgent and requires further study.

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