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RESEARCH ARTICLE

CORONAVIRUS INFECTION IN CHILDREN DURING A PANDEMIC. REVIEW

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ABSTRACT

The generalized data of publications on coronavirus infection in children, including neonatal and subsequent age periods, are presented in the review. Children are less likely to get sick than adults, but they are more often asymptomatic carriers of infection. The similarities and differences in the course of infection in adults and children are shown. A rarer incidence and a mild course of infection can be associated with the peculiarities of the activity of the immune system in children due to frequent age-related vaccinations and more frequent "contact infections". In addition, the difference in the expression sites of the APF2 receptor may play a role, facilitating the penetration of the pathogen of CoV-19 into the cell (in children - in the intestine, in adults - in the respiratory tract). Children develop gastrointestinal tract pathology more often than adults when infected with SARS CoV-2, typical and atypical manifestations of Kawasaki disease are found. The main recommendations of the Ministry of Health of the Russian Federation on the treatment and prevention of coronavirus infection are presented.

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INTRODUCTION

In March 2020, a pandemic of the new coronavirus infection COVID-19 was announced (Dhir *et al* 2020). As of February 13,2022, the total number of confirmed cases from the beginning of the pandemic in the world was 411,246,446 patients and in Russia 14,133,509 (3.4%) (The Official information about coronavirus, 2022). In addition, a significant number of pregnant women infected with SARS-CoV-2 have been described (Chi J, at Gong W, 2021). Clinicians pay great attention to the problem of the risk of infection of newborns (intrauterine, after childbirth), as well as to the problem of the influence of the type of childbirth (vaginal or via cesarean section) on the infection of newborns. Older children have a less severe course of infection compared to adults. This fact is noted by a number of researchers (Dhir *et al* 2020; Mena et Yadav 2020; Bai *et al*, 2020; Pericleous *et al*, 2020; Kampocas T, *et al*, 2020; Ludwigson JF, 2020; Osmanov IM, *et al*, 2021; Catagnoli R, *et al*, 2020; World Health Organization, 2020).

The causative agent of COVID-19 infection: The pathogen SARS-CoV-2 was isolated for the first time in Yuhani (China), causing severe atypical pneumonia with "severe acute respiratory syndrome" (COVID-19). This virus belongs to the Coronavirus family (Coronaviridae), the genus Betacoronavirus (β-coronavirus), the species SARS-CoV. Coronavirus RNA is the largest genome among RNA viruses. The genomic regions of SARS-CoV-2 have a structure 95% similar to the β-coronavirus found in bats (World Health Organization, 17 January 2020; Van Dorenaben W, *et al*, 2020).

The pathogens SARS-CoV and MERS-CoV also belong to the genus of betacoronaviruses. The SARS-CoV virus causes SARS atypical pneumonia, and the MERS-CoV virus causes the Middle Eastern respiratory distress syndrome MERS with a particularly severe course of the disease and high mortality (Centers for Disease Control and Prevention. Coronavirus (COVID-19); Junqiang L, *et al*. 2020). Currently, there are 5 variants of the SARS CoV-2 coronavirus that cause concern (Variants of Concern - VOC) as defined by the World Health Organization (WHO). These strains were named Alpha (line B.1.1.7), Beta (line B.1.351), Gamma (line B.1.1.248), Delta (line B.1.617.2) and Omicron (line B.1.1.529).

They have the following designations: Alpha strain SARS-CoV-2 (British), Beta strain SARS-CoV-2 (South African), Gamma strain SARS-CoV-2 (Brazilian), Delta strain SARS-CoV-2 (Indian) and Omicron strain SARS-CoV-2 (Botswana and South Africa) (UN Statement, 15.01.2021; UN Statement, 26.11.2021). Coronavirus contains 5 main structural proteins (Spike proteins): hemagglutinins, esterase protein, M-matrix protein, N-nucleocapsid and E-envelope protein. These proteins determine the antigenic properties of the virus. As a result of SARS-CoV mutations, nosy strains of the SARS CoV-2 coronavirus have appeared, including Omicron, which is especially rapidly spreading. (Kampocas T, *et al*, 2020; Fan S, *et al*, 2020; Fung TS, et Liu DX, 2019; UN Statement, 15.01.2021; UN Statement, 26.11.2021).

Mortality in SARS CoV infection is 8-10%, MERS is 15-38% (Zhu N, *et al*, 2019; Junqiang L., *et al*, 2020; European Centre for Disease Prevention and Control (ECDC), December 6, 2019). The mortality rate in COVID-19 (when infected with the SARS CoV-2) varies widely, it depends on the country and the period of the pandemic. The 411,246,446 people were infected and 5,830,835 people (1.4%) died in the world from the beginning of the pandemic according to statistics on February 13,2022 (Coronavirus, statistics, 2022). The factors of poor prognosis of coronavirus infection in adults (including pregnant women) and children are obesity, previous diseases (diabetes mellitus, hypertension, cardiovascular diseases). In adults, elderly age is also a risk factor. Human coronavirus causes a large number of different respiratory syndromes, neurological and systemic lesions: gastroenterological, renal, hepatic and others (Cui J, *et al*, 2019). There is evidence of facilitated penetration of SARS CoV-2 into the cell through angiotensin-2-converting enzyme (ACE-2) receptors, which in children are most expressed in the gastrointestinal tract, and in adults - in the upper respiratory tract (Li W, *et al*, 2003).

Ways of transmission of infection. The ways of transmission of infection in children are basically the same as in adults. This is airborne, with close contact, through hands, surfaces of objects (live viruses persist on steel surfaces for 6 hours, plastic 6-8 hours, cardboard - 3.5 hours). Frequent gastrointestinal symptoms in children and the corresponding transmission of infection through faeces, unlike adults, are important (Dhir SK, *et al* 2020; Pericleous E, *et al*, 2020). Particular attention of doctors is drawn to the issue of the transmission of coronavirus from mother to fetus or newborn. Most authors believe that there is no risk of infection of the fetus through the placenta (vertical pathway). However, there is evidence that such a risk exists in the pathology of the placenta, starting from the 1st trimester (miscarriages). At the same time, an increase in fibrin is detected in the placenta subchorially and inside the villi, which may be evidence of circulatory disorders in the placenta in women who have had an infection caused by SARS-CoV-2 in the 3rd trimester. There were many anomalies in the placenta, poor vascularization, oligohydroamnion (lack of water), absence of villi in the placenta, abnormal or damaged vessels and thrombosis around the villi, villi edema, fetal death, retroplacental hematoma, signs of acute and chronic inflammation, vascular thrombosis (Pericleous E, *et al*, 2020; Komine-Aizawa S, *et al*, 2020). The revealed changes in the placenta may be the cause of miscarriage of the fetus and neonatal pathology. Changes in the placenta may be a manifestation of systemic inflammation or hypercoagulation, which affect the pathology of the placenta. Vertical transmission of infection through the placenta is confirmed by the detection of antibodies in the fetal blood not only IgG, but also IgM, which cannot penetrate the placenta due to the large size of the molecule (Pericleous E, *et al*, 2020). Cases of infection of newborns during vaginal delivery with positive tests for SARS-CoV-2 in the mother's vaginal discharge are described. In this regard, in most cases, childbirth was carried out by caesarean section, followed by isolation of the newborn from the sick mother for 14 days. The detection of IgG against SARS-CoV in the fetus is regarded as a factor in protecting the fetus from infection, and vertical transmission of infection through the placenta from the mother to the fetus is considered possible only with placental pathology. This is more common in obesity, premorbid pathology, including cytomegalovirus and other viral and bacterial infections. Coronavirus infection in the fetus is more often observed in the pathology of the placenta infected with SARS-CoV than SARS-CoV-2 (Komine-Aizawa S, *et al*, 2020).

After childbirth, there is a risk of infection of the newborn from a sick mother, which necessitates the isolation of the newborn. Despite closer contacts, children get sick less often than adults, which can be explained by the significantly greater activity of acquired immune protection after frequent contact infections in children's groups (Pericleous E, *et al*, 2020). In particular, the frequency of hospitalizations of children is 0-2%, and adults 10-12%, and the disease in children proceeds much easier than adults. Children are often asymptomatic carriers of of coronavirus (Dhir SK., *et al* 2020). The problem of transmission of coronavirus through breast milk also attracts much attention. There are huge benefits of breastfeeding babies. Most publications report on the safety of breast milk, but there are publications on the detection of SARS-CoV-2 virus RNA in breast milk (Pericleous E, *et al*, 2020). And yet breast milk (native or expressed) should be given to infants when the clinical condition of the mother allows, there are negative tests for SARS-CoV-2, as well as with hand and respiratory hygiene (Dhir SK., *et al* 2020; Chi J, et Gong W, 2021; Pericleous E, *et al*, 2020;- Ludwigson JF, 2020).

Pathogenesis: SARS-CoV, SARS-CoV-2 and MERS-CoV are highly lethal viruses. They cause a sharp change in the immune status, severe lung pathology with a fatal outcome (Kampocas T, *et al*, 2020; Hui DSH, *et al*, Zumla A, 2019). SARS - CoV and SARS CoV-2 use the ACE-2 receptor (Angiotensin Converting Enzyme 2 receptor) as a target to facilitate virus entry into the cell. MERS-CoV also has a kind of gate to the cell through the location of dipeptidase-4, which is found on the surface of cells of the lungs, kidneys, small intestine, T-lymphocytes and macrophages. These are the target areas for MERS-CoV.

In severe cases, these viruses cause activation of the expression of pro-inflammatory cytokines: IL-6, tumor necrosis factor (TNF) (cytokine storm), as well as anti-inflammatory cytokine IL-10. The IL-6 is the most active cytokine. It participates in the excessive synthesis of other proinflammatory cytokines, activates ACE-2 receptors (the gateway for the virus), stimulates osteoclasts, causing the risk of osteoporosis and vitamin D deficiency. In addition, IL-6 induces the synthesis of acute-phase proteins in hepatocytes: CRP, fibrinogen, leptin and others, participates in the formation of respiratory distress syndrome (Henry *et al*, 2020). The IL-10 increases sharply with severe COVID-19 in the first days of the disease, being a marker of pronounced inflammation. This cytokine inhibits the synthesis of proinflammatory cytokines (tumor necrosis factor and IL-1ß) (Girndt M, 2003), interferon-gamma (Varma TK, 2001). IL-10 stimulates B-cell proliferation and antibody production (Lazear, *et al*, 2015).

The level of cytokines and chemokines is most elevated at the peak of the disease and gradually decreases during treatment. Recovering patients have a high level of specific neutralizing antibodies (AT) that contribute to the elimination of the SARS-CoV-2 virus. AT IgG are formed at a late stage of the disease (approximately in the second week) and after recovery. AT IgM are formed earlier, the peak concentration falls on the 2nd - 3rd week of the disease and remains up to 12 weeks after recovery. The hyaline membranes, fibrin exudate, epithelial damage, diffuse type II hyperplasia with all signs of alveolar damage are formed in the lungs with severe pneumonia with a fatal outcome. Bacterial infection also develops in some patients (Kampocas T, *et al*, 2020; Rodrigues-Mortales AJ, *et al*, 2020). When comparing infection caused by SARS-CoV-2 in pregnant and non-pregnant women, it was found that pregnant women are more likely to develop renal failure, disseminated intravascular coagulation and deaths occur (Kampocas T, *et al*, 2020; Hui DSH, et Zumla AA, 2019). In 25% of cases, premature birth, severe pneumonia, the need for artificial lung ventilation (ALV) in pregnant women, delayed fetal development, spontaneous miscarriages, combined with premature contractions, rupture of the amniotic membrane, fetal death or neonatal death, or there was a need for intratracheal intubation of the newborn. Infants had low birth weight and various perinatal complications (Kampocas T, *et al*, 2020). Thus, when pregnant women are infected with SARS-CoV-2, there is a high risk for the life of both the pregnant woman and the fetus. Vaccination of pregnant women and surrounding people significantly reduces this risk. The asymptomatic course of the disease in pregnant women is a source of infection transfer (Fan S, *et al*, 2020).

The clinical course of COVID-19. Fever, sometimes low, is one of the common symptoms of COVID-19 in children. The disease is characterized by persistent dry cough, sometimes a wet cough with moderate severity of the infection (Pericleous E, *et al*, 2020). In addition, other respiratory syndromes are described: nasal congestion, rhinitis, irritation in the throat. When using computed tomography (CT scan), many children showed signs of pneumonia, single or multiple "glass-like" seals (a symptom of "frosted glass"). In adolescents with covid pneumonia, lesions of up to 5 lobes of the lung were detected. The leading role of CT scan in the diagnosis of lung lesions in children has been established (sensitivity 97.5%) (Pericleous E, *et al*, 2020; Rodrigues-Mortales AJ, *et al*, 2020). The course of COVID-19 in children is also characterized by gastrointestinal symptoms. Abdominal pain, diarrhea, vomiting are observed in 10% of infected children, including newborns. Children also have lesions of the urinary system (cystitis, urethritis). Unlike older children, the course of COVID-19 in newborns was more severe: 40% of infected infants needed resuscitation and mechanical ventilation, 20% of newborns had fever. Only 33% of newborns had COVID-19 asymptomatic (Pericleous E, *et al*, 2020).

In severe cases of neonatal COVID-19, multiple symptoms were noted, including respiratory distress syndrome, neonatal encephalopathy, pneumonia, prolonged QT syndrome, tachycardia, shortness of breath, asphyxia, diarrhea, neonatal jaundice , moderate fever, neurological symptoms, muscle hypotension, hypoxia, low birth weight (Ludwigson JF, 2020). In adolescents infected with SARS-CoV-2, in a number of cases, symptoms of a severe condition called antidiuretic hormone deficiency syndrome were observed, which is characterized by severe dehydration, a decrease in sodium in the blood (as well as potassium and calcium). This condition was accompanied by polyuria with high urine osmolarity (2-7 times higher than normal), hypernatriuria. Severe dehydration and hypoxic state increases the activation of the renin-angiotensin-aldosterone system (RAAS) receptors in the carotid sinus, aorta, causing vasoconstriction, including in the lungs, where cytokines damage lung tissue and alveoli; oxygen saturation decreases (Ho KS, *et al*, 2021). Clinically, disorders of water-electrolyte metabolism against the background of cardio-pulmonal syndrome are characterized by seizures, disorientation, lethargy (Yuosaf Z, *et al*, 2020). At the height of the COVID-19 pandemic (namely, in April 2020), a message about children with hyperinflammatory shock appeared in England. The clinical picture had signs similar to Kawasaki disease and toxic shock syndrome. Symptoms of the disease developed 2-4 weeks after the acute course of COVID-19. All the children had serological signs of SARS-CoV-2 infection. In this regard, the syndrome has been associated with COVID-19. Clinical signs of this pediatric inflammatory syndrome, similar in symptoms to Kawasaki disease, included fever, rash, conjunctivitis, peripheral edema, gastrointestinal disorders, shock, and elevated markers of inflammation and heart damage (Morris SB, *et al*, 2020). This syndrome, similar in symptoms to Kawasaki disease, was registered as multisystem inflammatory syndrome in children (MIS-C) (Morris SB, *et al*, 2020). Further studies showed that the clinical picture of MIS-C was characterized mainly by shock, cardiac dysfunction, abdominal pain and noticeably high indicators of inflammatory markers. Nearly all patients had positive SARS-CoV-2 test results. The 64.4% of patients with MIS-C had manifestations that seemed to coincide with the acute period of COVID-19 (Morris SB, *et al*, 2020; Dufort EM, *et al*, 2020; Shana Godfred-Cato, *et al*, 2020; Feldstein LR, *et al*, 2020; Caro-Patón GL, *et al*, 2021). The average duration of hospitalization was 6 days; 64% of patients needed help in the intensive care unit, 1.8% of patients died. MIS-C in children with the COVID-19 pandemic occurred as toxic shock syndrome and atypical Kawasaki syndrome (with signs of gastrointestinal damage and cardiosymptoms). The patients also had high levels of C- reactive protein (CRP), procalcitonin, ferritin, troponin, D-dimer, IgG. and changes in the coronary arteries (Shana Godfred-Cato, *et al*, 2020). В разных публикациях авторы обращают внимание на совпадение симптомов MIS-C с симптомами заболевания COVID-19, вызванным SARS-CoV-2, а также типичным шоковым синдромом, бактериальным сепсисом и синдромом макрофагальной активности. Some, but not all,

tests were positive for COVID-19 in these patients (Pericleous E, *et al*, 2020; Shana Godfred-Cato, *et al*, 2020; Morris SB, *et al*, 2020; Caro-Patón GL, *et al*, 2021).

Kawasaki disease is described in detail in the publication by S.D. Kirilina (2021): "Kawasaki disease (vascular-cutaneous lymphonodular syndrome, is necrotizing systemic vasculitis with a predominant lesion of medium and small arteries, manifested by fever, changes in mucous membranes, damage to coronary and other arteries with the possible formation of aneurysms, thrombosis and vascular wall ruptures", deprived of elastic fibers" (Kirilina SD, 2021). Risk factors for Kawasaki disease are age from 3 months to 4 years, Asian origin, decreased cellular and humoral immunity, male sex (Pericleous E, *et al*, 2020). The clinical characteristics of Kawasaki disease include prolonged (7-10 days) fever that cannot be treated, signs of acute inflammation of the eyes, tongue, larynx, palms, and also diarrhea, vomiting, stomach pain, pneumonia, pleural effusion. Unlike COVID-19, there is swelling of the feet, hands, polymorphic erythema on the trunk, arthralgia. Unlike COVID-19, there is swelling of the feet and hands, polymorphic erythema on the trunk, arthralgia (Tubiana, *et al*, 2020; Dasgupta, at Finch, 2020).

The unknown factor causing Kawasaki disease activates the formation of immune complexes, activation of T-lymphocytes and the production of cytokines that damage the vascular wall by the type of cytokine storm. In addition, matrix metalloproteinases are activated, which damage the endothelium, vascular cells, there is an increase in vascular permeability and damage to the capillary wall (Tubiana J., *et al*, 2020). Vasculitis is generalized, especially pronounced in the coronary arteries in Kawasaki disease, At the site of the defect of the vessel, its obliteration may occur. Active inflammation for weeks or months is replaced by progressive fibrosis, scarring and vascular stenosis (Kirilina SD., 2021; Tubiana J., *et al*, 2020). Untreated Kawasaki disease in 25% of cases is complicated by aneurysms with a high risk of death. The syndrome is treated with high doses of immunoglobulins (at least 10 days). By all accounts, the symptoms of CoV-19 and Kawasaki disease are difficult to distinguish. There is no specific treatment for children. With multisystem syndrome in children, treatment is used similar to treatment for Kawasaki disease. The treatment complex includes oxygen and nutritional support, as well as water-electrolyte balance support (Verdon *et al*, 2020; Ouldali *et al*, 2020; Chitos *et al*, 2020; Shana Godfred-Cato, *et al*, 2020). According to the latest information, the new strain of Omicron coronavirus has an incubation period of 1-3 days and spreads 4-10 times faster than previous strains. Basically, the disease proceeds easily, limited to respiratory symptoms (nasal congestion, runny nose, sore throat, sneezing, cough), and there are also pain in the joints, weakness, taste sensations change less often and pneumonia develops, although in some cases pneumonia developed on the 9th-10th day of the disease. At risk are people with chronic diseases, the elderly, as well as children, although omicron is contagious for all age categories (UN Statement, 15.01.2021; UN Statement, 26.11.2021г).

Laboratory diagnostics: To diagnose diseases in children caused by SARS-CoV, MERS-CoV, SARS-CoV-2 viruses, according to most researchers, it is necessary to detect RNA viruses by porlimerase chain reaction (PCR). This test is most informative in the first week of illness.

However, this method can give false-positive and false-negative results (Sheridan C, 2020; Wynants L, 2020). When examining sputum, tampons with contents from the nose and pharynx at the beginning of the disease, positive PCR results are detected in 72%, 63% and 32%, respectively (Pericleous E, *et al*, 2020; Rodrigues-Mortales AJ, *et al*, 2020). The study of IgG and IgM blood virus neutralizing antibodies is informative for verifying the diagnosis of COVID-19. These indicators are used primarily to monitor recovery. The peak IgM content is observed between 2 and 3 weeks of illness and remains up to 12 weeks after recovery. IgG antibodies are synthesized more slowly, their peak content occurs after the 3rd week and remains elevated for longer. Upon admission to the hospital and during treatment, monitoring of oxygen saturation in the blood is important, as well as determining the activity of liver enzymes, myocardium, lactate dehydrogenase (LDH), creatine kinase. troponin, the blood content of erythrocytes, leukocytes, CRP, D-dimer, the state of the coagulation system and water-salt metabolism (the sodium content in the blood with LDH deficiency syndrome decreases to 112-117 mmol / l, potassium to 3.5-3.8 mmol / l, calcium to 2.17 mmol /l versus 141 mmol / l, 4.2 mmol /l and 2.5 mmol /l are normal, respectively).

According to changes in water-electrolyte metabolism, the symptoms are similar to those of renal diabetes insipidus. In severe cases of COVID-19, the glucose content in the blood was significantly increased (7.8-15.5 mmol/l at a rate of 4-6 mmol/l). At the same time, the lactate content in the blood did not exceed normal values, which can be explained by glucose metabolism via an alternative pathway with the formation of powerful pro-oxidant stress agents, including methylglyoxal. These metabolites characterize a high risk of endogenous intoxication (Yuosaf Z, *et al*, 2020; Kosmachevskaya OV, *et al*, 2018). The described changes in carbohydrate metabolism in COVID-19, even in patients who do not suffer from diabetes mellitus, may be one of the factors of a particularly severe course of COVID-19 in diabetics. It is also necessary to conduct routine urine tests. Prognostic indicators of severe, complicated course of infection are proinflammatory cytokines IL-6 and tumor necrosis factor (TNF), as well as anti-inflammatory cytokine IL-10 (Pericleous E, *et al*, 2020; Yuosaf Z., *et al*, 2020). Markers of inflammation in COVID-19 ‘ are LDH, D-dimer, procalcitonin, CRP, ferritin, IL-6 and IL10, the level of which is elevated in the blood (Ho KS, *et al*, 2021). These laboratory indicators are the most common diagnostic criteria for COVID-19.

Treatment (basic provisions): Effective measures for severe COVID-19 include resuscitation and respiratory support (oxygen mask, ALV), intravenous administration of human immunoglobulin against coronavirus (Pericleous E, *et al*, 2020). A clear detailed algorithm for the pharmacological treatment of COVID-19 is also presented in the "Temporary Methodological Recommendations" of the Ministry of Health of the Russian Federation (09/21/2021), which offers pharmacotherapy depending on the severity of the disease: (mild, severe and extremely severe form) and preventive measures.

For mild forms in outpatient settings, the use of expectorant and antitussive drugs (bromhexine, thermopsis, etc.), antiviral drugs – favipiravir (coronavir), capable of inhibiting RNA polymerase involved in virus replication, or ingavirin, viferon is recommended. In addition, interferon-alpha (IFN-alpha) has an antiviral effect, used in the form of nasal drops to reduce

virus replication and provide immunomodulatory effects (increased macrophage activity. As an antipyretic, it is proposed to use paracetamol. If there are signs of bacterial infection, antibiotics are prescribed (3-7 days): amoxiclav (flemoclav, flemoxin), levofloxacin or ceftriaxone. In the last months of 2021 and at the beginning of 2022, dexamethasone tablets are used on an outpatient basis in patients over 18 years of age while maintaining temperature, shortness of breath, and cough. The use of hormonal therapy should be combined with anticoagulant therapy for the prevention of thrombosis (eliquist, xarelto or, in their absence, curantil, dipyridamole, acetylsalicylic acid, clopidogrel). It is also necessary to observe a high-liquid regime (at least 1.5 liters of liquid per day). Veroshpiron is used (for ACE-2 receptor blockade), reducing pulmonary fibrosis, reducing the risk of complications. In order to reduce endogenous intoxication and the risk of pulmonary fibrosis, polyoxidonium and longidase are used, respectively. It is also recommended to take vitamin D, zinc preparations and multivitamins.

For patients with a high comorbidity index, human immunoglobulin against coronavirus, favipiravir is included in the treatment complex, levilimab or other analogues of recombinant human antibodies to the IL-6 receptor are used to combat the cytokine storm, blocking excessive cytokine production and synthesis of acute-phase proteins in hepatocytes (CRP, fibrinogen, leptin, etc.). Intravenous administration of hormones is connected.

When treating patients in a hospital with an extremely severe course of the disease (pneumonia, respiratory failure, respiratory distress syndrome), the previously mentioned drugs are connected to the intravenous administration of not only human immunoglobulin against coronavirus and human monoclonal antibodies to the IL-6 receptor (subtype IgG1) (sarilumab or tocilizumab).

Preventive measures. For healthy individuals and all persons over 60 years of age, it is recommended to use interferon-alpha-2b (IFNa-2b) in the form of nasal drops or take Favipirovir (Umifenovir) 200 mg 2 times a week for 3 weeks. Persons with a single contact with a confirmed COVID-19 patient are recommended to use not only IFNa-2, but also Favipirovir (Umifenovir) 200 mg once a day for 9-14 days for prevention. If necessary, preventive courses are repeated.

The vaccination debate: Due to the fact that children are less likely and easier to get sick with a new coronavirus infection, until mid-2021 it was considered inappropriate to vaccinate children under 18 from this infection. However, with the emergence of a new, extremely contagious strain of COVI-19 Omicron and a significant increase in the incidence of the disease among children, all over the world came to the conclusion that it is necessary to vaccinate all children aged 4-18 years. Moreover, the fact of frequent asymptomatic carriage and transmission of infection from children remains unchanged. In some countries, vaccination starts at the age of 2. B At the National Research Center for Epidemiologyand Microbiology named after the honoraryacademician N. F. Gamaleya created a special children's vaccine "Gam-COVID-Vac-M" (”Sputnik M"), which contains 1/5 of the dose of antigens compared to the adult version of Sputnik - V (Gam-COVID-Vac). N. F. Gamaleya National Research Center has received permission to use this vaccine due to the increase in childhood morbidity. Currently, in Russia, adolescents aged 12 to 17 years are vaccinated with the Sputnik M vaccine. Most vaccines against coronavirus infection are allowed to be used during pregnancy, as their effectiveness often exceeds the potential risk of possible complications. The transplacental transfer of antibodies from the mother to the fetus after vaccination can be considered as an indicator of the protection of newborns from infection. In addition, it was found that reproductive organs expressing the ACE-2 receptor (facilitating the entry of the virus into the cell) are a target for SARS-CoV-2 (Kalamokas *et al*, 2021). It has been confirmed that vaccination is preferable to the risk of infection with COVID-19 in pregnant women. A large number of vaccinated pregnant women and their fetuses were protected from COVID-19, which allows us to conclude about the benefits of vaccination and the need to encourage vaccination of pregnant women. (Kalamokas *et al*, 2021). Severe reactions to the vaccine (the possibility of thrombosis, high fever) may serve as a limitation. Such reactions to some vaccines produced in different countries make it necessary to carefully select safe options in each case. In Russia, vaccination of pregnant women with the domestic Sputnik-V or Sputnik - Light vaccine is successfully used, not only highly effective, but also practically without causing complications (Logunov DY, *et al*, 2021; Gushchin *et al*, 2021).

Conclusion

During the first 2 years of the coronavirus pandemic, the total number of reported cases of COVID-19 in children, including newborns, was significantly less than in adults, and the overall prognosis in children, as a rule, was favorable. Infection (PCR tests are positive) in older children is asymptomatic in most cases, which leads to an increased risk of transmission of infection, especially in close contact. In both infected adults and children, including newborns, respiratory symptoms were predominant. But high fever in children was noted infrequently. In 10% of cases, gastrointestinal manifestations occurred in children. Infection caused by SARS-CoV-2 in newborns was more severe than in other children and significantly more often (in 34%) they needed intensive care and ALV. Limited low-quality data available in numerous publications indicate that the risk of infection with SARS - CoV-2 in newborns is extremely low with a predominance of postpartum infection (contact, less often – vaginal) (Dhir SK, *et al*, 2020; Chi J, et Gong W, 2021). There are separate reports about the possibility of "vertical" infection through a pathologically altered placenta. In the early stages of pregnancy, such cases end with the death of the fetus and miscarriages, and in the later stages end with premature birth and obstetric complications (Dhir *et al*, 2020). A number of publications discuss the necessity and safety of breastfeeding, although the data are contradictory. Basically, there are reports of the absence of SARS-CoV-2 RNA in breast milk, however, in some reports there is information about the detection of such RNAs in breast milk As a rule, SARS-CoV-2 was in breast milk in women who had been ill with COVID-19. The same women had a high content of IgA and IgG antibodies, which was an immune defense for newborns (Kalamokas *et al*, 2021). It is necessary to take into account the huge advantages of breastfeeding. In this regard, most authors recommend using it for infants when the clinical condition of the mother and child allows, with careful observance of precautions (Dhir SK, *et al*, 2020). Currently, the safest and most reliable way to protect adults and children from infection with the SARS-CoV -2 strain is vaccination, which is actively carried out all over the

world. It is also important to carry out anti-COVID-19 anti-epidemiological measures: the use of masks, respirators, antiseptics, personal hygiene, distance in public places, isolation of patients with COVID-19 and carriers of SARS-CoV-2.

Glossary of Abbreviations

AB – antibodies
ACE-2 - Angiotensin Converting Enzyme 2 -
ALV - artificial lung ventilation
COVID-19 (CoV-19) –COronaVIrus Disease 2019
CRP - C - reactive protein
CT scan - computed tomography
IFNα-2b - interferon-alpha-2b
IL-6 – interleukin - 6
IL-10 – interleukin – 10
LDH - lactate dehydrogenase
MERS - Middle East respiratory syndrome
MERS-CoV – Middle East respiratory syndrome-related coronavirus
MIS-C - multisystem inflammatory syndrome in children
PCR - polymerase chain reaction
SARS - Severe Acute Respiratory Syndrome
SARS CoV - Severe acute respiratory syndrome coronaviru
SARS CoV-2 Severe acute respiratory syndrome-related coronavirus 2
TNF - tumor necrosis factor
WHO - World Health Organization
LDH - lactate dehydrogenase

REFERENCES

Dhir S.K, Rumar J, Meena J. *et al*. Clinical features and outcome of SARS CoV-2 infection in Neonates: systematic review. J Top Pediatr. 2021 Jul 2;67(3):fmaa059. doi 10.1093/tropej/fmaa059.

The Official information about coronavirus in Russia. https://cdn.stopcoronovirus.ru/stopcoronavirus.rf/ai/html/3/attach/2022-02-13_coronavirus_government_report.pdf

Chi J, Gong W. Clinical characteristics and outcomes of pregnant women with COVID-19 and the risk of vertical transmission: a systematic review. Arch Gynecol Obstet. 2021. 303 (2): 337-345. Doi 10. 1007/ s00404-020-05889-5.

Mena J, Yadav J. Clinical features in children: a systematic review and meta analisys. Indian Pediatr. 2020.57(9): 820-826. doi: 10.1007/s13312-020-1961-0.

Bai Y, Yao L, Wei T. *et al*. Presumed, asymptomatic carrier transmission of CoVID-19. JAMA. 2020. 323(14): 1406-1407. Doi: 10. 1001/ jama2020. 2565/.

Pericleous E, Tsalkidis A, Bush A. *et al*. Coronavirus global pandemic: An overview of current findings among pediatric patients. Pediatr Pulmonol. 2020. 55(12): 3252-3267. doi: 10.1002/ppul.25087.

Kampocas T, Rapani A, Papageorgiou M. *et al*. The current evidence regarding CJVID-19 and pregnancy: Where Are We Now and Where Should We Head to Next? Viruses 13(10):2020. DOI:10.3390/v13102000.

Ludwigson JF. Systematic review of COVID019 in children shows milder cases and better prognosis then aldults. Acta Pediatr. 2020; 109: 1089-1095. doi: 10.1111/apa.15270.

Osmanov IM, Mazankova LN, Samitova ER. *et al*. New coronavirus infection (COVID-19) in children. Pediatrician's practice. 2021; .3: 8-11.

Catagnoli R, Volto M, Licari A. *et al*. Severe acute reshiratory syndrome coronavirus 2 (SARS COV2) infection in children and adolecens. Systemic review. JAMA Pediatr. 2020; 174(49): 882-889. Doi: 10.1001/jamapediatrics. 2020. 1467.

World Health Organization. Laboratory testing for 2019 novel coronavirus (2019–nCoV) in suspected human cases: interim guidance, 17 January 2020. Electronic resource. Date of application February 13,2022.

Van Dorenaben W, Bashmaker T, Morus H. *et al*. Aerosol and surface stability SARS COV2 as compared with SARS COV1. N.J.Engl Med. 2020; 382(16): 1564-1567. doi: 10.1056/NEJMc2004973.

Centers for Disease Control and Prevention. Coronavirus (COVID-19). (Electronic resource). https://www.cdc.gov/coronavirus/2019-ncov/index.html/. February 13,202.

Junqiang L, *et al*. CT Imaging of the 2019 Novel Coronavirus (2019-nCoV) Pneumonia. Radiology. 2020; 1: 18.

Statement on the work of the sixth meeting of the International Health Regulations Committee (2005) on the emergency situation in connection with the coronavirus pandemic (COVID-19). Date of application 15 January 2022 World Health Organization, official website, https://news.un.org/ru/story/2021/11/1414572, Appeal 15.01.2021.

UN Statement, 26.11.2021. A new strain of coronavirus has been given the name "Omicron". UN News. 26.11.2021, https://news.un.org/ru/story/2021/11/1414572. Date of application 22 January 2022.

Distribution of confirmed cases of MERS-CoV by place of infection and month of onset, from March 2012 to 2 December 2019. *ecdc.europa.eu*. European Centre for Disease Prevention and Control (ECDC) (December 6, 2019). https://www.ecdc.europa.eu? Date of application 22 January 2022.

Fan S, Yan S, Liu X. *et al*. Human coronavirus infection and pregnancy. Maternal-Fetal Medicine. 2021; 3(**1**): 53–65. DOI:10.1097/FM9.0000000000000071

Fung TS., Liu DX. Human Coronavirus: Host-Pathogen Interaction// Annu Rev Microbiol. 2019; 73: 529-557. DOI: 10.1146/annurev-micro-020518-115759.

Zhu N, Zhang D, Wang W. *et al*. A novel coronavirus from patients with pneumonia in China 2019. N. Engl J. Med. 2020;382 (8): .727-733. doi:10. 1956/NEJMoa 20010/7.

European Centre for Disease Prevention and Control (ECDC), An agency of the European Union. https://www.ecdc.europa.eu/en. December 6, 20196.

Coronavirus statistics. Electronic resource: https://coronavirusstat.ru; https://www.yandex.ru/search/?text=коронавирус+статистика&lr=213&clid=9582. Date of application February 11, 2022.

Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses// Nat. Rev. Microbiol. 2019; 17 (30): 191-192. Doi: 10, 1038/341579-018-0118-9.

Li WN, Moor MJ, Vasilieva N. *et al*. Angiotensin converting enzyme 2 is a functional receptor for the SARS coronavirus. Natur.. 2003; 426 (6965): 450-454. Doi: 10. 1038/ Nature 2145.

Komine-Aizawa S, Takola K, Kalinis B. *et al*. Placental barrier against CoV-19. Placenta. 2020; 99: 45-49. doi: 10.1016/ j.placenta 2020/07. O22.

Hui DSH, Zumla A A. severe acute respiratory syndrome:historical, epidemiologic and clinical a features. Infect Dis Clin North Am. 2019; 33(4): 869-889. doi: 10.1016/j.idc.2019.07.001.

Henry BM, Lippi G, Pltbani M. Laboratory abnormalities in children with novel cjronavirus diseases./Clin.Chem. Lab. Med. 202;. 58(7):.1135-1138. DOI: 10.1515/cclm-2020-0272.

Girndt M. Humoral immune responses in uremia and the role of IL-10. Blood Purification: journal. 2003; 20 (5): 485—488. doi:10.1159/000063553.—PMID 12207099.

Varma T K, Toliver-Kinsky T E, Lin C Y., Koutrouvelis A P., Nichols J E, Sherwood E R. Cellular mechanisms that cause suppressed gamma interferon secretion in endotoxin-tolerant (Mice). Infection and Immunity: journal. 2001;. 69 (9): 5249—5263.

Lazear H M, Nice T J, Diamond M S. Interferon-λ: Immune Functions at Barrier Surfaces and Beyond. Immunity. Cell Press, 2015; 43(1): 15—28.

Rodrigues-Mortales AJ, Cardona-Ospina JM, Gutiérrez-Ocampo E. *et al*. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis.Travel Med Infect Dis. 2020; 34: 101623. doi: 10.1016/j.tmaid.2020.

Ho KS., Marasimhan B, Kumer A. *et al* Syndrome of innapopriate antidiuretic hormone is the initial presentation of CoV-19: a novel case report. Nephrologia. 2021; 41(2): 210-226. DOI:10.4103/2230-8210.84870

Yuosaf Z, Al-Shokri SD, Soub H. *et al*. Covid-19 associated SIADH a clue in the times of pandemic. Am J Endocrinpl Metabol. 2020; 318(6): . E882-E885. doi: 10.1152/aipendo. 00178.2020

Morris SB, Schwartz NG, Patel P, Abbo L, Beauchamps L, Balan S, Lee EH, et al. Case Series of Multisystem Inflammatory Syndrome in Adults Associated with SARS-CoV-2 Infection - United Kingdom and United States, March-August 2020. MMWR Morb Mortal Wkly Rep. 2020 Oct 9;69(40):1450-1456.

Dufort EM, Koumans EH, Chow EJ, Rosenthal EM, Muse A, Rowlands J, Barranco MA, *et al*. Multisystem Inflammatory Syndrome in Children in New York State. N Engl J Med. 2020; Jul 23;383(4): 347-358. doi: 10.1056/NEJMoa2021756. Epub 2020 Jun 29. N Engl J Med. 2020. PMID: 3259883

Shana Godfred-Cato, Bobbi Bryant, Jessica Leung, Matthew E Oster, Laura Conklin,Joseph Abrams, Katherine Roguski*et al*. COVID-19-Associated Multisystem Inflammatory Syndrome in Children - United States, March-July 2020/ MMWR Morb Mortal Wkly Rep. 2020; Aug 14;69(32):1074-1080.DOI: 10.15585/mmwr.mm6932e2.

Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, Newburger JW, *et al* Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. Overcoming COVID-19 Investigators; CDC COVID-19 Response Team.Feldstein LR, *et al*. Engl J Med. 2020; 383(4):334-346. doi: 10.1056/NEJMoa2021680. Epub 2020 Jun 29. N Engl J Med. 2020.

Caro-Patón GL, de Azagra-Garde AM, García-Salido A, Cabrero-Hernández M, Tamariz A, Nieto-Moro M. Caro-Patón GL, *et al*. Shock and Myocardial Injury in Children With Multisystem Inflammatory Syndrome Associated With SARS-CoV-2 Infection: What We Know. Case Series and Review of the Literature. J Intensive Care Med. 2021; 36(4): 392-403. doi: 10.1177/0885066620969350. Epub 2020 Nov 5. J Intensive Care Med. 2021. PMID: 33148089 Review.

Kirilina SD. Kawasaki syndrome in children - current. Pediatrician's practice. 2021; 4: 5-11.

Riphagen S, Gomez X, González Martínez C G, Wilkinson N. . Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. 2020; .395 (10237): 1607-1608. DOI: 10.1016/S0140-6736(20)31094-1.

Tubiana J, Poirault C, Cjrsia A. *et al*. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. B.M.J. 2020; 369: m2094. doi: 10.1136/bmj.m2094.

Dasgupta K, Finch SE. A case of hediatric multisystem inflammatory syndrome temporally associated with COVID-19 in South Dacot. South Dakota journal of medicine. 2020. 73(6). P.246-251.

Verdoni I., Mazza A., Gervasoni A. *et al*. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020; 395(10239): 1771-1778. doi: 10.1016/s0140-736(20) 31103-X.

Ouldali N, Pouleti M, Matiani P. *et al*. Emergence of Kawasaki disease related to SARS-CoV-2 infection in an epicentre of the French COVID-19 epidemic: a time-series analysis. The Lancet Child & Adolescent Health. 2020; 4(9): 662-668. DOI:https://doi.org/10.1016/S2352-4642(20)30175-9.

Chitos K, Bassiri H, Behrens EM. *et al*. Multisystem inflammatory syndrome in children during the coronavirus 2019 pandemic: a case series. J Pediatric Infect Dis Soc. 2020; 9(3): 393-398. doi: 10.1093/jpids/piaa069.

Sheridan C. Coronavirus and the race to distribute reliable diagnostics. Nat. Biotechnol. 2020; 38 (4): 382–384. DOI: 10.1038/d41587-020-00002-2..

Wynants L, Calster BV., Bonten M.M.J. *et al*. Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal .BMJ. 2020; 369: m1328. DOI: 10.1136/bmj.m1328-1367.

Kosmachevskaya OV, Shumaev KB, Topunov AF. Carbonyl stress: from bacteria to humans. Petrozavodsk: Publisher Markov NA., 2018. 225p.

Kalamokas N, Rapani A, Papageorgiou M. *et al*. The current evidence regarding COVID-9 and pregnancy: where are we now and where should we head to next? Viruses. 2021; 13(10): .2000. doi: 10.3390/v13102000.

Logunov DY, Dolzhikpva IV, Shcheblyakov DV. *et al*. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. Lancet. 2021; 397(10275: 671-681. doi: 10.1016/S0140-6736(21)00234-8.

Gushchin VA, Dolzhikova IV., Shchetinin AM. *et al*. Neutralizing activity of sera from Sputnik V-vaccinated people against variants of concern (VOC: B.1.1.7, B.1.351, P.1, B.1.617.2, B.1.617.3) and Moscow endemic SARS COV-2 variants. Vaccines. 2021; 9(7): 779-791. DOI:10.3390/vaccines9070779.

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