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ENTEROVIRUSES ISOLATED FROM CHILDREN FROM MIGRANTS' FAMILIES IN THE NORTH-WEST OF RUSSIA

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The goal of the study was to compare non-polio enteroviruses isolated from children from migrants' families and from resident children in the North-West of Russia. Isolation of viruses was performed according to the Polio Laboratory Manual, WHO, 2005. The genome region VP1 of certain isolated enterovirus strains was partially sequenced in order to identify virus serotype. WHO Subnational Poliomyelitis Laboratory in St. Petersburg is responsible for 14 administrative territories with the population of more than 20 million people. Annually we investigate nearly three hundred samples from children with acute flaccid paralysis, enterovirus infection, healthy resident children and healthy children under five who arrive in the North-West of Russia from unsafe territories, mostly from Central Asia.

The percentage of enterovirus isolation from healthy children from migrants' families was practically the same as from resident patients with enterovirus infection (about 10%). Enteroviruses frequently circulating in the North-West of Russia are Echoviruses 6, 9, 11, 13, 30, Coxsackieviruses A4, A6, A10, A16 and Coxsackieviruses B1–6. We found all these enteroviruses in the samples from children from migrants' families. In addition to these enteroviruses we also detected enteroviruses which had not been previously isolated in the North-West of Russia, such as Coxsackieviruses A13, 17, 24, Enteroviruses 75, 99 and 120, Echoviruses 18 and 29. Phylogenetic analysis showed that serotypes of enteroviruses which were isolated from migrants' children had a different origin when compared to the viruses of the same serotype regularly detected in the North-West of Russia. Nucleotide sequences of Coxsackieviruses A13 and A17 strains isolated from the children from Tajikistan differed dramatically from sequences presented in GenBank. This may indicate that Coxsackieviruses A strains circulating in the countries of Central Asia have their specific genotype.

Our study proved that the spectra of nonpoliomyelitis enteroviruses isolated from children from migrants' families and from resident children were significantly different. In order to prevent the circulation of imported new enterovirus serotypes and genotypes it is necessary to examine systematically the groups at risk, such as children under 5 who arrive in the North-West of Russia from unsafe territories.

3.23

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DYNAMICS OF MORBIDITY OF THE WEST NILE FEVER IN THE ASTRAKHAN REGION

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The variety and wide prevalence of arbovirus infections, the possibility of adverse outcomes determine the relevance of their study. In the territory of the Astrakhan re-

gion the epidemic focus of West Nile Fever is registered. The purpose of this study was to analyze the dynamics of the morbidity of the West Nile Fever in the Astrakhan region from 2014 to 2017. The analysis of "Data on infectious and parasitic diseases" (Form 1) in the Astrakhan region was carried out.

As our research has shown, West Nile Fever in the Astrakhan region is currently characterized by a low intensity of the epidemic process. 5 people in the Astrakhan region were affected by the West Nile Fever in 2014, the morbidity rate per 100 000 of the population was 0.5. The number of cases increased by 3.0 and 4.8 times respectively in 2015 and 2016. 15 people fell ill with West Nile Fever in 2015, and 24 people — in 2016. The mortality rate per 100 000 of the population was equal to 1.5 and 2.4 respectively. It should be noted that the number of people with West Nile Fever in Russian Federation as a whole increased by 1.5 and 4.9 times in 2015 and 2016, compared to 2014. The source of infection in West Nile Fever is mainly wild birds. The increase in the incidence rate in 2015 and 2016 in the Astrakhan region and in Russia may be associated with increased infection of migratory birds during their seasonal migration from the natural foci of West Nile Fever. Only one case of West Nile Fever was registered in the Astrakhan region in 2017, the mortality rate per 100 000 of the population decreased in 24 times compared to the previous year and amounted to 0.1. Children under the age of 14 years were 11.1% of all the patients with this arbovirus infection from 2014 to 2017.

Thus, the natural focus of the West Nile Fever remains in the Astrakhan region, which activity depends on both the sources of infection and its vectors influenced by the intensity of the epidemic process in endemic foci, seasonal migration of sources of infection and climatic conditions.

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DETECTION OF PARVOVIRUS INFECTION MARKERS IN RISK GROUPS

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Parvovirus infection (PVI) caused by Parvovirus B19 (B19V) is transmitted by airborne, parenteral and vertical routes. The virus affects the precursor cells of erythrocytes. PVI can cause serious complications, up to a lethal outcome, in people at risk who are hematological patients, patients with immunosuppression, people requiring blood derived product etc. Despite the high prevalence data on the incidence of B19V in people at risk and the clinical manifestations of the disease is not enough.

The aim of the study was to investigate the frequency of occurrence of B19V markers and the effect of PVI on the clinical course and the outcome of initial disease in patients with hematologic profile — malaria patients, children after hematopoietic stem cell transplantation (allo-HSCT).

Plasma/serum samples of malaria patients (n = 316) and patients who underwent allo-HSCT (n = 54) at the age of 0.6–19 years were examined for the presence of B19V DNA by PCR and IgG-antibodies to B19V by ELISA method.

In patients with co-infection with B19V and *P. falciparum*, the rates of complications and mortality were significantly higher: observed in $72.7 \pm 2.7\%$ of cases compared to $37.9 \pm 3.0\%$ in the group of malaria patients without PVI. Moreover the disease led to death in 6 ($10.9 \pm 4.4\%$) cases within the first group and in 2 ($0.8 \pm 0.5\%$) cases in the second group. Most of cases of complicated malaria with PVI-coinfection falls on patients under 5 years. Important that 6 out of 8 deaths occur in the same group, that is significantly higher than in the absence of PVI.

In patients with allo-HSCT, a high incidence of detecting PVI markers in plasma was demonstrated. IgG antibodies to B19V were detected in 68.5–80.4% of cases, which is 2 times higher than among healthy population of the same age. Non-zero viral load values were observed in 28–30.4% of cases. The B19V DNA detection in the blood by the 30th day was associated with febrile neutropenia in these terms in 100% of cases versus 68% in patients with no DNA.

Parvovirus infection B19V is widespread in people at risk and can cause a complicated course of the underlying disease.

3.25

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CYTOKINE PROFILE IN ADULTS WITH RESPIRATORY SYNCYTIAL VIRAL INFECTION

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Respiratory syncytial viral (RSV) infection often has a complicated course. Studies show the possibility of viral persistence which leads to chronic bronchitis and asthma. It is extremely important to predict development of complications in patients with this infection, especially in risk groups: HIV-infected, hematological patients and elderly people.

48 patients with RSV infection aged 15 to 59 years were enrolled in the study. The diagnosis was confirmed by immunofluorescence or immunochromatography. All patients underwent interferon and cytokine status studies with determination of serum IFN α , IFN γ , IL-1, IL-2, IL-4, IL-5, IL-6, IL-12, TNF α .

Cytokine status of patients with RSV infection reflects high pathogenic role of pro-inflammatory cytokines and predominance of cytokine profile of the humoral immune response. Anti-inflammatory cytokine IL-4 and pro-inflammatory IL-1 have been shown to be the most important in the course of a complicated RSV infection. From the second week of the illness, a significant increase in the levels of IL-4 and IL-1 in the serum indicates a favorable trend in the development of the infection.

The progression of bronchitis is indicated by the growth of the cytokine coefficient (IL-1/IL-4) in the second week of the disease (above 0.5). The increase in IL-5 levels above 50 pg/ml after first 3 days of the illness indicates development of acute tonsillitis as a complication. During the first days of the disease high levels of IL-12 (more than 2000 pg/ml) indicate a higher possibility of tonsillitis and bronchitis. While after the 9th day it accompanies resolution of pneumonia. The level of induced production of IL-6 by leukocytes above 20 000 pg/ml in the first 3 days of the illness indicates risk of complications, and its growth in the second-third week coincides with the onset of recovery in pneumonia.

Cytokine levels in blood serum of patients with RSV infection have significant deviations. In the first days of the disease, a high level of induced IL-12 and IL-6, an increase in the level of IL-5 indicate a high risk of complications. From the 10th day of the illness, high values of induced IL-12 and IL-6, serum IL-4 and IL-1, as well as a decrease in IL-5 values, indicate the onset of the recovery. Imbalance of the cytokine profile in RSV infection has an important pathogenetic and prognostic value in the development of complicated forms of the disease.

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SURVEILLANCE OF POLIOMYELITIS AND ACUTE FLACCID PARALYSIS IN THE SOUTH OF THE RUSSIAN FEDERATION IN 2013–2017

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The main indicators of sensitive surveillance of poliomyelitis and acute flaccid paralysis (AFP) on the administrative territories of the South of Russia which are under responsibility of Stavropol Regional Center for epidemiological surveillance of poliomyelitis and acute flaccid paralysis in 2013–2017 corresponded to the recommended level. The morbidity index for AFP among children under 15 were 1.6–2.2 for 100 000 of these children. The predominant diagnosis among AFP cases (71.4%) was polyneuropathy. The percentage of AFP cases with two stool samples was 100%, the percentage of samples examined not later than 14 days after onset of paralysis was 97.9%. The samples of good quality constituted 96.1%, they arrived at the laboratory during 72 hours in 97.9% of cases. The virological investigation showed that from 313 patients we isolated 12 polioviruses (3.8%) and 13 nonpoliomyelitis enteroviruses (4.2%). Half of polioviruses belonged to type 3, the 3 mixed samples contained polioviruses of type 2 and type 3, polioviruses of type 1 were isolated from two samples and poliovirus type 2 from one sample (in 2013–2014). Enteroviruses were represented in 30.7% by enterovirus 71, 15.4% of viruses belonged to Coxsackieviruses B1–6, 7.7% to Coxsackievirus A4, Echoviruses 3 and 29, 30% of enteroviruses were not identified. In order to search wild polioviruses on the territories which did not reach the appropriate number of revealed AFP we investigated 310 samples from healthy children under 5 and confirmed the absence of wild polioviruses. In the frame of supplementary surveillance 1625 samples from groups at risk were examined, vaccine derived or wild polioviruses were not found. The percentage of poliovirus and enterovirus detection varied during the years from 3.6% till 6.8%. Vaccine polioviruses of three types were isolated in 1.7% of cases and the majority of them (53.6%) belonged to type 3. Nearly half of isolated enteroviruses were represented by Coxsackieviruses B1–6 (49%), Coxsackieviruses A constituted 7.5%, Echoviruses were detected in certain cases and nearly 40% of enteroviruses were not identified.

The system of sensitive epidemiological surveillance combined with good quality virological surveillance allowed to confirm polio free status of the territories in the South of Russia.