

it causes a range of illnesses from hand-foot-and-mouth disease (HFMD) to severe neurological manifestations. EV-A71 strains have been phylogenetically classified into genogroups: A to G. Whereas canonical genogroups B and C have been reported worldwide, new genogroups E and F were recently identified in Africa and Madagascar, respectively. The recent identification of the new Genogroups E and F raised the question of their cross-antigenicity and immunogenicity with the canonical ones.

We compared antigenic and immunogenic features of EV-A71 strains, which belong to the canonical (B-C) and the new (E-F) genogroups. The level of cross-protection induced by a given EV-A71 genogroup against viruses of other genogroups was estimated using a seroneutralization assay with human and rabbit *sera*, as well as a mouse monoclonal antibody.

Neutralization assays performed with diverse standardized human, rabbit, and mouse anti-EV-A71 sera or antibodies successfully neutralized all available isolates indicating a broad overall cross-antigenicity between the canonical genogroups B and C and the newly described genogroup E and F. By using collections of human sera from Cambodian patients with neutralizing antibodies against EV-A71 genogroup C, we evaluated the epidemiological risk of a population affected by a canonical EV-A71 genogroup from being protected against the new genogroups E and F. All human *sera* showed rather similar cross-neutralization activities between isolates of genogroups B, C, E and F.

Taken together, our results indicate that the antigenic features of all tested genogroups are quite similar among the serotype EV-A71. They also suggest that the neutralizing antibody response induced by strains of the canonical genogroups B and C is likely to be protective against the new genogroups E and F. Our findings provides valuable informations in terms of public health and EV-A71 vaccine development.

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#### CLINICAL-LABORATORY CHARACTERISTICS OF INFLUENZA INFECTION IN HOSPITALIZED ADULT PATIENTS IN THE EPIDEMIC SEASON 2017–2018

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Despite advances in the field of modern influenza vaccination and antiviral therapy, influenza and acute respiratory infections remain the most common diseases. The annual incidence is 19–20 thousand per 100 000 and the economic loss of about 90% of the losses from all infectious diseases. The death rate from influenza in the world is 0.01–0.2%, increasing in children under 2 years and those over 65 years of age, as well as in the development of pneumonia, as complications. We conducted a clinical and laboratory analysis of cases of influenza infection in the epidemic season 2017/18 in adult patients hospitalized in the Botkin Clinical Infectious Diseases Hospital. 423 medical charts were reviewed, with confirmed influenza infection by PCR. The analysis of the obtained results was carried out using the statistical package SPSS 17.0RU for Windows. The etiological composition was presented by influenza A viruses — 56%, 25% of them H1N1, H3N2 — 64%, undifferentiated influenza A viruses — 9%, influenza A+B — 2%, and influenza B viruses — 44%, 85% of them Yamagata, Victoria — 0.7% and 14.3% undifferentiated influenza B. At admission to the hospital, the condition of most patients was regarded

as of moderate severity. More than 50% of patients were hospitalized before the 3<sup>rd</sup> day of illness. Among those admitted to the hospital 51.2% were men and 48.8% were women. The median age was 30.5 years. Comorbidity diseases were absent in most patients (65%). All patients received standard pathogenetic therapy. The clinical pattern was characterized by a marked intoxication syndrome, the median temperature of the body was 39.0 degrees. The duration of the intoxication syndrome was 5.6±0.4 days, and catarrhal syndrome was 8.1±0.5 days. 50% of the patients had complications: 12.5% of them — pneumonia, 12.5% — sinusitis and 18.3% — bronchitis. Duration of the hospitalization was 6.3±0.6 days. There were no lethal cases among the observed patients. In conclusion, it should be noted that influenza A viruses prevailed in the observed patients (56%), and among viruses influenza A-H3N2 (63%), among viruses of influenza B — Yamagata type viruses (85%). Hospitalization was in the early days. The clinical pattern was characterized by severe intoxication and catarrhal syndrome, frequent complications, including pneumonia (12.5%).

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#### VACCINE PROPHYLAXIS, DIAGNOSTICS AND GENOTYPES OF MUMPS (EPIDEMIC PAROTITIS) VIRUS

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Epidemic parotitis (EP, mumps) is an acute anthroponotic viral infection. Mumps virus is single-strand negative RNA genome virus. Its genome contains 7 genes encoding 5 internal proteins (P, L, M, V, I), the transmembrane protein SH and 2 surface proteins — hemagglutinin/neuraminidase (HN) and fusion protein F. It is important to emphasize that only antibodies to proteins F and HN have neutralizing activity.

Vaccination against mumps was introduced in the Russian Federation in 1981, that highly affected morbidity. Indeed, in 1970–1980 in Russia, 300 to 600 thousand cases of mumps were registered annually, while in 2015 as little as 127 cases were detected. The mass rejection of vaccinations in Western European countries affected the incidence of mumps in Russia. In 2017, 4443 people became ill. Among them, children under 14 were prevailed, although there were a lot of adults as well. Mumps is a serious viral disease; in 30–40% of cases it may be asymptomatic. It leads to the development of orchitis in 25% of diseased boys. The risk of miscarriage in mumps-infected is higher than even at rubella. For verification of mumps diagnosis in the Russian Federation mainly ELISA (domestic and foreign test systems) are used. However, a study of the blood of patients for the presence of specific antibodies of the IgG or IgM class is not enough either to establish the fact of active replication of EP, or to confirm both manifest and asymptomatic forms of the disease.

At present, there are 12 genotypes of the EP virus circulating in the world: A, B, C, D, E, F, G, H, I, J, K, L and Leningrad-3 (L-3), which has been assigned to a special group. The contagiousness of patients with mumps is not high, but the susceptibility is universal, it reaches 100% and lasts for a lifetime. Mumps outbreaks are recorded in populations with both high and low vaccine coverage.

Today in the world, more than 120 countries have introduced immunization schedules against mumps in their vaccination calendars, and in 72 countries they are absent. Advances in vaccine prevention are undoubtful. Over 37 years, 215 million people have been vaccinated in the

Russian Federation, 2500 lives have been saved, 2.5 million cases of serous meningitis have been prevented, tens of thousands of cases of orchitis (the probability of male infertility), pancreatitis, and diabetes have been prevented.

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### INFLUENCE OF THE NEWCASTLE DISEASE VIRUS ON SOME INDICES OF CELL-MEDIATED IMMUNITY IN TUMOR-BEARING RATS

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The use of oncolytic viruses for biotherapy of tumors is a promising approach. It is assumed that the administration of some kinds of viruses into the tumor-bearing organism induces both direct and indirect antitumor effect. The potential use of Newcastle disease virus (NDV) in this field attracts attention of the researchers.

Our aim was to study the effect of the administration of NDV vaccine strain on some indices of cell-mediated immunity in rats after transplantation of carcinoma.

The experiment was performed on 19 white mongrel male rats with Guerin's carcinoma. The NDV vaccine strain La-Sota was inoculated once 5000 doses paratumorally 2 times a week, 4 times in total: in the first group of rats the course of NDV was started after tumor transplantation, in the second group — one week before tumor transplantation. Tumor growth was observed and lymphocytes' subsets were counted in peripheral blood samples collected from the femoral vein of animals in the dynamics of the course of NDV administration. The per cent of T- and B-lymphocytes were estimated by flow cytometer BD CantoII. The results showed stimulating effect of the NDV on the T-cell link of rats' immune system and made it possible to establish differences in the type of the immunological changes developing in tumor-bearing rats, depending on the time of administration of the virus relative to the time of tumor transplantation and their possible significance for obtaining a prophylactic effect on transplanted tumors in some animals. So the administration of NDV previous to tumor transplantation caused a marked increase of CD3<sup>+</sup>CD25<sup>+</sup> (T cells expressing an early activation marker) and CD3<sup>+</sup>CD4<sup>+</sup> lymphocytes' levels which persisted after tumor transplantation while the levels of CD3<sup>+</sup>CD8<sup>+</sup> and CD3<sup>+</sup>RT1b (T cells expressing a late activation marker) cells were decreased. This was the only group where in some rats tumor formation after transplantation was not observed or early regression was detected. On the contrary, in the control animals the highest CD3<sup>+</sup>CD8<sup>+</sup> and the lowest CD3<sup>+</sup>CD25<sup>+</sup> cells' levels were observed during the whole period. Administration of NDV to the rats of the first group after tumor transplantation produced effect neither on tumor growth nor on potentially antitumor factors of cell-mediated immunity. Thus we consider that if NDV is able to induce any antitumor effect it should be used before tumor transplantation; activation of Th cells should be achieved.

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### THE EFFECT OF PARVOVIRUS B19 INFECTION ON RESULTS OF CHEMOTHERAPY IN PATIENTS WITH LYMPHOMA

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Parvovirus B19 infection (B19V) can cause severe complications in patients with hematological malignancies which explains the importance of understanding

the influence of B19V on the results of chemotherapy (CT). The purpose of the study was to reveal the prevalence of B19V in patients with lymphomas and the influence of B19V on the CT results.

The study included 41 patients aged 48.9±2.3 years: 12 patients with Hodgkin's lymphoma (HL) and 29 with Non-Hodgkin's lymphoma (NHL) (21 aggressive, 8 indolent). Patients received CT according to the tumor immunophenotype. B19V DNA was determined in plasma and in bone marrow (BM) by qPCR, B19V IgM and IgG in the serum by ELISA.

78.0% of patients had B19V IgG, mean concentration was 158.1±12.9 U/mL. B19V DNA in plasma was detected in 7.3%, in BM in 48.8%. Viral load in plasma was 68.7±35.8 IU/mL, in BM — 438 240.0±281 316.8 IU/mL. Seroprevalence and the mean concentration of B19V IgG was higher in NHL than in HL (79.3% vs 75.0% and 161.4±16.3 vs 153.6±20.5, p>0.05). In NHL, the number of seropositive patients and the mean level of B19V IgG were higher in aggressive than in indolent tumors (81% vs 75% and 177.9±19.3 U/mL vs 114.4±22.8 U/mL, p = 0.052). B19V IgM were not found. B19V DNA in plasma was found only in NHL patients (10.3%). The frequency of B19V DNA detection in plasma was higher in indolent (12.5%) than in aggressive lymphomas (9.5%), while DNA concentration was higher in aggressive lymphomas (102.5±20.5 IU/mL vs 1.0±0.0 IU/mL, p > 0.05). B19V DNA detection frequency in BM was similar in HL (50.0%) and NHL (48.3%, p>0.05), but the mean B19V DNA concentration was higher in NHL than in HL: 624 496.9±395 398.3 IU/mL vs 3640.5±1649.2 IU/mL, p > 0.05. In NHL, B19V DNA in BM was more frequent in indolent than in aggressive lymphomas (50.0% vs 47.6%), and the average concentration was higher in aggressive lymphomas (865 689.2±541 738.6 IU/mL vs 21 516.3±19 352.8 IU/mL, p > 0.05). Complete remission was observed in 68.3% of patients, partial remission 17.0%, stabilization 4.8%, progression 9.9%. CT results depended neither on serostatus and B19V IgG concentration nor on B19V DNA presence in BM or plasma (p > 0.05).

All parameters of the viral infection (B19V IgG, DNA) were higher in NHL than in HL (p > 0.05). The mean concentration of B19V IgG was higher in aggressive NHLs than in indolent ones (p = 0.052). B19V infection did not influence results of antitumor CT (p > 0.05).

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### ASSOCIATION BETWEEN HERPES VIRUS INFECTION AND INDICATORS OF OXIDATIVE STATUS OF TUMOR TISSUE IN GASTRIC CANCER

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Viral infection and oxidative stress are recognized as aggravating factors contributing to the neoplastic tissue transformation. Our purpose was to determine the influence of viral infections of tissues on the processes of the free radical oxidation in stomach cancer (SC).

We studied tumor tissues (TT) and intact tissues from the resection line (IT) obtained from 25 SC patients (mean age 62.8±2.1 years). DNA of CMV, EBV and HHV6 was determined by qPCR. Levels of malondialdehyde (MDA) were measured to assess the intensity of the oxidative stress; the function of the antioxidant component was evaluated by catalase, superoxide dismutase and glutathione peroxidase activities and levels of reduced glutathione.