

The specificity of examined sandwich-ELISA variants was high, the sensitivity widely varied. The best result (7 ng/ml of purified AV 6 type) was obtained with capture MAbs #1 and PX conjugate of these MAbs. For AV antigens detection in infected cell the most promising is MAbs #2 FITC conjugate that allows to detect AV of epidemic types in infected cells in form of nuclear localized clear fluorescence. Usage of MAbs for development of high sensitivity and specificity test-kits for differential diagnosis of AV infection provides new possibilities for medical practice. Diagnostic properties of developed sandwich-ELISA and MAbs #2 FITC conjugate will be investigated with clinical samples.

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### THE ROLE OF MOLECULAR-GENETIC RESEARCH IN THE SYSTEM OF EPIDEMIOLOGICAL SURVEILLANCE OVER ENTEROVIRUS INFECTION IN THE RUSSIAN FAR EAST AND SIBERIA

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A seasonal peak of enterovirus (EV) incidence is typical for majority of the constituent entities of the Russian Far East and Siberia. The spectrum of identified EV is diverse. Genetic variability of EV leads to emergence of new sub-subtypes.

The goal of the research was to evaluate the role of genotyping and phylogenetic analysis in epidemiological surveillance over enterovirus infection (EVI).

Epidemiological analysis was performed based on the official reporting forms. A total number of 1474 environmental samples, biomaterial from patients with EVI and exposed persons were analyzed via molecular-genetic methods. Reconstruction of genetic affinity was performed using Bayesian modeling.

Circulation of Russian and foreign EV strains was registered in the Russian Far East and Siberia. The most epidemiologically significant strains were as follows — Coxsackie B-4, B-5, ECHO-6, 9, 30. During the last four years Coxsackie A, mostly Coxsackie A-6 was also identified. The breakouts of Coxsackie A-6-infection were registered in children's ensembles in the Amur, Sakhalin and Khabarovsk Regions. Most EV had a genetic relation to reference sequences obtained from the GenBank database. This indicates the possibility of importation of EVI from different countries. Epidemiological investigations confirmed that some cases were imported. That said, during the summer season of 2017 EVI was diagnosed in patients arrived from resorts located in Turkey, Vietnam and Tunisia. The diseases were caused by Coxsackie A-6, Coxsackie A-2, EV-A71C1 variants as well as EV-C104 that was never registered in Russia before.

Molecular-genetic research not only promotes the enhancement of diagnostic subsystem of epidemiological surveillance, but also improves evaluation of epidemiological situation in the constituent entities of the country, facilitates identification of territorial peculiarities of genetically isolated and epidemiologically significant EV variants circulation, helps to identify imported cases of EVI.

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### CONTROL OF INFLUENZA VIA VACCINES: CHALLENGES AND PERSPECTIVES AS VIEWED BY VARIOUS STAKEHOLDERS

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Influenza remains one of the principal challenges of modern healthcare on a global scale. Despite vaccination efforts, morbidity and mortality — especially among high-risk groups during seasonal epidemics — are high. Each year more emerging and re-emerging strains of animal origin are designated as having pandemic potential. Vaccines are the cornerstone of influenza control, including mitigation of yearly epidemics and out-of-season outbreaks, as well as prepandemic preparedness. Challenges, however, still remain, and here we explore varying views of different stakeholders (international agencies, regulators and manufacturers) as one of the reasons why.

Influenza virus is constantly evolving, thus, recommended strains for seasonal vaccines are regularly updated. Current WHO position includes 3- and 4-valent vaccines; and a nominal 25% increase in manufacturing capacities is needed for the switch to the latter. Moreover, even a single change in strain recommendation would require manufacturers to develop a new process within 6 months at most, and strain yield and HA activity for the candidate virus may be lower than had been anticipated. Separate WHO recommendations for tropical countries (similarly to northern and southern hemispheres) are still highly debatable. Until then local authorities at the country level should make the decision; however, current-season vaccines may already (or yet) be unavailable.

Though effectiveness, safety and economical feasibility for influenza vaccines has been proved numerous times, manufacturing capacities worldwide are still lacking. Current technology is classic at best and utilizes chicken embryos, whereas promising approaches (e.g. cell cultures) would require overhauling of the whole monitoring (e.g. GISRS) and manufacturing system. Academia could generate a breakthrough (e.g. next generation vaccines), but the transition from a prototype even to a preclinical setting is a very high-risk and money-intensive endeavor. Similarly, since there is no guaranteed market for prepandemic influenza vaccines, except periodic stockpiling by international or national bodies, R&D activities in this area for manufacturers are not a priority. Finally, we have lately seen a surge of support for the anti-vaccination movement.

Thus, combined efforts of all stakeholders are urgently needed to advance control of influenza via vaccines to the next stage and as part of the universal health coverage paradigm.

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### CROSS-ANTIGENIC AND IMMUNOGENIC FEATURES OF CANONICAL AND NEW GENOGROUPS OF ENTEROVIRUS 71

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Enterovirus 71 (EV-A71) is a member of the *Enterovirus A* species. EV-A71 is a leading public health problem, because

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