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RISK FACTORS FOR SARI AND INFLUENZA VACCINE EFFECTIVENESS IN SENTINEL SURVEILLANCE SYSTEM IN RUSSIA, THE SEASON 2017–2018E.A. Smorodintseva¹, A.A. Sominina¹, K.A. Stolyarov¹, A.A. Melnikova², E.B. Ezhlova²¹Smorodintsev Research Institute of Influenza, St. Petersburg, Russia; ²Federal Service for Surveillance on Consumer Rights Protection and Human Well-Being, Moscow, Russia

The influenza sentinel surveillance system (ISS) in Russia includes 19 hospitals and 14 polyclinics located in Kaliningrad, St. Petersburg, Lipetsk, Moscow, Samara, Stavropol, Novosibirsk, Chita, Khabarovsk, Vladivostok. The standard definitions for SARI, ILI and ARI (according to WHO case definition) and case-based reporting were used in the study. The on-line data submission into the electronic database of the Smorodintsev Research Institute of Influenza from each Sentinel Site (SS) at the FBUZ Centers for Epidemiology and Hygiene was conducted on a weekly basis. Case-based form for each patient included the data on age, sex, date of disease onset, sampling for PCR, co-morbidity, ICU placement, the status of vaccination, treatment by antivirals, results the PCR detection of influenza viruses and other 7 respiratory viruses, outcome of the disease. Laboratory confirmed influenza (LCI) was registered in average in 20.8% of patients with SARI and in 16.3% of ILI/ARI patients. Severity of the clinical course of SARI determined as the proportion of SARI patients placed in the Intensive Care Unit of total SARI cases was estimated as 7.6%, LCI SARI cases as 2.3%. Influenza A(H3N2) virus caused 51.0% of SARI cases, influenza B (Yamagata lineage) and A(H1N1) pdm09 viruses were determined in 33.3 and 15.8%, respectively. The general trend of greater significance of LCI among SARI compared to the ILI/ARI was confirmed this season. Among 400 SARI patients with LCI only 17 (4.25%) patients were vaccinated. Among 320 LCI outpatients with ILI/ARI 22 (6.9%) patients were vaccinated. The effectiveness of vaccination assessed by the case-control method was estimated as 11% in prevention of admission with LCI SARI cases and 58% in prevention of LCI ILI/ARI cases. The concomitant somatic pathology and pregnancy were identified in 57.5% of SARI patients with LCI. This indicator was significantly higher (by 23.1%) in LCI SARI than in SARI caused by other respiratory pathogens. The leading role of pregnancy as a risk factor for hospitalization with LCI SARI (27.3% of SARI patients with influenza against 5.7% of SARI patients with other etiology) was confirmed in this season. In addition, significant increase ($p < 0.05$) of percentage of LCI SARI with cardiovascular diseases (16.5%) and diabetes (5.5%) compared to patients with SARI of other etiology (11.7 and 2.8% respectively) was established, and these patients' categories were assigned to the risk groups.

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RESULTS OF MOLECULAR DETECTION AND CHARACTERIZATION OF INFLUENZA AND OTHER RESPIRATORY VIRUSES IN RUSSIA, SEASON 2017–2018A.A. Sominina¹, D.M. Danilenko¹, A.B. Komissarov¹, A.V. Fadeev¹, M.M. Pisareva¹, K.A. Stolyarov¹, L.S. Karpova¹, E.I. Burtseva², A.V. Vasin¹¹Smorodintsev Research Institute of Influenza, St. Petersburg, Russia; ²N.F. Gamaleya FRC Epidemiology and Microbiology, Moscow, Russia

The influenza season 2017–2018 started significantly later than any of the seasons analyzed in the last five years. The epidemic lasted for 12 weeks (weeks 6–17), was of me-

dium intensity and involved 10.4% of the population of the country with children aged 3–6 years being the most affected group. The average hospitalization rate of patients with ILI and ARI was 2.6% and was the highest in infants aged 0–2 years (5.4%). The number of influenza-associated deaths was two times higher this season compared to 2016–2017 which can be attributed to the circulation of A(H1N1) pdm09 viruses that still is the major cause of lethal influenza outcomes in the country. A total 72 759 patients were investigated by RT-PCR in 55 collaborating RBLs and 12 149 (20.7%) were positive for influenza, of which 39.3% were influenza A(H1N1)pdm09 viruses, 29.6% were A(H3N2) and 31.1% influenza B (Yamagata lineage) viruses. The first cases of influenza viruses were detected at the very beginning of the season (weeks 40–45.2017), however a distinct increase in the rate of detection was registered only from the week 2.2018 with the peak on the week 13–14.2018 and subsequent gradual decline. The certain differences in the etiology of morbidity between Federal Districts were registered. The impact of influenza and other ARI agents in different stage of, epidemic was determined. In the pre-epidemic period, the incidence growth was occurred mainly due to ARI (about 32.7%), especially due to rhinoviruses (RhV) and RSV(10.2 and 8.0% cases, respectively) while LCI were registered in 3.4% only. During the epidemic, the rate of laboratory confirmed influenza cases (LCI) detection increased up to 29.2% at simultaneous decrease in frequency of parainfluenza, adenovirus, bocavirus, coronavirus and, especially, RhV, to a lesser extent RSV infection. In the post-epidemic period, the role of influenza A(H1N1)pdm09, A(H3N2) and B viruses dropped up to 6.1; 6.9 and 3.6%, respectively, with increase of RhV (9.5% of diseases). Genetic analysis of influenza A(H1N1)pdm09 and A (H3N2) viruses circulating in 2017–2018 season showed that all analyzed viruses by the structure of surface genes encoding antigenic determinants corresponded to the vaccine strains recommended by WHO for the Northern Hemisphere for 2017–2018 epidemic season. However, significant changes in the internal genes of circulating viruses were revealed.

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PROSPECTS FOR MONOCLONAL ANTIBODIES USING IN DIFFERENTIAL DIAGNOSIS OF ADENOVIRUS INFECTION

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More than 50 types of adenoviruses (AV) cause human diseases. There are serological evidences that more than 80% of population suffer from AV infection. The variety of clinical manifestations of AV infection complicates its differential diagnosis. Currently polyclonal sera are widely used for these purposes in Russia. The development of highly sensitive and specific enzyme-linked immunosorbent (ELISA) and immunofluorescence (IF) tests with using monoclonal antibodies (MAbs) is an urgent task.

Highly sensitive and specific MAbs #1 and #2 were obtained at the laboratory of biotechnology. MAbs were conjugated with horseradish peroxidase (PX) and fluorescein isothiocyanate (FITC). Sensitivity and specificity of various combinations of MAb #1 or #2 and its PX conjugates for detection of purified AB type 6 was examined by sandwich-ELISA. The ability of FITC conjugates to detect AV 3, 4, 6 types in infected A549 cells was examined by IF. Respiratory syncytial virus was used as negative control.

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