

LAIVs were attenuated for mice. These data indicate that the 4M2e insertion did not affect LAIV virus replication characteristics. The expression of M2e epitopes by the recombinant viruses was confirmed by ELISA with M2e-specific antibody 14C2 (ab5416). The results of immunogenicity and cross-protective efficacy of the new LAIV-4M2e viruses will be presented.

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CIRCULATION OF COXSACKIEVIRUS A IN HAND-FOOT-MOUTH DISEASE IN SOUTHERN VIETNAM, 2015–2016

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Hand, food and mouth disease (HFMD), a common contagious disease that usually affects children, is normally mild but can have life-threatening manifestation. It can be caused by enteroviruses, particularly Coxsackieviruses (CA) and human enterovirus 71 (EV71) with highly variable clinical manifestation.

In 2011–2014, EV71 and CA16 were responsible for the HFMD outbreak in South Vietnam. However, CA6 and CA 10 were observed increased dramatically from 2015–2017. In 3 years, 1488 cases were detected positive for enterovirus from 3277 HFMD cases, the results are the more frequently presented serotypes as 908 EV-71 (61%) and 580 other EV none EV71 (39%).

The HFMD cases which were detected as other EV positive, had been sequenced and serotyped with results: CA6 (196.34%), CA10 (75.13%), CA16 (146.25%) and CA2.4, 5.8, 9; CB3.4, 5; ECHO6.9, 11.16, 25.30... (163, 28%).

Furthermore, serotype of CA 6, CA 10 replacement every year.

CA10 increased in 2016 and the presence of CA10 were 68% (69/102) in the group of Enterovirus non EV71. Our study demonstrates variety of enterovirus genotypes as viral pathogens in causing HFMD in Southern Vietnam. CA10 and CA6 were co-circulating together with EV-71 and CV-A16 in recent years.

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EPIDEMIOLOGY OF ADENOVIRAL INFECTION IN ST. PETERSBURG

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The modern methods of laboratory diagnostic for different virus significantly expanded etiological spectrum of acute gastroenteritis. Along with wide spread rota- and noroviral gastroenteritis, a large amount of cases with adenoviral etiology is registered. According to the published data, the adenoviral acute intestinal infections constitute from 1 till 15% of all diarrheal diseases and depends on the region.

The purpose of this study was to find the prevalence of adenoviral acute intestinal diseases in St. Petersburg, to estimate the significance of this problem, find the risk groups and other epidemiological features.

We used the official data from St. Petersburg center for registration of infectious and parasitic diseases in 2016–2017. Epidemiological investigation of 344 cases of adenoviral infection was performed by standard contact investigation. Molecular diagnostics was performed using PCR based tests.

The incidence level of adenoviral infection in St. Petersburg in 2016 was 4.1 per 100 000; in 2017 — 2.4 per 100 000. Adenoviral infection was registered in 90.0% in hospital patients, because of using high technology laboratory methods. Findings among outpatients were rare and were only in depth examination. From 2016–2017 adenoviral infection was found in 34 (9.8%) outpatients only. Adenoviral gastroenteritis was registered in all districts of our city, in 2016 more frequently in Viborgsky, Central and Primorsky districts of St. Petersburg; in 2017 more frequently in Kalininsky, Primorsky and Krasnogvardeisky districts. All the patients with this infection were recovered.

Monthly trend showed autumn-winter seasonality, in summer the incidence decreased. Analysis of the age structure of adenoviral infection showed that 60% cases were in the age group from 0 to 14 years. In children from 0 to 2 years old — 30% cases were registered, from 3 to 6 — 24.4%. The incidence level in the age group from 0 to 2 was 24.1 per 100 000 in 2017 (6 times increase from common level of this infection); in children from 3 to 6–18 per 100 000 (4 times increase from common level of this infection). We found the same tendency in 2016. Adenoviral infection is also registered among people of active age (in the age group 20–29 we found 12.9% cases; 30–39 — 7.1); in the elderly patients we found decreasing trend. It was only 3.2% cases of adenoviral infection in patients after 60. Diagnostic investigations on the etiology of acute intestinal infections were organized on different agents simultaneously. So 38% cases in this investigation were with associations of adenovirus with over etiologic viral and bacterial agents. Viral-viral associations were in 54% of all mixed cases. More frequently associative epidemic foci were forming with adenovirus and rotavirus (32%); adenovirus and norovirus (16%); with over viruses — 6% cases. The part of viral-bacterial associations in the adenoviral foci was 43% (33 cases). Among bacterial agents adenovirus more frequently associated with *Escherichia*, *Campylobacter*, opportunistic flora, rarely with *Klebsiella* and *Yersinia* associations with 3 etiologic agents was found in 4% cases. Two patients had adeno-, roto- and norovirus at the same time. We also found epidemic foci with mixed adenovirus, rotavirus and campylobacter infections. All mixed cases were found in hospital patients. Mixed infections had more serious clinic without specific clinical manifestation, and additional laboratory methods were required for identification.

This investigation showed significance of the problem of adenoviral infection in St. Petersburg; children from 0 to 2 years old were found to be a risk group for this disease. Autumn-winter seasonality was found. Epidemiological specific feature of adenoviral infection is forming mixed foci with other (viral and/or bacterial) etiologic agents in 38% cases.

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CHALLENGES FOR POLIO ERADICATION. RISK OF RE-EMERGENCY OF INFECTION IN POLIO FREE COUNTRIES

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The risk of importation of wild polioviruses (WPV) into polio-free countries remains till poliomyelitis is eradicated. Other risks of Polio Eradication Initiative are: circulating vaccine-derived polioviruses (VDPV) with nucleotide substitutions and recombinant profile; appearance of vaccine associated paralytic poliomyelitis (VAPP) and escape of polioviruses from polio vaccines.

Wild type 1 poliovirus, the causative agent of poliomyelitis outbreak in Tajikistan where vaccine coverage dramatically decreased, was imported into Russia and was isolated from poliomyelitis cases and healthy migrants' from Tajikistan. We isolated WPV1 from three children who arrived in Russia from Tajikistan. The percentage of migrants' children who were seronegative to three types of poliovirus was 30 times higher than it was among resident Russian children. We isolated twice as many polioviruses from healthy migrants' children as from patients with acute flaccid paralysis in Russia.

The transmission of pathogenic revertant type 2 poliovirus from the unvaccinated paralytic patient to four healthy contacts in a hospital illustrated the emergence of VDPV with increased transmissibility. The vaccine-derived poliovirus of type 3 which displayed 1.1% nucleotide substitutions in the genomic region VP1 was isolated from a patient with VAPP who received two doses of oral polio vaccine (OPV). Another VAPP patient excreted polioviruses of types 1 and 2 after vaccination with OPV. A month later he stopped to excrete poliovirus of type 2, but he continued to excrete poliovirus of type 1 for more than 4 months. We also revealed the excretion of vaccine poliovirus of type 2 from VAPP patient till 105th day after receiving four doses of oral polio vaccine. Vaccine poliovirus of type 3 was detected in the sample of unvaccinated 11-week-old patient with VAPP. We isolated the same poliovirus from the patient's sister who received 3 doses of inactivated polio vaccine and had high antibodies titers to polioviruses. She was the only possible source of poliovirus for the VAPP patient.

These data illustrate how poliovirus can persist in the population and confirm the possibility of limited spread of VDPV among well-immunized population. Reemergence of poliomyelitis can compromise Polio Eradication Initiative. It is indispensable to continue accurate surveillance and maintain polio free status of Russia as well as of other polio free countries.

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ROLE OF DIFFERENT TYPES OF ENTEROVIRUSES IN ETIOLOGY OF INFECTION ON CERTAIN TERRITORIES OF RUSSIA

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Epidemic peaks of enterovirus infection with the prevalence of different clinical forms of infection depend on different etiological factors. Outbreaks of hand, foot and mouth disease registered in the North-West of Russia in 2011–2012 were connected with Coxsackievirus A16 not detected previously in the region. The identification of two genetic variants closely related to strains isolated in France in 2010 and in Japan in 2011 suggested that Coxsackieviruses A16 implicated in these outbreaks had been brought to the North-West of Russia by two importation events. Echovirus 30 lineage which largely circulated in Russia in 2013 and caused outbreaks of meningitis in the North-West of Russia belonged to genotype H new for the region. Viruses implicated in outbreaks were closely related to the strains of genotype H detected in China in 2010–2013. Since earlier we detected in the country only Echovirus 30 of genotype Ec2 it is likely that Echovirus 30 of genotype H was imported into Russia from South-East Asia.

In 2016 Echovirus 30 of different variants of genotype H was implicated in epidemic peaks of enterovirus meningitis in Saratov and Kostroma regions. But a year later in Saratov

region another type of enterovirus provoked a peak of enterovirus meningitis. It was Echovirus 18 which differed from viruses of the same type occasionally circulating in the North-West of Russia. In Murmansk and Leningrad regions in 2016 Coxsackieviruses A6 belonging to different genetic variants were the etiological factor of hand, foot and mouth disease. In Murmansk region and in the Komi Republic the cases of enterovirus infection with exanthema in 2017 were also connected mainly with Coxsackievirus A6. The strains of Coxsackievirus A6 identified in the North-West of Russia belonged to three sub-genotypes of pandemic genotype of Coxsackievirus A6.

Thus we detected Echoviruses 30 and 18 on territories where enterovirus meningitis was the leading form. On territories where enterovirus exanthema dominated the etiological factor of infection was Coxsackievirus A6. Our studies proved that surveillance of enterovirus infection aimed at acquiring new information about circulation of enteroviruses among population on different territories in different years is indispensable for prevention of propagation of enterovirus infection and for limitation of circulation of enteroviruses including the imported new serotypes/genotypes by means of using virological and molecular methods.

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MOLECULAR-GENETIC CHARACTERISTICS OF THE COXSACKIE A10 ENTEROVIRUS THAT WAS CIRCULATING IN THE CONSTITUENT ENTITIES OF THE RUSSIAN FAR EAST

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The 2017 epidemic season of enterovirus infection (EVI) was conditioned by circulation of Coxsackie A10 (CA10) in several constituent entities of the Far Eastern Federal District (FEFD) — the Khabarovsk, Primorsky Territories, Republic Sakha (Yakutia), Jewish Autonomous Region (JAR), Amursk and Magadan Territories. During the previous years the CA10 was identified in individual cases and only in 2016 it was the cause of outbreaks in the Amursk city (the Khabarovsk Territory).

A total number of 90 strains of CA10 were sequenced. A following phylogenetic analysis with the aid of BEAST program software and reference sequences obtained from the GenBank database was executed. A model of molecular clock was used to perform the evolutionary analysis.

Two genetic lines of CA10 (A and B) were circulating in the observed constituent entities of the FEFD. The line A included enteroviruses (EV) isolated in the Republic Sakha (Yakutia) and Khabarovsk Region during 2016 as well as those that circulated in different regions of Russia in 2009–2013 and Europe in 2003–2010. The presented genetic variant was the source of the outbreaks in the Amursk city (the Khabarovsk Territory) registered in 2016. Divergence of the characteristics between Far Eastern and other Russian EV strains most likely took place in 2011 (CI: 2009–2012). The genetic line B was presented by CA10 isolated in the FEFD in 2016–2017. The B-line strains isolated in the FEFD were divided into two clusters. First cluster was presented by the strains that circulated in the Khabarovsk, Primorsk, Magadan Territories and JAR in 2017 as well as those isolated in China in 2015. The most recent common ancestor (MRCA) for EV of the first cluster existed in 2013 (CI: 2012–2015). The second cluster included strains from the Republic Sakha (Yakutia) and Amur region isolated in 2016. However, this CA10 variant did not circulate in the constituent entities of the FEFD in 2017.