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## MEASLES IN YEKATERINBURG: THE HISTORICAL PATH FROM THE PERIOD BEFORE VACCINATION TO THE STAGE OF ELIMINATION OF THE INFECTION

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Measles is still salient due to the reports of its outbreaks in many regions of the world, including in the Russian Federation.

The aim of the study is to characterize the manifestations of the epidemic process of measles in a large industrial center with different strategies of vaccination.

The research is based on statistical reports on the incidence of measles in Yekaterinburg from 1950 to 2016. The manifestations of the epidemic process were analyzed for 6 periods: the period before vaccination (1950–1961), the period of selective immunization (1962–1965), routine vaccination of children under the age of 8 years (1966–1972), prolongation of the age for measles vaccination to 14 years (1973–1986), the revaccination of children and adolescents (1987–2001) and the period of elimination of infection (2002–2016).

In the period before vaccination the mean annual incidence was 1381.7±162.9 ‰, the seasonal rise was in December-May, children prevailed in the structure of cases. The incidence was anti-persistent with the Hurst index (H) 0.472. In the period of selective vaccination, the incidence decreased to 1082.8±189.1 ‰.

During routine vaccination of children under the age of 8 years, the incidence reduced to 219.8±110.8 ‰, with the annual decline rate of –53.0%, the trend stability of the incidence is confirmed by the Hurst index (0.529). The incidence reduced in almost all age groups, seasonality was similar to the previous periods.

While the vaccinated population under the age of 14 years increased, the incidence decreased to 89.9± 39.1 ‰. However, 2 outbreaks (in 1979 and 1984) were reported in this period. The incidence of measles in this period was anti-persistent (H = 0.381).

The revaccination against measles led to a significant decrease in incidence to 5.7±1.6 ‰, offset of seasonal rises to February-May, while cases among adolescents and adults prevailed.

In the period of elimination of infection (2001–2015), the morbidity was sporadic (0.06±0.02 ‰), due to introduction of measles from other regions without spread. In 2016, there was an outbreak of infection in the city with 72 cases.

Thus, in the historical context the strategy of vaccination determined the situation with measles. However, at the stage of elimination of infection, the possibility of outbreaks of measles remains among unvaccinated children and adults, which requires rethinking of evaluation criteria of epidemiologic safety and their constant adjustment.

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## GENERATION AND CHARACTERIZATION OF GENETIC REASSORTANTS BETWEEN POTENTIALLY PANDEMIC VIRUSES (A/H9N2 OR A/H5N8) AND THE A/HONG KONG/1/68/162/35 (H3N2) MASTER DONOR VIRUS

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In this work, reassortants based on potentially pandemic viruses (A/H9N2 or A/H5N8) and the A/Hong Kong/1/68/162/35 (H3N2) (A/HKca) master virus were generated and characterized. The A/HK/HK/6:2/2016 (H9N2) (RA-52) and A/UNL/HK/2:6/2017 (H5N8) (RA-54) strains were obtained by genetic reassortment of wild viruses (A/Hong Kong/1073/99 (H9N2) or A/Common tern/Uvs-Nuur Lake/26/2016 (H5N8)) and A/HKca attenuated high yield virus, which serves as a donor of internal protein gene segments [Tsybalova, 2012]. The RA-52 reassortant was obtained after 10 passages in 10–12 day-old embryonated chicken eggs (CE); the RA-54 was obtained after 7 passages. The reassortants inherited 2 surface proteins genes from wild viruses and 6 internal protein genes from the donor strain. Genetic compositions were confirmed using restriction fragment length polymorphism analysis. The antigenic identities of reassortants and wild-type strains was confirmed by haemagglutinin inhibition reaction. Full-genome sequencing showed one amino acid substitution in the PB2 protein sequence (M475I) in RA-54, in comparison with the donor strain. RA-52 had no amino acid substitutions. Both reassortants are high virus yield in CE. The RA-52 yield was 8.5 log $EID_{50}$/0.2 ml; the RA-54 yield was 7.75 log $EID_{50}$/0.2 ml. To confirm that both were cold-adapted and temperature sensitive, the reproductive capacities at different temperatures were measured at 26°C and 39°C. The $RCT_{26}$ for RA-52 was 1.0 log $EID_{50}$; for RA-54, it was 2.25 $EID_{50}$. The $RCT_{39}$ values were 7.0 log $EID_{50}$, and 7.5 log $EID_{50}$, respectively. These properties were retained after 5 passages (CE), which indicates their stability.

The results show that the reassortants are antigenically identical to wild-type strains and that they inherited high yields, cold adaptation, and temp. sensitivity from the master strain. They can be used for development of both inactivated and live influenza pandemic vaccines. Both reassortants were deposited in the State Collection of Viruses under the numbers 2884 (RA-52) and 2885 (RA-54). Nucleotide sequences have been deposited in GISAID under numbers EPI_ISL_321099 (RA-52) and EPI_ISL_321098 (RA-54).

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## FURTHER DEVELOPMENT OF "IgY-TECHNOLOGY": AN ELISA SYSTEM BASED ON SPECIFIC ANTIBODIES FROM EGG YOLKS AS A SURROGATE VARIANT OF THE NEUTRALIZATION TEST

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Neutralization test (NT) remains the "gold standard" in seroepidemiological and diagnostic studies of infections associated with poliovirus (PV). This is due to functional nature of the NT, which reflects the real immune status of the test serum. However, the NT uses cell cultures and live viruses, which requires compliance with relevant biosafety requirements. In accordance with the plans of the WHO Polio Eradication Initiative, work with PV (wild or Sabin strains) in the near future will be sharply limited (and is already limited for PV Sabin type 2) by the requirements of the containment and will be possible only in a small number of specially accredited institutions.

In this report, we present the results of the development of blocking ELISA as a surrogate variant of NT for the detection of antibodies to PV based on the use of specific IgY antibodies isolated from egg yolks of chickens immunized with PV and inactivated standard poliovirus antigen.

The results of comparison of two tests (NT and blocking ELISA) are presented when titrating 90 blood serums of children who received 2 doses of IPV following 3 doses