– they were mostly registered in the children’s organized groups (86.2%) including 12.0% cases in child-care facilities;
– they occurred more frequent in autumn-winter (46.2%) and spring (38.4%) periods of a year and were associated with consumption of vegetable salads in 72.4% cases;
– violation of sanitary-and-hygienic mode and technology of meal preparation from uncooked vegetables was noted in all outbreaks;
– laboratory confirmation of the diagnosis was set in 39.5% of the patients by PCR assay in the first days; bacteriological and serological diagnosis was confirmed in 14.1 and 64.6% after 2–3 weeks;
– Yersinia pseudotuberculosis was revealed in the population of synanthropic and wild small mammals in 52.9%, in transmission factor — in 46.7% from the total number of the studied outbreaks;
– all epidemic Y. pseudotuberculosis strains were O:1b serotype, possessed ypm gene of super-antigen, lacked of high-pathogenicity island (HPI), and belonged to plasmid content to single plasmid (pYV 47 MDa) and two-plasmid (pYV 47 MDa and pVM 82 MDa) strains with the identical frequencies;
– the peculiarity of clinical manifestation of pseudotuberculosis caused by Y. pseudotuberculosis with two-plasmid and chromosomal tcpY1 gene (phagocytosis inhibitor) was the presence of the intoxication symptoms, fever, rash, damage of gastrointestinal tract, liver and joints with prevalence of medium-severe and severe course specific for Far Eastern scarlet-like fever (FESF);
– we discovered one more form of FESF clinical course caused by Y. pseudotuberculosis with pYV plasmid and lacking tcpY1 gene. In this case all observed symptoms were poorly expressed, and pseudotuberculosis was developed in “minor” easier form mainly in children.

The revealed peculiarities of pseudotuberculosis outbreak are necessary to take into consideration in epidemiological surveillance.

5.4 doi: 10.15789/2220-7619-2018-4-5.4
INTRASPECIFIC DIVERSITY OF YERSINIA PESTIS CHAPERONE/USHER SECRETION APPARATUSES
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The Post-Antibiotic Era requires replacement of antibiotics with alternative antibacterials aimed at alternative molecular targets. One of such alternative approaches to treat infections are remedies targeting virulence. Yersinia pestis as many other Gram-negative bacterial pathogens use the chaperone/usher (CU) pathway to assemble virulence-associated surface fibers termed pilus or fimbriae. Y. pestis has two well-characterized CU operons: the caf genes coding for the F1 capsule and the psa genes coding for the pH 6 antigen. There are eight additional CU secretion systems capable of assembling Y. pestis pilus fibers. When choosing new targets for effective treatment of infectious diseases, it is necessary to search for pathogenicity factors possessing structural conservatism, since polymorphism gives pathogens the opportunity to evade interaction with the drug.

Searches and comparisons of amino acid sequences of CU proteins from Y. pestis strains belonging to SNP-types 0.PE2, 0.PE3, 0.PE7, 0.PE4, 0.PE5, 1.ori, 1.ANT, 2.ANT, and 2.MED were conducted using the databases of the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov) by MAUVE (http://darlinglab.org), BLAST (https://blast.ncbi.nlm.nih.gov), ProtParam tool (https://web.expasy.org/protparam), and protein sequence analysis (http://molbiol.ru/scripts/01_18.html). The usher genes for two of chaperone/usher pathways (yp1539–1544 and yp0406–1563) were disrupted in all of the studied Y. pestis strains by an insertion sequence or premature stop codon, and thus these pathways are not expected to be functional. The phylogenetic-group-specific polymorphisms of amino acid sequences of the proteins from the Y. pestis CU secretion systems is inherent in five ushs (yp0562, y1858, y1871, y2390, y3480), three molecular chaperone (y2392, y3479, caf1M) and three adhesin subunits (caf1, y2388, y3478). These polymorphic proteins are excluded from the list of potential Y. pestis molecular targets.

This research was supported by the Russian Science Foundation (grant 14-15-0039).

5.5 doi: 10.15789/2220-7619-2018-4-5.5
THE OUTER MEMBRANE PROTEIN A (ompA) OF YERSINIA PESTIS IS NOT REQUIRED FOR VIRULENCE IN MICE AND RATS
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The plague bacterium Yersinia pestis has a number of well-described strategies to protect itself from the both cellular and humoral factors of the host's innate immunity. OmpA in several pathogens has been shown to mediate resistance to complement and antibacterial peptides, as well as play a role in invasion and intracellular survival. In this study, we sought to determine whether deletion of the ompA would render fully virulent Y. pestis strain attenuated in the mouse and rat models of plague.

Y. pestis ΔompA mutant was constructed using the knockout mutagenesis. SDS-PAGE and Western blot analyses with anti-OmpA serum showed the absence of OmpA in Y. pestis ΔompA cell lysates and outer membranes preparations. We could not detect any differences between Y. pestis wild type strains and their ΔompA derivatives using a serum killing assay. The OmpA deficient mutants were 2 times less resistant to bacterial action of polymyxin B as compared with the wild type strains. To assess the biological significance of OmpA in fully virulent Y. pestis strain in vivo, studies in a mouse and rat models of bubonic and pneumonic plague were performed. Inbred mice and rats were infected subcutaneously or intranasally to mimic bubonic or pneumonic plague and observed for 21 days. Comparative study of the virulence of Y. pestis mutant strains using subcutaneously and intranasally challenged mice and intranasally challenged rats did not reveal differences in their LD50. The average survival time of mice and rats that succumbed to infection with the strain 231 or its isogenic derivative did not differ from each other. The estimated LD50 of the ompA mutant for subcutaneously challenged rats was approximately 10-fold higher than the LD50 of the wild type 231 strain.

The main outcome of our investigation is the finding that the loss of the ability to produce OmpA antigen did not influence virulence of ΔompA mutant of Y. pestis. This argues against the usefulness of using OmpA as a molecular target for plague prophylaxis and therapy.

This study was supported by the Sectoral Scientific Program of the Russian Federal Service for Surveillance on Consumer Rights Protection and Human Wellbeing.