

colitica), only one *Y. pseudotuberculosis* strains (1.7%) was detected by the bacteriological method. The set of pathogenicity factors of this strain didn't prove to be usual for the strains isolated in the Russia which in most have the YPM genes (the superantigen *Y. pseudotuberculosis*-derived mitogen) and responsible for the typical pseudotuberculosis symptoms (rash, skin desquamation, red tongue). The obtained strain proved to have "high pathogenicity islands" (HPI) genes with ypm being absent. These "european" strains cause pseudotuberculosis with such symptoms as mesenteric lymphadenitis, acute appendicitis and gastrointestinal features. The traditional bacteriological technique proved to be effective both in theory and in practice.

Necessity of using both classical bacteriological and PCR methods thus proves to be important for understanding the symptoms yersiniosis.

5.9

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ONCE UPON A TIME IN THE FAR EAST: ON THE 50TH ANNIVERSARY OF THE DISCOVERY OF "REAL PSEUDOTUBERCULOSIS" AMONG HUMANS

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After the first description of pseudotuberculosis and its pathogen in 1884, the infection was for a long time considered a classic zoonosis. Single cases of human disease usually resulted in death. In the mid twentieth century W. Masshoff and W. Knapp (1953, 1954) described rare sporadic cases of the appendicitis caused by infection of mesenteric lymph nodes. However, the decisive turn in the discovery of the true face of human pseudotuberculosis occurred only after the unusual events in the Far East of the USSR. It all started with the fact that in Vladivostok in the spring of 1959 an infection affected more than 300 young sailors of one military unit. 200 people with a severe form of the disease were placed in the hospital. Epidemiologists believed that the cause of this outbreak could be massive foodborne infection.

The clinical findings of the disease were very polymorphic, which made diagnosis difficult. Most patients in the early days had mainly typical symptoms of scarlet fever, some — signs of hepatitis, others — appendicitis or arthritis. A new disease was called "Far Eastern scarlet fever — FESF" before the discovery of etiology (I. Grunin, G. Somov, I. Zalmover, 1960). Similar collective outbreaks began to be recorded annually in other regions of the Far East.

However, the nature of the infection remained a mystery for several years, until in 1966 the naval bacteriologist Vladimir Znamenskij did announce that he and his colleagues found in the feces of patients *Yersinia pseudotuberculosis*. However, authoritative scientists refused to believe a little-known provincial microbiologist. On the recommendation of reviewers, the scientific journal rejected the article sent. So, in order to prove his rightness, Dr. Znamenskij in January 1967 in Leningrad infected himself with the culture of *Y. pseudotuberculosis*, taken from a patient. After 6 days, he developed a severe septic form of FESF.

Doctors of the Military Medical Academy studied it in details and successfully cured. The results fully confirmed Znamenskij's hypothesis that FESF is a previously unknown form of human pseudotuberculosis. From then a new stage in the study of pseudotuberculosis began, which significantly changed the old ideas about this infection and its pathogen.

5.10

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MONITORING OF VACCINAL PROCESS IN HUMANS RESIDING IN THE ALTAI HIGH-MOUNTAINOUS NATURAL PLAGUE FOCUS

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The Altai high-mountainous natural plague focus has high epidemic potential; in 2014–2016 three cases of bubonic plague are registered in local residents.

The aim of this work — complex immunological examination of the humans residing at the territory of Gorno-Altai high-mountainous natural focus, vaccinated with a live plague vaccine.

Sixty volunteers earlier non-vaccinated against plague and living in the focus took part in the experiment. Blood sampling was performed before vaccination/revaccination after 1, 3 and 6 months.

Immunological efficiency of vaccination was estimated by: lymphocyte subpopulational composition; index of CD4⁺/CD8⁺ cells; IFN γ , TNF α , IL-4 production; NST-test; specific antibody titer to *Yersinia pestis* F1; typing of HLA class II genes. Processing of statistical data was performed using parametrical and nonparametric criteria.

No pathological alterations in lymphocyte subpopulational composition were revealed. Decrease of T-lymphocyte was registered in 3 months after revaccination due to increase of CD3⁻CD19⁺-cells. Increase of T-helper percentage, raising immunoregulatory index value and the general tendency to functional activity increase of immunocompetent cells in the NST-test in 1 month after revaccination indicates the presence of adaptive cellular immunity.

Positive seroconversion in the overwhelming majority of the vaccinated humans taking part in the testing indicates the adequate immune reconstruction of the body and development of specific antibody in reply to plague vaccine introduction. Increase of TNF α and IFN γ production, and also IFN γ /IL-4 ratio after vaccination indicate the increase of Th1-cell activity and development of the cellular immune response in humans. At the same time, decrease of IFN γ /IL-4 ratio and also TNF α associated with Th-1-cells occurs after revaccination indicating the shift to humoral immunity.

Commonly encountered HLA-DRB1 (*03, *04, *07, *08, *11, *13), HLA-DQB1 (*02, *03:01) and HLA-DQA1 (*05:01) gene alleles are defined. Possible associations of these alleles with TNF α and IL-4 production level and also with relative T-helper content and CD3⁻CD16⁺-cells are revealed.

Comparative analysis permitted to detect a number of the major parameters indicating to activation of cellular and humoral immunity in humans vaccinated against plague. Further immunological monitoring of the vaccinal process is necessary.