Intestinal dysbiosis of male Wistar rats was induced by ampicillin and metronidazole. Indigenous enterococci (group E), lactobacilli (group L), bifididobacteria (group B) were isolated from feces before the antibiotic usage and then separately or as mixture of three strains (group M) were given to the animals for 4 days. Rats from control group 1 (C1) didn`t receive autoprobiotics. Animals from control group 2 (C2) didn`t receive antibiotics and autoprobiotics. The study of fecal samples, collected on 4th and 9th days of experiment, was performed by RT-PCR and by metagenome 16S rRNA analysis. The cluster differentiation of lymphocytes was analysed using flow cytometry.

Dysbiosis is characterized (on 4th day) by excessive abundance of filum *Gammaproteobacteria*, *Proteus* spp. (Pr) and, *Klebsiella* spp. (K), and decrease of *Faecalibacterium* sp. (F), *Prevotella* spp. (Pv), *Bacteroides* spp., *Lactobacillus* spp. populations. The decrease abundance of opportunistic enterobacteria was minimal in groups C1 and M. Low efficacy against Pr and K, main decrease of *Lactobacillus* spp. and *Paraprevotella* spp. content in M group coincided with maximum shifts in cluster differentiation of lymphocytes: increase of B-cells, NK-cells, decrease of T-cells and $CD3^+CD8^+$ T-lymphocyte. Surprisingly no significant changes in the immunogram of rats from the group C1 could be detected.

Indigenous enterococci stimulated growth of bacteroides and inhibited growth of lactobacilli and Pv. This autoprobiotic demonstrated low antagonistic activity against Pr. Indigenous lactobacilli inhibited the growth of the Pr and restored the number of Pv. and F. Significant decrease of both K and Pr percentage abundance and the increase of F were observed in group B.

Changes in the composition of microbiota correlated with changes of immunity in different experimental groups. The increase in the abundance of F correlated with the increase of $ThCD3^+$.

$CD25^-FoxP3^+$ content in the spleen in groups L and B. It was found that content of Th $CD44^+62L^+$ lymphocytes in the blood, which was reduced in group B and E inversely correlated with the abundance of *Gammaproteobacteria*.

It should be noted that implementation of autoprobiotics besides the influence on microbiota have a significant effect on immunity, which varies depending of the type of autoprobiotic. The mechanisms of immunomodulatory effects of autoprobiotcs are not yet clear and require further studies.

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POTENTIAL INFLUENCE OF IMMUNOMODULATORS ON THE PRODUCTION OF INTERFERON-GAMMA AND INTERLEUKIN-10 IN LABORATORY ANIMALS VACCINATED AGAINST PLAGUE

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The improvement of specific prophylaxis of infectious diseases involves the search for new highly effective immunomodulators to influence the activation of the factors of active and adaptive immunity. As potential components that increase the effectiveness of live plague vaccine, polyoxidonium and Ingaron (Interferon gamma human recombinant), preparations with a stimulating effect on immune system are of some interest.

The comparatives analysis of polyoxidonium and Ingaron effect on interferon-gamma and interleukin-10 production in BALB/c mice when immunized with culture of *Yersinia pestis* vaccine strain EV line NIIEG were studied.

200 BALB/c mice were subcutaneously immunized with a *Y. pestis* EV NIIEG culture at dose of 2.5×10^4 (group 1), in combination with polyoxidonium at dose of 4 μg (group 2), or with Ingaron in dose of 150 IU (group 3), intact mice (group 4) served as controls. The content of cytokines in blood was determined by enzyme immunoassay on the 3rd, 7th, 21st and 90th days after injection of preparation using commercial test systems (eBioscience, Austria).

On the 3rd day of the experiment, significant increase in the level of both interferon-gamma and interleukin-10 was established in all animals of experimental groups (1 — 58.3 and 29.0; 2 — 57.2 and 65.9; 3 — 83.2 and 45.6 pg/ml, respectively), compared with intact mice (26.2 and 11.1 pg/ml). An increase in the level of cytokines by 3–4 times was noted in the experimental group at 7 and 21 days after immunization. A significant decrease in the amount of interferon-gamma (1 — 48.4; 2 — 35.6 and 33.2 pg/ml in 3 group) was showed after 3 months, but it remained high compared to control (16.3 pg/ml). Content of interleukin-10 in blood of group 1 and group 3 mice decreased sharply by 90th day of observation (to 16.5 and 12.7 pg/ml), while in group 2 remained at high level (34.6 pg/ml), which indicates a possible prolonged action of polyoxidonium on production of cytokines — biomarker for anti-plague immunity.

Thus, potentiating effect of immunomodulators in laboratory animals vaccinated against plague has been established.

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NEUTROPHIL/LYMPHOCYTE DISBALANCE AS A PREDICTOR OF VAGINITIS

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Infectious vaginosis or cervicitis is a frequent cause of ginecologist's appointment. Vaginitis is vaginosys of bacterial, viral or fungal etiology. During this inflammation vagina or cervix surface leucocytes count increases significantly. We were interested how white blood cells (WBC) count changes in peripheral blood during vaginitis and/or cervicitis.

The aim of the study was to estimate absolute and relative WBC count in peripheral blood from patients with and without vaginitis.

A total of 26 (mean age 40±19) women visited IDC ginecologist between 28 April to 12 June 2018. Informed agreement was received from all patients. Blood samples were collected in 5 ml K3 EDTA Vacuette tubes. Alifax Roller was used to erythrocyte sedimentation rate (ESR) determination, Sysmex XN was used to complete blood cell count (CBC) determination. The ginecologic slides were heat-fixed and stained with azur-eosine.

Microscopic exam of normal cervix slides shows not more 15 leucocytes in field-of-view (fov) at 1000 total magnification. Normal vagina slides contains 0–10 leucocytes in fov. Peripheral WBC rates was graded according to age. So we divided patients into 4 groups: with normal leukocyte count in the blood and urogenital tract (n = 10), with normal WBC in blood and elevated WBC in cervical and/or vaginal slides (n = 8), with normal blood and increased WBC values in the urogenital tract (n = 4) and abnormal WBC in hole blood and normal urogenital parameters (n = 4).

Parameters of peripheral blood in this group were compared with the group with normal values. The most numerous group had abnormal parameters both in blood and in cervix or vagina.

Nonparametric comparison in the groups with the Mann–Whitney test showed a statistically significant ($p = 0.0062$) increase in the absolute number of peripheral blood lymphocytes in patients with inflammation in the urogenital tract.

The imbalance of peripheral blood lymphocytes/neutrophils as a possible immunity disorder allows infection to cause vaginitis. Therefore, periodic monitoring of the complete blood cell count and measures leading to the normalization of the CBC can help prevent the inflammation of the urogenital tract.

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THE TRECs AND KRECs FREQUENCY IN THE BLOOD IN A POPULATION OF ST. PETERSBURG

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TRECs (T-cell receptor excision circles) and *KRECs* (kappa-deleting recombination excision circles) are surrogate markers of maturation of T-cells and B-cells. *TRECs* and *KRECs* quantification can be used for detection of primary or acquired immunodeficiency. However, to detect immunodeficiency, it is required to know the population values of the excision rings concentration.

The aim of this work was to determine the values of *TRECs* and *KRECs* in the blood of healthy donors in St. Petersburg.

Blood of healthy volunteers aged from 0 to 95 years (total 160 people) was used in the research. *TREC/KREC* copies were assessed by quantitative PCR. Calibrators for PCR are kindly provided by the Institute of chemical biology and fundamental medicine (Novosibirsk, Russia).

There was no significant correlation between the concentration of *TRECs* or *KRECs* from sex. At the same time there was a significant negative correlation between the number of copies of *TREC*/10^5 lymphocytes (Spearman correlation coefficient $r = -0.836$; $p < 0.0001$) or the number of copies of *KREC*/10^5 lymphocytes ($r = -0.641$; $p < 0.0001$) from age.

All group was divided into 7 age groups: newborns, 3 months – 9 years, 10–19 years, 20–29 years, 30–39 years, 40–49 years, older than 50 years. There was statistically significant reduction of the content of *TREC*s in the blood after 10 years and after 30 years. The number of *KREC*s was significantly decreased after 10 years. Then there are no significant differences in the number of *KREC*s between groups of 20–29 years and groups older than 30 years. At the same time the number of *KREC*s in the group of 10–19 years is significantly higher compared to adults over 30 years. Further experiments are needed to clarify whether the number of excision rings in human blood stabilizes after a certain age.

Thus, for first population values of excision rings concentration in blood of healthy donors of St. Petersburg were determined in this work. These data can be used to detect various immunodeficiency states.

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COMPARATIVE ESTIMATION OF SENSITIVITY OF SEROLOGICAL REACTIONS FOR ESTIMATION OF IMMUNITY AGAINST THE CAUSATIVE AGENT OF TULAREMIA

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Tularemia is an anthropozoonotic natural focal acute infection. According to Russian biological safety regulations compulsive immunization and specific immunity estimation is carried out in accordance with established regulations for all the employees, who work with the causative agent of tularemia. Immunological efficacy of vaccination as well as specific diagnosis of tularemia is carried out using serological reactions (ELISA, MAT, IHAT) and/or skin allergic test, which causes extra body burden of antigens. Accordind to methodological guidelines 4.2.2939-11 (RU) for estimating of post-vaccination immunity it is allowed to apply one of the serological methods. It is widely recognized that ELISA is the most sensitive serological assay, including for tularemia. Serological reactions are carried out *in vitro*.

The purpose of the work was to compare sensitivity and specificity of ELISA and IHAT designed for detection of antibodies to *F. tularensis* antigens.

Blood serum samples were obtained from people, who had been immunized with live tularemia vaccine 1 month and 5 years before the assay. As a negative control the blood sera of donors with no anamnesis of a natural infection or vaccination against tularemia were used.

Detection of specific antibodies was carried out using tularemia serodiagnostic test produced by the Stavropolsky Antiplague Scientific Research Institute, an experimental ELISA test system, and "ELISA classic Francisella tularensis IgG" (SERION, Germany) to be considered for reference, following the manufacturers' guidance. To obtain the experimental ELISA test system, LPS extracted by Westphal method [1965] was used.

Of the 16 donors' samples in the ELISA, 7 turned out significant titres that exceeded the dilution of 1: 400, and 9 — negative. The data obtained in the ELISA were completely correlated with the results of "ELISA classic Francisella tularensis IgG", which was used as a verification test. In IHAT, positive reactions were found in 15 donors, negative in one. False positive reactions of IHAT can be associated with the immobilization of whole *F. tularensis* cells on the erythrocytes with antigens capable of cross reactivity The use of IHAT is justified for the diagnosis of tularemia if it is the case of antibody titres increase in dynamics. To estimate the effectiveness of immunologic adjustment after vaccination, ELISA seems to be preferable.

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THERAPEUTIC EFFICACY OF MONOCLONAL ANTIBODIES AGAINST LETHAL TOXIN OF *BACILLUS ANTHRACIS* IN A MOUSE MODEL

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Despite insignificant number of anthrax cases in the Russian Federation, the antitoxic drug development is going on. That's connected with the threats of terrorist acts and the presence of a large number of cattle burial grounds in the Russian Federation. The inhalational and intestinal form of the disease is enhanced by complexity of diagnosis, thus anthrax may be particularly dangerous. At the late stages of anthrax infection antibiotic therapy turns out to be ineffective and the patient has a risk of quick death due to a large amount of the lethal toxin accumulated in the patient's blood. At this stage antibodies capable of neutralizing, primarily, the lethal toxin (LT)