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Contents

Editorial Board Contents

C.
(P.)
1
2-5

Review (Dedicated to the birthday of I.I. Mechnikov)

6-10

Metchnikoff at Rockefeller: a legacy of phagocyte- microbial interactions

Siamon Gordon, William Dunn

In 1909, Elie Metchnikoff presented a signed portrait of himself to Simon Flexner, the first scientific director of the newly formed Rockefeller Institute in New York. It was eventually passed on, at Rockefeller, to Rene Dubos, a French microbiologist, and then to his successors, James G Hirsch and Zanvil A Cohn; Metchnikoff's spirit continued to pervade the laboratory directed subsequently by Ralph M Steinman. Over 50 years, 1960-2010, this became one of the premier research laboratories in the world to investigate the immune interactions of microbes with granulocytes, monocyte-macrophages and dendritic cells, respectively, at all times under the benign presence of Metchnikoff. I was fortunate to join the laboratory as a student of Zanvil Cohn during 1966-1976, which initiated me into a life-long love affair with macrophages, lasting to the present day at Oxford. In this year of his 175th birthday, I would like to record the legacy that Metchnikoff left to my generation during that period at Rockefeller University.

Keywords: I.I.Mechnikov, Phagocyte-microbial interactions, history

11-34

Ilya Ilyich Mechnikov: life and work

Minukhin V. V., Kolotova T. Yu., Skliar N. I., Voronkina I.A., Davidenko M.B., Kazmirchuk V.V.

On May 15, 2020, we celebrated the 175th anniversary of the Ilya Metchnikoff, the author of the hypothesis about parenchymella, the father of cellular immunology and inflammation theory, founder of gerontology, aging and longevity science. The article discusses the main milestones in the life and scientific work of Ilea Metchnikoff. Ilya Metchnikoff working originally in Russia, later in Italy, and then at the Pasteur Institute in Paris. His initial observations on phagocytic cells were made in the marine biology laboratories in Messina on starfish. Ilya Ilyich, as a result of observations of intracellular digestion in sponges, coelenterates and some flatworms, stretches a thread between phagocytosis and evolution (phagocytella), inflammation, cellular immunity, regeneration and the aging process. This thread is the quintessence of his work. Metchnikoff devoted many years to studying the comparative development of the embryonic layers of lower animals. Ilya Ilyich demonstrated that cnidarians gastrulate by introgression of cells which move from the blastula wall into the interior blastocoel and formed parenchymella or phagocytella. According to Metchnikoff, the hypothetical ancestor of multicellular organisms was similar to phagocytella. Metchnikoff is rightly famous for his theories of phagocytosis and inflammation. He proposed that macrophages evolved first to regulate development, and that these function are the stage for their evolution into the cells of innate immunity. It is very important to aware that cells and microorganisms according to Metchnikoff were taken up by an active process, involving living, and not only dead organisms. The humoral theory claimed that the phagocytes caused the spread of disease in the body and thus would harm the host, rather than defend it, against bacterial invasion. Metchnikoff devoted much of his scientific work to the revealing of the role of phagocytosis in inflammation. He observed diapedesis through vessel walls and aggregation of leukocytes at sites of inflammation. Phagocytosis not only destructs of infectious microbes but uptake of host cells, e.g. erythrocytes, from diverse species as well. More broadly phagocytes are the cells which preserving the integrity and defining the identity of the organism. Metchnikoff believed that the disabilities of old age are the work of phagocytes transformed from defenders against infection into destroyers of tissues by autotoxins derived from putrefactive bacteria residing in the colon. Such degenerative changes, he believed were nearly always premature and potentially prevented by procedures directed against the putrefactive bacteria. Until recently it was generally assumed that phagocytic removal of neurons occurs only after neuronal death. But now it has been convincingly proved that stressed but viable neurons reversibly exposed the "eat-me" signal leading to their phagocytosis by microglia; this neuronal loss was prevented in the absence of microglia. As a result these data breathe life into the Metchnikoff's ageing theory. Metchnikoff's hypothesis from the very beginning met with fierce criticisms. It required 25 years of intense effort to achieve recognition of the phagocytosis theory. This struggle culminated in 1908 with the awarding of the Nobel Prize

Keywords: evolution, natural selection, parallel evolution, complexity, parenchymella, phagocytella, gastrula, phagocytes, inflammation, innate immunity, macrophage, probiotics, ageing theory

Experimental works

Study of the efficiency of using disinfectants «Adalux» to provide paper material with bactericidal properties

35-40

Zinchenko I., Babich O., Tsytlshvili K., Shostenko O., Kononenko K.

Introduction. The issue of environmental management and protection of the environment from pollution are of paramount importance. Today, there is a big problem associated with the accumulation of polymer waste, which catastrophically pollutes the planet. Most plastic waste is not recyclable, but can be decomposed in landfills for decades. As an alternative to plastic products, world experts suggest the use of paper, biodegradable (biopolymer), reusable packaging. Many countries are now working to develop and produce packaging from affordable and environmentally friendly and natural materials that can degrade in soil or compost. **The purpose of this work** is to determine the resistance of paper samples of different densities to microbiological contamination after treatment with bactericidal agent «ADALUX». **Objects of research** - samples of paper which are widely used in the industry, with a density of 80 g/cm², 52 g/cm², 50 g/cm²; liquid bactericidal drug «ADALUX» (hereinafter - the drug) - a disinfectant that does not contain chlorine compounds. **Research methods and techniques.** The paper samples were treated with a 0.1% solution of the drug in the form of an aerosol and stored at room temperature for a

month and monitored. Raw paper samples were stored in the same conditions. The study of samples for microbiological contamination was performed for 7, 14 and 30 days on the following indicators: total microbial count (TMC), bacteria of the *Escherichia coli* group (BECG), enterococci (EC), fungi and yeast-like microorganisms. The resistance of paper samples to microbiological contamination, or bactericidal properties of the paper treated with the drug, was determined by the following methods: contact (disk), agar filling, artificial contamination of the paper surface - test object - *Escherichia coli B* (hereinafter - *E. coli B*). By comparing the number of colonies that grew in the variants with treated and untreated paper samples, the resistance of the test paper samples to high bacterial contamination was determined. **Results and discussion.** On paper samples that were not treated with an antibacterial agent, growth of saprophytic bacteria (GSB) was observed during the storage period, mold and yeast-like fungi were also found, and a small number of bacteria belonging to the group of *E. coli* were found. Processing of paper samples with 0.1% solution «ADALUX» provided bactericidal and bacteriostatic properties of the paper. They especially manifested themselves on the day of treatment and after 7 days of storage. Bacteriological crops from the surface of the samples on the day the paper was treated with a bactericidal agent showed a complete absence of microorganisms on the surface of all the studied paper samples. After 7 days of storage, the contamination of the treated samples with saprophytic microorganisms was observed 1.6 - 2.9 times less than in untreated ones. After 14 and 30 days of paper storage, the bactericidal effect against TMC and BECG decreased, but the development of bacteria on the surface of the samples was slower than on untreated paper samples. Molds and yeast-like fungi were observed on both processed and untreated paper samples of various densities. Probably, the 0.1% solution «ADALUX» has a more pronounced bactericidal effect, but its fungicidal properties are much less. Microscopic studies of colonies grown on a selective medium for fungi showed a predominance of growth of yeast-like fungi and less mold. On all investigated paper samples (processed and unprocessed), stored for more than 14 days, colonies of microorganisms belonging to spore bacteria were identified. Morphological features and microscopy of the colonies of these microorganisms suggested that they belong to the spore bacteria of the genus *Bacillus*, tentatively of the species - *Bacillus subtilis* (hay bacillus), which are widespread in the environment. Due to the ability to form spores, these microorganisms easily tolerate adverse living conditions and continue to live on the surface of the paper. After processing paper samples with «ADALUX» disinfectant (0.1% solution), paper with a density of 80 g/cm² had the most bactericidal properties, least of all with a density of 50 g/cm². A study of the resistance of treated paper samples to artificial bacterial contamination with the *Escherichia coli B* test-object (at a concentration of ~ 10³ - 10⁶ cells/ml) showed that after 7 days of storage, there was no growth of the test object on paper samples with a density of 80 g/cm² and growth retardation on paper samples with a density of 52 g/cm². Studies of paper samples during storage for 30 days showed that all paper samples (processed and unprocessed) did not have resistance to artificial bacterial contamination upon contact with the test object, which resulted in fouling of paper samples with colonies of *E. coli* bacteria. **Conclusions.** Based on the results, it was found that the disinfectant «ADALUX» (chlorine-free) in a concentration of 0.1% has a bactericidal effect when processing paper samples for seven days and bacteriostatic effect (inhibition of bacterial growth) when stored for a month against saprophytic microorganisms and BECG, but not very effective against microscopic fungi. It is likely that paper products that have been treated with such a disinfectant, on the one hand, have bactericidal properties for some time, on the other hand, in case of impossibility of recycling after their direct use, as waste can decompose naturally without harming the environment.

Keywords: bactericidal agent «ADALUX», microbiological contamination of paper, bactericidal properties of paper, bacteriostatic properties.

Biopharmaceutical research on the choice of a non-steroidal anti-inflammatory agent in the development of combination gel for mastopathy therapy 41-47

Zuikina S. S., Vyshnevskaya L. I.

According to the International Agency for Research on Cancer (IARC) at WHO, more than 1.7 million women are diagnosed with breast cancer annually. In Ukraine, according to the National Cancer Registry, in 2013, BC was first identified in 16,624 women (in 2012 – 16,660), which is 72.2 cases (in 2012 – 67) for every 100,000 women in the country. The global death toll from this disease is growing and is killing more than 500,000 women worldwide annually. According to experts from the National Cancer Institute, a diagnosis of breast cancer by the end of 2020 may become a reality for almost 17% of Ukrainian women, which gives reason to view it as a socially significant epidemiological problem. The aim of the study was to substantiate the choice of NSAIDs and their concentration for use in the development of combination gel for the treatment of mastopathy and prevention of breast cancer. The methods of literary analysis, marketing research and biopharmaceutical methods in vitro were used. The results of marketing studies and pharmacological studies of the level and types of activity of NSAIDs allowed indometacin to be selected as the active pharmaceutical ingredient (API). According to the results of biopharmaceutical studies, the concentration of the active substance in the composition of the gel is established.

Keywords: breast cancer, mastopathy, gel, indometacin, release.

Improving vaccine efficacy based on non-covalent photoinactivation of microorganisms - sources vaccine antigens (MSVA) 48-53

Martynov A., Farber B., Osolodchenko T., Klein I.

One of the most promising methods for non-covalent inactivation of vaccine-producing microorganisms is the use of photoinactivation using riboflavin derivatives. The study used a dynamic combinatorial derivative of riboflavin - succinyl-maleinyl riboflavin. Corpuscular vaccines are divided into the following groups: from 2AB to 5AB - bacteria were inactivated by riboflavin derivative and blue light, and groups from 6AB to 9AB were inactivated by formalin (0.1% formalin in 9 log CFU was kept for 2 weeks in an thermostat and then sterility was determined - bacterial growth was not observed). A dynamic derivative of riboflavin at a final concentration of 0.02% can photo inactivate 6 time more bacteria *P. Aeruginosa* and *E. coli* than riboflavin. The minimum effective blue light emitter power (450 nm) for the photodynamic inactivation of both *P. aeruginosa* and *E. coli* is 1024.2 mW / cm². In groups of mice pre-vaccinated intraperitoneally with corpuscular photo inactivated vaccines based on suspensions of and *E. coli* at doses of 0.5-1.0 ml 4 log (CFU) / mL, 100% survival of all animals was observed, whereas in control group with the same type of vaccines but formalin-treated vaccines, it failed to achieve a 100% protective effect.

Keywords: vaccines; non-covalent inactivation; photodynamic; riboflavin derivatives; visible light; *E. coli*; *P. aeruginosa*, TRIZ

Study of the antibacterial activity of new modified galenic and novogalenic phytosubstances from *Vaccinium vitis-idaea* leaves 54-57

Tsamenko K.V., Kyreev I.V., Osolodchenko T.P.

The purpose of the work is to study the antibacterial activity of new modified galenic and novogalenic phytosubstances from *Vaccinium vitis-idaea* leaves. **Materials and methods.** The object of our research new modified galenic and novogalenic phytosubstances from *Vaccinium vitis-idaea* leaves. Pharmacopoeia agar diffusion method biological method for determining the activity of antibiotics, based on the ability of molecules antibiotic substances diffuse in agar media and form zones of inhibition, in which the test microorganisms used do not develop sensitive to the antibiotic under study. The study of antibacterial activity of the phytosubstances was in the laboratory of biochemistry of microorganisms and nutrient medium of the Mechnikov Institute of Microbiology and Immunology under the direction of candidate of biological sciences Osolodchenko T.P. The reference drug was Inurek, recommended by the European Association of Urology for the prophylactic treatment of urinary tract infections. **Results.** We have identified the most active phytosubstance, which is the glycosides

of phenolic compounds in combination with the arginine, dissolved in 50% alcohol. It has been established that polysaccharides from the leaves of *Vaccinium vitis-idaea* leaves may have a low antibacterial effect, and in the complex with phenolics, they do not infuse an antibacterial effect on the antibacterial effect. It has been established that phenolics from half of the leaves of lingonberry extraordinarily exhibit a greater antibacterial effect in the presence of glucosides. **Conclusions.** A screening study of the antibacterial activity of 13 new modified galenic and novogalenic phyto-substances from *Vaccinium vitis-idaea* leaves carried out. The most active was phytosubstance 12, which is a complex of glycosides of phenolic compounds with arginine. It has been proven that it is phenolic compounds in the form of glycosides that have a more pronounced effect in the main relations of uropathogens than their aglycones..

Keywords: new modified galenic and novogalenic phytosubstances, leaves, *Vaccinium vitis-idaea*, antibacterial activity

Reproduction and apoptosis of EBV- latent infected cells under influence a TRIZ-created antiviral drugs 58-67 Farber B, Martynov A, Klein I.

Introduction. We had worked persistently and in 1997, the first model of such a structure based on oligopeptides of horse albumin was revealed. We named this project and called Albuvir (combined from the word Albumin and the word virus) and applied in veterinary medicine, where viral infections represent more than 95% of all pathologies. In 2000 an application was filed for the first modification of this drug. Subsequently, for the production and sale of this product, registration certificates of the State Committees in Veterinary Medicine of Eastern European countries were obtained. In 2010, we signed a license agreement to transfer of limited rights in the field of veterinary medicine for the production and sale of Albuvir in Eastern Europe. The drug was produced commercially and was successfully used to cure hundreds of thousands of chickens, rabbits, sheeps, cows, pigs, pigeons, fish (industrial - sturgeon), cats, dogs, geese, ducks, and other types of farm birds and animals. Thus, the task of this work was to study the ability of Albuvir to inhibit EBV reproduction and induce apoptosis of latently infected cells in the culture. **Materials and methods.** Cell culture. The inhibitory effect of Albuvir on EBV was studied in the following cell cultures: Raji - cell culture of the B-phenotype of Burkitt's lymphoma. Namalwa is a B-phenotype cell culture from Burkitt's lymphoma that lacks the EBV genome. B95-8 is a marmoset monkey B-lymphocyte cell line containing the complete EBV genome, producing complete viral particles. To control cell viability, a 0.4% trypan blue dye (Sigma, United States) was used. EBV was isolated from a lymphoblastoid culture of B95-8 cells (B-lymphocytes of monkeys-marmazetka), which produces this virus, according to the method of Walls, Crawford. Investigated substances. Albuvir (N. 1) - dynamic acylated acidic peptides - antagonists of signal peptides of nuclear (nucleolar) localization and polyribosomes. Lysine tris-succinamide (N. 2). Acyclovir was used as a reference drug (references data) MTT test. The cytotoxic concentration was determined in the Raji lymphoblastoid cell system using the colorimetric MTT method. This method is widely used to determine the CC50 of potential drugs in the study of the cytopathic action of viruses in vitro. Raji cells were plated into 96 well culture plates, 100 μ l per well, 25 μ l MTT (final concentration 5 μ g / ml) was added and incubated for 3 h at 37 ° C in an atmosphere of 5% CO₂. After incubation, cells were washed with PBS and resuspended in 96% ethanol to dissolve formazan. The results were analyzed spectrophotometrically on a Dynatech reader (Sweden) at a wavelength of 540 nm. Polymerase chain reaction. The degree of influence of drugs on EBV reproduction was determined using PCR test systems "AmpliSens-100-R". A fragment encoding the VCA protein of the virus with a size of 290 nucleotide sequences was the chosen genome region of the Epstein-Barr virus. The control was cells that, after infection with the virus, were incubated in the growth medium without the addition of the substances that were studied. We determined the percentage of inhibition of the level of accumulation of viral DNA in the samples treated with the test substances in relation to the control sample, the value of which was taken as 100%. **Results and discussion.** Effect of the dynamic antiviral drug Albuvir on reproduction and apoptosis latently infected with the Epstein-Barr virus cells in vitro. Modern approaches to the treatment of herpes infection, in particular the Epstein-Barr virus (EBV), include the use of ethyotropic drugs, as well as sensitizing therapy. The range of drugs active against EBV remains very limited to ganciclovir and acyclovir. The search for new compounds active against EBV remains relevant. The aim of this study was to find out the anti-EBV activity of the drug Albuvir in Raji, B95-8, Namalwa lymphoblastoid cells. The cytotoxicity index (CC50) was determined, which was 3000 μ g/mL, and the concentration of the drug that inhibits the reproduction of the virus (EC₅₀) was 0.1 μ g/mL. The ability of the drug Albuvir to inhibit the reproduction of the Epstein-Barr virus in all studied cell cultures was revealed. When the economic efficiency of creating static drugs in accordance with the S-shaped curve decreases, the need arises for a transition to a supersystem, namely, the creation of dynamic drugs systems. It has been proven that the drug Albuvir is able to inhibit the reproduction of the Epstein-Barr virus in Raji, B95-8 and Namalwa cell cultures. It is determined that the drug has a high activity in the culture of Raji cells (SI 8400), respectively, the drug is promising enough to develop as a treatment for EBV-associated diseases.

Keywords: TRIZ, laws of system evolution, dynamization, S-curve, Epstein-Barr virus, cell culture, antiviral action, albumin.

Bilateral Optic Neuritis in a Child Associated Multiple Sclerosis 68-72 Dwita Permatasari, Lukisiari Agustini, Gatot Suhartono

Introduction: Optic neuritis can be associated with multiple sclerosis (MS). Therefore, accurate diagnosis, risk assessment and management of patients with optic neuritis associated multiple sclerosis should be assessed. **Method:** A 5 years old girl suddenly blurred vision in both eyes and headache within 4 days before admitted in outpatient clinic. Patient had no fever and neurologic deficit. Visual acuity in first day were hand movement, color vision difficult to be evaluated in both eyes and right eye positive relative afferent pupillary defect. Posterior segment evaluation showed bilateral edema optic nerve. MRI showed bilateral optic neuritis, chronic plaque in right parietal lobe, right and left centrum semiovale. VEP showed demyelinating lesion in bilateral visual pathway. Patient was given intravenous methylprednisolone 500 mg divided 4 times a day and continued with oral prednisone start on the sixth days. **Result:** After treatment with intravenous corticosteroid until fifth days follow up, BCVA and color vision improve gradually. At the ninth days follow up, BCVA on right eye (RE) 5/5 and left eye (LE) 5/8.5 pinhole not improve. Ishihara on RE 12/14 and LE 10/14. Ophthalmoscopy examination showed disc edema subsided in the follow up. A month follow up, BCVA and Ishihara on both eye were 5/5 and 14/14. Ophthalmoscopy examination showed normal optic nerve head. **Conclusion:** Bilateral optic neuritis in a child associated multiple sclerosis is a challenging case. Intravenous methylprednisolone is the first line drug therapy give better visual outcome.

Keywords: bilateral optic neuritis, multiple sclerosis, methylprednisolone

Study of stability when storing of tablets under the conditional name "Ap-helmin" as one of the factors of pharmaceutical development 73-75

Semchenko K. V., Vyshnevskaya L. I.

Introduction. According to the World Bank, economic losses from helminthiasis of the digestive system rank fourth in the overall structure of diseases and injuries of the world's population. To meet the existing needs of the population of Ukraine in effective anthelmintic drugs, there were developed a complex anthelmintic drug in the form of coated tablets under the conditional name "AP-helmin", the active ingredients of which are albendazole and praziquantel in the ratio (1:4). One of the main ways to assess the quality of the drug is to maintain its stability during storage. Thus, the purpose of this work is to study stability during the storage of coated tablets under the conditional name "AP-helmin" on the basis of compliance of quality indicators with the requirements of SPhU and the developed project of quality control methods. **Materials & methods.** As the object of the study there were investigated 5 series of coated tablets for the treatment of helminthiasis of the digestive system under the conditional name "AP-helmin". The well-known SPhU methods were used to assess the stability of the established indicators. **Results & discussion.** The proper quality and stability of the drug is confirmed throughout the study

period. Yet, there is a tendency to reduce the resistance to crushing and reduce the quantitative content of active substances after 27 months of storage. **Conclusion.** It was found that throughout the study period of storage samples of the drug met the requirements of the project MCYA and HFC. Therefore, the most rational is to establish the shelf life of coated tablets under the conditional name "AP-helmin" for at least 24 months in a dry dark place at room temperature.

Keywords: tablets; stability; pharmaceutical development; Ap-helmin; albendazole; praziquantel

Features of disease course of some forms of herpesvirus infection

76-78

Sorokina O.G., Popov M.M., Liadova T.I., Malanchuk S.H., Dorosh D.M., Sorokina A.V.

Among the many factors that directly affect the immune system, infections caused by the herpes virus deserve special attention. In recent years, there has been an increase in the number of patients suffering from chronic recurrent herpesvirus infections, which in many cases are accompanied by severe general malaise and a number of therapeutic complaints. Today about 80-95% of the population is infected with Epstein-Barr virus EBV. Primary infection of EBV leads to lifelong persistence of the pathogen with possible periodic reactivation under the action of various immunosuppressive factors, which leads to chronic forms of the disease. EBV can cause chronic manifest and erased forms of the disease, running on the type of chronic mononucleosis. Thus, the study of the nature of clinical and laboratory changes in patients with chronic EBV infection and the peculiarities of the disease is an urgent problem of our time. The aim of this work was to study the features of the course of chronic EBV infection. We performed a comprehensive clinical and laboratory examination of 128 patients with chronic EBV infection (reactivation period). The diagnosis of chronic EBV infection was established on the basis of medical history, complaints, the presence of specific antibodies to EBV antigens and the detection of virus DNA in the blood. Studies of clinical blood tests of patients with chronic EBV infection and the control group showed differences. Thus, in patients with chronic EBV infection, a significantly elevated ESR level was found - 12.6 ± 1.8 versus 4.5 ± 1.1 in the control group ($p < 0.05$). The levels of erythrocytes, hemoglobin and platelets did not differ significantly from the control group. In patients with chronic EBV infection, there was a decrease in the level of leukocytes ($5.13 \pm 0.22 \times 10^9/l$ against $(6.20 \pm 1.8) \times 10^9/l$ in the control group ($p > 0.05$), but these changes did not go beyond the norms established for healthy people. Analysis of the leukocyte formula revealed the presence of patients with chronic WEB infection with a significant increase in the relative content of lymphocytes - $42.50 \pm 2.0\%$ against $33.70 \pm 2.68\%$ ($p < 0.05$) and monocytes - $11.15 \pm 0.9\%$ vs. $3.0 \pm 0.6\%$ ($p < 0.05$), which was the basis for confirming the presence of a chronic infectious process. In general, 94.8% of patients with chronic EBV infection had lymphocytosis and 82.5% had monocytosis. The relative number of neutrophils in patients with chronic WEB infection averaged $45.35 \pm 4.1\%$ against $61.7 \pm 3.8\%$ in the control group ($p < 0.05$); the relative number of eosinophils and basophils was within normal limits. When studying the absolute number of lymphocytes and monocytes in patients with chronic EBV infection, there was a tendency to increase them and their level was on average $(2.13 \pm 0.7) \times 10^9/l$ and $(0.51 \pm 0.08) \times 10^9/l$ against $(2.39 \pm 0.7) \times 10^9/l$ and $(0.47 \pm 0.08) \times 10^9/l$ in the control group ($p > 0.05$). The absolute number of neutrophils in patients with chronic WEB infection was significantly lower than in the control group and was $2.70 \times 10^9/l$ versus $4.21 \times 10^9/l$ ($p < 0.05$). The study of the absolute number of eosinophils and basophils in patients with chronic EBV infection did not reveal statistically significant differences compared with the control group. Thus, according to the results of our study, we found that patients with chronic EBV infection among the clinical manifestations were most often chronic tonsillitis, chronic fatigue syndrome and peripheral lymphadenopathy. Analysis of the results of laboratory studies revealed a significant increase in ESR, relative lymphocytes and monocytes, as well as a decrease in absolute and relative neutrophils, compared with the control group of patients, indicating a shift in white blood cell count, characteristic of the viral etiology of the disease what associated with the EBV.

Keywords: herpesvirus infections, chronic EBV infection, course of the disease, clinical and laboratory parameters, immune system.