

ABSTRACT

of the PhD dissertation titled: «Changes in intestinal hemo-and lymphodynamics and contractile function of lymph nodes in abdominal inflammation» by

Yeshmukhanbet Anar submitted for the degree of Doctor of Philosophy (PhD) on the educational program «8D05102-Biomedicine»

General characteristics of the work. The dissertation studies structural and morphofunctional changes in the intestinal lymph nodes, lymph flow, cellular composition of lymph and blood, biochemical and physicochemical parameters, contractile activity of the lymph nodes during inflammation of the abdominal cavity, as well as their microbiological parameters *in vitro* in order to identify their sensitivity to new antibiotics.

The relevance of the work: Inflammatory processes in the abdominal cavity can lead to serious complications that disrupt the functioning of internal organs and can cause death. The lymphatic system, due to its anatomical and functional features, plays an important role in water-salt metabolism and immune reactions, as well as in maintaining the stability of the internal environment of the body. All parts of the lymphatic system - capillaries, vessels and lymph nodes - participate in these processes.

Some pathologies can develop with the participation of the lymphatic system, which, due to its protective, drainage and transport functions, can change the course of the disease and the general condition of the body. Modern research highlights the transport of interstitial fluid and metabolites as an important task in the fight against toxic infections of various origins. Inflammation, for example, in the abdominal cavity, can cause disturbances of complex physiological functions. Despite the achievements of medicine, inflammatory processes in organs such as the kidneys, stomach, spleen and intestines remain a pressing and serious problem.

The aim of the study: Experimental study of structural and functional changes in the lymphatic system: lymph flow rate, biochemical parameters of lymph and blood composition, dynamics of contractile activity of lymph nodes during abdominal cavity inflammation.

To achieve this goal, the following tasks were solved:

1. To study lymph flow, cellular composition of lymph and blood, biochemical and physico-chemical parameters in abdominal cavity inflammation.
2. To study the bacterial microflora in abdominal inflammation and to determine their sensitivity to antibiotics *in vitro*.
3. To study morphometric changes in the small intestine in normal and experimental animals with abdominal cavity inflammation.
4. To study structural and morphofunctional changes in lymph nodes in abdominal cavity inflammation using light microscopy.
5. To study the contractile activity of lymph nodes in normal and in abdominal cavity inflammation.

Object of research. The studies in accordance with the set objectives were carried out on white laboratory rats of the Sprague Dawley (SD) line. Lymph, lymph nodes, blood.

Research Methods. To induce an experimental inflammatory process, 10% fecal solution was injected into the abdominal cavity of male Sprague Dawley (SD) rats at a rate of 0.5 ml per 100 g of body weight (Lazarenko, 2008). The rate of lymph flow and its rheological properties were studied in the control and experimental groups of rats. The following were determined in the lymph and blood of all groups of animals: blood and lymph clotting time according to Sukharev, viscosity using a VK-4 viscometer. Biochemical analyses were performed in blood and lymph samples on an automatic biochemical analyzer COBOS INTEGRA 400 (USA) using standard kits. The cellular composition of the blood and lymph was determined on a hematological analyzer "SYSMEX KX-2199" (Japan, 2003). Electrolytes in lymph and blood plasma were determined using an AVL 9180 analyzer (ROCHE DIAGNOSTICS, Austria, 2012). Lymph and blood coagulation was assessed using a TS4000 coagulometer (HTI, USA, 2013), and biochemical parameters of urine were determined using an analyzer (High Technology, USA, 2013). Contractile activity of isolated lymphatic vessels and nodes was studied using a generally accepted technique. The morphology of the lymph nodes was studied by making semi-thin (1 μm) and ultra-thin sections 50-70 nm thick on a Leica EM UC7 ultratome (Leica Microsystems, Germany). The experiments used a Leica DME light microscope (Germany), ImageJ morphometric analysis (Wayne Rasband, USA), and statistical data processing and analysis using Statistica 6.0 (StatSoft, USA).

Scientific novelty of the research work For the first time, our understanding of the role of the lymphatic system in the drainage-compensatory and adaptive reactions of the body during inflammation of the internal organs of the abdominal cavity is expanded, which allows us to develop measures to prevent and reduce its negative impact on the visceral functions of the body. For the first time, the following were determined: morphofunctional and structural state, morphometric parameters of the lymph node during inflammation of the abdominal cavity. A decrease in lymph flow was determined by a violation of general biochemical parameters and rheological properties of the lymph. Destructive changes in the adrenergic innervation of the lymph nodes during inflammation of the abdominal cavity, a decrease in spontaneous and induced contractile activity of the lymph nodes to vasoactive substances were revealed, which in turn led to a decrease in the transport function of the lymphatic system.

Scientific and practical significance of the work. A feature of the work is the analysis of changes in microbiological parameters occurring in the body, in particular the lymphatic system, by introducing a fecal solution under experimental conditions. And also determination of sensitivity of microflora to antibiotics of the new group in vitro. In inflammatory process, revealed in internal organs of the body, adaptive functions of the lymphatic system are shown. The lymphatic system, including lymph nodes, plays a key role in inflammatory processes and is important for functioning of the whole organism. Modern research aimed at

studying antibiotics of the new group makes a significant contribution to this area. The results of our research both in theoretical and practical aspects are important and expand our knowledge about physiology and pathophysiology of the lymphatic system. The results of the work are included in the course of lectures on disciplines: 'Human Physiology' of the 2nd year of the educational programme "6B05108-Biomedicine" of the Faculty of Biology and Biotechnology of the Department of Biophysics, Biomedicine and Neuroscience of Al-Farabi KazNU, in the course of lectures, seminars on the educational programme "Biology" of the 2nd year of Master's degree of Zhetysu State University "Adaptive Physiology" (Act on the introduction of completed research work in the educational process, Appendix B).

Basic principles put forward during the defense:

1. Hemo- and lymphodynamics were studied during abdominal cavity inflammation, and violations of physicochemical parameters of lymph and blood, an increase in enzymes, total amylase, ALT, AST and bilirubin and a decrease in total protein during inflammatory processes were revealed.

2. The bacterial microflora of animals of the experimental group was studied, as a result microorganism strains of *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* were isolated. High sensitivity of microorganisms isolated during inflammation to cephalosporins and aminoglycoside antibiotics was revealed.

3. Destructive and necrotic changes, increased oedema of the intestinal wall and its layers, changes in exocrinocytic cells of the epithelial layer, a sharp decrease in the number of cells in them, irregularity of crypts and development of microabscesses in them were revealed in the wall of the small intestine.

4. In inflammatory processes of the abdominal cavity the decrease of immune function of mesenteric lymph nodes due to structural changes of paracortical regions of abdominal lymph nodes, decrease of lymphopoiesis processes and decrease of germinative centre ratio in lymphoid nodes were studied. According to the data of histological and morphometric analyses, mesenteric lymph nodes are characterised by a change in the ratio of cortical and brain matter in lymph nodes. An increase in the number of macrophages in the cerebral layer of lymph nodes and a decrease in the size of the cortical layer were revealed.

5. It was established that with inflammation of the abdominal cavity, there is a decrease in the contractile activity of the lymph nodes and the magnitude of the effect of vasoactive substances, which in turn indicates inhibition of the sensitivity of the receptors of the lymph nodes.

The personal contribution of the dissertation author to the implementation of the results of the research work presented for defense: All results of the dissertation were obtained with the personal participation of the author. The dissertation candidate independently conducted an analysis of literary data on the research topic, experiments, processing and analysis of research results, wrote and formatted the dissertation manuscript.

Approbation of the work. The main provisions of the dissertation and the

research results were presented at the following international scientific conferences and symposia:

- International scientific conference of students and young scientists “Farabi’s World” (Almaty, Kazakhstan, 2021);
- Materials of the International Scientific and Practical Conference “Current Problems of Biology and Biotechnology”, dedicated to the 70th anniversary of Professor S.T. Tulekhanov, corresponding member of the National Academy of Sciences of the Republic of Kazakhstan, Doctor of Biological Sciences (Almaty, Kazakhstan, 2021);
- XV International Scientific and Practical Conference «Trends in the development of science and practice». European conference (Madrid, Spain, 2021)
- International scientific conference of students and young scientists “Farabi’s World” (Almaty, Kazakhstan, 2022);
- I International Scientific and Practical Conference “Integration of Sciences: Biophysics, Biomedicine, Neuroscience” (Almaty, Kazakhstan, 2022);
- Materials of the XV International Scientific and Practical Conference named after Academician Yu.I. Borodin “Lymphology: from fundamental research to medical research (Novosibirsk, Russia 2023);
- International research competition “New Science”, research work of the year (Petrozavodsk, Russia, 2023);
- XXIV Congress of the Physiological Society named after I.P. Pavlov (St. Petersburg, Russia, 2023);
- BIO Web of Conferences, Morphometric changes in the blood and lymphatic channels during inflammation (Almaty, Kazakhstan, 2024);
- IEEE Ural-Siberian Conference on Computational Technologies in Cognitive Science, Genomics and Biomedicine, CSGB 2023 – Proceedings. (Novosibirsk, Russia, 2023)

The main results of the dissertation were heard annually at the Scientific and Technical Council of the Faculty of Biology and Biotechnology of Al-Farabi Kazakh National University, at meetings of the Department of Biophysics, Biomedicine and Neuroscience.

Publications of articles: The results of the study on the topic " Changes in intestinal hemo-and lymphodynamics and contractile function of lymph nodes in abdominal inflammation " were published 12 scientific articles, of which 1 article was published in a journal included in the Scopus database (Q1 percentage indicator 85), 1 article was published in journals included in the Web of Science database (Q4), Hirsch index -1, as well as 3 articles in republican scientific journals on the list of the Committee for Control in the Sphere of Education and Science of the Republic of Kazakhstan, 5 in international and republican scientific and practical conferences of Kazakhstan, 2 monographs were published.

The structure of the doctoral dissertation: The thesis consists of normative references, notations and abbreviations, introduction, literature review, research materials and methods, as well as research results and their discussion, conclusion, used sources, tables and figures and appendices. The volume of the work is 128 pages, including 4 tables, 33 figures, 265 literature sources and 5 appendices.