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INTERCELLULAR INTERACTIONS AND THE LEVEL OF AGGREGATION OF BLOOD CELLS IN THE AREA OF INFLAMMATION IN PEOPLE LIVING IN THE EUROPEAN NORTH

The immunological results of 242 people with bronchitis and 198 people with colitis, as well as 47 practically healthy people aged 21 to 55 years at the time of examination were analyzed in order to study intercellular interactions and the relative proportion of neutrophil aggregation in the area of inflammation in people living in the North. Against the background of neutropenia in the area of inflammation, the level of migration of monocytes and lymphocytes is less pronounced. In conditions close to physiological, in the exudate of the "skin window", no significant differences in the level of leukocyte migration were revealed. With neutropenia in peripheral venous blood, the content of neutrophil aggregates in the area of inflammation is higher. Aggregation of neutrophils leads to significantly more active exosecretion, degranulation and lysis of aggregate cells, which may be one of the mechanisms for the formation of neutropenia in people living in the North.

Keywords: aggregation, neutrophils, monocytes, lymphocytes, neutropenia, bronchitis, colitis.

Introduction. In response to any change in the intercellular environment that carries a potential threat to the cell or blood loss, a reaction of changes in the microcirculatory unit develops with a change in blood filling, blood flow velocity. In this case, the cells release a complex complex of biologically active substances that cause reactions from a number of humoral effector systems. The set of lysosomal enzymes is highest in polymorphonuclear neutrophil granulocytes. Neutrophil granules of neutrophil include lysozyme, lactoferrin and alkaline phosphatase, active only in a neutral medium. Reducing the pH value to 4 is optimal for the activity of enzymes of azurophilic granules – myeloperoxidase and acid hydrolases. Azurophilic granules contain a large amount of elastase, which can be a factor of destruction; two metalloproteinases (collagenase and gelatinase) can cause degradation of the extracellular matrix [22, 28].

An increase in the content of proteolytic enzymes of active substances in the intercellular medium and blood in the area of trouble causes a reaction from the plasma protease system with the activation of Hageman factor, the conversion of precallikrein into kallikrein and the subsequent formation of plasma bradykinin and tissue kinin (lysyl-bradykinin or kallidin). An increase in the content of kinin causes the expansion of the vessel lumen in the microcirculation area with an increase in permeability, by contracting smooth muscles and endothelial cells.

Serotonin, histamine, kinins and prostaglandins are involved in the formation of edema during inflammation. The further continuation of the reaction involves the complement system; vasodilation and elevation of the vascular wall reproduces the product of activation of the C1, C4, C2 complement system (C-kinin). C-kinin differs from kinins in that it is inactivated rather than initiated by trypsin. The complement system also supplies the main chemotaxis factor C5, which is formed by neutrophil enzymes and enhanced by platelet reaction.

Tissue hypoxia with a decrease in O2 partial pressure, changes in microcirculation and vascular permeability cause an increased level of neutrophil adhesion in venules [24-26]. The adhesion of leukocyte blood cells is enhanced by a whole series of biologically active substances produced by activated neutrophils themselves [19].

In the study of intercellular interactions in peripheral venous blood in practically healthy residents of high latitudes, it was previously found that the activity of aggregation of peripheral venous blood cells in Arctic residents is 1.5-1.7 times higher than that of people living in more favorable climatic conditions. Erythrocytes and platelets aggregate most often (20.92 and 18.95%, respectively), peripheral blood leukocytes form aggregates actually 2 times less often (neutrophil granulocytes in 10.45%, lymphocytes in 7.19%) [21]. The level of neutrophil aggregation activity is associated with a decrease in the content of these cells in the circulating blood and an increase in the concentration of sCD56 adhesion molecules. The facts of the release of specific leukocyte granules into the pseudopod region associated with increased secretion of adhesion molecules, selectins, their ligands and chemotactic receptors in the adhesion region are known [7, 20, 29, 31, 34]. In residents of high latitudes, the content of the extracellular pool of signaling molecules, receptors and their ligands is significantly higher than in people living in more favorable climatic conditions. The dependence of this phenomenon on northern climatic conditions is demonstrated by the highest levels of extracellular pool content in residents of Arctic regions [2, 13]. Even in practically healthy people living in the North, the concentrations of free adhesion molecules and the L-selectin ligand (respectively sCD54, sCD62 and sCD62L) are significantly higher.

A higher level of adhesion activity and subsequent migration of activated neutrophil granulocytes in the inhabitants of the North is necessary due to the low level of vascular permeability and clearance of metabolic products [5, 8]. Neutrophils are involved in the clearance of cell waste products and their apoptosis. Phagocytosis of apoptotic bodies by granulocytes occurs very quickly and does not cause inflammatory reactions [4]. A high level of chemoattractants contributes to a constant migration flow of granulocytes, which is often manifested by a decrease in the content of circulating and actively

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phagocytic neutrophils in the blood [18]. If there is a sufficient concentration gradient of the chemoattractant, the location of the receptors on the surface of the cell membrane becomes asymmetric, concentrates on one of the poles in the form of a cap (capping) and determines the direction of its movement [23].

Leukocytes normally have a fairly significant viscosity, compared, for example, with the level of this property in erythrocytes and platelets. Studies have shown that the mouth of the capillaries is not so rare, even normally, leukocytes clog, but after a short time the blood flow is restored. With inflammation, such effects are recorded much more often [16]. During inflammation, accumulations of leukocytes are recorded near the walls of blood vessels (venules), which is associated with an unfavorable course of the inflammatory process. The phenomenon of granulocytes sticking to the vascular endothelium in the area of inflammation with the formation of cell aggregates is the earliest manifestation of the neutrophil reaction to changes in homeostasis or tissue damage. The phenomenon of clumping (aggregation) of granulocytes has been proven in vivo in pulmonal vascular leukostasis, interstitial edema and pulmonary insufficiency, as well as in Arthus phenomenon and complications of hemodialysis [24-26]. Irreversible aggregation of neutrophils is involved in the formation of leukostasis and leukopenia due to a decrease in the content of cells in the circulating pool and their transition to marginal. A high level of aggregation (clumping) involving C5a is already associated with neutrophil lysis and can lead to granulocytopenia [16].

In connection with the above, the aim of the study was to study intercellular interactions and the relative proportion of neutrophil aggregation in the area of inflammation in people living in the North.

Materials and methods. The immunological results of the preanalytical and analytical stages of the examination of 242 people with bronchitis and 198 people with colitis living in Arkhangelsk who applied to the Biolam center for professional diagnostics with a previously established diagnosis, as well as 47 practically healthy people aged 21 to 55 years at the time of the examination were analyzed. The survey was carried out with the written consent of the respondents in compliance with the basic norms of biomedical ethics in accordance with the document "Ethical principles for medical research involving human subjects" (WMA Declaration of Helsinki 1964, amended in 2013), and also approved and approved by the Commission on Biomedical Ethics at the Institute of Physiology of Natural Adaptations of FECIAR UrB RAS (Protocol No. 5 of 11.02.2022).

Peripheral venous blood, sputum, and feces were examined. A hemogram was determined in peripheral venous blood using the XS-1000i hematological analyzer (Sysmex, Japan). The deficiency of neutrophil granulocytes (neutropenia) was established at a content of <2.0×10⁹ cells/l in peripheral venous blood. Preparations for microscopy of feces were prepared after preliminary preparation of an emulsion with a saline solution (1/1), both the sediment and the supravaginal fluid were examined [10]. Cytological examination of sputum was studied after centrifugation of 1 ml of sputum and application of 0.5 ml of sediment to a slide [12]. Cytogram and phagocytosis were studied in smears stained according to Romanovsky-Giemse and Gram; counting was performed at the rate of 100 cells. Leukocyte aggregation was studied by light

Table 1

Comparative analysis of the content of cells and their phagocytic activity in peripheral venous blood and biomaterial from the area of inflammation, depending on the presence or absence of neutropenia in the examined (M±m)

Parameters studied	Bronchitis		Colitis	
	Neutropenia, n=124	Normal neutrophil content, n=118	Neutropenia, n=135	Normal neutrophil content, n=63
1	2	3	4	5
Venous blood				
Neutrophils, %	45.93±0.38	56.18±0.54	46.29±0.43	59.25±0.37
% of active phagocytes	44.32±0.57**2-3	55.37±0.52	42.55±0.68**4-5	59.31±0.56
Phagocytic number	8.61±0.27*2-3	6.23±0.32	12.23±0.31**4-5	7.46±0.44
Monocytes, %	10.29±0.21	6.87±0.25	12.69±0.45	8.34±0.46
% of active phagocytes	19.29±0.13	18.87±0.25	23.23±0.34	21.32±0.46
Phagocytic number	8.52±0.22*2-3	5.34±0.33	9.85±0.31*4-5	6.71±0.41
Lymphocytes, %	29.42±0.58	27.51±0.53	37.39±0.48	29.22±0.53
Sputum		Feces		
Neutrophils, %	31.36±1.22**2-3	36.24±0.78	32.42±1.23**4-5	39.23±1.35
% of active phagocytes	51.24±1.53**2-3	58.36±1.24	49.83±1.12**4-5	56.45±1.32
Phagocytic number	9.53±0.56*2-3	7.32±0.43	11.64±0.62**4-5	8.32±0.79
Monocytes, %	9.52±0.47***2-3	19.36±0.52	15.23±0.51**4-5	21.43±0.65
% of active phagocytes	22.24±1.05**2-3	29.53±0.73	25.37±0.66*4-5	28.42±0.69
Phagocytic number	6.23±0.26*2-3	5.08±0.32	7.93±0.34*4-5	6.32±0.42
Lymphocytes, %	29.45±0.61	25.31±0.67	34.42±1.21*4-5	38.23±1.65
Aggregation of neutrophils, %	25.86±0.92***2-3	13.64±0.63	31.34±1.53**4-5	23.48±1.45

* p<0.05, ** p<0.01, *** p<0.001.

microscopy [3, 9]. The study of neutrophil migration in physiological conditions was carried out by the "skin window" method [33].

Statistical processing of the obtained data was carried out using the application software package "Statistica 10.0" (Stat-Soft, USA). The level of statistical significance of the differences (p) in the work was assumed to be 0.05.

Results and discussion. At the initial stages of the development of inflammation, neutrophils and mononuclears are mobilized, which can be manifested by a decrease in the total content of leukocytes in the blood due mainly to neutrophils and monocytes.

It was of interest to study in comparative terms the content of leukocytes and their phagocytic activity in the area of inflammation (table 1).

The inflammatory exudate clearly shows the ability of cells to stick together with the formation of aggregates of 3-5 cells. When calculating the number of neutrophil aggregates per 200 neutrophils, it was found that with neutropenia, the ability of granulocytes to stick together is noticeably higher. In sputum smears of patients with bronchitis, the differences in the activity of the formation of aggregates from neutrophils are on average almost 2 times greater (fig. 1, 2). Against the background of neutropenia in the area of distress, the level of migration of monocytes and lymphocytes is less pronounced. It is known that the rate of chemotaxis of polymorphonuclear granulocytes into the area of trouble is at first much higher, and then it drops rapidly; the process of penetration of monocytes into the lesion is slow, but longer. The migration of lymphocytes cannot actually be differentiated by morphological methods of investigation from the recirculation that these cells are capable of [35].

Under conditions close to physiological, in the exudate of the "skin window", no significant differences in the level of leukocyte migration were revealed (table 2). Consequently, the significant decrease in the migration activity of neutrophils and monocytes to the focus of inflammation in neutropenia is associated with a decrease in the content of their circulating pool. An increase in the content of aggregated neutrophils and monocytes in neutropenia indicates an increase in the level of irreversible aggregation or inability to dissociate aggregates under these conditions. Since the dissociation of the aggregate occurs before the secretion of acid hydrolases and cathepsin [30, 32], it can be assumed that the process of reversibility of aggregation is disrupt-
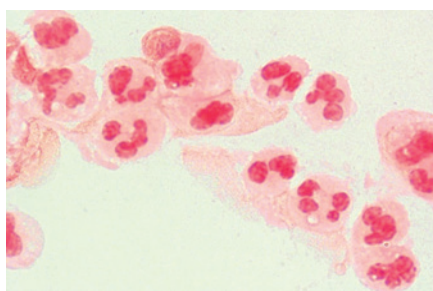
Table 2

Comparative composition of blood cells in the exudate of the "skin window" of practically healthy people 12 hours after scarification, depending on the level of neutrophils in the blood (M±m)

Indicator	Neutropenia, n=22	Normal neutrophil content, n=25
Neutrophils, %	67.34±2.18	62.77±2.38
Monocytes, %	14.52±0.38*	17.43±0.33
Lymphocytes, %	16.23±0.64*	18.65±0.52
Eosinophils, %	1.41±0.28	1.15±0.22
Aggregation of neutrophils, %	22.13±0.27***	14.53±0.19
Aggregation of monocytes, %	19.53±0.31***	11.23±0.26

* $p<0.05$, ** $p<0.01$, *** $p<0.001$.

Fig. 1. A smear of sputum at bronchitis with neutropenia. Gram staining. × 1000. Neutrophil aggregation
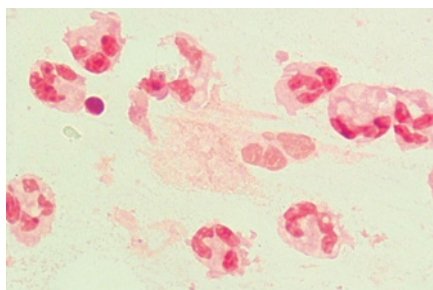

Fig. 2. A smear of sputum at bronchitis with normal neutrophil content. Gram staining. × 1000. Neutrophils

ed in neutropenia. Glucocorticoids are involved in this process, which prevent the degranulation of enzymes working in an acidic environment and the release of cathepsin and elastase.

Cell adhesion on the surface of the endothelium or other surface of the extracellular matrix and their aggregation may be related processes. The adhesion of leukocytes to the endothelium, which regulates the size of the marginal pool, on the one hand, is initiated by the aggregation of cells on the surface of the endothelium, on the other hand, is determined by the production of various adhesion molecules, selectins and their ligands

by endotheliocytes [7, 29, 34]. Adhesion ensures the attachment of neutrophils to the endothelium and other surface of the extracellular matrix, then aggregation is assimilated with the release of biologically active substances by neutrophils with subsequent activation of enzymatic systems, including the complement system.

The formation of sockets is based on the interaction of cells under the influence of C3 activation products, which initiate not only adhesion, conglutination, but also the formation of sockets. Activating factors can be trypsin-like enzymes, lipopolysaccharides, polysaccharides, C-reactive protein, Fc-aggregated Ig. Cluster-forming cells can be neutrophils, monocytes and lymphocytes [1, 11]. Upon contact of cells with cluster-forming cells, proteolytic and hydrolytic enzymes and reactive oxygen species are released [6, 15, 36]. Enzymes and biologically active substances in cases of rosette lysis are also isolated by platelets (hydrolases, cathepsins, collagenases) [14]. Intercellular interactions of neutrophils, monocytes, erythrocytes and platelets are one of the forms of participation of these cells in preventive reactions and inflammation. Cytolysis and phagocytosis, which follow the formation of rosettes, are a mechanism for protecting organs and tissues from the damaging influence of factors and actions that activate the complement system [17, 27].

Conclusion. So, with neutropenia in peripheral venous blood, the content of neutrophil aggregates in the area of inflammation is higher. Aggregation of neutrophils leads to significantly more active exosecretion, degranulation and lysis of aggregate cells, which may be one of the mechanisms for the formation of neutropenia in people living in the North.

Reference

1. Bel'chenko D.I., Krivosheina E.L. Sootnoshenie intensivnosti ekzocitarnogo lizisa eritrocitov v autorozetkah perifericheskoj krovi i haraktera techeniya ostrogo limfoblastnogo lejkoza [The ratio of the intensity of exocytic lysis of erythrocytes in peripheral blood autosets and the nature of the course of acute lymphoblastic leukemia]. Gematologiya i transfuziologiya [Hematology and transfusiology. 1999; 3:13-5. (in Russ.)].

2. Dobrodeeva L.K., Samodova A.V., Karyakina O.E. Vzaimosvyaz' urovnej soderzhaniya mozgovogo natrijureticheskogo peptida v krovi i aktivnosti immunnyh reakcij u lyudej [Relationship between levels of brain natriuretic peptide in blood and immune response in subjects] Fiziologiya cheloveka [Human physiology. 2016; 42(6):106-15. (in Russ.)]. DOI: 10.7868/S0131164616050052.

3. Zupanets I.A., Misyureva S.V., Propisnova V.V. et al. Klinicheskaya laboratornaya diagnostika: metody issledovaniya [Clinical laboratory diagnostics: research methods Kharkiv: Zolotye stranitsy, 2005. (in Russ.)].

4. Il'in M.V., Maltseva P.A., Romanov V.A., Khrustalev O.A. Izmeneniya pokazatelej okislitel'nogo stressa i apoptoza nejtrofilov pri diffuznoj i limitirovannoj formah sistemnoj sklerodermii [Changes in oxidative stress and neutrophil apoptosis in diffuse and limited forms of systemic scleroderma] Tsitokiny i vospalenie [Cytokines and inflammation. 2011; 10(3):79-81. (in Russ.)].

5. Kim L.B. Transport kisloroda pri adaptacii cheloveka k usloviyam Arktiki i kardiorespiratornoj patologii [Oxygen transport during human adaptation to Arctic conditions and cardiorespiratory pathology. Novosibirsk: Nauka, 2015. (in Russ.)].

6. Lebedeva T.N., Sobolev A.V., Minina S.V. et al. Cirkuliruyushchie immunnye kompleksy v diagnostike allergicheskoj reakcii immunokompleksnogo tipa [Circulating immune complexes in the diagnosis of allergic reactions of immune complex type] Klinicheskaya Laboratornaya Diagnostika [Clinical laboratory diagnostics. 2004; 11:11-3. (in Russ.)].

7. Pal'tsev M.A., Ivanov A.A. Mezhkletochnye vzaimodejstviya [Intercellular interactions. Moscow: Meditsina, 1995. (in Russ.)].

8. Pashinskaya K.O., Samodova A.V., Dobrodeeva L.K. Vliyanie soderzhaniya apoA-1 v perifericheskoj krovi na sostoyanie immunnogo gomeostaza u lic, prozhivayushchih v ekstremal'nyh usloviyah Arktiki [The effect of the content of ApoA-I in peripheral blood on the state of immune homeostasis in people living in extreme climatic conditions of the Arctic] Klinicheskaya Laboratornaya Diagnostika [Clinical laboratory diagnostics. 2021; 66(9):539-45. (in Russ.)]. DOI: 10.51620/0869-2084-2021-66-9-539-545.

9. Petrishcheva N.N., Papayan L.P. Gemostaz. Fiziologicheskie mekhanizmy, principy diagnostiki osnovnyh form gemorragicheskih zabolevanij [Hemostasis. Physiological mechanisms, principles of diagnosis of the main forms of hemorrhagic diseases. Saint-Petersburg, 1999. (in Russ.)].

10. Pismennaya S.V. Issledovaniye soderzhimogo kishechnika: uchebno-metodicheskoye posobiye [Study of the contents of the intestine: a teaching aid. Arkhangelsk, 2013. (In Russ.)].

11. Podberezin M.M. Sovremennye metody diagnostiki autoimmunnyh gemoliticheskih anemij [Modern methods of diagnosis of autoimmune hemolytic anemia. Gematologiya i transfuziologiya [Hematology and transfusiology. 1998; 1:15-8. (in Russ.)].

12. Roitberg G.E., Strutynsky A.V. Vnutrennie bolezni. Laboratornaya i instrumental'naya diagnostika: ucheb. Posobie [Internal diseases. Laboratory and instrumental diagnostics: studies. manual. Moscow, 2013. (in Russ.)].

13. Samodova A.V., Tsypysheva O.B. Sootnoshenie vnekletochnogo pula receptorov i urovnya immunnyh reakcij u lyudej, prozhivayushchih v usloviyah Zapolyar'ya [Correlation of Receptors' Extracellular Pool and Immune Response Level in Individuals Living in Arctic Conditions. Ekologiya cheloveka [Human ecology. 2015; 12:21-7. (in Russ.)].

14. Smirnova E.A., Belchenko D.I., Krivosheina E.L. Ispol'zovanie opredeleniya chastoty ekzocitarnogo lizisa eritrocitov v kostnomozgovyh eritroklazicheskih klasterah dlya prognozirovaniya haraktera i vybora terapii idiopaticheskoj trombocitopenicheskoj purpury u detej [Exocytic erythrocytes lysis in bone marrow erythroclazic clusters – determination of its incidence for pediatric thrombocytopenic purpura prognosis and for choice of therapy] Pediatriya [Pediatrics. 1997; 76(4):63-5. (in Russ.)].

15. Starikova E.A., Kiseleva E.P., Freidlin I.S. Geterogennost' mononuklearnyh fagocitov: subpopulyacii ili proyavleniya plastichnosti [Heterogeneity of mononuclear phagocytes: subpopulations or manifestation of their plasticity]. Uspekhi sovremennoy biologii [Successes of modern biology. 2005; 125(5):466-77. (in Russ.)].

16. Chernukh A.M. Vospalenie [Inflammation. Moscow: Meditsina, 1979. (in Russ.)].

17. Bessis M.C. Erythroblastic island, functional unity of bone marrow. Rev Hematol. 1958; 13:8-11.

18. Boulay F., Mery L., Tardif M. et al. Expressing cloning of a receptor for C5a anaphyloxin on differentiated HL-60 cells. Biochemistry. 1991; 30:2993-9. DOI: 10.1021/bi00226a002.

19. Clark R.A. Chemotactic factors trigger their own oxidative inactivation by human neutrophils. J Immunol. 1982; 129:2725-31.

20. Clark R.A., Volpp B.D., Leiddal K.G., Nauseef W.M. Two cytostatic components of the human neutrophil respiratory burst oxidase translocate to the plasma membrane during cell activation. J Clin Invest. 1990; 85(3):714-21. DOI: 10.1172/JCI114496.

21. Dobrodeeva L.K., Samodova A.V., Balashova S.N., Pashinskaya K.O. Intercellular interactions in peripheral venous blood in practically healthy residents of high latitudes. BioMed Research International. 2021; 2021:7086108. DOI: 10.1155/2021/7086108.

22. Eipper S., Steiner R., Lesner A. et al. Lactoferrin is an allosteric enhancer of the proteolytic activity of cathepsin G. PLoS One. 2016; 11(3):e0151509. DOI: 10.1371/journal.pone.0151509.

23. Ford W.L., Gowans J.L. The Traffic of Lymphocytes. Semin Hematol. 1969; 6(1):67-83.

24. Graddock P.R., Fehr J., Dalmasso A.P. et al. Hemodialysis leukopenia. Pulmonary vascular leukostasis resulting from complement activation by dialyzer cellophane membranes. J Clin Invest. 1977; 59(5):879-88. DOI:10.1172/JCI108710.

25. Graddock P.R., Hammerschmidt D.E., White J.G. et al. Complement (C5a)-induced granulocyte aggregation in vitro. A possible mechanism of complement-mediated leukostasis and leukopenia. J Clin Invest. 1977; 60(1):260-4. DOI: 10.1172/JCI108763.

26. Hammerschmidt D.E., White J.G., Craddock P.R., Jacob H.S. Corticosteroids inhibit complement-induced granulocyte aggregation. A possible mechanism for their efficacy in chock states. J Clin Invest. 1979; 63(4):798-803. DOI: 10.1172/JCI109365.

27. Jandl J.H., Tomlinson A.S. The destruction of red cells by antibodies in man. II. Pyrogenic, leukocytic and dermal responses to immune hemolysis. J Clin Invest. 1958; 37(8):1202-28. DOI: 10.1172/JCI103710.

28. Korkmaz B., Moreau T., Gauthier F. Neutrophil elastase, proteinase 3 and cathepsin G: physicochemical properties, activity and physiopathological functions. Biochimie. 2008; 90(2):227-42. DOI: 10.1016/j.biochi.2007.10.009.

29. Li S.H., Burns D.K., Rumberfer J.M. et al. Consensus repeat domains of E-selectin enhance ligand binding. J Biol.Chem.1994; 269(6):4431-7. DOI: 10.1016/s0021-9258(17)41798-4.

30. Massberg S., Grahl L., von Bruehl M-L. et al. Reciprocal coupling of coagulation and innate immunity via neutrophil serine proteases. Nat Med. 2010; 16(18):887-96. DOI: 10.1038/nm.2184.

31. Mitchell R.A., Hong L., Chesney J. et al. Macrophage migration inhibitory factor sustains macrophage proinflammatory function by inhibiting p53: Regulatory role in the innate response. Proc Natl Acad Sci USA. 2002; 99(1):345-50. DOI: 10.1073/pnas.012511599.

32. Pham C.T.N. Neutrophil serine proteases: specific regulators of inflammation. Nat Rev Immunol. 2006; 6(7):541-50. DOI: 10.1038/nri1841.

33. Rebuck J.W., Crowley J.H. A method of studying leukocytic functions in vivo. Ann N Y Acad Sci. 1955; 59(5):757-805. DOI: 10.1111/j.1749-6632.1955.tb45983.x.

34. Rodeberg D.A., Bass R.C., Alexander J.W. et al. Neutrophils from burn patients are unable to increase the expression of CD11b/ CD18 in response to inflammatory stimuli. J Leucot Biol. 1997; 61(5):572-82. DOI: 10.1002/jlb.61.5.575.

35. Springer T.A. Traffic signals for lymphocytes recirculation and leukocyte emigration: the multistep paradigm. Cell. 1994; 76(2):301-14. DOI: 10.1016/0092-8674(94)90337-9.

36. Theofilopoulus A.N., Dixon F.J. Immune complexes in human diseases: a review. Am J Phathol. 1980; 100(2):529-94.