

Analysis of the Complex of Adaptive and Compensatory Changes in Chronic Inflammation of the Reproductive System Based on the Evaluation of the Features of the Spectrum of Cytochemical Indicators of the Activity of Circulating and Tissue Leukocytes

Iryna Sokolovska^a, Nataliia Prybora^b, Valentyna Nechyporenko^a, Olena Pozdniakova^a, Nataliia Hordiienko^a, Kostiantyn Nechyporenko^a, Yuliia Siliavina^a, Iryna Antonenko^a, Nataliia Serhata^a, Valentyna Zarytska^c, Iryna Ievstigneieva^c, Tetiana Hryshyna^c, Igor Zazirny^d, Oleksandr Pokropyvnyi^d, Olena Ibrahimova^d, Lesya Yanitka^e, Iryna Kryachok^f, Iryna Tytorenko^f, Maryna Varakuta^g, Valerii Bulanov^h, Vitalii Mavrin^a, Tatyana Govorukhaⁱ, Yaroslav Kmetyuk^d

^aMunicipal Institution of Higher Education «Khortytsia National Educational and Rehabilitational Academy» of Zaporizhzhia Regional Council, Naukovogo Mistechka, 59, Zaporizhzhia, 69017, Ukraine, ^bDragomanov Ukrainian State University, ^cClassical private university, ^dKL "Feofania" DUS», ^eBogomolets National Medical University, ^fNational Cancer Institut, Dnipro Humanitarian University^g, National University Zaporizhzhia Polytechnic^h, MNCE "Kyiv City Clinical Oncology Center"ⁱ

irinasokol10@meta.ua

Keywords *adaptation, compensatory changes, cytochemical parameters, circulating and tissue leukocytes, chronic inflammation.*

Physiological processes occurring in the human body are reflected in cellular metabolism. One of the criteria for assessing the state of human health is the study of the features of the cytochemical indicators of the activity of circulating and tissue leukocytes, which react especially subtly to functional and pathological changes, reflecting multifactorial internal processes that affect the organism of the subject and provide important information about the reactivity of the organism and the severity of the course disease. The state of the cytochemical spectrum of these cells reflects reactive changes in the macroorganism, and makes it possible to determine the depth and direction of the pathological process. These studies at the cellular level can detect adaptive and compensatory changes in metabolism even when the cells do not change morphologically.

Introduction

Chronic inflammation of the genital system is one of the urgent medical problems that significantly affect the reproductive health of millions of women and men of childbearing age. At the current stage, the state of health of the Ukrainian nation, and especially reproductive health, is characterized by a low birth rate against the background of a high level of the main component of the threat to human reproduction - infertility. Every year, about 300,000 teenagers enter the reproductive age in our country, the harmonious development of which largely determines the state of their reproductive potential [1]. People with chronic inflammation of the genital organs make up 60-70% of patients who seek medical help in our country [2]. Chronic inflammation is characterized by a protracted, often erased course, a tendency to relapse, the presence of complications and resistance to therapy. The development and formation of inflammatory diseases are based on interconnected processes that begin with acute inflammation and end with destructive changes, Bacterial invasion is the main trigger of the inflammatory process of the genitals. The development of inflammation is determined by the microbial factor. The etiological structure of nonspecific inflammatory diseases of the genital organs is diverse. The cause of nonspecific inflammatory diseases can be streptococci, staphylococci, enterococci, chlamydia, mycoplasma, ureaplasma, Escherichia coli,

Candida fungi, klebsiella, proteus, viruses, actinomycetes, trichomonads (**Figure 1**)



Figure 1. Syphilis, spirochaete, Treponema, Gonococcus, Gonorrhoea, Chlamydiosis, Chlamydia, Mycoplasma, Ureaplasma. Bacterial infection. Sexually transmitted diseases

Currently, opportunistic microorganisms, as well as associations of microorganisms with a predominance of anaerobic, non-spore-forming microorganisms, play an important role in the occurrence of these diseases [3]. Due to changes in the clinical picture, it is not always possible to accurately determine the severity of the disease, to predict the development of local and general complications, therefore the issue of developing an individual approach to the treatment of patients based on objective changes and easily measurable laboratory indicators is relevant and important [4]. Circulating and tissue leukocytes react especially subtly to pathological changes, therefore an important indicator of the body's natural non-specific resistance is the functional state of neutrophilic leukocytes, which are responsible for the process of phagocytosis and intracellular digestion of bacterial agents [5].

The role of neutrophils in inflammatory processes Neutrophils are the largest group of

leukocytes, which make up 50-75%[6]. After leaving the bone marrow, neutrophils circulate in the blood for only a few hours (on average, about 10 hours). Then, after leaving the blood stream, they remain among the connective tissue elements of most organs for several days. Here, neutrophils are able to capture and digest microorganisms. A mature neutrophil has segmented nuclei, an immature one has a rod-shaped or bean-shaped nucleus [7].

Neutrophils contain large amounts of glycogen and lipids in the cytoplasm, which provide neutrophils with energy (Figure 2)

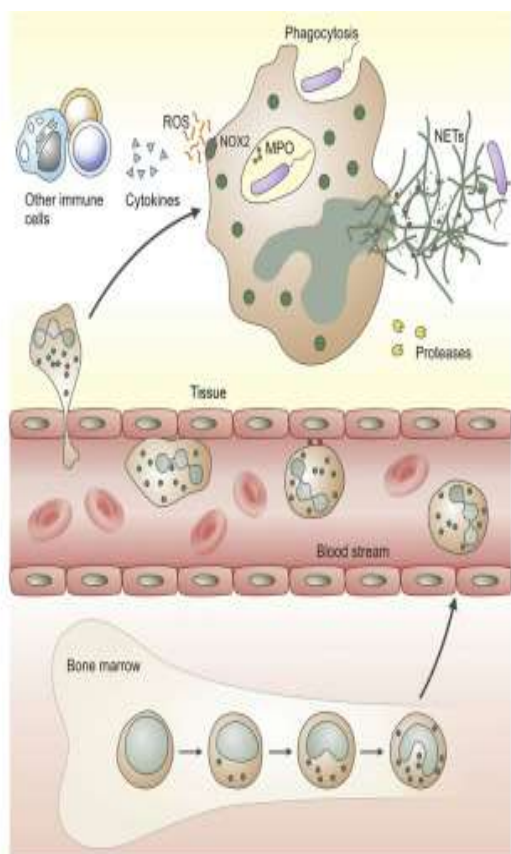


Figure 2. The Neutrophil.

The grain is fine, it is not easily visible both in fresh and in fixed colored preparations. Neutrophils contain a complete set of substances with which they destroy phagocytosed

microorganisms [8]. They include active chemical substances. Neutrophils perform the following functions: high migratory activity, phagocytosis, adhesion, digestion of pathogenic cells, strengthening of the antibacterial effect, ability to recognize foreign agents [9]. With the help of receptors, the neutrophil recognizes bacteria, using oxygen and anoxic mechanisms to destroy bacteria (Figure 3).

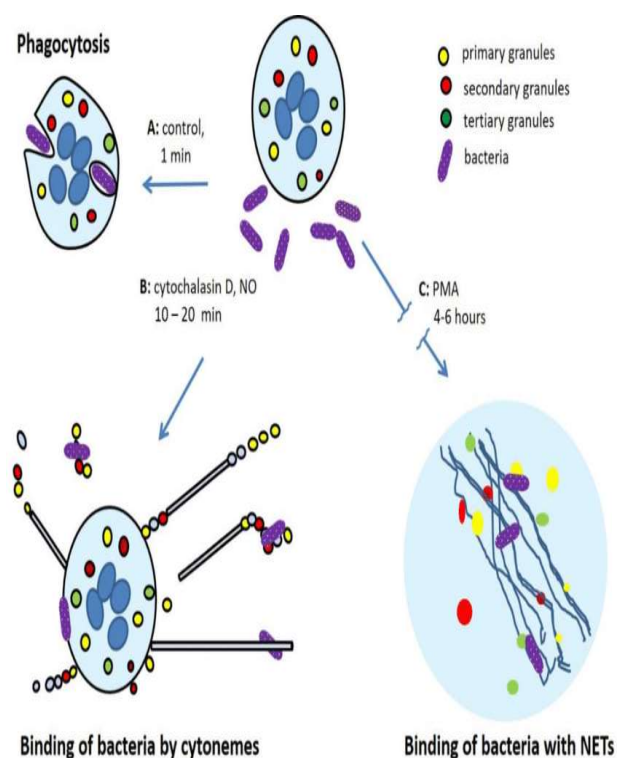


Figure 3. Mechanisms of interactions of human neutrophils with bacteria: (A) phagocytosis; (B) extracellular binding of bacteria by cytonemes of living neutrophils; (C) binding of bacteria by neutrophil extracellular traps (NETs) composed of nuclear DNA and granular proteins released by dead neutrophils.

Cytochemical studies. It is known that cytochemical techniques make it possible to differentiate intracellular biostructures; their advantages are determined by: availability; technical adequacy; minimum requirements for the volume of the researched material; high

informativeness. They make it possible to detect such changes in intracellular components that are difficult, and sometimes impossible, to identify using other, more complex methods [10]

The specified methods allow: to consider the mechanisms of the participation of hemoelements in the development of the disease; trace the stages of formation of intracellular disorders under the influence of infectious agents (disruption of metabolic tension, enzyme spectrum of coordination of exchange processes) [11].

This contributes to a clearer understanding of the possibilities of compensatory reactions. Cytochemical changes in neutrophils and monocytes act as an objective criterion for assessing natural resistance at various stages of the development of the inflammatory process. Therefore, from the perspective of the above, it seems very promising to determine the activity of cytochemical indicators of leukocytes, which reflect the energy state and structural integrity of cells.

Experimental part

1. *Clinical examination.* 95 clinically healthy persons (50 men and 45 women) and 180 patients with chronic inflammation of the genital system aged 18-50 years were examined. The clinical condition of the patients was evaluated based on the survey, collection of complaints, history, examination of the skin of the genital organs, and in women - of the mucous membrane of the vagina using a gynecological mirror. For

biochemical, general clinical and cytological research, blood and scrapings from the mucous membrane of the urogenital tract were taken before the start of the treatment course. Blood was taken from a vein and stabilized with a five percent sodium citrate solution. Scrapings from the mucous membrane of the genitals were taken in men - from the middle part and navicular fossa of the urethra, in women - from the urethra, posterior vault of the vagina and cervical canal. Clinical examination of patients and collection of biomaterial for laboratory research were carried out in conjunction with the dermatovenerologist of the city hospital

The control group (C) of the examined consisted of 95 clinically healthy persons (part-time donors), of whom 50 were men and 45 were women (**Table 1**). By age, the composition of the control was as follows: 18-28 years - 30 people, 29-39 years - 35 and 41-50 years - 30 people. The groups of subjects included 180 patients with chronic inflammation, of which 83 were men and 97 were women (**Table 1**). Patients were divided by age as follows: 18-28 years - 60, 29-39 years - 58 and 40-50 years - 44 patients.

Table 1. Distribution of examined persons by age and sex

Group	C1	C2	C3	1	2	3
Age (year)	18-28	29-39	40-50	18-28	29-39	40-50
Men	15	20	15	28	30	25
Women	15	15	15	32	28	19

2. *Study of the state of systemic and local non-specific protection of patients with chronic*

inflammation of the genital system in the context of adaptive and compensatory changes

All the individuals examined underwent a general clinical blood test [12]. The counts of erythrocytes, leukocytes, and platelets were determined using Goryaev's counting chamber. The concentration of hemoglobin in the blood, as well as the color indicator, were determined. Blood cells in smears were morphologically studied using the Romanovsky-Giemsa staining method. The leukogram was calculated using a unified method, and the erythrocyte sedimentation rate (ESR) was determined. Additionally, cytochemical indicators of leukocytes in blood smears were examined. The myeloperoxidase activity of polymorphonuclear leukocytes was assessed using the Graham-Knollie method [13], while the content of cationic proteins (CP) was determined according to V.G. Shubich's method, and the average cytochemical coefficient was calculated.

To assess monocyte (MON) activity, the activity of the naphthyl acetate esterase enzyme was determined using the Leffler method [14]. The percentages of positively reactive cells, as well as esterase-positive lymphocytes (likely T cells), within the total lymphocyte pool were calculated.

An idea of the state of systemic nonspecific protection of the body can be obtained by analyzing the quantitative and qualitative indicators of the composition of leukocytes and the sedimentation rate of

erythrocytes of peripheral blood (ESR). Integral hematological indicators can change already in the pre-pathological period, or in the early stages of the disease, when preventive measures to regulate protective reactions are most effective [15]. Also, formalized integrative indicators can change in the case of a sluggish, chronic course of the disease, when the indicators of the general blood analysis do not go beyond fairly wide limits of normal values. In addition, the use of calculated indicators makes it possible to tentatively assess the activity of various links of the system of non-specific reactivity without complex additional examinations.

Based on leukogram data and peripheral blood erythrocyte sedimentation rate, integral indicators were calculated using mathematical formulas. Calculation of integral formalized indicators of leukograms of peripheral blood was carried out using a special computer program.

The state of local non-specific protection was evaluated when examining smears-scrapings of the mucous membrane of the genital organs of patients with chronic inflammation. Analysis of the smear allows to judge the presence or absence of an inflammatory process, as well as to see infectious agents in the smear. Leukocytes serve as a criterion for inflammation. The normal number of leukocytes in a smear: no more than 10 - 15 in the field of vision. An increase in the number of leukocytes indicates inflammation. Moreover, the more leukocytes, the more

pronounced the inflammatory process (**Figure 4**).

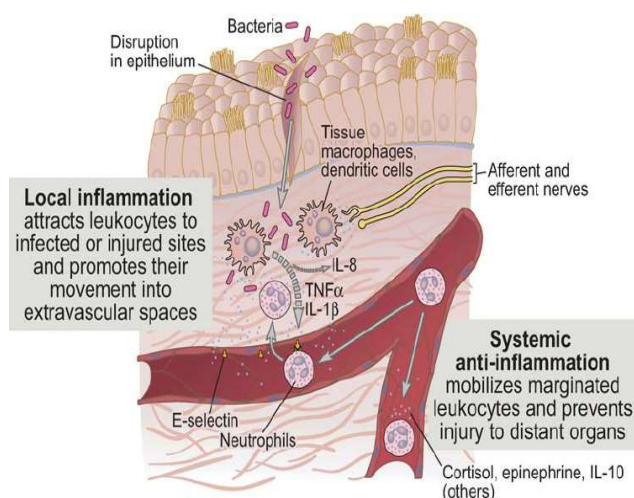


Figure 4. Local inflammation and systemic anti-inflammation hypothesis. When bacteria invade through an epithelial barrier, they are usually sensed by tissue-resident macrophages, dendritic cells, and/or mast cells. These cells release mediators that attract neutrophils to the site of infection, promote adhesion of the neutrophils to local vascular endothelium, and facilitate their diapedesis into the infected site

In the smear, causative agents of some sexually transmitted diseases can be detected, such as gonococci (causing gonorrhoea), trichomonads (trichomoniasis, trichomonosis), gardnerella (gardnerellosis, vaginal dysbacteriosis), candida (candidiasis, thrush).

Representatives of opportunistic flora may also be detected: staphylococci, streptococci, diplococci, bacteria (*Escherichia coli*). Some causative agents of sexually transmitted infections, such as chlamydia, mycoplasma, ureaplasma, are not detected in the general smear. Therefore, a high level of leukocytes in the smear, in the absence of visible pathogens, may indicate the presence of these hidden infections [16].

The average number of leukocytes in smears stained by the Romanovsky-Giemsa

method and their percentage ratio were calculated, cytochemical indicators were additionally determined: myeloperoxidase activity and the content of cationic proteins of polymorphonuclear leukocytes, naphthyl acetate esterase activity of mononuclear monocytes (MON) and lymphocytes.

Results and discussion

Cytochemical studies are normal.

Cytochemical analysis of enzyme systems, determination of the content of lipids, hydrocarbons, proteins and other substances in cells is one of the promising directions [17]. These studies at the cellular level can detect adaptive and compensatory changes in metabolism even when the cells do not change morphologically. Semi-quantitative evaluation of results is most often used during cytochemical research [18].

Alkaline phosphatase (K.F.3.1.3.1.)

Alkaline phosphatase is found in neutrophil granulocytes, starting with metamyelocytes. However, its largest amount is in mature neutrophils[19]. Alkaline phosphatase belongs to the group of hydrolytic enzymes with optimum action at pH 9.6; carries out hydrolysis of monosubstituted esters of orthophosphate. The activity is associated with specific granules, determined by the azo coupling method according to Keplow in the modification of M. G. Shubich. **Table 2** presents the normal values of the average cytochemical coefficient (ACC) of neutrophil alkaline phosphatase.

Table 2. Normal values of the average cytochemical coefficient of neutrophil alkaline phosphatase

Age, years	Women	Men
16–35	0,47±0,07	0,47±0,07
36–60	0,68±0,10	0,74±0,10
61–90	0,42±0,07	0,22±0,05

Acid phosphatase (K.F.3.1.3.2.)

Acid phosphatase belongs to the group of hydrolytic enzymes with an optimum pH of 5,2. It is determined in the cytoplasm, mainly, of neutrophils and lymphocytes, as well as other cells containing nuclei, and platelets. Localization of the enzyme in neutrophils is associated with primary granules, but not with secondary and tertiary granules. That is, younger cells of the neutrophil series give a more intensive reaction to acid phosphatase. For semiquantitative determination of acid phosphatase activity, Burston's azo coupling method is used. In neutrophils, the reaction appears in the form of diffuse staining or small granules, in lymphocytes - large single granules. **Table 3** presents the normal values of ACC acid phosphatase of neutrophils.

Table 3. Normal values of ACC acid phosphatase of neutrophils

Age, years	Men	Women
16–35	0,79±0,02	0,81±0,09
36–60	0,68±0,11	0,64±0,04
61–90	0,44±0,02	0,41±0,02

Normally, the percentage of positively reacting lymphocytes is 26. We investigated the activity of acid phosphatase of neutrophils and lymphocytes of 95 donors. ACC in neutrophils was 1.02±0.08 (0.82–1.21). The percentage of

positively reacting lymphocytes is 51.0±6.7 (30.9–71.1).

Myeloperoxidase (K.F. 1.11.1.7.)

Myeloperoxidase is an iron porphyrin enzyme that catalyzes in the presence of hydrogen the oxidation of various specific substrates, including phenols, amino acids, and some aromatic acids. Peroxidases were detected in specific granules of cells of different maturity of granulocytic rows and not always - in the cytoplasm of monocytes. Myeloperoxidase plays an essential role in phagocytosis. The enzyme is one of the main oxygen-dependent microbicidal systems of the phagocyte.

Myeloperoxidase is a marker of myeloid cells. Determination of enzyme activity is based on the oxidation of benzidine into colored oxybenzidine. The reaction manifests itself in the form of diffuse coloration or small granules. An increase in activity occurs during inflammatory processes, a decrease in activity when taking corticotropin, (**Table 4**) presents the normal values of ACC myeloperoxidase of neutrophils

Table 4. Normal values of ACC myeloperoxidase of neutrophils

Age, years	Women	Men
16–35	2,24±0,10	2,49±0,09
35–60	2,55±0,11	2,35±0,12
61–90	2,24±0,08	2,23±0,11

Nonspecific esterases.

Nonspecific esterases (NSE) are a group of enzymes capable of hydrolyzing simple esters of N-free alcohols and organic acids. Enzymes are localized mainly in the lysosomes of monocytes and lymphocytes. In monocytes,

activity is manifested in the form of fine granularity, or diffuse staining, in lymphocytes - in the form of large single granules. In granulocytes, enzyme activity is practically not detected. The determination of alpha-naphthyl esterase activity is based on the hydrolysis of alpha-naphthyl acetate to free phenol, which with diazotium salts gives a colored color.

Normal values: ACC in monocytes - 0.95 ± 0.01 , the percentage of positively reacting lymphocytes is 18.0 ± 0.4

Cationic protein. Cationic protein is a non-enzymatic protein that plays an important role in the process of phagocytosis. It, being adsorbed on the surface of the microbial cell, facilitates the penetration of lysosomal enzymes into the cytoplasm of the absorbed particle. Diachromic cationic dyes are used to study cationic proteins. Normal values: ACC in adults is 1.58 ± 0.03 , the decrease in the indicator occurs during inflammatory processes.

Glycogen.

Glycogen is localized in the cytoplasm and plays an important role in the energy supply of cells. For its determination, glycogen oxidation methods are used with the help of potassium periodate with the formation of aldehyde compounds that react with schiff-iodic acid. Glycogen is found in neutrophils in the form of diffuse staining of the cytoplasm or fine granularity, in lymphocytes - in the form of single large grains, in megakaryocytes in the form of granules resembling a cluster of blood

platelets. **Table 5** presents the normal values of the ACC glycogen of neutrophils.

Table 5. Normal values of ACC glycogen of neutrophils

Age, years	Men	Women
16–35	$2,52 \pm 0,12$	$2,04 \pm 0,12$
36–60	$1,91 \pm 0,15$	$2,17 \pm 0,14$
61–90	$1,97 \pm 0,12$	$1,89 \pm 0,17$

Normally, the percentage of lymphocytes containing glycogen is 10.4 ± 2.3 ; megakaryocytes - 62.0 ± 3.6 , increase of ACC glycogen in neutrophils occurs during inflammatory processes, reduction of ACC glycogen in neutrophils occurs under the action of ionizing radiation, toxic impact of bone marrow by industrial, agricultural, household chemical compounds, use of myelodepressive agents.

Lipids.

Lipids are usually associated with protein in cells, that is, they are in the composition of lipoproteins, which are part of cell membranes, mitochondria and other organelles that play an important role in the transport of lipids. Determined mainly in neutrophils. Cytochemical research is based on the use of fat-soluble substances (sudan III, sudan IV, black sudan). A decrease in the content of lipids in neutrophils occurs during inflammatory processes, (**Table 6**) presents the normal values of ACC lipids of neutrophils.

Table 6. Normal values of ACC lipids of neutrophils

Age, years	Men	Women
16–35	$2,42 \pm 0,12$	$2,28 \pm 0,12$
36–60	$2,40 \pm 0,13$	$2,63 \pm 0,12$
61–90	$2,49 \pm 0,11$	$2,50 \pm 0,08$

Conclusions.

Cytochemical indicators of the activity spectrum of circulating and tissue leukocytes in examined persons with a chronic inflammatory process.

During the microscopic examination of smears of scrapings from the mucous membrane of the genitals of patients with chronic non-specific inflammatory diseases of the genital organs of different age groups, an inflammatory reaction was observed, the type and severity of which slightly depended on the degree of insemination by pathogenic flora and epithelial dystrophy[20]. The number of leukocytes varied from 5 to 20 in the field of vision, detritus and mucus were determined. There were no significant differences in the ratio of different types of leukocytes in the groups of patients (Table 7).

When patients were divided into groups depending on the type of pathogen in the 2nd group (with trichomoniasis) compared to the others, the relative numbers of lymphocytes and monocytes in smears from the mucous membrane of the genitals were probably lower.

Table 7. The content of leukocytes in smears of scrapings from the mucous membrane of the genitals in patients with chronic nonspecific inflammation

Indicator	Group					
	1m	2 m	3m	1w	2w	3w
Number of neutrophils, %	91, 1 ± 3,1	91, 9 ± 3.5	88, 2 ± 6.7	88, 5 ± 5,8	85, 1 ± 7,2	88, 6 ± 4,3
Number of lymphocytes, %	6,4 5 ± 3,1 7	6,0 0± 2.9 3	8,9 2 ± 5.3 8	8,1 1 ± 4,4 0	11, 66 ± 6,5 6	7,4 1 ± 3,3 0
Number of histiocytes, %	2.1 4 ± 1,4 6	2.1 0 ± 1,3 3	2,6 7 ± 1,8 8	3,2 4 ± 2,2 2	2,9 3 ± 1.9 9	4,1 4 ± 2.7 1

Notes:

- 1m - men of the 1st group,
- 1w - women of the 1st group,
- 2m - men of the 2nd group,
- 2w - women of the 2nd group,
- 3m - men of the 3rd group,
- 3w - women of the 3rd group

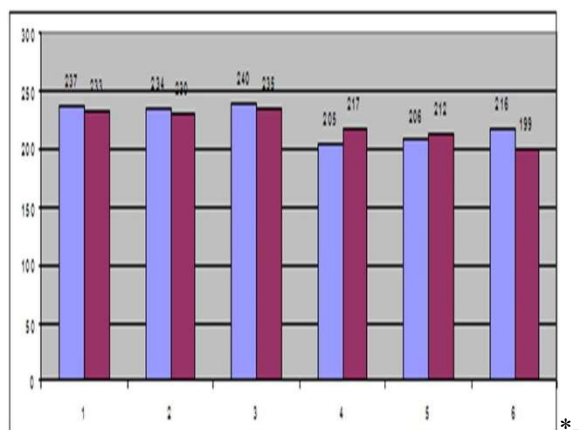
That is, local protective reactions, even with a chronic course of inflammation in trichomoniasis, to a greater extent occur due to microphagocytosis (Table 8). Cytochemical indicators of circulating leukocytes in clinically healthy women and men were at the same level.

Table 8. The content of leukocytes in smears of scrapings from the mucous membrane of the genital organs of patients with various sexually transmitted infections

Indicator	Group					
	1	2	3	4	5	6
Number of neutrophils, %	88,6 ± 6,0	91,0 ± 4,9	86,9 ± 7,2	88,6 ± 12,3	88,4 ± 5,1	88,2 ± 6,8
Number of lymphocytes, %	8,1 ± 5,0	7,6 ± 0,44	8,81 ± 0,52	7,44 ± 4,40	8,22 ± 0,5	9,44 ± 0,56
Number of histiocytes, %	3,26 ± 0,27	1,88 ± 0,13	2,96 ± 0,16	3,59 ± 0,22	3,11 ± 0,2	2,38 ± 0,15

Note.

* - p<0.05 in comparison with other groups



Notes:

- 1-3 – men Control (C1-C3);
- 1'-3' – women Control (C1-C3);
- 4-6 – men of the 1st, 2nd, 3rd groups of patients;
- 4'-6' – women of the 1st, 2nd, 3rd groups of patients

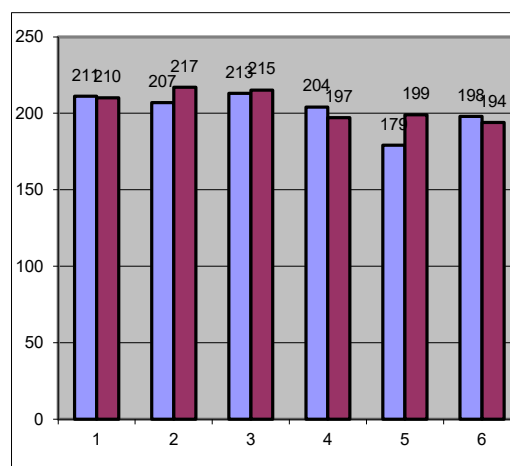
5. σ - standard deviation from the mean value.

Figure 5. The average cytochemical coefficient (ACC) of myeloperoxidase activity of peripheral blood neutrophils in patients with chronic nonspecific inflammation of the genitals

In patients with chronic non-specific inflammation of the genitals, ACC myeloperoxidase in the circulating pool of polymorphonuclear leukocytes was significantly reduced compared to controls, except for the 1st group of women. Thus, in sick men of the 1st, 2nd, and 3rd groups, the ACC of myeloperoxidase of polymorphonuclear leukocytes was reduced by 1,16, 1,16, and 1,10 times, respectively (p<0.05).

In women of the 2nd and 3rd groups, it was reduced by 1,10 and 1,17 times, respectively (p<0.05) (**Figure 5**).

ACC of cationic proteins of the circulating pool of polymorphonuclear leukocytes was significantly reduced in men of the 2nd group by 1.18 times (**Figure 6**).



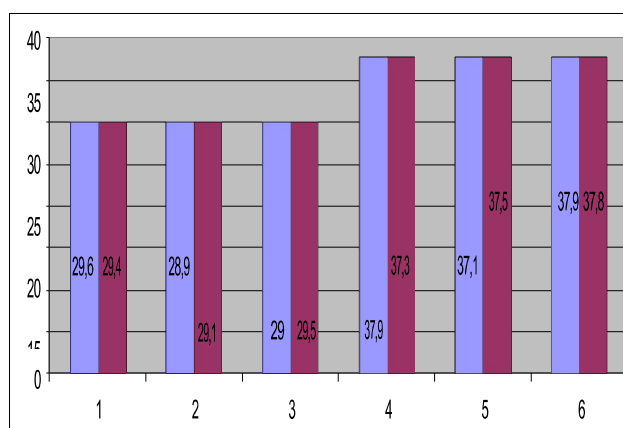
Notes:

- 1-3 – men Control (C1-C3);
- 1'-3' – women Control (C1-C3);
- 4-6 – men of the 1st, 2nd, 3rd groups of patients;
- 4'-6' – women of the 1st, 2nd, 3rd groups of patients

5. σ - standard deviation from the mean value.

Figure 6. The ACC of CP of peripheral blood neutrophils in patients with chronic nonspecific inflammation of the genitals

The percentage of positively reacting cells to non-specific esterases of the circulating pool was increased in both men and women of all groups. Thus, in sick men of the 1st, 2nd and 3rd groups, the percentage of cells positively reacting to non-specific esterases of lymphocytes was increased by 1.28, 1.25 and 1.34 times, respectively ($p < 0.05$) (**Figure 7**). In women of the 1st, 2nd, and 3rd groups, it exceeded such control by 1.27, 1.27, and 1.28 times, respectively ($p < 0.05$). This indicates an increase in the relative content of probably T-lymphocytes in the circulating pool of lymphocytes.



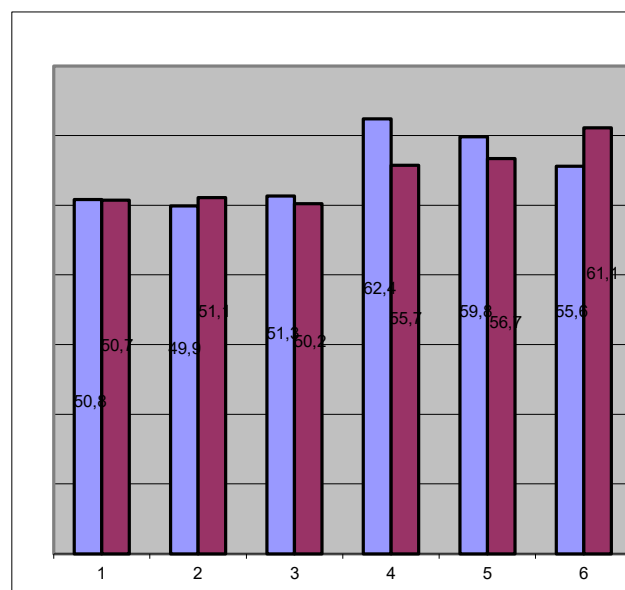
Notes:

- 1-3 – men Control (C1-C3);
- 1'-3' – women Control (C1-C3);
- 4-6 – men of the 1st, 2nd, 3rd groups of patients;
- 4'-6' – women of the 1st, 2nd, 3rd groups of patients
- \square - standard deviation from the mean value.

Figure 7. The percentage of cells positively reacting to non-specific esterases in the pool of circulating lymphocytes of peripheral blood in patients with chronic non-specific inflammation of the genital

Regarding the percentage of cells positively reacting to non-specific esterases of the circulating pool of monocytes, a significant

increase was observed in men of the 1st and 2nd groups and in women of the 3rd group (**Figure 8**) in 1.22, 1.18 and 1.21 times, respectively ($p < 0.05$).

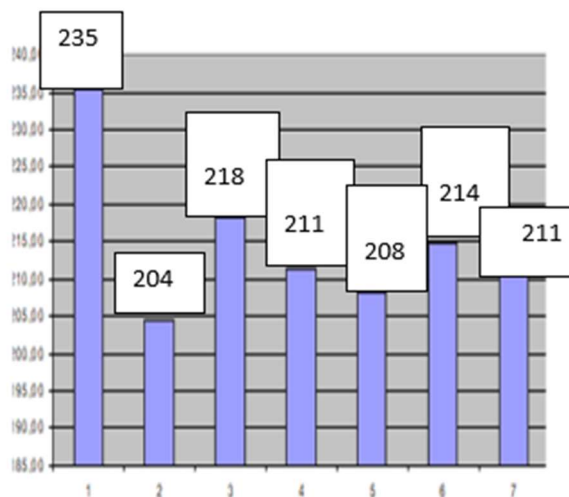


Notes:

- 1-3 – men Control (C1-C3);
- 1'-3' – women Control (C1-C3);
- 4-6 – men of the 1st, 2nd, 3rd groups of patients;
- 4'-6' – women of the 1st, 2nd, 3rd groups of patients
- \square - standard deviation from the mean value.

Figure 8. The percentage of cells positively reacting to nonspecific esterases in the pool of circulating monocytes of peripheral blood in patients with chronic nonspecific inflammation of the genitals

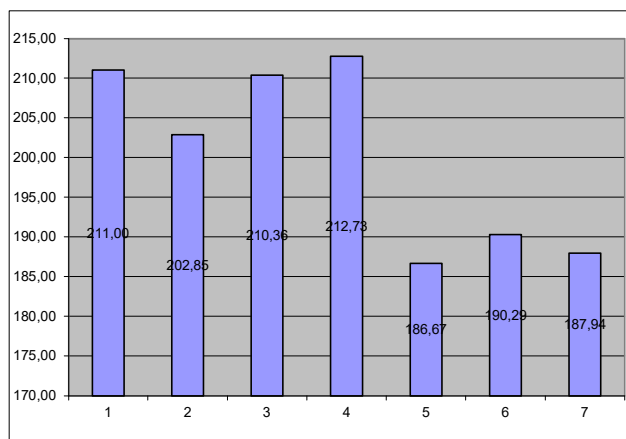
In groups of patients with different types of infectious agents, the preservation of myeloperoxidase activity is determined (**Figure 9**). In groups of patients with various types of infection, a decrease in the content of cationic proteins in the circulating pool of polymorphonuclear leukocytes is determined in groups 4, 5, 6 (by 1.13, 1.11 and 1.12 times) (**Figure 10**).



Notes:

1. Control;
2. 2-7 patients of 1-6 groups;
3. σ - standard deviation from the mean value.

Figure 9. The average cytochemical coefficient (ACC) of myeloperoxidase activity of circulating neutrophils in patients with chronic nonspecific inflammatory process of the genitals with various types of sexually transmitted infections

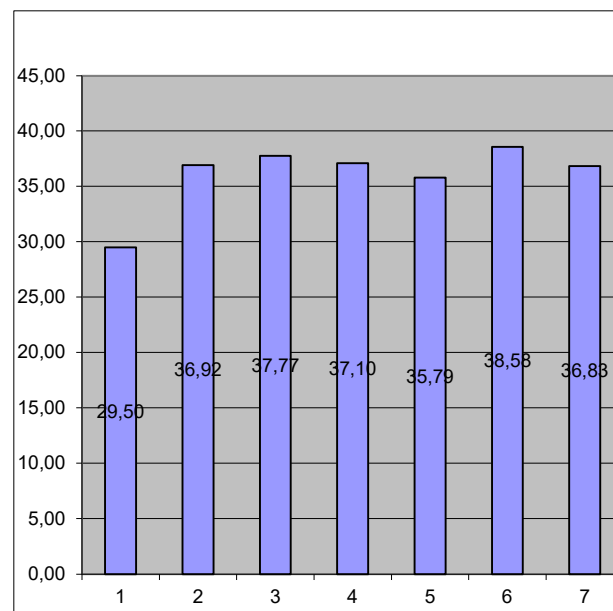


Notes:

1. Control;
2. 2-7 patients of 1-6 groups
3. σ - standard deviation from the mean value.

Figure 10. The ACC of cationic proteins of circulating neutrophils in patients with chronic nonspecific inflammatory process of the genitals with various types of sexually transmitted infections

Regarding the activity of non-specific esterase of circulating monocytes (**Figure 11**), it was significantly increased in patients of all groups with various infectious agents by 1.2 times compared to the control.



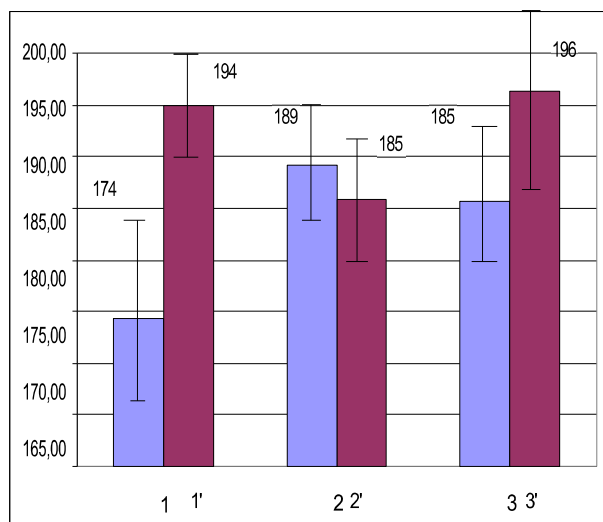
Notes:

1. Control;
2. 2-7 patients of 1-6 groups
3. σ - standard deviation from the mean value

Figure 11. The percentage of cells positively reacting to non-specific esterases in the pool of circulating monocytes in patients with chronic non-specific inflammatory process of the genitals with various types of sexually transmitted infections

Thus, in patients with chronic nonspecific inflammatory process of the genitals with various types of sexually transmitted infections, there was a decrease in the phagocytic activity of neutrophils of the oxygen-independent type in groups of patients with chlamydial, viral and mixed flora. The phagocytic activity of

circulating monocytes and the relative content of probably T-lymphocytes in the circulating lymphocyte pool probably increased in patients of all groups with different types of infectious agents.



Notes:

1. 1-3. men of 1-3 groups;
2. 1'-3' - women of 1-3 groups;


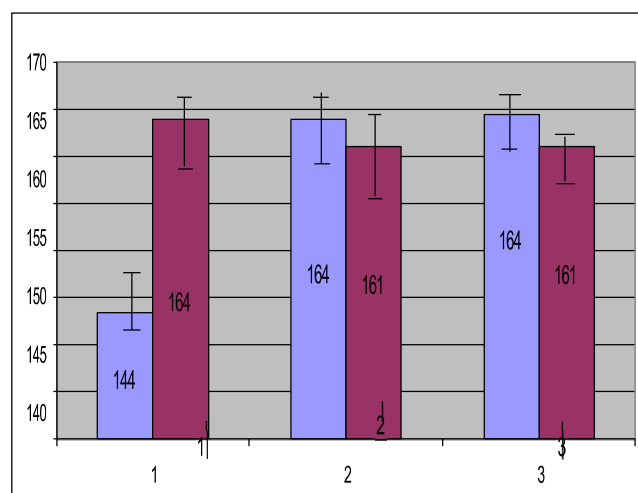
3.  - standard deviation from the mean value.

Figure 12. The ACC of myeloperoxidase activity of tissue neutrophils in patients with chronic nonspecific inflammatory process of the genitals

The average cytochemical coefficient of myeloperoxidase activity of tissue polymorphonuclear leukocytes in sick men was not significantly different from that in controls (**Figure 12**).

The ACC of the cationic proteins (CP) of the tissue pool of polymorphonuclear leukocytes in all groups of patients was significantly ($p < 0.05$) smaller, on average by 1,2 times, than the circulating one (**Figure 13**).



Notes:

1. 1-3. men of 1-3 groups;
2. 1'-3' - women of 1-3 groups;


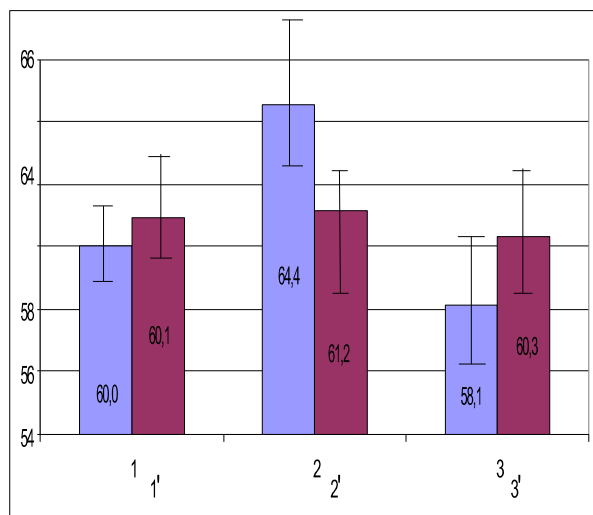
3.  - standard deviation from the mean value.

Figure 13. The ACC average of the content of cationic proteins in tissue neutrophils in patients with a chronic nonspecific inflammatory process

This indicates a decrease in the phagocytic activity of tissue polymorphonuclear leukocytes by an oxygen-independent mechanism in comparison with the activity of circulating polymorphonuclear leukocytes.

At the same time, the percentage of cells positively reacting to non-specific esterases of tissue lymphocytes in all groups of patients was significantly on average 1,6 times ($p < 0.05$) higher than that in the circulating pool (**Figure 14**).



Notes:


- 1-3. men of 1-3 groups;
- 1'-3' - women of 1-3 groups;
-  - standard deviation from the mean value.

Figure 14. The percentage of cells positively reacting to non-specific esterases in the pool of peripheral blood tissue lymphocytes in patients with chronic non-specific inflammatory process

That is, in the focus of inflammation, the relative content of T-lymphocytes in the lymphocyte pool is probably increased compared to the circulating blood.

In patients with various types of infections, there was a decrease in the average cytochemical coefficient of myeloperoxidase activity of tissue polymorphonuclear leukocytes, which was probably lower than that in comparison with the circulating pool of polymorphonuclear leukocytes of the same group of patients by 1,5 times ($p < 0.05$). In the 4th group of patients, the average cytochemical coefficient of myeloperoxidase activity of polymorphonuclear leukocytes was probably

lower than that of patients in the 1st-3rd and 5-6th groups ($p < 0.05$).

The average cytochemical coefficient of cationic proteins of the tissue pool of polymorphonuclear leukocytes in all groups of patients with various sexually transmitted infections was also lower than that in the circulating pool by an average of 1,2 times ($p < 0.05$).

1. Thus, in sick men and women, a weakly expressed inflammatory reaction was determined both systemically and locally in the focus of the lesion. The phagocytic activity of polymorphonuclear leukocytes is reduced mainly by an oxygen-dependent mechanism, and tissue - by an oxygen-independent mechanism. As an exception, in patients with chlamydial infection, the phagocytic activity of tissue polymorphonuclear leukocytes was also reduced by an oxygen-dependent mechanism. In patients with trichomoniasis, oxygen-independent mechanisms of phagocytosis were maintained at the highest level. In patients with a chronic non-specific inflammatory process, a preference was found for the macrophage component of the phagocytosis system, T lymphocytes probably predominated among the cells of the immune system.

2. It has been established that the content of cationic proteins in neutrophils correlates with the severity of the disease: a high content ensures an acute clinical course with the development of complications, a low content indicates the

functional inferiority of polymorphonuclear leukocytes, which contributes to the transition of inflammation to a chronic form.

References

- [1] Pongratz G, Straub R. The sympathetic nervous response in inflammation. *Arthritis Research & Therapy* 2014;16(6):1-12.
- [2] Sokolovskaya I, Nechiporenko V, Gordiyenko N, Pozdnyakova O, Volkova S, Cymbal V, Makurina G. Lipid peroxidation during chronic inflammation. *French-Ukrainian Journal of Chemistry* 2018;6(2):38-53.
- [3] Cerqueira É, Marinho DA, Neiva HP, Lourenço O. Inflammatory effects of high and moderate intensity exercise - a systematic review. *Frontiers in Physiology* 2020;10:1550.
- [4] Wen Y, Zhu Y, Zhang C, Yang X, Gao Y, Li M, Yang H, Liu T, Tang H. Chronic inflammation, cancer development and immunotherapy. *Frontiers in Pharmacology* 2022;13:1-16.
- [5] He Y, Yue Y, Zheng X, Zhang K, Chen S, Du Z. Curcumin, Inflammation, and Chronic Diseases: How Are They Linked? *Molecules* 2015;20(5):9183-9213.
- [6] Sokolovska I, Maryukhnich N, Zarytska V, Kyrpychenko O, Nechiporenko V, Pozdnyakova O, Gordiyenko N, Tsymbal V. The state of lipid exchange and thrombotic link of hemostasis in patients with chronic non-specific inflammatory diseases of genitals. *French-Ukrainian Journal of Chemistry* 2019;7(1):34-45.
- [7] Weiss G, Goldsmith L, Taylor R, Bellet D, Taylor H. Inflammation in Reproductive Disorders. *Reproductive Sciences* 2009;16(2):216-229.
- [8] Sokolovskaya I, Kutsak A, Zarytska V, Nechiporenko V, Gordiyenko N, Siliavina Y, Horash K, Plakhotnik O. Investigation of aspects of the interaction of the indicators of lipid exchange, trombocitarian block of hemostasis, total body reactivity and their influence on the psychosomatic harmonization of the man in chronic inflammatory processes. *French-Ukrainian Journal of Chemistry* 2019;7(2):120-137.
- [9] Nedeva C. Inflammation and Cell Death of the Innate and Adaptive Immune System during Sepsis. *Biomolecules* 2021;11(7):1011.
- [10] Sokolovskaya I, Prybora N, Nechyporenko V, Pozdnyakova O, Hordiienko N, Nechyporenko K, Siliavina Y, Serhata N, Mavrin V, Semeniv I, Kotuza A, Pokropyvnyi O, Ibrahimova O, Kryachok I, Tytorenko I, Yanitka L, Zarytska V, Bulanov V, Muz N, Kudinova M, Essandoh M. Peculiarities of the State of the Body's Immunoprotective Functions, Bacterioscopic and Cytological Studies in the Presence of a Chronic Inflammatory Process of the Reproductive System. *French-Ukrainian Journal of Chemistry* 2023;11(1):60-73.
- [11] Sellami M, Gasmi M, Denham J, Hayes L, Stratton D, Padulo J, Bragazzi N. Effects of Acute and Chronic Exercise on Immunological Parameters in the Elderly Aged: Can Physical Activity Counteract the Effects of Aging? *Frontiers in Immunology* 2018;9:1-17.
- [12] Kienle K, Lämmermann T. Neutrophil swarming: an essential process of the neutrophil tissue response. *Immunological Reviews* 2016;273(1):76-93.
- [13] Sokolovskaya I, Kryachok I, Chorna I, Semeniv I, Kotuza A, Hryhorieva N, Plakhotnik O, Zarytska V, Zhuravel V, Kmetyuk Y, Kondratiuk A. Influence of exogenous, physiological and factors of chronic inflammatory process on indicators of disturbances of adaptive processes of the person. *French-Ukrainian Journal of Chemistry* 2020;8(2):183-202.
- [14] Kaufmann S. Immunity to Intracellular Bacteria. *Annual Review of Immunology* 1993;11(1):129-163.
- [15] Sokolovskaya I, Prybora N, Valentyna Nechiporenko V, Pozdnyakova O, Hordiienko N, Nechiporenko K, Siliavina Y, Mavrin V, Kotuza A, Kliusov O, Kryachok I, Tytorenko I, Zub V, Yanitka L, Hordienko N, Kudinova M, Mamedli Z, Hordiienko L, Kmetyuk Y, Sprynchuk N. Assessment of the State of Platelet Haemostasis and Adhesive - Aggregation Properties of Platelets as a Factor of Increasing the Tendency to Thrombosis in Chronic Inflammation. *French-Ukrainian Journal of Chemistry* 2022;10(2):22-36.

[16] Kutikhin A, Tupikin A, Matveeva V, Shishkova D, Antonova L, Kabilov M, Velikanova E. Human Peripheral Blood-Derived Endothelial Colony-Forming Cells Are Highly Similar to Mature Vascular Endothelial Cells yet Demonstrate a Transitional Transcriptomic Signature. *Cells* 2020;9(4):876.

[17] Ullyot J, Bainton D. Azurophil and specific granules of blood neutrophils in chronic myelogenous leukemia: an ultrastructural and cytochemical analysis. *Blood* 1975;45(4):469-482.

[18] Sokolovskaya I, Prybora N, Nechyporenko V, Pozdniakova O, Hordiienko N, Antonenko I, Nechyporenko K, Serhata N, Siliavina Y, Zarytska V, Bielan O, Pokropyvnyi O, Yunger V, Yanitka L, Galtseva T, Kryachok I, Tytorenko I, Varakuta M, Mavrin V, Kmetyuk Y. Assessment of the Nature of Dyslipoproteinemias and Correlations of Indicators of General Reactivity and Lipid Metabolism in Patients with Chronic Nonspecific Inflammation of the Reproductive System. *French-Ukrainian Journal of Chemistry* 2023;11(2):77-94.

[19] Kadota H, Gono T, Shirai Y, Okazaki Y, Takeno M, Kuwana M. Immune Checkpoint Inhibitor-Induced Myositis: a Case Report and Literature Review. *Current Rheumatology Reports* 2019;21(4):81.

[20] Arrey F, Löwe D, Kuhlmann S, Kaiser P, Moura-Alves P, Krishnamoorthy G, Lozza L, Maertzdorf J, Skrahina T, Skrahina A, Gengenbacher M, Nouailles G, Kaufmann S. Humanized Mouse Model Mimicking Pathology of Human Tuberculosis for in vivo Evaluation of Drug Regimens. *Frontiers in Immunology* 2019;10:89.