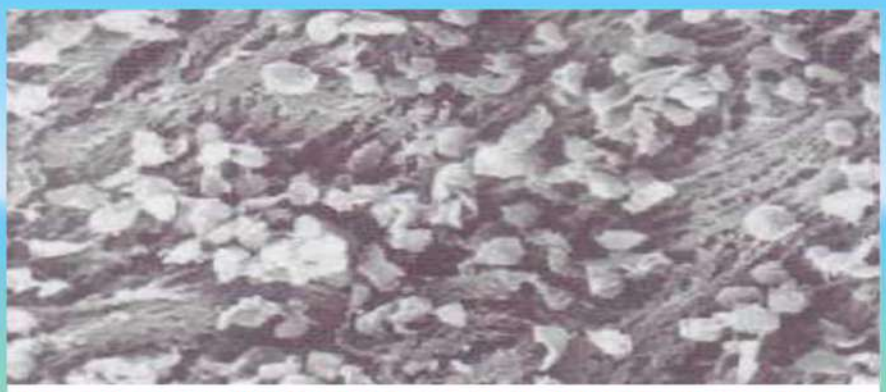
French-Ukrainian Journal of Chemistry

www.kyivtoulouse.univ.kiev.ua/journal

Vol 10, No 2 (2022)

Chemistry beyond frontiers



The role of von Willebrand factor in the bloodstream. Adhesion of blood platelets to the damaged vessel wall

free open access publication

ISSN: 2312-3222

Joint publication of the Taras Shevchenko National University of Kyiv and University Toulouse 3-Paul Sabatier

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

Irina Sokolovska[a*], Nataliia Prybora[b], Valentyna Nechyporenko[a], Olena Pozdniakova[a], Nataliia Hordiienko[a], Iryna Antonenko[a], Kostiantyn Nechyporenko[a], Nataliia Serhata[a], Yuliia Siliavina[a], Valentyna Zarytska[c], Olha Bielan[d], Oleksandr Pokropyvnyi[e], Olena Ibrahimova[e], Vitaliy Yunger[e], Lesya Yanitka[f], Tetyana Galtseva[g], Iryna Kryachok[h], Iryna Tytorenko[h], Maryna Varakuta[i], Vitalii Mavrin[a], Yaroslav Kmetyuk[e]

[a]Municipal Institution of Higher Education «Khortytsia National Educational and Rehabilitational Academy» of Zaporizhzhia Regional Council, Naukovogo Mistechka,59, Zaporizhzhia, 69017, Ukraine, [b]National Pedagogical Dragomanov University, [c]Classical private university, [d]University of Economi cs Department «Economics and Organisation of Tourism», Varna, Bulgaria, [e]KL "Feofania" DUS, [f]Bogomolets National Medical University, [g]Oles Honchar Dnipro National University, [h]National Cancer Institut, [i]Dnipro Humanitarian University

irinasokol10@meta.ua

Keywords: *nature of dyslipoproteinemias, correlation relationships, general reactivity of the body, integral leukogram indicators, lipid metabolism, immunopathological mechanisms, atherosclerosis.*

Metabolic disorders can occur at all levels of biological organization - from molecular and cellular to the level of the organism as a whole. These changes may result from disruptions in hormonal mechanisms, actions of pathogenic factors, or infections. Primary metabolic disorders are the basis of many diseases, such as diabetes, obesity, and atherosclerosis, while secondary disorders accompany most pathological processes. Disruption of lipid metabolism leads to changes in their functions and the development of pathological processes, such as dyslipoproteinemia, and also contributes to the development of atherosclerosis. Various intracellular infectious agents play a significant role in the development of dyslipoproteinemias and atherosclerosis, for example, chlamydia can alter the lipid metabolism in macrophages under the influence of low-density lipoproteins, leading to the formation of 'foam-like' cells. This, in turn, contributes to the development of atheromatous plaques-a favorable environment for chlamydia, where it can survive for an extended period and trigger immunopathological mechanisms.

Introduction

The treatment of inflammatory diseases, both infectious and aseptic, continues to be a prominent research topic in clinical medicine. Numerous studies on the inflammatory process have identified its vascular component as a universal protective reaction to harmful influences. At the same time, it is noted that this process can have both protective effects against the inflammatory syndrome and damaging effects on the patient's organs and systems [1, 3]. Therefore, inflammation should be viewed in the context of a universal protective reaction, namely the systemic inflammatory response syndrome.

Acute and chronic inflammation. Acute inflammation is characterized by an intense progression and resolution, usually within one to two weeks (depending on the damaged organ or tissue, the degree and scale of their alteration, the body's reactivity); with moderately pronounced tissue alteration and destruction, exudative and proliferative changes at the injury site, characterized by a normergic inflammation response **(Figure 1**).

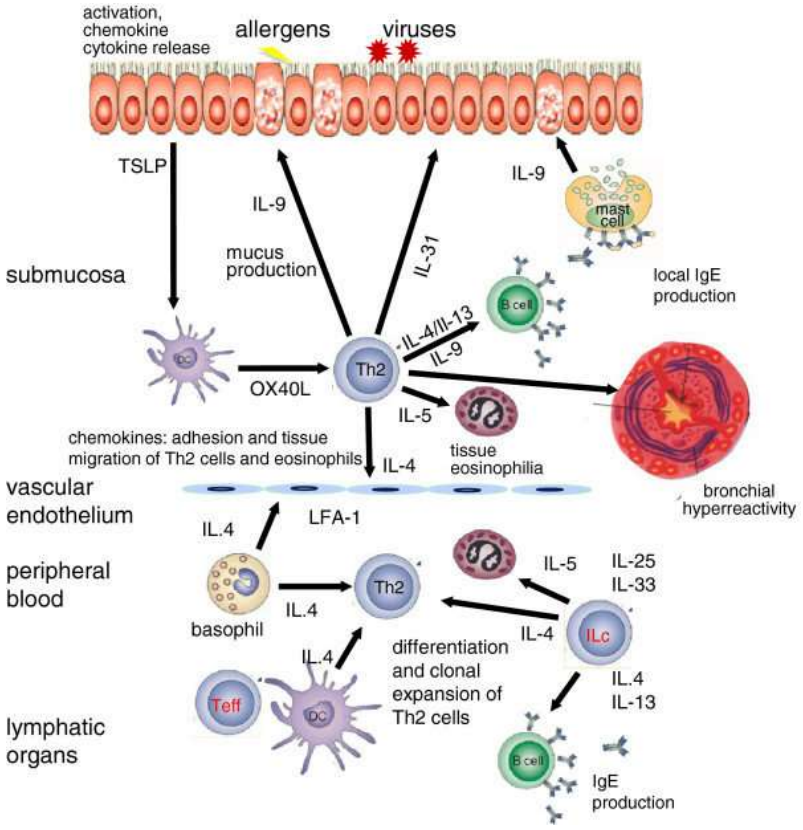


Figure 1. Characteristics and consequences of acute and chronic inflammatio: demonstrating the activation of epithelial cells by allergens, viruses, bacteria and pollutants.

In its hyperergic flow, alteration and destruction of tissues dominate at the site of inflammation. Chronic inflammation can originate primarily or secondarily. If inflammation becomes protracted following an acute period, it is designated as "secondary chronic". Inflammation that is initially persistent, sluggish, and prolonged is termed "primarily chronic". Chronic inflammation, characterized by a high presence of mononuclear phagocytes

and lymphocytes at the inflammation site (including specific forms in various infectious diseases) is termed as mononuclear-infiltrative.

Chronic inflammation is marked by several characteristics, including the formation of granulomas (for example, with tuberculous, brucellosis, or syphilitic inflammation); infiltration at the inflammation site by various types of leukocytes, predominantly monocytes and lymphocytes, and the formation of a fibrous capsule (for example, in the presence of a foreign body in the tissue or the deposition of calcium salts), and the development of necrosis at the core of chronic inflammation site **(Figure 2)**.

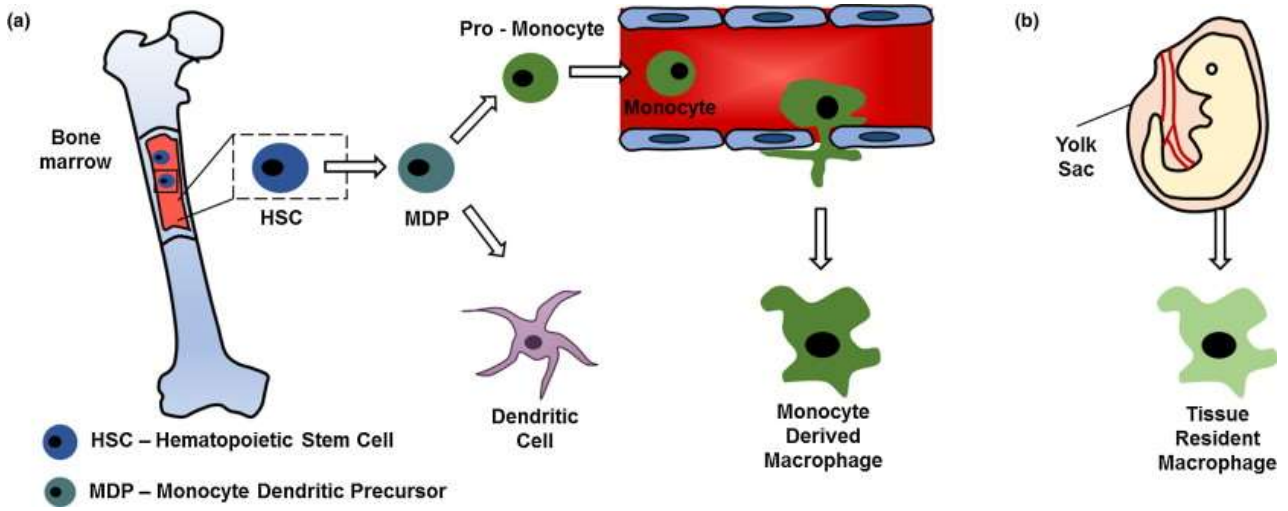


Figure 2. Infiltration of the focus of inflammation by various types of leukocytes. Origin of macrophages. (a) Circulating monocytes are primarily derived from committed progenitor cells in the bone marrow (derived from HSC), which migrate to peripheral blood. Monocytes extravasate through blood vessels when recruited as part of tissue homeostasis or injury events, where they subsequently differentiate into monocyte derived macrophages. (b) In contrast, tissue resident macrophages are derived in utero in the yolk sac and populate tissues such as the brain (microglia), liver (kuppfer cells) and the heart.

The causes of chronic inflammation are diverse and can be categorized into several groups: various forms of phagocytic insufficiency; prolonged stress and other conditions that lead to increased concentration of catecholamines and glucocorticoids in the blood. These groups of hormones suppress the processes of proliferation, maturation and activity of phagocytes, potentiate their destruction.

Recent years have witnessed a notable increase in the incidence of chronic inflammatory diseases of the reproductive system in Ukraine.

There are many diseases in this category, attributed to a wide variety of pathogens and possible localizations of cells; thus, inflammation can occur in any organ of the reproductive system. Without proper treatment, the pathology may become chronic and potentially lead to serious complications, including infertility and systemic intoxication.

A diverse range of microorganisms directly cause inflammatory diseases of the

genital system. This is basically a group of sexually transmitted infections: trichomonads, gonococci, chlamydia, ureaplasma, mycoplasma, herpes viruses, cytomegalovirus, papilloma virus. The causative agents include various types of staphylococci (such as golden, epidermal, pyogenic), group B streptococci, Escherichia coli, proteus vulgaris, enterococci, Klebsiella, anaerobic bacteria (including bacteroids, peptococci, peptostreptococci), gardnerella, yeast-like fungi of the genus Candida, actinomycetes, among other microorganisms.

Pelvic inflammatory diseases constitute a significant social problem, owing to their direct impact on the reproductive health and quality of life of women.

In these diseases, the primary etiological factor is infectious, predominantly represented by pathogens of sexually transmitted infections. Of particular concern is the recent widespread emergence of multiresistant L-forms of bacteria, which exhibit altered biological properties due to the uncontrolled use of antibiotics and hormonal drugs **(Figure 3**).

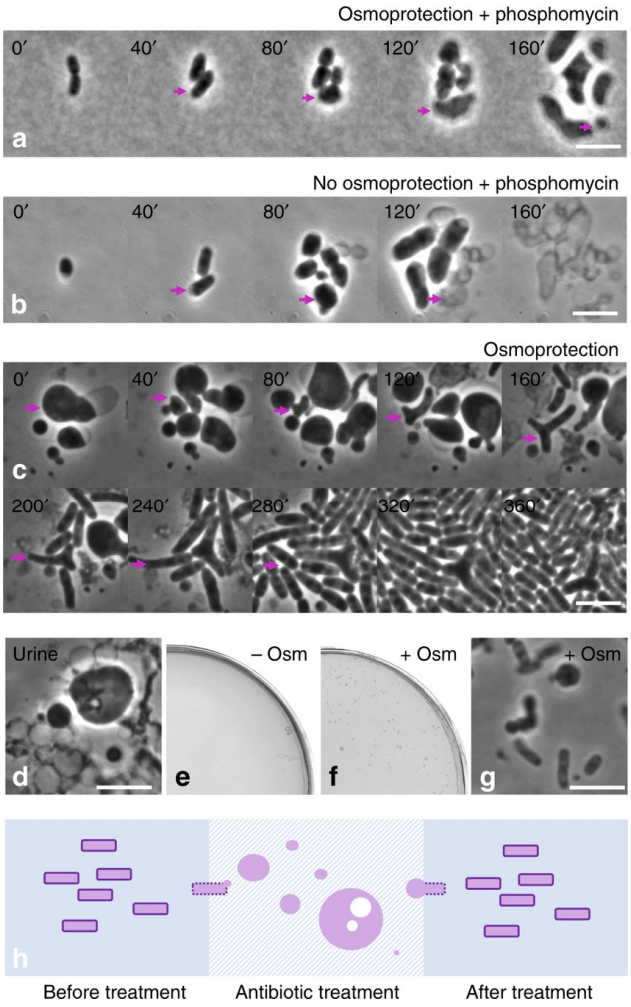


Figure 3. Model showing L-form switching as a mechanism for the recurrence of bacterial infections. Bacteria causing UTI are treated with cell-wall-targeting antibiotics. This leads to elimination of the cell wall and emergence of L-forms, which are not detectable by standard clinical culture methods. Following antibiotic treatment the bacteria can regenerate the wall and potentially cause recurrence of a full-blown infection.

The violation of the macroorganism's immune protection mechanisms plays a key role in the generalization of the infectious process and its subsequent spread to the upper parts of the genital tract [3]. During immunoinflammatory processes, a lipid imbalance occurs, which can be caused by an imbalance between the pro- and antioxidant systems [2]. Specifically, the role of

intracellular infectious agents in the development of dyslipoproteinemias and atherosclerosis has been established [4].

Thus, chlamydia can alter lipid metabolism in macrophages under the influence of low-density lipoproteins, leading to the formation of "foam-like" cells. This process, in turn, contributes to the formation of atheromatous plaques - a favorable environment for chlamydia to survive for extended periods and trigger immunopathological mechanisms [5]. In the course of research, it was established that a low level of high-density lipoprotein cholesterol (HDL) is a risk factor for the development of atherosclerosis [6, 7]. The prevailing explanation for the inverse relationship between HDL concentration and atherosclerosis development is HDL's role in the reverse transport of cholesterol **(Figure 4).**

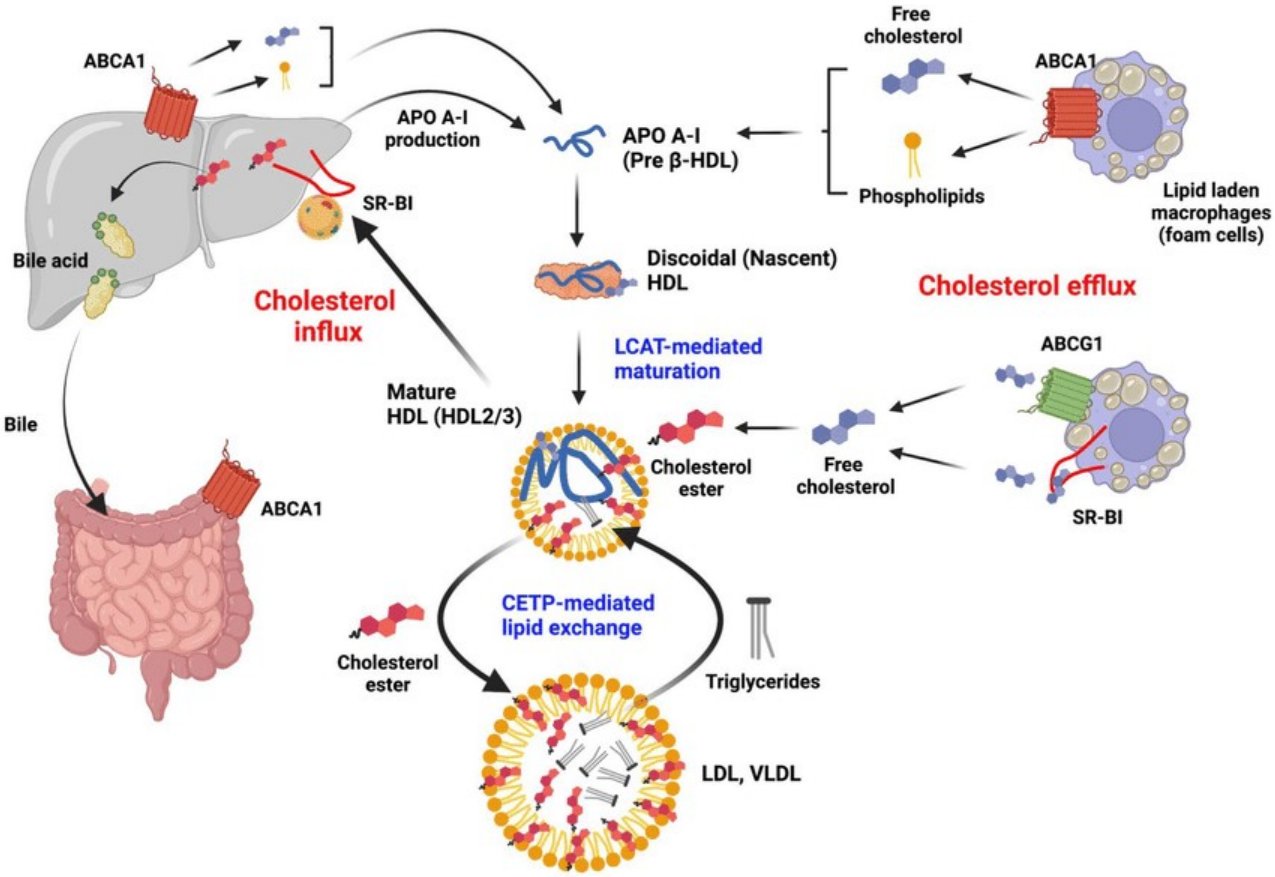


Figure 4. HDL-mediated reverse cholesterol transport. Cholesterol efflux: macrophages localize to fat deposits on the walls of blood vessels, forming lipid laden foam cells — both foam cell and hepatic ABCA1 contribute to HDL formation.

In this process, HDL assists in removing excess cholesterol (CHOL) from cells and transporting it to the liver for further catabolism. However, some properties of HDL, such as antioxidant, anti-inflammatory, anti-thrombotic and others, may contribute to its atheroprotective role. Conversely, chronic inflammation, a hallmark of atherosclerosis can result in the loss of HDL's protective properties and even lead to the emergence of HDL with altered

characteristics. These altered HDLs are termed dysfunctional **(Figure 5)**.

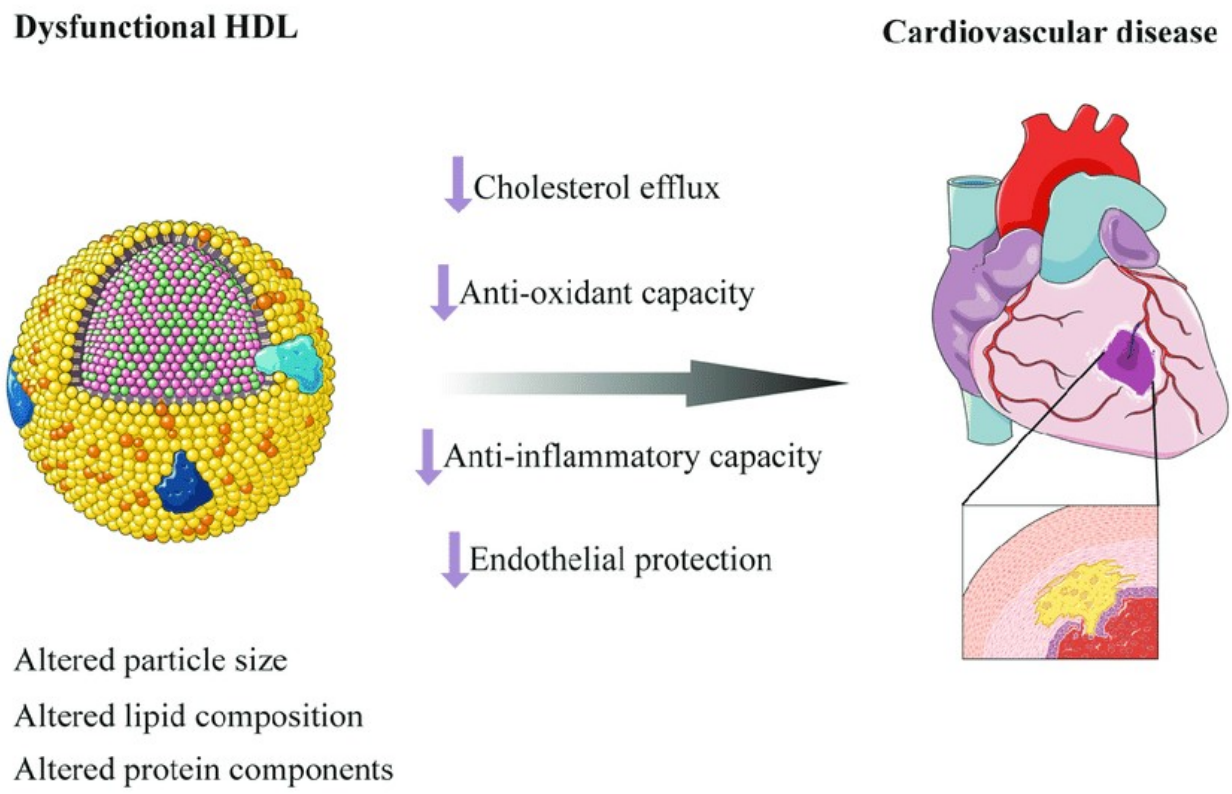


Figure 5. Dysfunctional HDL and cardiovascular disease. Altered lipid composition, protein components, and sizes result in dysfunctional HDL. Decreased cholesterol efflux from macrophages, antioxidant and anti-inflammatory capacity, and endothelial protective function of HDL induce atherosclerosis and cardiovascular diseas.

Therefore, the purpose of our study was to investigate the state of lipid metabolism, the nature and types of dyslipoproteinemias, their correlation with nonspecific reactivity, and the alteration of these properties under conditions of systemic inflammation. This investigation is crucial for understanding the progression, complication development, and treatment effectiveness of infectious inflammatory diseases of the genital system.

Experimental part

Methods of studying lipid metabolism and assessing the type of dyslipoproteinemia. Total cholesterol content was determined using the spectrophotometry method, employing reagent sets of the «Filisit diagnostics», Dnipro. The presence of chylomicrons and very low-density lipoprotein cholesterol (VLDL) was determined by imaging the sample post-exposure to blood plasma at a temperature of 0°-+4° C, the concentration of low-density lipoprotein cholesterol (LDL) was determined according to the method of Burshtein and Samai [8]. High-density lipoprotein cholesterol (HDL) concentration was measured using a reagent set from company "Cormay", and triglycerides were assessed using a reagent set from "Lahema", Czech Republic. Phenotypes for

dyslipoproteinemias were verified following the methodological recommendations for the diagnosis of cardiovascular diseases (**Figure 6).**

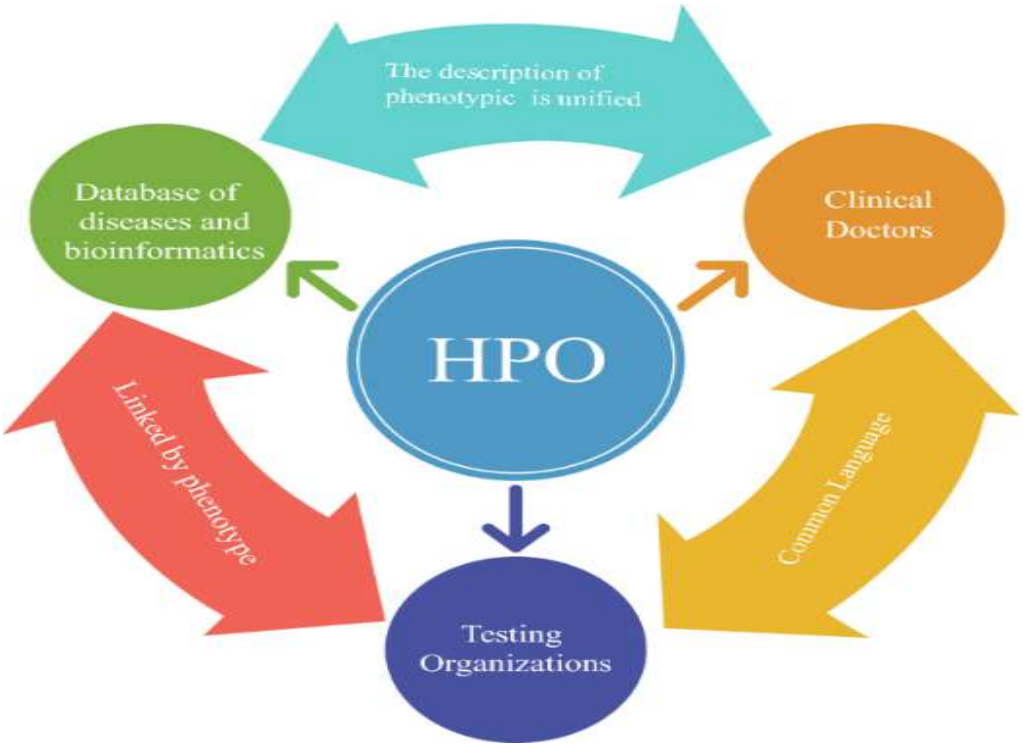


Figure 6. Phenotypes of Cardiovascular Diseases. Cardiovascular diseases (CVDs) are a large group of diseases and have become the leading cause of morbidity and mortality worldwide.

The intensity of lipid peroxidation was assessed by the concentration of malondialdehyde (MDA), determined through reaction with thiobarbituric acid [9].

All the individuals examined underwent a general clinical blood test [10]. 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 [11], 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 [12]. The percentages of positively reactive cells, as well as esterase-positive lymphocytes (likely T cells), within the total lymphocyte pool were calculated. Insight into the state of the body's

systemic non-specific reactivity can be gained by analyzing both the quantitative and qualitative indicators of leukocyte composition and erythrocyte sedimentation rate (ESR). Using leukogram parameters enables the evaluation of leukocyte indicators, which hold diagnostic and prognostic value. These indicators facilitate the assessment of the immune system's effectiveness and the level of immunological reactivity, crucial in forming non-specific adaptive reactions [10]

Integral hematological indicators can change during the pre-pathological period, or in the early stages of the disease, a phase where preventive measures to regulate protective reactions are most effective. Additionally, formalized integrative indicators may change in cases of a sluggish, chronic disease course, even when general blood analysis indicators remain within normal value ranges. Furthermore, employing calculated indicators allows for a preliminary assessment of the activity within the non-specific reactivity system, bypassing the need for complex additional examinations. Integral indicators were computed based on leukogram data and peripheral blood erythrocyte sedimentation rate using mathematical formulas. The calculation of integral formalized indicators for peripheral blood leukograms was performed using a specialized computer program.

LD - leukocyte shift index, LG - lymphocyte-granulocyte index, LESR - lymphocyte and ESR ratio index, LER - lymphocyte and eosinophil ratio index, LMR - lymphocyte and monocyte ratio index, NLR - neutrophil and lymphocyte ratio index, NMR - neutrophil index and monocyte ratio index, GI - general index (**Figure 7**).

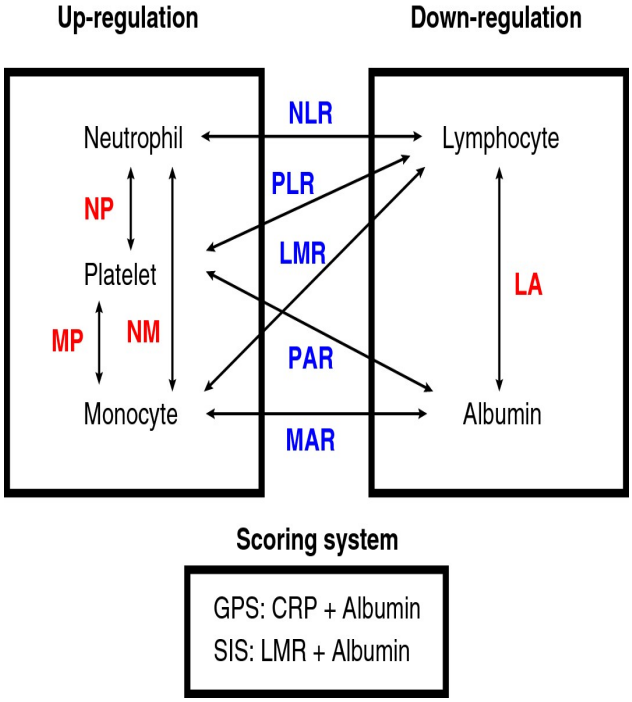


Figure 7. A schema of the inflammation-related markers adopted in the present study. As systemic inflammatory factors, we chose 4 parameters (neutrophil, lymphocyte, platelet, monocyte).

Clinical Characteristics of Patient Examinations: The study included 95 clinically healthy individuals (50 men and 45 women) and 180 patients with chronic non-specific inflammatory diseases of the genital organs. The clinical condition of patients was evaluated based on a survey, collection of complaints, medical history, and examination of the genital skin and women's vaginal mucosa using a gynecological mirror. The clinical examination of patients and collection of biomaterials for the laboratory

survey were conducted by dermatovenerologist I.O. Lankina at City Hospital №6 in Zaporozhye.

The control group (K) comprised 95 clinically healthy non-donor individuals, including 50 men and 45 women (**Table 1**). The age distribution was as follows: 18-28 years - 30 individuals, 29-39 years - 35 individuals, and 41-50 years - 30 individuals. The study group included 162 patients with chronic nonspecific inflammatory diseases of the genital organs, comprising 83 men and 79 women. (**Table 1**). The age distribution among the patients was as follows: 18-28 years - 60 individuals, 29-39 years - 58 individuals, and 40-50 years - 44 individuals.

Table 1. Distribution of surveyed individuals by age and sex.

Group	K1	K2	K3	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

Results and discussion

Lipoproteins are complex particles, featuring a central core containing cholesterol esters and triglycerides, and are surrounded by free cholesterol, phospholipids, and apolipoproteins, that facilitate their formation and function. Plasma lipoproteins are categorized into seven classes, differentiated by size, lipid composition, and apolipoproteins (chylomicrons, chylomicron remnants, VLDL, IDL, LDL, HDL, and Lp (a). Chylomicron remnants, VLDL, IDL, LDL, and Lp (a) are pro-atherogenic, whereas HDL is anti-atherogenic.(**Figure 8**).

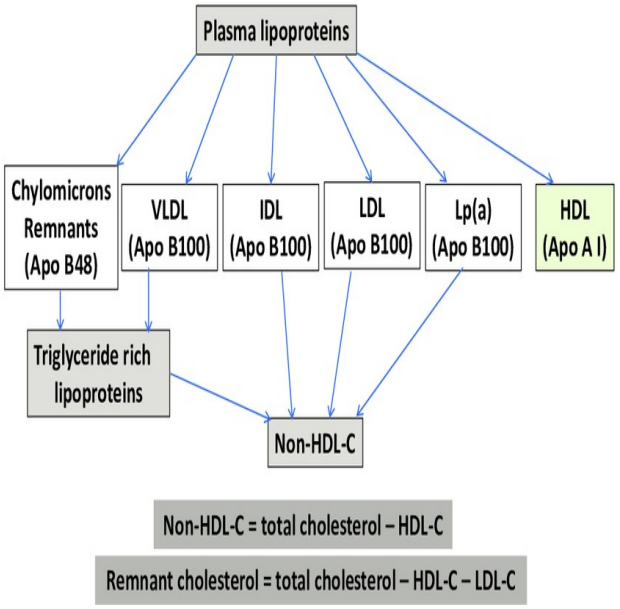


Figure 8. Plasma lipoproteins. CM-chylomicrons, VLDL-very low density lipoprotein, IDL-intermediate density lipoprotein, LDL-low density lipoprotein, HDL-high density lipoprotein, Lp(a)-lipoprotein(a),

In the study of the lipid spectrum in the blood plasma of patients with chronic inflammation of the reproductive system, significant differences were noted compared to the indicators of clinically healthy individuals. In the third group, the concentration of total cholesterol in the blood plasma of affected women was 1.2 times higher ($p<0.05$) than in the control group **(Table 2).**

It is noteworthy that the increase in blood plasma cholesterol concentration in both affected women and men corresponded with the patients' rising average age in the groups, a trend not observed in the control group. The visual identification of chylomicrons in the blood plasma of patients from both genders in the 2nd and 3rd groups was notably more frequent (9 out

of 58 and 10 out of 54, respectively) compared to the control group (1 out of 35). The frequency of visually detecting very low-density lipoprotein cholesterol (VLDL) in the blood plasma of both female and male patients in the 1st group (5 out of 64) showed an increasing trend. In the 2nd (12 out of 58) and 3rd (22 out of 44) groups, this frequency was significantly higher ($p<0.05$) than in the control group (1 out of 30 and 0 out of 35, respectively).

The level of LDL in the blood plasma of women of the 1st and 2nd groups tended to increase, and in the women of the 3rd group it was 1.4 times higher ($p<0.05$) than in K.

It is noteworthy that the LDL content in the blood plasma of women correlated positively with the increase in the average age within the group. There were no changes in the concentration of LDL in the blood plasma of sick men. In the third group, affected women exhibited a significant decrease in HDL concentration in blood plasma, by 1.4 times ($p<0.05$). No significant changes in HDL concentration were observed in male patients across all three age groups.

In affected women, the concentration of triglycerides (TRIG) in blood plasma rose with increasing average age. Specifically, in women of the 2nd and 3rd groups, this increase was significant, at 1.3 times ($p<0.05$). For men in the 2nd group, a 1.2-fold increase ($p<0.05$) in TG concentration in blood plasma was observed compared to the control group. Similarly, in patients of group 3, the increase was significant, at 1.3 times ($p<0.005$) **(Table 2)**.

Table 2. Lipid spectrum of blood plasma of patients with chronic nonspecific inflammation of the reproductive system

Group		CMs)n	LDL n	LDL, mmol*l^{-1}	HDL, mmol*l^{-1}	CHOL mmol*l^{-1}	*TRIG* mmol*l^{-1}	MDA, μmol*l^{-1}
K1	M	0	0	3,42±0,29	1,35±0,11	4,70±0,51	0,98±0,07	3,88±0,31
	W	0	0	2,83±0,37	1,33±0,14	4,13±0,41	1,25±0,12	3,18±0,36
K2	M	0	0	3,85±0,40	1,40±0,15	5,20±0,54	1,23±0,5	4,02±0,38
	W	0	0	3,09±0,27	1,37±0,13	4,52±0,38	1,27±00,7	3,21±0,33
K3	M	0	0	3,69±0,32	1,75±0,20	5,45±0,43	1,35±0,12	4,0±0,34
	W	0	0	3,31±0,29	1,40±0,29	4,60±0,33	1,33±0,15	3,26±0,30
1	M	0	2	3,90±0,31	1,32±0,18	5,25±0,58	1,29±0,09	4,92±0,21*
	W	0	3	3,34±0,61	1,60±0,14	4,99±0,32	1,45±0,15	3,84±0,33
2	M	4*	5*	4,17±0,55	1,28±0,19	5,45±0,44	1,42±0,08	6,41±0,73*
	W	5*	9*	3,90±0,38	1,44±0,05	5,44±0,62	1,62±0,12*	5,23±0,44*
3	M	5*	12*	4,12±0,44	1,20±0,07	5,32±0,47	1,58±0,06*	6,47±0,71*
	W	5*	10*	4,49±0,23*	1,02±0,12*	5,51±0,45*	1,68±0,05*	5,93±0,62*

Notes.

1 n - the number of positive results;

2*- $p<0.05$, the reliability of the differences in comparison with the control group:

Analysis of features of dyslipoproteinemia types.

In analyzing the types of dyslipoproteinemias (DLP) among the examined subjects, it was found that DLP, predominantly type II, was frequently detected in male patients of the 1st group (youngest age), with types IIb and III observed in isolated cases **(Table 3).** In female patients of the 1st group, types IIa, IIb, and III DLP, known for their high atherogenicity, were identified in isolated cases.

Type IIa dyslipoproteinemia was significantly more common in men of the 1st group (7 out of 22) ($p<0.05$) compared to women (1 out of 38), likely attributable to the higher estrogen levels in women aged 18-28 years IIn the 2nd group (average age), type IIa DLP (18 out of 58) was more prevalent in both men and women compared to controls (0) ($p<0.05$), with types IIb and III occurring in isolated cases. Type V dyslipoproteinemia was observed in several instances, being significantly more frequent in women (5 out of 28) ($p<0.05$) than in the 1st group and controls (0).

Table 3. Peculiarities of dyslipoproteinemia types in patients with chronic nonspecific inflammation of the reproductive system

Group		Number of people in the group	Number of persons without DLP	Number of persons with DLP				
				IIa type	IIв type	III type	IV type	V type
К	M	50	50	-	-	-	-	-
	W	45	45	-	-	-	-	-
1	M	22	12	7*	2	1	-	-
	W	38	33	1*	3	1	-	-
2	M	30	13	11	2	1	-	3
	W	28	12	7*	3	1	-	5^
3	M	22	2	3*	7*	5*	-	5^
	W	22	5	3*	5*	3	2	4^

Notes:

1.* - $p<0.05$ reliability of differences, in comparison with K

2. ^ - $p<0.05$ in comparison with the control group and group 1.

A significant increase in the level of MDA was observed in sick women of the 2nd and 3rd groups and in sick men of all groups: in men of the 1st group by 1.3 times ($p<0.05$), and in the 2nd and 3rd groups - 1.6 times; in women of the 2nd and 3rd groups - 1.6 times ($p<0.05$).

In the 3rd group of patients (the oldest age group), type IIa DLP was observed significantly less frequently (6 out of 44) ($p<0.05$) compared to the 2nd group (18 out of 58), in both men and women. At the same time, DLP II в (12 out of 44) and III (8 out of 44) types were found more often in both men and women of the 3rd group than in K. DLP type V in the 3rd group of patients was found significantly more often (9 out of 44) ($p<0.05$) than in the 1st group and K (0). Two women of this group were also diagnosed with DLP type IV.

The analysis of hypercholesterolemia (H) prevalence among patients, based on gender and age, revealed the following findings (**Table 4).**

Table 4. The frequency of hypercholesterolemia based on gender and age of patients

Group	Number of examined persons					
	M			W		
	The total number of	With H		The total number of	With H	
		With a subnormal level of CHOL	With a high level of CHOL		With a subnormal level of CHOL	With a high level of CHOL
1	28	5	3	36	11	1
2	30	20*	3	30	9	2
3	25	12	4	29	9	1

Note. * - $p<0.05$ in comparison with all other groups;

We observed an increased detection frequency of DLP, including DLP with high atherogenicity, corresponding to the increasing age of patients.

The number of affected women with H across all age groups was consistent, comprising 29 out of 95 with a subnormal level of CHOL, and 4 out of 105 with a high level of CHOL.

In the 1st group of men (youngest age), H with a subnormal level of CHOL was observed less frequently (5 out of 28) compared to the other groups. In men, the frequency of H with a subnormal level of CHOL was significantly higher in the 2nd (20 out of 30) and 3rd (12 out of 25) groups than in the 1st group. H with a high level of CHOL was consistent across all male groups (10 out of 83), exceeding that in women. Among the reasons for the high frequency of H in men, particularly in the 2nd group, are factors such as lifestyle, nutrition, and sexually transmitted infections.

Correlation relationships of indicators of the general reactivity of the body of the examined persons and lipid metabolism **(Figure 9*).***

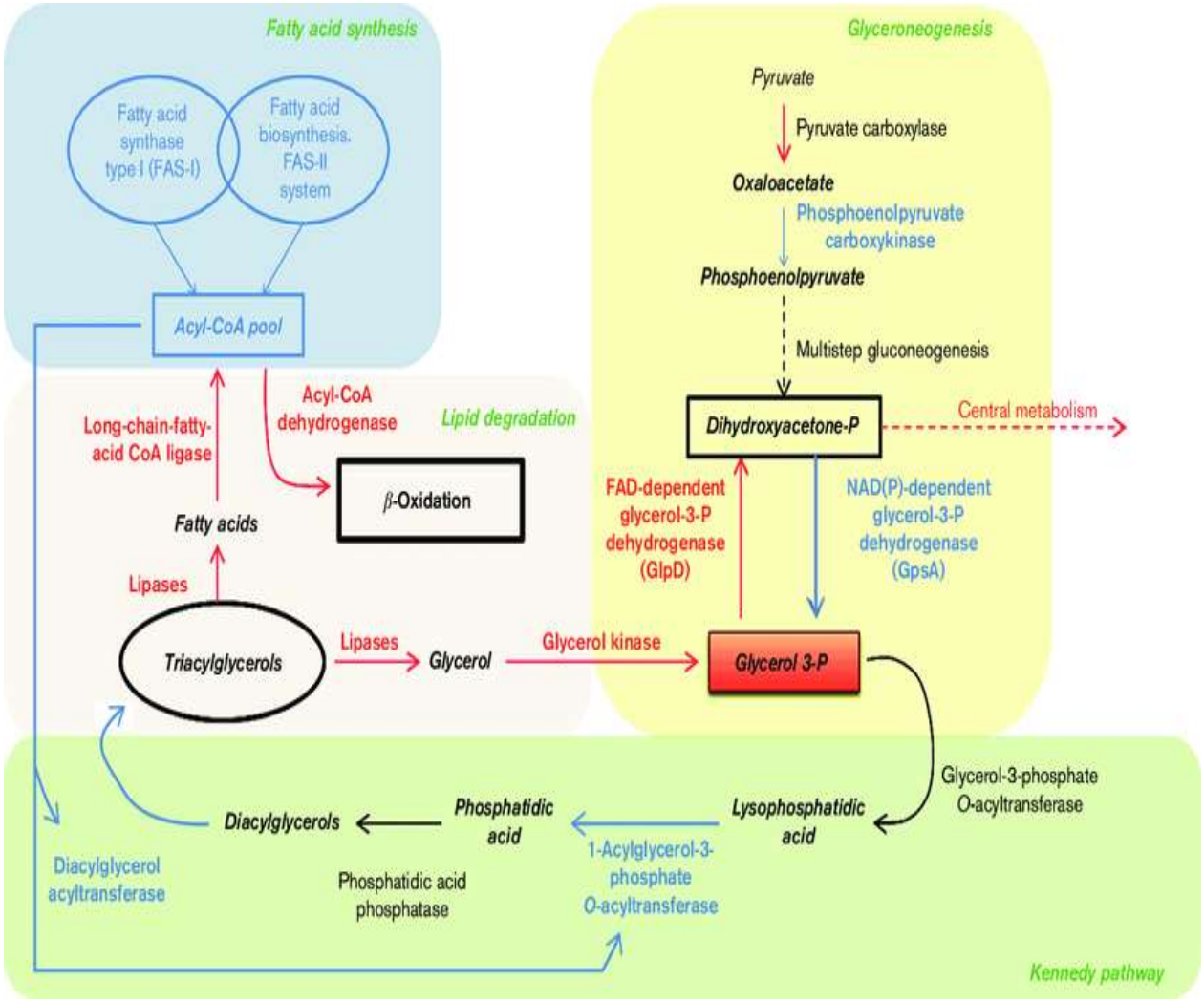


Figure 9. Overview of reactions involved in lipid metabolism. Metabolites are shown in black. Enzymes in red were upregulated, whereas enzymes in blue were downregulated.

A correlational analysis was conducted on indicators characterizing nonspecific reactivity and lipid metabolism in patients with chronic inflammation of the reproductive system.

Strong direct correlations between the content of LDL in blood plasma and the percentage of α-naphthyl acetate esterase (ANAE)-positive cells in circulating MON (r = 0.54), LESR (r = 0.81), LG (r = 0.65), GI (r = 0.76), as well as strong inverse correlations of LDL content and LD (r = -0.71), NLR (r = -0.77), (p<005) **(Table 5).**

Thus, the increase in LDL content in the blood plasma of patients was associated with the predominance of MON in the macrophage phagocytosis system and the cellular components of specific immune mechanisms.

Regarding the content of total CHOL, there were strong direct correlations of this indicator with the percentage of positive-reacting ANAE cells in circulating LYM (r = 0.90) and MON (r = 0.75), LESR (r = 0.83), LG (r = 0.87), GI (r = 0.91), and inverse with the average cytochemical coefficient of myeloperoxidase (MPO) (r = -0.79) and CP (r = -0.53) of

circulating polymorphonuclear leukocytes (PMNs), LD (r = -0.89), LMR (r = -0.94), NLR (r = -0.60), ($p<0.05$).

This means that the increase in the level of total cholesterol also occurred in parallel with the advantage of the MON-macrophage link in the phagocytosis system against the background of reduced phagocytic activity of circulating PMNs and the advantage of the cellular link in the mechanisms of specific protection.

HDL content was strongly directly related to the average cytochemical coefficient of myeloperoxidase MPO (r = 0.52) of circulating PMNs, LD (r = 0.79), NLR (r = 0.85), NMR (r = 0.53) and conversely - with the percentage of positive-reacting ANAE cells circulating LYM (r = 0.63) and MON (r = -0.56), LESR (r = -0.74), LG (r = -0.70), GI (r = -0.76), ($p<0.05$).

Therefore, it can be thought that the decrease in HDL content was also parallel to the superiority of the MON-macrophage link in the phagocytosis system against the background of reduced phagocytic activity of circulating PMNs and the advantage of the cellular link in the mechanisms of specific protection.

The presence of strong and moderate direct correlations between TG content in blood plasma and LESR (r = 0.65), as well as inverse correlations between TG concentration and NLR - (r = -0.50) were determined.

Table 5. Correlation coefficients of indicators of nonspecific reactivity and lipid metabolism in patients with chronic nonspecific inflammatory process of the reproductive system

Indicator, unit of measurement	LDL $mmol.l^{-1}$	CHOL $mmol.l^{-1}$	HDL, $mmol.l^{-1}$
The average cytochemical coefficient of MPO of circulating PMNs	-0,30*	-0,79*	+0,52*
Percentage of positive-reacting ANAE cells in circulating LYM	+0,44*	+0,90*	-0,63*
Percentage of positive-reacting ANAE cells in circulating MON	+0,54*	+0,75*	-0,56*
LD	-0,71*	-0,89*	+0,79*
LESR	+0,81*	+0,81*	-0,74*
LG	+0,65*	+0,87*	-0,70*
GI	+0,76*	+0,91*	-0,76*
NLR	-0,77*	-0,94*	+0,85*
NMR	-0,21	-0,60*	+0,53*

Note. * - $p<0.05$.

The analysis to determine the correlation between non-specific body defense indicators in patients with chronic inflammation affected by various sexual infections and lipid metabolism metrics revealed a robust, direct correlation. This was evident in the blood plasma concentrations of CHOL and MDA, which were strongly and positively correlated with the percentage of ANAE-positive cells (r = +0.93 and +0.90), circulating MON (r = +0.93 and +0.90), and inversely correlated with circulating LYM (r = +0.84 and +0.90), LG (r = +0.83 and +0.81), and

GI (r = ±0.92 and +0.92). Furthermore, a strong inverse relationship was observed with NLR (r = -0.83 and -0.81) and NMR (r = -0.61 and -0.57). (**Table 6**).

Table 6. Correlation coefficients of indicators of nonspecific reactivity and lipid metabolism in patients with various types of sexually transmitted infections

Indicator, unit of measurement	Percentage of positive-reacting ANAE cells in circulating MON	Percentage of positive-reacting ANAE cells in circulating LYM	LG	GI	NLR	NMR
CHOL mmol.l^{-1}	+0,93*	+0,84*	+0,83*	+0,92*	-0,83*	-0,61*
MDA, mmol.l^{-1}	+0,90*	+0,90*	+0,89*	+0,92*	-0,81*	-0,57*

Note. * - p<0.05.

Thus, the enhancement of atherogenic properties of the blood plasma of patients with chronic inflammation of the reproductive system was associated with the superiority of the MON-macrophage link in the system of phagocytosis and the cellular link of specific protection.

Conclusions

In patients with non-specific inflammation of the reproductive system, there are established violations of LP metabolism: in women of the third older age group, a 1.2-fold increase in total cholesterol concentration was observed. Additionally, an increased frequency of chylomicronemia in the second and third groups was noted in patients of both sexes (9 out of 58 and 10 out of 44), the presence of VLDL (14 out of 58 and 22 out of 44) in comparison with K, an increase in the concentration of TG by 1.3 times, MDA by 1.6 times, in the older group of sick women – an increase in the level of LDL by 1.4 times and a decrease in the level of HDL by 1.4 times (p<0, 05).

In both female and male patients, the total frequency of DLP with a high risk of atherogenesis increased according to age: 15 cases out of 60 occurred in the younger group, 25 out of 58 in the middle group, and 26 out of 44 in the older group (p<0.05). DLP IIa type was more often detected in men of the younger (7 out of 22) and middle (11 out of 30) groups compared to the older (3 out of 22) group (p<0.05) and in patients with chlamydia (7 out of 28) and viral infection (5 out of 19) (p<0.05), in comparison with patients of other groups The summarized data of the correlation analysis allow us to assume that the increase in atherogenic properties of the blood plasma of patients with chronic inflammation occurred together with damage to the vascular endothelium.(**Figure 10**).

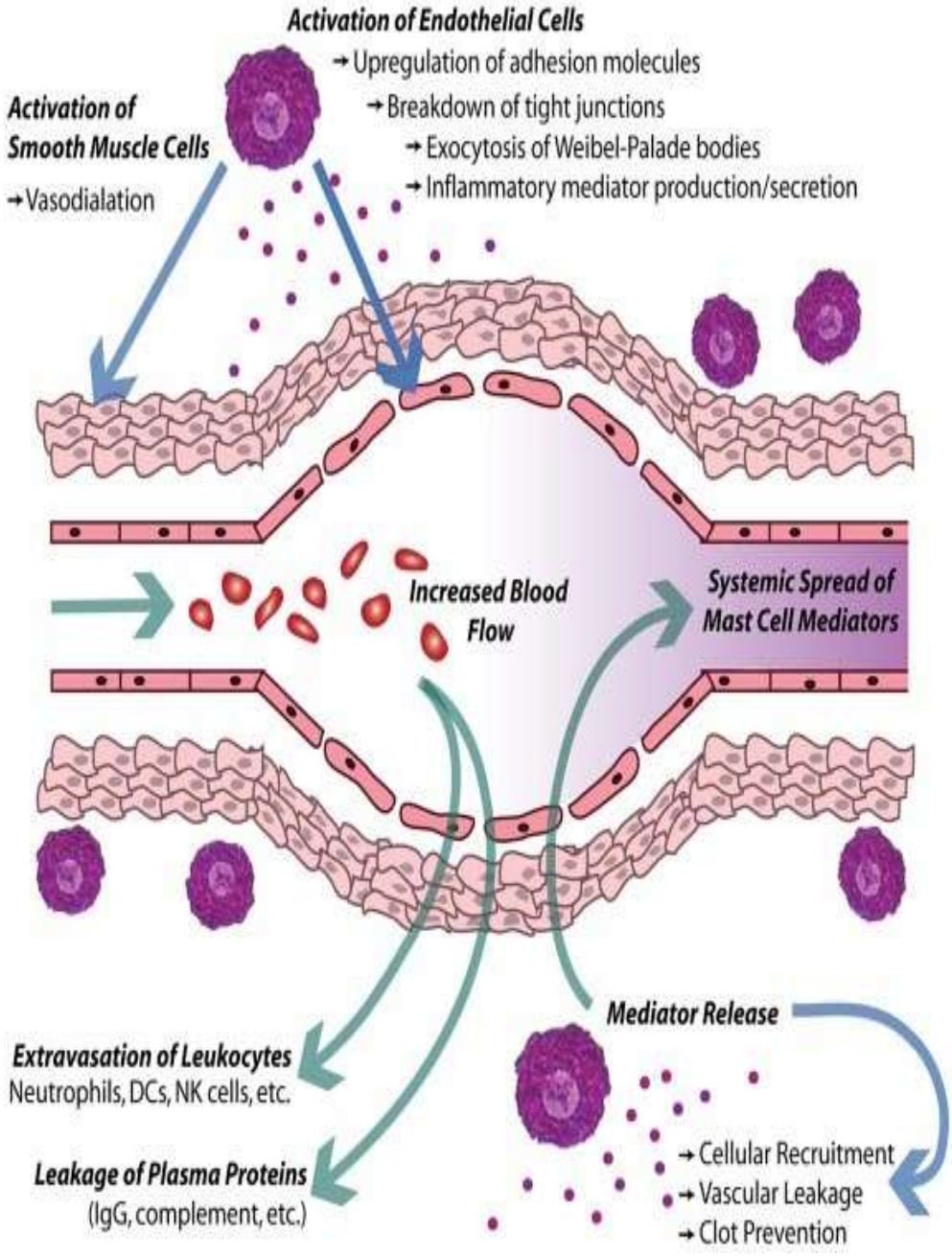


Figure 10. Local action on the vascular network in acute inflammation. Activated mast cells release inflammatory mediators, which then cause changes in the vascular endothelium. Some of these mediators directly act on smooth muscle cells, contributing to the expansion and permeability of blood vessels.

These disturbances occurred in parallel with the superiority of the MON-macrophage link of phagocytosis against the background of reduced activity of neutrophils

Correlation analysis of indicators characterizing lipid metabolism and non-specific reactivity in patients with chronic inflammation allowed us to establish that the increase in the level of atherogenic lipoproteins and MDA with a parallel decrease in the concentration of anti-atherogenic HDL occurs in accordance with the superiority of the MON-macrophage link in the

system of phagocytosis and the cellular link specific protection. HDL content was strongly directly related to the average cytochemical coefficient of myeloperoxidase MPO (r=0.52) of circulating PMNs, LD(r=0.79), NLR (r=0.85), NMR (r=0.53) and conversely - with the percentage of positive-reacting ANAE cells circulating LYM (r=0.63) and MON (r= -0.56), LESR (r= -0.74), LG (r= -0.70), GI (r= -0.76), ($p<0.05$).

References

[1] Jellinger P. American Association of Clinical Endocrinologists/American College of Endocrinology Management of Dyslipidemia and Prevention of Cardiovascular Disease Clinical Practice Guidelines. Diabetes Spectrum 2018;31(3):234-245.

[2] Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L. Corrigendum to: 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. European Heart Journal 2019;41(44):4255-4255.

[3] Rhee E, Kim H, Kim J, Lee E, Kim B, Kim E, Song Y, Lim J, Kim H, Choi S, Moon M, Na J, Park K, Oh M, Han S, Noh J, Yi K, Lee S, Hong S, Jeong I. 2018 Guidelines for the management of dyslipidemia in Korea. The Korean Journal of Internal Medicine 2019;34(5):1171-1171.

[4] Hasheminasabgorji E, Jha J. Dyslipidemia, Diabetes and Atherosclerosis: Role of Inflammation and ROS-Redox-Sensitive Factors. Biomedicines 2021;9(11):1602.

[5] Zhang T, Chen J, Tang X, Luo Q, Xu D, Yu B. Interaction between adipocytes and high-density lipoprotein:new insights into the mechanism of obesity-induced dyslipidemia and atherosclerosis. Lipids in Health and Disease 2019;18(1):223.

[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] Pang J, Chan D, Watts G. The Knowns and Unknowns of Contemporary Statin Therapy for Familial Hypercholesterolemia. Current Atherosclerosis Reports 2020;22(11):64.

[8] Daiber A, Chlopicki S. Revisiting pharmacology of oxidative stress and endothelial dysfunction in cardiovascular disease: Evidence for redox-based therapies. Free Radical Biology and Medicine 2020;157:15-37.

[9] Sokolovskaya I, Prybora N, Valentyna Nechyporenko V, Pozdniakova O, Hordiienko N, Nechyporenko 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.

[10] Andrabi S, Bekheirnia M, Robbins-Furman P, Lewis R, Prior T, Potocki L. SMAD4 mutation segregating in a family with juvenile polyposis, aortopathy, and mitral valve dysfunction. American Journal of Medical Genetics Part A 2011;155(5):1165-1169.

[11] Scheuer H, Gwinner W, Hohbach J, Gröne E, Brandes R, Malle E, Olbricht C, Walli A, Gröne H. Oxidant stress in hyperlipidemia-induced renal damage. American Journal of Physiology-Renal Physiology 2000;278(1):F63-F74.

[12] 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.

[13] 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.

[14] Villadangos J, Young L. Antigen-Presentation Properties of Plasmacytoid Dendritic Cells. Immunity 2008;29(3):352-361.

[15] 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.

[16] Oguntibeju OO. Type 2 diabetes mellitus, oxidative stress and inflammation: examining the links. Int J Physiol Pathophysiol Pharmacol. 2019;11(3):45-60.

[17] Ginsberg H. Lipoprotein Physiology and Its Relationship to Atherogenesis. Endocrinology and Metabolism Clinics of North America 1990;19(2):211-228.

[18] Chait A. The role of lipoprotein receptors in lipid transport and in the pathogenesis of the hyperlipoproteinemias. Spec Top Endocrinol Metab. 1983;5:1-53.