Interplay of Lipid Peroxidation, Chronic Inflammation, and Platelet Aggregation in the Pathogenesis of Human Diseases

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Lipid peroxidation is a key manifestation of oxidative stress and an important mechanism of cellular injury. Excessive production of reactive oxygen species promotes membrane lipid oxidation and the accumulation of toxic lipid peroxidation products. Chronic inflammation further amplifies oxidative stress, creating a self-perpetuating cycle that promotes platelet activation, adhesion, and aggregation. Together, these processes represent closely interconnected pathogenic mechanisms contributing to endothelial dysfunction and the progression of chronic inflammatory diseases.

Introduction

Oxidative stress is closely associated with the development of chronic inflammation, forming a so-called "vicious cycle" in which reactive oxygen species (ROS) stimulate the production of pro-inflammatory cytokines, while inflammatory cells, in turn, generate additional free radicals [1].

This reciprocal interaction sustains prolonged activation of the inflammatory response, promotes endothelial dysfunction, impairs microcirculation, and contribu tes to the progression of tissue damage. (**Figure 1**).

Platelet activation also represents a critical component of this pathogenic process [2].

Under the influence of lipid peroxidation products and inflammatory mediators, platelet reactivity increases, leading to enhanced adhesion to the damaged endothelium and increased platelet aggregation [3].

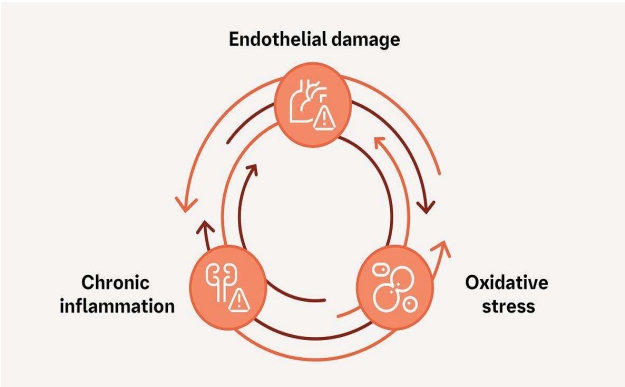

Figure 1. The relationship between oxidative stress and chronic inflammation. Excessive formation of reactive oxygen species stimulates the synthesis of pro-inflammatory cytokines, while activated inflammatory cells produce new portions of free radicals, forming a "pathological circle" that supports chronic inflammation, endothelial dysfunction and microcirculation disorders.

Simultaneously, thromboxane A_2 (TXA_2) synthesis is elevated, whereas the bioavailability of nitric oxide (NO) and prostacyclin (PGI_2) - physiological inhibitors of platelet aggregation and potent vasodilators - is reduced [4].

As a consequence, a prothrombotic state develops, which is accompanied by endothelial dysfunction, perpetuates chronic inflammation, and contributes to the pathogenesis of cardiovascular and metabolic disorders (**Figure 2**).

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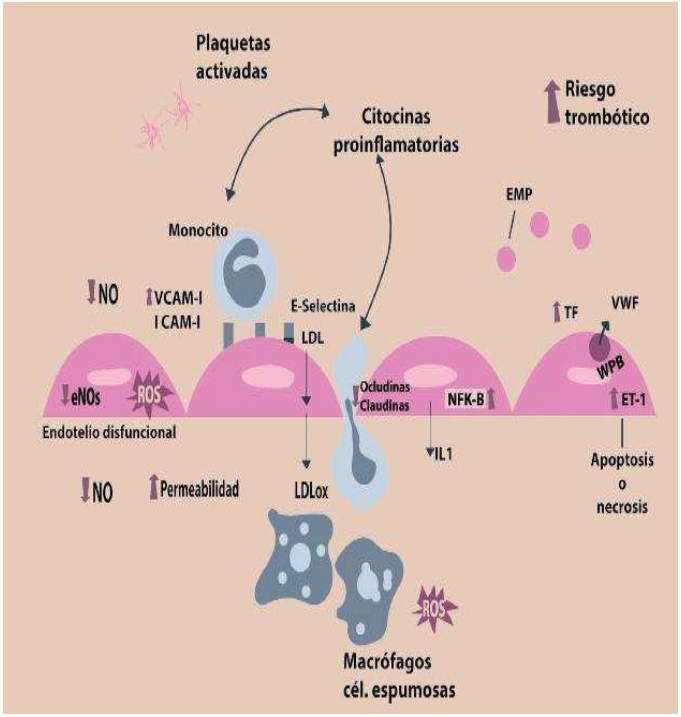

Figure 2. Mechanisms of platelet activation under oxidative stress. Lipid peroxidation products and pro-inflammatory mediators enhance platelet adhesion and aggregation, increase the synthesis of thromboxane A_2, reduce the bioavailability of nitric oxide (NO) and prostacyclin (PGI_2), which contributes to the development of endothelial dysfunction and the formation of a prothrombotic state

Therefore, excessive activation of lipid peroxidation represents one of the major pathogenetic mechanisms underlying oxidative stress and is closely linked to the maintenance of chronic inflammation and disruption of vascular homeostasis [5]. Excessive accumulation of lipid peroxidation products stimulates the synthesis of prostanoids and leukotrienes, induces endothelial dysfunction, increases vascular permeability, promotes platelet adhesion and aggregation, and enhances the release of pro-inflammatory mediators [6].

These events establish a self-perpetuating vicious cycle in which oxidative stress sustains chronic inflammation, while the inflammatory response further increases the generation of reactive oxygen species and intensifies lipid peroxidation [7]. This interplay constitutes a key pathogenic mechanism in the development and progression of cardiovascular, metabolic, inflammatory, and degenerative diseases and significantly contributes to the occurrence of their complications (**Figure 3**).

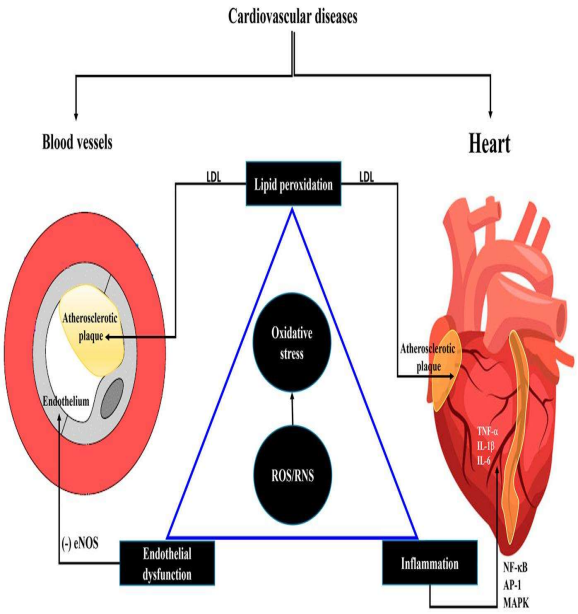

Figure 3. Pathogenetic relationship between lipid peroxidation, oxidative stress, chronic inflammation, endothelial dysfunction and platelet activation. The enhancement of lipoperoxidation processes supports the formation of reactive oxygen species, stimulates the synthesis of prostanoids and leukotrienes, contributes to the development of vascular disorders and the progression of cardiovascular, metabolic and inflammatory diseases.

Biochemical Mechanisms of Lipid Peroxidation. During inflammation, activated phagocytes produce increased amounts of reactive oxygen species (ROS) [8]. Their interaction with polyunsaturated fatty acids initiates lipid peroxidation (LPO), one of the major biochemical mechanisms responsible for cellular damage (**Figure 4**).

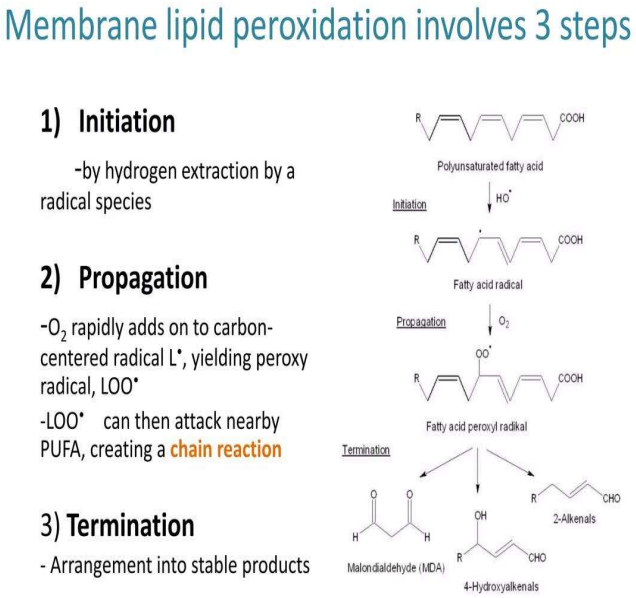

Figure 4. Scheme of peroxidation of cell membrane lipids under the action of reactive oxygen species

Under physiological conditions, lipid peroxidation occurs at a low intensity and is essential for the normal functioning of biological systems. Its activity is maintained by a dynamic balance between pro-oxidant and antioxidant defense mechanisms [9]. Moderate lipid peroxidation contributes to the renewal of biological membranes, maintenance of their structural and functional properties, participation in energy metabolism, cell proliferation, and the synthesis of biologically active compounds[10].

The principal substrates of lipid peroxidation are polyunsaturated fatty acids present in membrane lipids. In the bloodstream, fatty acids are transported as components of lipoproteins by specific carrier proteins known as apolipoproteins [11]. Lipid peroxidation mainly

occurs at the interface between the aqueous and lipid phases. Within low-density lipoproteins (LDL), reactive oxygen species primarily oxidize unsaturated fatty acids containing multiple double bonds (**Figure 5**).

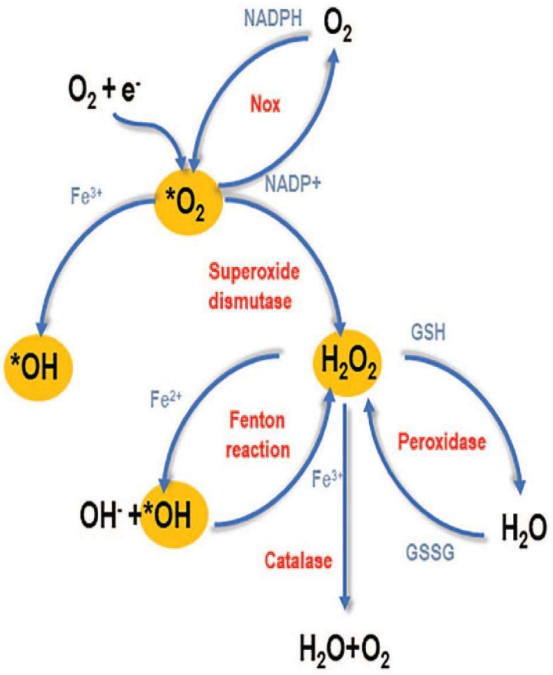

Figure 5. Main reactive oxygen species and their formation pathways in the cell

The antioxidant defense system consists of enzymatic and non-enzymatic components that protect cells against free radicals and their toxic metabolites [12].

The enzymatic antioxidant system includes superoxide dismutase (SOD), which catalyzes the dismutation of the superoxide anion into hydrogen peroxide, glutathione reductase, glutathione peroxidase, ceruloplasmin, and catalase (**Figure 6**).

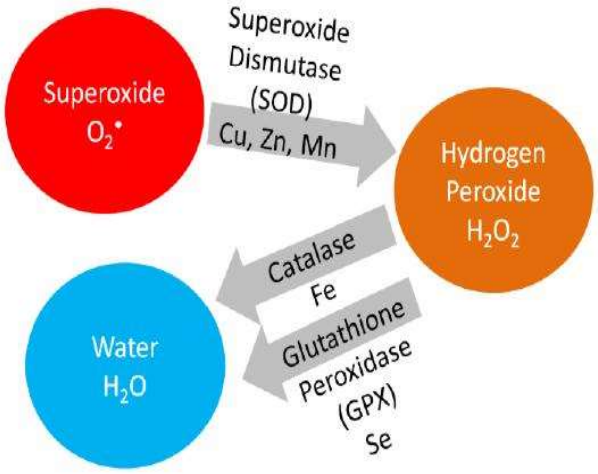

Figure 6. Enzymatic system of antioxidant defense of the body (superoxide dismutase, catalase, glutathione peroxidase).

Catalase is responsible for decomposing hydrogen peroxide into water and molecular oxygen, thereby preventing the accumulation of toxic peroxide compounds [13].

The non-enzymatic antioxidant system comprises lipid-soluble antioxidants, including α-tocopherol, ubiquinone, naphthoquinones, carotenoids, retinoids, steroid hormones (particularly estrogens), as well as water-soluble antioxidants such as glutathione, ascorbic acid, sodium thiosulfate, citric acid, and nicotinic acid [14].

Proteins containing sulfhydryl (thiol) groups, including cysteine and methionine residues, also contribute significantly to antioxidant protection [15].. These compounds inhibit free-radical oxidation by scavenging reactive oxygen species and neutralizing intermediate oxidation products[16].

Catalase is an iron-containing heme enzyme that plays a key role in hydrogen

peroxide metabolism and protects cells against oxidative damage (**Figure 7**).

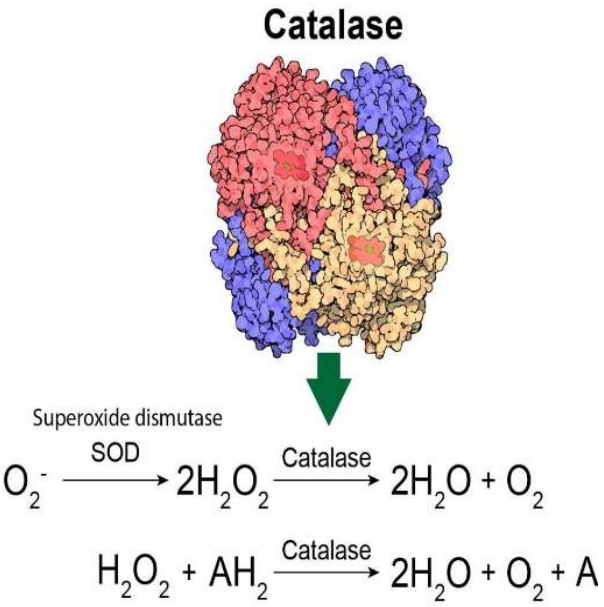

Figure 7. Catalytic cleavage of hydrogen peroxide by the enzyme catalase**.**

Effects of Lipid Peroxidation on Cellular Structures and Inflammatory Responses.

Excessive activation of lipid peroxidation (LPO) induces a wide range of structural and functional alterations within cells. In addition to damaging membrane lipids, it causes oxidative modification of amino acid residues, oxidation of thiol-containing compounds, inhibition of numerous enzymatic systems, and disruption of cellular energy metabolism by uncoupling oxidative phosphorylation (**Figure 8**).

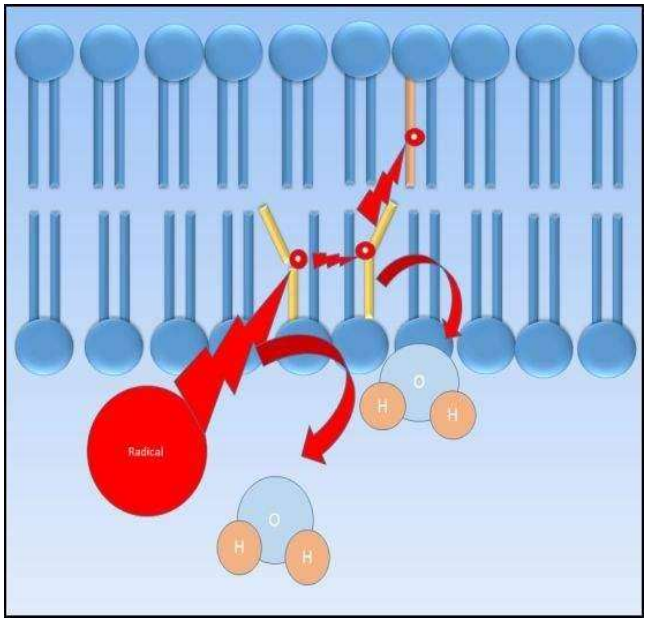

Figure 8. Schematic representation of the mechanism of lipid peroxidation. Reactive oxygen species (ROS) initiate chain reactions of oxidation of polyunsaturated fatty acids of membranes, which is accompanied by the formation of lipid radicals, hydroperoxides and secondary oxidation products.

Free radical-mediated reactions profoundly affect the physicochemical properties of biological membranes [17]. They increase the rigidity and viscosity of the lipid bilayer, alter membrane phase behavior, reduce electrical resistance, and impair phospholipid translocation between membrane leaflets (flip-flop movement) (**Figure 9**).

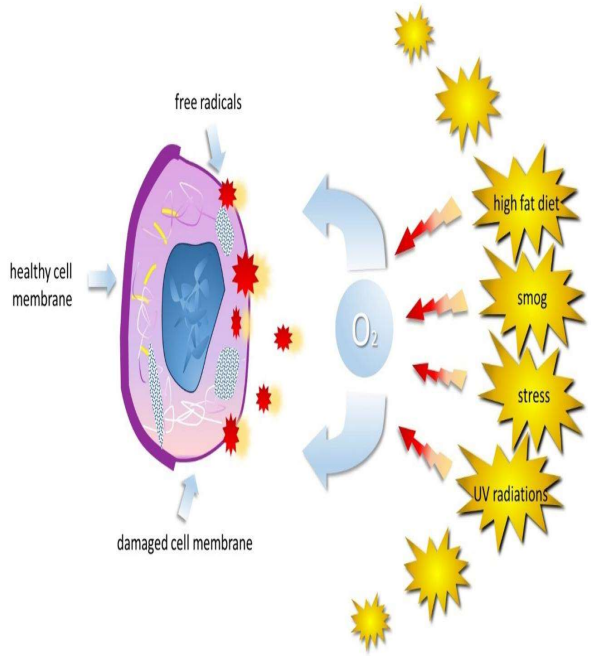

Figure 9. Oxidative damage to the cell membrane. Excessive formation of reactive oxygen species leads to disruption of the structure of the phospholipid bilayer, changes in membrane permeability and loss of their functional integrity.

Oxidative damage also restricts the lateral mobility of membrane proteins, thereby disrupting the activity of receptors, enzymes, and transport systems [18]. At the organelle level, these alterations result in mitochondrial swelling, destabilization of intracellular membranes, impaired ATP synthesis, and reduced cellular energy production [19].

Excessive lipid peroxidation overwhelms the mechanisms responsible for cellular homeostasis [20]. Consequently, toxic degradation products of membrane lipids accumulate, disrupting intracellular metabolism and promoting tissue injury [21]. Under these conditions, cells undergo either necrosis or apoptosis, particularly in the presence of additional harmful stimuli such as microbial pathogens, ionizing radiation, or other environmental stressors [22].

Cell destruction is accompanied by the release of intracellular proteins and non-protein molecules into the bloodstream [23]. Having lost their physiological functions, these compounds become endogenous pathogenic molecules that must be eliminated from the body. Low-molecular-weight compounds (less than 60 kDa) are removed through renal glomerular filtration and excreted in urine, whereas larger molecules require prior denaturation followed by phagocytic clearance (**Figure 10).**

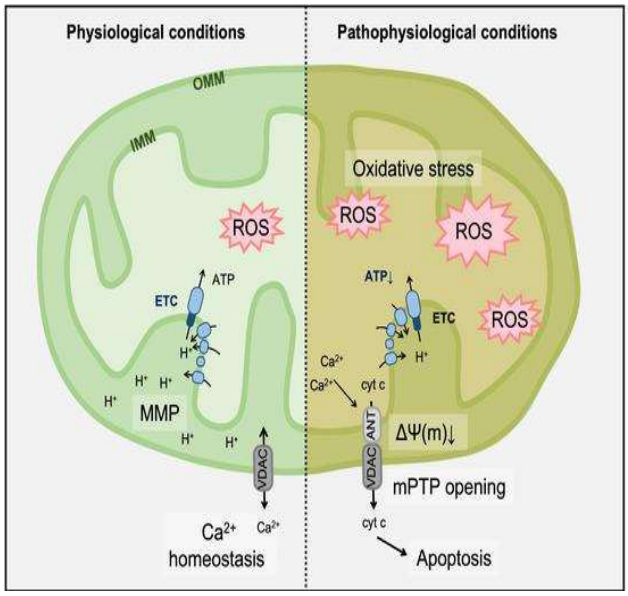

Figure 10. Mitochondrial dysfunction under conditions of oxidative stress. Excess reactive oxygen species causes damage to mitochondrial membranes, decreased ATP synthesis, impaired oxidative phosphorylation and activation of programmed cell death.

Cells of loose connective tissue play a pivotal role in this process by producing reactive oxygen species. ROS induce oxidative modification of proteins, resulting in the formation of pathological epitopes [24].

These altered structures are recognized by the complement system, facilitating their identification and subsequent removal by phagocytic cells. Following endocytosis, modified macromolecules accumulate within the arterial intima, interact with the proteoglycan-rich extracellular matrix, and are internalized by resident macrophages through scavenger receptor-mediated endocytosis [25].

At the same time, excessive ROS production contributes to endothelial dysfunction. Oxidative damage decreases the content of polyunsaturated fatty acids in membrane phospholipids, promotes fragmentation of integral membrane proteins, and impairs receptor-mediated signaling as well as membrane transport.

These changes increase vascular permeability, enhance transcytosis, and compromise endothelial barrier function. Ultimately, damaged molecules are degraded within lysosomes of macrophages, completing the process of eliminating endogenous and exogenous pathogenic substances (**Figure 11**).

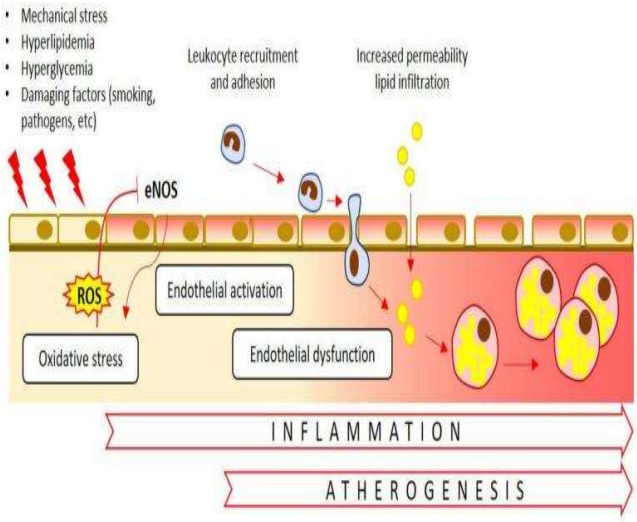

Figure 11. Participation of reactive oxygen species in the development of endothelial dysfunction and inflammatory response. Oxidized low-density lipoprotein molecules accumulate in the vascular wall and are taken up by macrophages through scavenger receptors, which contributes to the maintenance of chronic inflammation and the progression of vascular lesions.

Another important consequence of oxidative modification is activation of the adaptive immune response. Reactive oxygen species and secondary lipid peroxidation products covalently modify apolipoprotein B-100 (apoB-100) of low-density lipoproteins (LDL), generating novel pathological epitopes. These structures are recognized as foreign antigens by immunocompetent cells, leading to the production of autoantibodies and the formation of circulating immune complexes that further contribute to chronic inflammation.

Overall, excessive lipid peroxidation represents one of the principal mechanisms underlying oxidative stress.

It stimulates the production of prostanoids and leukotrienes, alters vascular reactivity, increases endothelial permeability,

enhances platelet aggregation, and promotes inflammatory responses. Collectively, these pathological events play a significant role in the development and progression of numerous inflammatory, cardiovascular, metabolic, and degenerative diseases [2].

Experimental part

Material and methods

he study included 95 apparently healthy volunteers (50 men and 45 women; age range 18–50 years), who served as the control group, and 180 patients diagnosed with chronic non-specific inflammatory diseases of the genital tract aged 18–50 years. The duration of the disease ranged from 2 to 20 years, and all patients had previously received conventional treatment without achieving sustained clinical improvement.

Clinical examination included medical history assessment and physical examination. In female patients, gynecological examination of the vaginal mucosa was performed using a speculum by a certified gynecologist and dermatovenereologist.

Bacterioscopic and cytological examinations were performed using genital mucosal scrapings stained according to the Romanowsky–Giemsa method.

Biochemical analyses were carried out in the accredited Clinical Diagnostic Laboratory of Zaporizhzhia. Total cholesterol (TC) concentration was determined spectrophotometrically using commercially available diagnostic kits. Concentrations of low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), very-low-density lipoprotein cholesterol (VLDL-C), triglycerides (TG), and the presence of chylomicrons were determined using standard laboratory methods. Dyslipidemia was classified according to the World Health Organization (WHO) criteria and the Fredrickson classification.

The intensity of lipid peroxidation was evaluated by measuring malondialdehyde (MDA) concentrations using the thiobarbituric acid reactive substances (TBARS) assay.

Platelet Hemostasis. Platelet hemostatic function was assessed by determining platelet adhesion, ADP-induced platelet aggregation, and disaggregation in platelet-rich plasma using standard laboratory techniques. Plasma von Willebrand factor (vWF) activity was also determined as an indicator of endothelial and vascular function.

In patients with chronic nonspecific inflammatory diseases of the female genital tract, the concentration of von Willebrand factor (vWF) was additionally determined in platelet-poor plasma. The assay was performed according to the Evans and Osten method modified by O.A. Tsyhuliova using formalin-fixed donor platelets [19].

The method is based on evaluating the ability of plasma vWF to induce ristocetin-mediated aggregation of washed formalin-fixed platelets obtained from healthy donors. Quantitative assessment was performed using a calibration curve generated from serial dilutions of standard platelet-poor plasma.

The principle of the assay relies on the ability of platelets treated with dilute formaldehyde to retain sensitivity to ristocetin in the presence of von Willebrand factor while remaining unresponsive to other physiological platelet agonists, including adenosine diphosphate (ADP), adrenaline, thrombin, and spontaneous aggregation. This characteristic provides high analytical specificity for vWF determination.

Reagents. The following reagents were used:

1. 3.8% sodium citrate solution;
2. phosphate buffer (pH 7.6);
3. EDTA-formalin buffer;
4. EDTA buffer solution;
5. ristocetin solution (10 mg/mL).

Venous blood obtained from healthy donors was immediately mixed with the EDTA-formalin solution during collection. Following initial centrifugation, platelet-rich plasma was separated and subjected to a second centrifugation step to obtain a platelet pellet.

The platelet pellet was washed twice with EDTA buffer and subsequently resuspended in phosphate buffer without EDTA to achieve a final concentration of approximately 2×10^5 platelets/μL.

For long-term preservation, the prepared platelets were suspended in phosphate buffer (pH 7.4) containing 0.01% sodium azide.

The suspension was aliquoted into sterile vials and stored at −10 to −12 °C for up to 2–3 months.

Before use, the platelet suspension was thawed and washed twice with EDTA-free phosphate buffer to remove the preservative solution completely.

Preparation of Platelet-Poor Plasma and Determination of von Willebrand Factor

Preparation of Platelet-Poor Plasma. Platelet-poor plasma was prepared from venous blood collected into siliconized tubes containing 3.8% sodium citrate at a blood-to-anticoagulant ratio of 9:1.

The samples were initially centrifuged at 1500 rpm for 7 minutes to obtain platelet-rich plasma. Subsequently, the plasma underwent a second centrifugation step at 4000 rpm for 20 minutes to produce platelet-poor plasma. The resulting plasma was transferred into clean siliconized or plastic tubes and used for subsequent laboratory analyses.

Assay Procedure. The assay was performed using photometric cuvettes with an optical path length of 5.65 mm and a total volume of 2.5 mL. Each test cuvette contained 1.0 mL of washed formalin-fixed platelet suspension, 0.4 mL of platelet-poor plasma obtained from the study participant, and 0.4 mL of EDTA-free phosphate buffer. An additional 0.6 mL of buffer was added to the control cuvette.

After baseline optical density had been adjusted to zero at a wavelength of 630 nm, 0.2 mL of ristocetin solution was added to the test sample. The mixture was gently homogenized, and the reaction time was recorded. Changes in optical density were measured after 2 minutes and were interpreted as an indicator of ristocetin-induced platelet aggregation.

Construction of the Calibration Curve. Quantitative determination of von Willebrand factor was performed using a calibration curve generated from pooled platelet-poor plasma obtained from healthy donors.

The reference plasma was serially diluted with EDTA-free phosphate buffer at dilution ratios ranging from 1:2 to 1:32. Ristocetin-induced platelet aggregation was then assessed for each dilution using the procedure described above.

The endpoint was defined as the highest plasma dilution capable of producing detectable platelet aggregation, corresponding to approximately 2–3% of normal von Willebrand factor activity.

The obtained values were plotted on logarithmic coordinates. Under appropriate experimental conditions, the calibration curve demonstrated a linear relationship in a bilogarithmic coordinate system. This standard curve served as the basis for calculating von Willebrand factor concentrations in patient plasma samples. To improve analytical accuracy, selected specimens were additionally analyzed at two or three different dilution levels.

Hematological and Cytochemical Analysis. All participants underwent a complete blood count, including erythrocyte, leukocyte, and platelet counts, hemoglobin concentration, erythrocyte sedimentation rate (ESR), and leukocyte differential count. Morphological evaluation of blood cells was performed on Romanowsky–Giemsa-stained blood smears.

The functional activity of neutrophils was assessed by cytochemical analysis. Myeloperoxidase activity, reflecting oxygen-dependent phagocytic mechanisms, was determined using the Graham–Knoll method. The content of cationic proteins was evaluated as an indicator of neutrophil bactericidal activity. In addition, integrated inflammatory indices were calculated based on leukocyte counts and ESR values.

Patient Stratification. Healthy individuals were divided into three age groups: 18–28 years, 29–39 years, and 40–50 years. Patients with chronic non-specific inflammatory diseases of the genital tract were similarly stratified according to age and sex.

According to microbiological findings, patients were classified into six etiological groups: bacterial infection, trichomoniasis, fungal infection, chlamydial infection, viral infection, and mixed infection.

Statistical analyses were performed using Microsoft Excel and Statistica software. Data are presented as mean ± standard deviation (SD). Comparisons between groups were performed using Student's *t*-test for independent and paired samples where appropriate. Correlation analysis was applied to evaluate relationships between biochemical, hematological, and hemostatic parameters. A p value <0.05 was considered statistically significant.

Results and discussion

For biochemical and general clinical analyses, blood was collected before the start of the treatment course. The collection was carried out from a vein, after which the blood was stabilized with a 5% sodium citrate solution. Clinical examination of patients and selection of biological material for laboratory studies were carried out together with a doctor from the Zaporizhia City Hospital. The control group (C) consisted of 95 practically healthy individuals (non-staff donors), among whom there were 50 men and 45 women (**Table 1**). The age distribution in the control group was as follows: 18–28 years - 30 people, 29–39 years - 35 people, 41–50 years - 30 people [25]. The main groups of the study included 180 patients with chronic nonspecific inflammatory diseases of the genital organs, including 83 men and 79 women (**Table 1**). The patients were distributed by age as follows: 18–28 years - 60 people, 29–39 years - 58 people, 40–50 years - 44 patients.

Table 1. Distribution of Study Participants by Age and Sex

Group	CG 1	CG2	CG3	1	2	3
Age (years)	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

The table summarizes lipid metabolism parameters and the level of lipid peroxidation in men (M) and women (W) from the control group (CG) and three study groups (Groups 1–3) [13].

The analyzed indicators include ultra-low-density lipoproteins (ULDLn), very-low-density lipoproteins (VLDLn), low-density lipoprotein cholesterol (LDL, mmol·L^{-1}), high-density lipoprotein cholesterol (HDL, mmol·L^{-1}), total cholesterol (CHOL, mmol·L^{-1}), triglycerides (TG, mmol·L^{-1}), and malondialdehyde (MDA, μmol·L^{-1}) [25]. Results are presented as mean ± standard error (**Table 2**).

Table 2. Plasma Lipid Profile in Patients with Chronic Inflammatory Diseases of the Genital Tract Compared with Healthy Controls

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

Notes:

1. n – number of observations (participants) or positive cases, as indicated.

2.Statistically significant difference compared with the control group ($p < 0.05$).

The correlation analysis demonstrated a close relationship between lipid metabolism parameters, platelet hemostasis, and markers of non-specific immune reactivity in patients with chronic non-specific inflammatory diseases of the genital tract. An

increase in the atherogenic properties of blood plasma was associated with enhanced platelet activation and signs of endothelial dysfunction, as reflected by elevated von Willebrand factor (vWF) levels.

These alterations occurred simultaneously with activation of the monocyte–macrophage phagocytic system and reduced functional activity of circulating neutrophils, indicating the persistence of chronic inflammation and oxidative stress.

The obtained findings support the concept that disturbances in lipid metabolism contribute not only to oxidative modification of lipoproteins but also to platelet hyperreactivity and vascular endothelial injury. Correlation analysis was performed to evaluate the relationships between lipid profile parameters, platelet hemostasis, and endothelial function in patients with chronic non-specific inflammatory diseases of the genital tract (**Table 3**).

Table 3. Correlations between lipid profile parameters, platelet function, and von Willebrand factor in patients with chronic non-specific inflammatory diseases of the genital tract

Parameter	Platelet count (×10⁹/L)	Onset of ADP-induced platelet aggregation (s)	Maximum platelet aggregation (%)	von Willebrand factor (%)
HDL-C (mmol/L)	–0.73*	–0.52*	–0.48*	–0.52*
Total cholesterol (mmol/L)	–0.61*	–0.74*	0.89*	0.86*
LDL-C (mmol/L)	0.73*	0.51*	0.63*	0.64*

Note. * $p < 0.05$.

High-density lipoprotein cholesterol (HDL-C) demonstrated significant negative correlations with platelet count ($r = –0.73$, $p < 0.05$), the onset of ADP-induced platelet aggregation ($r = –0.52$, $p < 0.05$), and plasma von Willebrand factor (vWF) levels ($r = –0.52$, $p < 0.05$). These findings suggest that higher HDL-C concentrations are associated with reduced platelet activation and a lower degree of endothelial dysfunction. A positive correlation was observed between HDL-C and the maximum intensity of platelet aggregation ($r = 0.48$); however, this association did not reach statistical significance ($p > 0.05$).

Total cholesterol (TC) showed significant negative correlations with platelet count ($r = –0.61$, $p < 0.05$), the onset of ADP-induced

platelet aggregation (r = –0.74, $p < 0.05$), and plasma vWF concentration (r = –0.86, $p < 0.05$). In contrast, TC exhibited a strong positive correlation with the maximum intensity of platelet aggregation (r = 0.89, $p < 0.05$), indicating enhanced platelet reactivity in patients with elevated cholesterol levels (**Table 3**).

Low-density lipoprotein cholesterol (LDL-C) was positively correlated with platelet count (r = 0.73, $p < 0.05$), the onset of ADP-induced platelet aggregation (r = 0.51, $p < 0.05$), and plasma vWF levels (r = 0.64, $p < 0.05$). Conversely, a significant negative correlation was observed between LDL-C concentration and the maximum intensity of platelet aggregation (r = –0.63, $p < 0.05$).

Overall, the correlation analysis demonstrated close associations between lipid metabolism, platelet function, and endothelial status in patients with chronic non-specific inflammatory diseases of the genital tract. The strongest correlations were observed between total cholesterol and maximum platelet aggregation, as well as between LDL-C, platelet count, and von Willebrand factor levels, indicating that disturbances in lipid metabolism are closely related to alterations in platelet hemostasis and endothelial function.

Conclusions

Patients with chronic inflammatory diseases of the genital tract exhibited pronounced alterations in plasma lipid metabolism compared with healthy controls. The most prominent abnormalities were observed in the older age groups. In women aged 29–39 and 40–50 years, total cholesterol (TC) concentrations were approximately 1.2-fold higher than those in age-matched healthy controls ($p < 0.05$). In addition, the prevalence of chylomicrons and very-low-density lipoprotein cholesterol (VLDL-C) was increased. Women aged 40–50 years also demonstrated a 1.4-fold elevation in low-density lipoprotein cholesterol (LDL-C) accompanied by a 1.4-fold reduction in high-density lipoprotein cholesterol (HDL-C) compared with controls ($p < 0.05$). Triglyceride (TG) concentrations were significantly increased (approximately 1.3-fold) in women aged 29–50 years and in men aged 40–50 years. Overall, increasing age was associated with progressive elevation of proatherogenic lipoproteins (VLDL-C and LDL-C), reduced HDL-C concentrations, and higher TG levels, indicating an age-dependent deterioration of the lipid profile. The frequency of dyslipidemia associated with increased cardiovascular risk also increased with age. Type IIa dyslipidemia occurred significantly more frequently in men of all age groups and in women aged over 29 years than in healthy controls. Moreover, Type IIb and Type III dyslipidemia were more prevalent in men aged 40–50 years. Young men demonstrated a higher prevalence of Type IIa dyslipidemia than women of the same age, which may be related to sex-specific lifestyle factors and the protective effects of endogenous estrogens in premenopausal women. Malondialdehyde

(MDA), a marker of lipid peroxidation and oxidative stress, was significantly elevated in women aged 29–39 years and in both men and women aged 40–50 years, reaching approximately 1.6 times the control values ($p < 0.05$).

These findings indicate activation of lipid peroxidation and suggest that oxidative stress becomes more pronounced with increasing age and chronic inflammation. The observed age-related increases in total cholesterol, LDL-C, TG, and MDA are consistent with previous reports demonstrating enhanced lipid peroxidation, impaired antioxidant defense, and progressive dyslipidemia during aging (**Figure 12**).

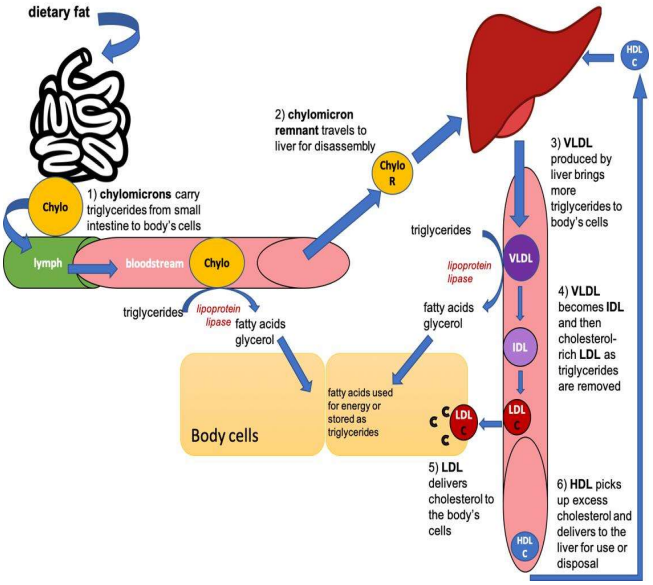

Figure 12. Age-related alterations in plasma lipid profile in patients with chronic inflammatory diseases of the genital tract.

Progressive increases in total cholesterol, LDL-C, VLDL-C, and triglycerides, together with reduced HDL-C levels, contribute to the development of an atherogenic lipid profile and increased cardiovascular risk.

The simultaneous elevation of triglycerides and atherogenic lipoproteins suggests that chronic inflammatory diseases of the genital tract may contribute to the development of secondary dyslipidemia and thereby increase cardiovascular risk. Evaluation of platelet function demonstrated significantly enhanced platelet activation in patients with chronic inflammation.

Platelet adhesion increased by approximately 20% in men aged 29–39 years and by 10% in women aged 40–50 years compared with healthy controls ($p < 0.05$). The onset of ADP-induced platelet aggregation occurred significantly earlier in men aged 18–39 years and women aged 29–50 years, whereas the maximal intensity of platelet aggregation was approximately 1.9-fold higher in all patient groups [5]. These findings indicate increased platelet reactivity and enhanced thrombotic potential in patients with chronic inflammatory diseases of the genital tract. The enhanced adhesive and aggregatory activity of platelets is likely associated with persistent inflammatory activation.

During chronic inflammation, activated neutrophils, monocytes/macrophages, natural killer cells, platelets, and endothelial cells produce large amounts of inflammatory mediators, including platelet-activating factor (PAF), thromboxane A_2 (TXA_2), cytokines, and adhesion molecules. Although local microthrombus formation may restrict the spread

of infection, systemic platelet hyperreactivity increases the risk of thrombotic complications and vascular events. Plasma von Willebrand factor (vWF), an established marker of endothelial dysfunction, was markedly decreased in all patient groups, reaching only 30–62% of control values.

These findings indicate impaired endothelial integrity in patients with chronic inflammatory diseases of the genital tract and further support the close relationship between chronic inflammation, oxidative stress, endothelial dysfunction, and platelet activation.

Overall, the obtained results demonstrate that chronic inflammatory diseases of the genital tract are associated with significant disturbances in lipid metabolism, activation of lipid peroxidation, enhanced platelet reactivity, and endothelial dysfunction. The progressive increase in total cholesterol, LDL-C, VLDL-C, triglycerides, and malondialdehyde levels, together with a reduction in HDL-C concentrations, indicates the development of an atherogenic lipid profile accompanied by oxidative stress formation of the secondary lipid peroxidation product, malondialdehyde (MDA) (**Figure 13**).

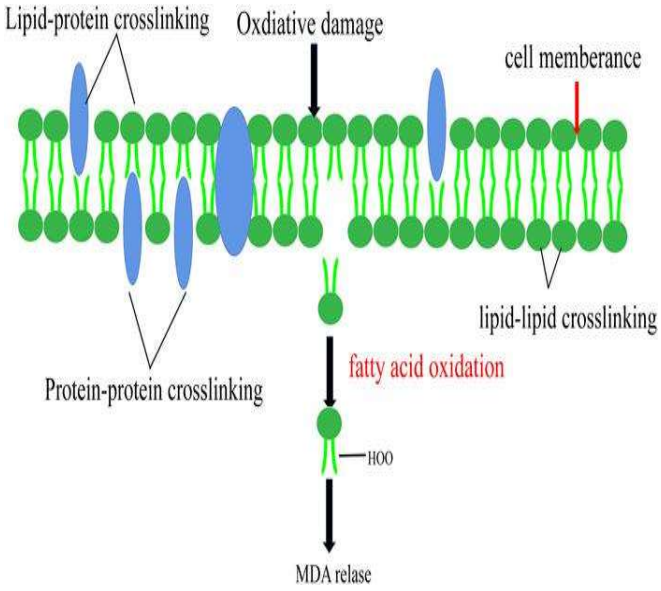

Figure 13. Mechanism of oxidative damage to the cell membrane involving lipid–protein cross-linking, lipid peroxidation of fatty acids.

Furthermore, chronic inflammation was associated with increased platelet adhesion and aggregation, as well as impaired endothelial function reflected by altered von Willebrand factor levels.

Sexually transmitted infections (STIs) trigger the activation of the inflammatory response, leading to significant alterations in platelet function. The inflammatory process stimulates the release of pro-inflammatory cytokines and other mediators, which enhance platelet activation and contribute to endothelial dysfunction.

One of the earliest changes is an increase in platelet adhesion, which rises from 40.6% to 57.2%**,** indicating enhanced platelet interaction with the vascular endothelium and an increased tendency toward thrombus formation. At the same time, the onset time of ADP-induced platelet aggregation is shortened from 14.9 s to

9.1–11.4 **s**, reflecting a more rapid platelet response to activating stimuli.

In addition, the maximum platelet aggregation increases markedly from 19.9% to 43.4%**,** demonstrating enhanced platelet reactivity and aggregation capacity.

Collectively, these changes indicate the development of a prothrombotic state associated with systemic inflammation and endothelial dysfunction induced by STIs.

Overall, activation of the inflammatory response in sexually transmitted infections results in increased platelet adhesion, accelerated ADP-induced aggregation, and enhanced maximal platelet aggregation. These alterations contribute to impaired microcirculation, endothelial injury, and an elevated risk of thrombotic and cardiovascular complications.

These changes suggest that lipid metabolism disorders, oxidative stress, platelet activation, and endothelial injury are closely interconnected and mutually reinforce one another(**Figure 14**).

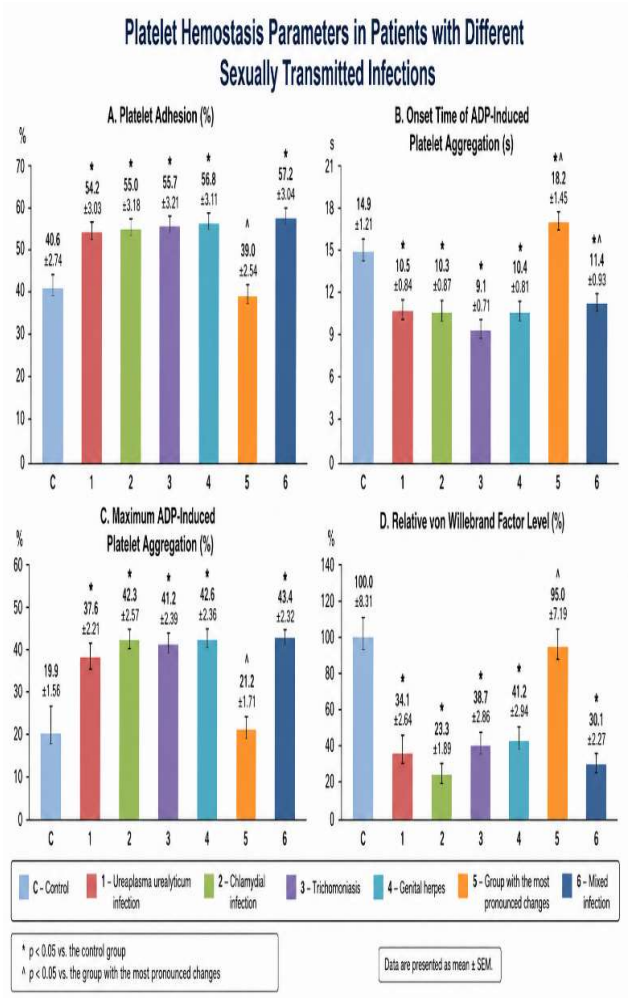

Figure14. Platelet Hemostasis Parameters in Patients with Different Sexually Transmitted Infections. (A) Platelet adhesion (%); (B) onset time of ADP-induced platelet aggregation (s); (C) maximum ADP-induced platelet aggregation (%); (D) relative plasma von Willebrand factor level (%). C – control; 1 – Ureaplasma urealyticum infection; 2 – chlamydial infection; 3 – trichomoniasis; 4 – genital herpes; 5 – mycoplasmal infection; 6 – mixed infection. Data are presented as mean ± SEM. $p < 0.05$ versus the control group; ^$p < 0.05$ versus the group with the most pronounced pathological changes.

Consequently, persistent lipid peroxidation may represent a key pathogenic mechanism linking chronic inflammation with platelet hyperactivity and vascular dysfunction, thereby contributing to the progression of inflammatory diseases and increasing the risk of

thrombotic, cardiovascular, and metabolic complications.

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