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

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In recent decades, considerable progress has been made in understanding the functional mechanisms of platelets and the correction of platelet haemostasis. Platelets are considered the most important participants in both the normal and pathological thrombotic processes characteristic of a variety of diseases and conditions. Alterations in various limbs of haemostasis are found in many somatic diseases (atherosclerosis, coronary heart disease, stroke), surgical procedures, oncological and immunological diseases. Inflammation underlies most diseases and remains an urgent problem in medicine. In the leukocyte infiltration of the inflammatory focus, the mechanism of its self-preservation is of great importance. The activation of haematopoiesis during inflammation is triggered by factors released by stimulated leukocytes of the focus and peripheral blood. Therefore, the problem of the state of the haemostasis system should be the focus of constant attention of clinicians, and with the help of laboratory monitoring of the state of the haemostasis system, it is possible to carry out drug correction of the haemocoagulation potential.

Introduction

Regarding platelet haemostasis disorders in inflammation, it is now proven that a complication of many inflammatory and non-inflammatory diseases is a violation of systemic and local microcirculation, thrombosis and thromboembolism. Especially in inflammatory diseases of the genital organs, disturbances of the microcirculation are observed [1].

Activation of the endothelium and dysregulation of the relationship between endothelial and dendritic cells has been shown to accelerate the development of atherosclerosis and cardiovascular diseases [2], as dendritic cell adhesion and migration promotes atherogenesis.

Inhibition of nitric oxide synthesis by endothelial cells, hypoxia, oxidized low dispersed lipids and tumour necrosis factor (TNF, **Figure 1)** also increase dendritic cell adhesion and migration during inflammation.

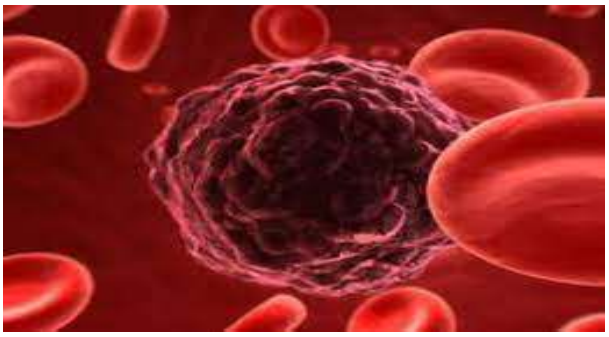

Figure 1. Tumour necrosis factor effect on blood cells.

The interaction of activated endothelial cells and inflammatory cells is thus extremely complex. In this context, the study of the wall effects of the endothelium is of great importance.

An increase in the plasma level of von Willebrand factor is considered as a marker for endothelial activation and/or damage (**Figure 2**) [3].

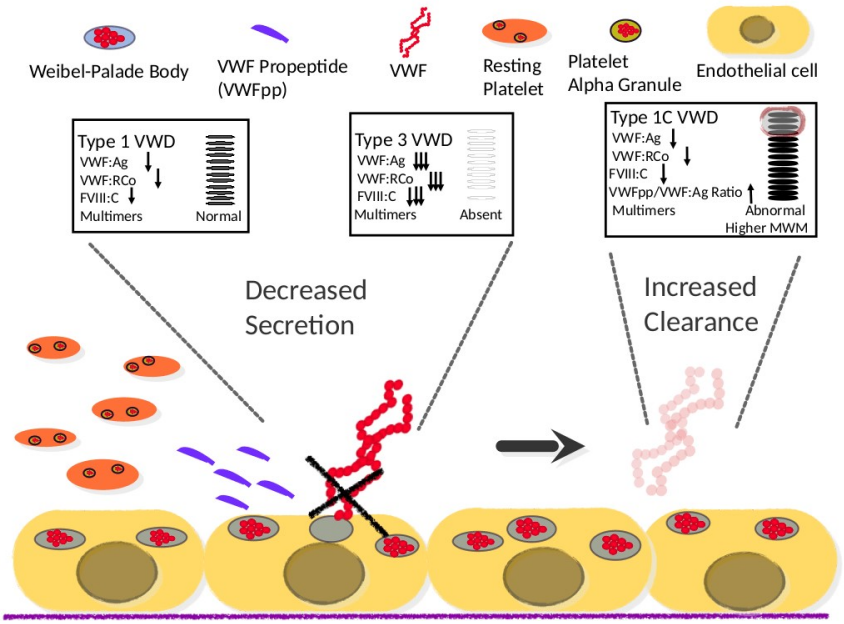

Figure 2. Quantitatived effects of von Willebrand factor.

The von Willebrand factor *is by nature a glycoprotein* (between 500 thousand and 2 million daltons). The subunits of von Willebrand factor contain domains for binding to platelet glycoprotein receptors, collagen, heparin and VIII coagulation factor. The main object of von Willebrand factor synthesis is endothelial cells. At the same time, most of the synthesized von Willebrand factor is deposited in the granules of the Veibel - Palade endothelial cells and can be rapidly released into the extracellular medium - the blood - when the cells are activated.

The role of von Willebrand factor in the bloodstream is to transport the procoagulant coagulation factor VIII, ensuring its stability and accumulation at sites of vascular damage and thrombosis. **(Figure 3).**

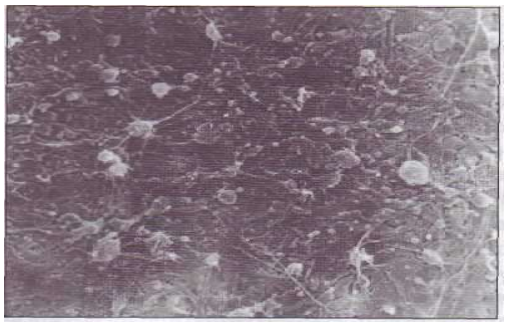

Figure 3. Platelet clot that forms on a damaged vessel wall.

However, the most important value of the von Willebrand factor is its involvement in the interaction between vessels and platelets. In the phases of platelet adhesion, flattening and aggregation, von Willebrand factor acts as a "bridge" between the subendothelial structures of the damaged vessel wall **(Figure 4)** and the platelets, as well as between the individual platelets.

Figure 4. Adhesion of blood platelets to the damaged vessel wall.

Currently, there are two methods for determining von Willebrand factor: 1) determination of factor antigen levels with specific antibodies; 2) ristocetin-induced aggregation of standard or formalized platelets. The diagnostic value of von Willebrand factor as a marker of endothelial dysfunction has been proven for some diseases. It was first demonstrated by Boneu B. and his co-authors (1975), who observed an increase in the concentration of von Willebrand factor in ischaemic limb injury and sepsis. An increase in von Willebrand factor was also found in the blood plasma of patients with hypertension, ischaemic stroke and pulmonary hypertension. A decrease in von Willebrand factor in blood plasma has been observed in patients after thrombolysis using tissue plasminogen activator [3].

In addition, there is evidence in the literature of shifts in the functioning of other limbs of haemostasis in inflammatory diseases

(prostaglandins, prostacyclin, thromboxane A2 (TxA2), etc.). It is known that cyclic endoperoxides formed as a result of the activation of lipid peroxidation in inflammatory processes **(Figure 5)** serve as a substrate for the synthesis of thromboxane A2 in platelets and prostacyclin in vascular endothelium.

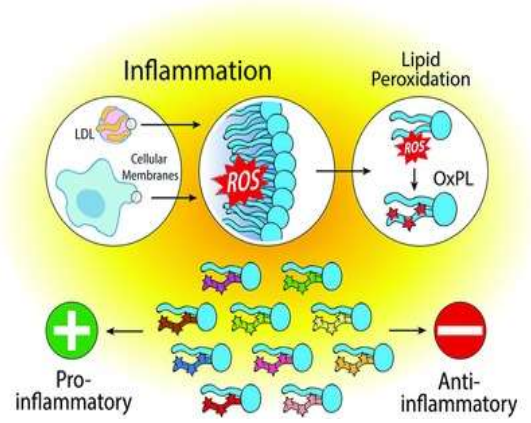

Figure 5. The process of activation of lipid peroxidation in inflammatory processes.

Thromboxane A2 is a strong activator of platelet aggregation and causes vasospasm, whereas prostacyclin, in contrast, inhibits platelet aggregation and dilates blood vessels. Changes in the balance between thromboxane A2 and prostacyclin in the direction of prostacyclin lead to activation of the coagulation system and thrombosis. Especially in chronic glomerulonephritis, there is a tendency to decrease the level of plasminogen activator and increase the level of its inhibitor, as well as antigen VIII von Willebrand factor and platelet ristocetin aggregation [4]. A correlation between increased platelet aggregation function and oxidative "stress" (increased levels of diene conjugate and malondialdehyde in the blood) has been found in patients with chronic nephritis [5]. Deterioration of local microcirculation has been noted in children with vasomotor rhinitis [6]. In lupus nephritis, there is depletion of the fibrinolytic system, first of the local renal vascular bed, then of the systemic one, depending on the severity of the disease [7]. Studies of the functions of microcirculatory haemostasis in patients with bronchial asthma have shown that platelet numbers and their ability to respond to the action of aggregating agents are increased, and thromboxane A2 levels are elevated [8]. In steroid-dependent asthma and chronic obstructive pulmonary disease, the authors observed activation of total plasma fibrinolytic activity to the point of developing a disseminated intravascular coagulation syndrome. In patients with skin inflammation, both allergic contact dermatitis and atopic damage or as a result of skin irritation, CS-1 fibronectin expression was found in inflamed vascular endothelial cells [8]. In psoriasis, platelet haemostasis activity is increased against a background of a decrease in fibrinolytic activity of the blood, and at the same time platelet factors are significantly involved in the implementation of psoriatic inflammation [9]. The authors found a correlation between endothelial activation and the release of adhesion molecules, impaired haemostasis, immunity as well as indicators characterizing the development of

atherosclerosis in rheumatoid arthritis [10]. Patients with appendicitis experience unfavourable disturbances in the lipid spectrum of platelet membranes, which increase their platelet potential. Obliterative endarteritis is associated with a significant increase in the adhesion and aggregation properties of platelets in the lesion pool and carries a high risk for the development of a generalised form of haemostasis [11].

In hypertension, platelet-induced dysfunction of the endothelium occurs with the involvement of proinflammatory cytokines, indicating the immuno-inflammatory nature of endothelial damage in hypertension [12]. An increase in spontaneous platelet aggregation has been found in insulin-dependent diabetes mellitus. These processes are thought to depend on the lack of nitric oxide secretion from damaged endothelial cells [13]. In the fight against sexually transmitted infections, which can lead to inflammation of the genitals, haemostasis disorders and signs of endothelial damage are also observed. In addition, most haemoblastoses and aplastic anaemias are complicated by an impairment of the immune system, the development of mycoses associated with a haemorrhagic syndrome. The bleeding is caused not only by thrombocytopenia due to bone marrow aplasia, but also by the tropism of the fungal pathogen for blood vessels. Some fungi, including yeast-like fungi and especially moulds, are capable of invading blood vessels and developing necrotizing angiitis, which is manifested by necrosis, infarction and haemorrhage in various cavities, organs and tissues [14, 15].

In secondary syphilis, spontaneous and induced platelet aggregation and von Willebrand factor levels are increased, characterizing haemostasiological endothelial dysfunction.

In patients with endothelial inflammation, fibrinolytic properties are reduced and resistance to thrombolysis develops, which plays an important role in the occurrence of infarcts.

Thrombin, which is activated during the inflammatory response, plays the role of an important mediator of neutrophil-dependent damage and is involved in the multicomponent system of the inflammatory cascade as an important link between inflammation and thrombosis.

Thus, inflammation causes a cascade of reactions that are firstly a factor and secondly a consequence of vascular endothelial activation and/or damage **(Figure 6)**. This process is multifactorial.

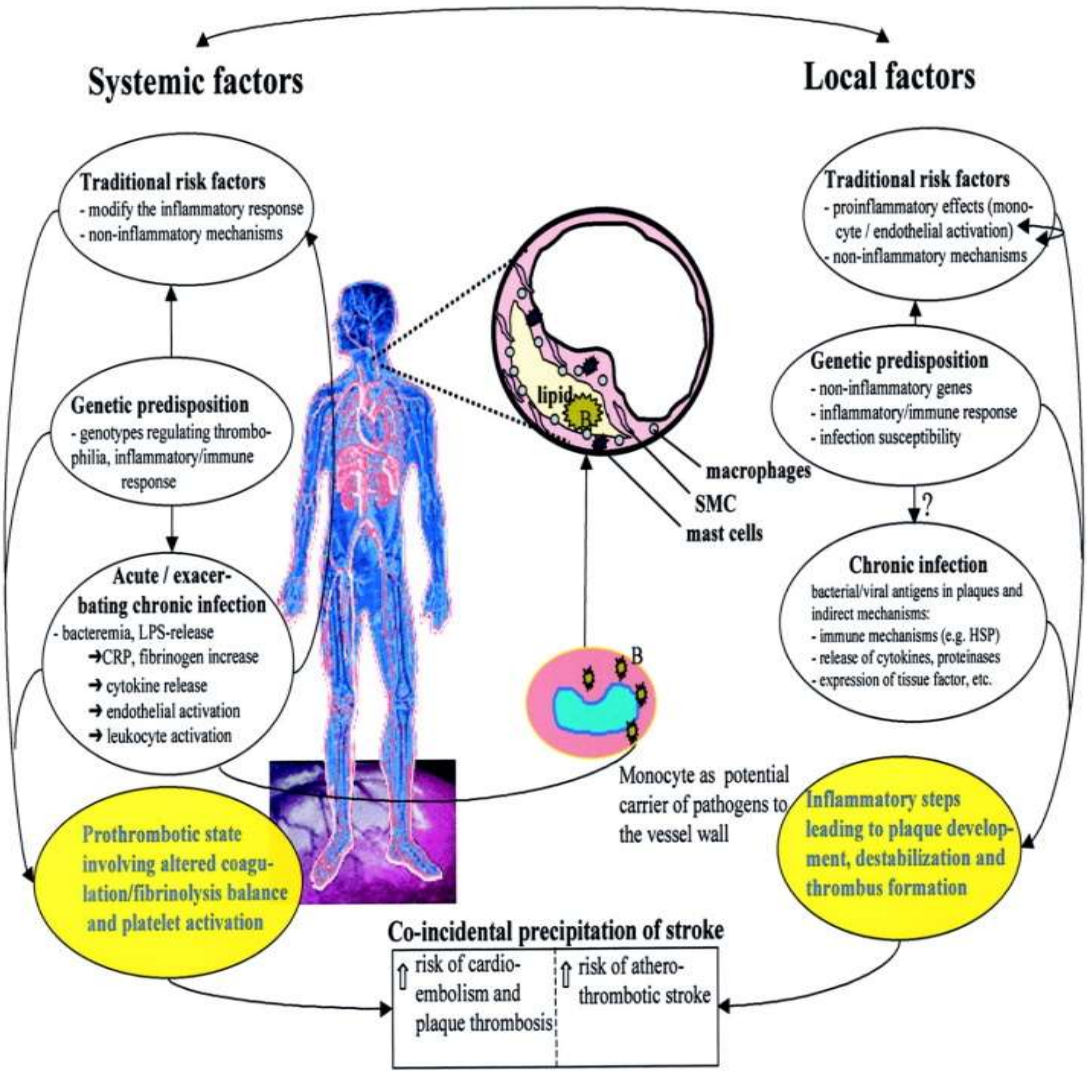

Figure 6. The relationship between inflammation and infection by vascular endothelial damage

Circulating blood cells, endothelial cells [and dendritic cells are involved. The most important humoral factors are interleukin-1, interleukin-6, tumour necrosis factor (TNF), chemoattractant-1, adhesion molecules, phagocyte enzymes and C-reactive protein, anti-endothelial antibodies, platelet activating factor (PAF), lipid mediators, active oxygen radicals and lipoperoxidation products, prostanoids, leukotrienes, von Willebrand factor, thrombin, etc. As a result of activation and/or damage to the endothelium, the function of the endothelial cells is disturbed and the endothelium itself acts as a producer of pathogenic factors. Endothelial dysfunction develops, which is manifested by an imbalance between the factors that ensure normal homeostasis: between the factors of relaxation and constriction of the blood vessels, the pro- and anti-haemostatic mediators, the stimulants and the growth inhibitors.

Experimental part

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 aged 18 to 50 years. The clinical condition of the patients was assessed by interview, survey of complaints, medical history, examination of the skin of the genital organs, in women of the vaginal mucosa, with the aid of a gynaecological mirror.

For biochemical, general clinical and cytological examinations, blood and smears were taken from the mucous membrane of the genitourinary tract before the start of treatment. Blood was collected from a vein and stabilized with 5% sodium citrate solution. Swabs from the genital mucosa were taken from the middle part and the fossa palatina of the urethra in men and from the urethra, the posterior vaginal vault and the cervical canal in women.

Clinical examination of patients and collection of biomaterial for laboratory examination was carried out together with a dermatovenerologist of the city hospital №6 in Zaporizhzhya (Zaporizhzhya, Lankina I.O.). The control group (C) consisted of 95 clinically healthy individuals (non-staff donors), including 50 men and 45 women **(Table 1).** By age, the composition of C was as follows: 18-28 years - 30 people, 29-39 years - 35 and 41-50 years - 30 people. The groups of study subjects included 162 patients with chronic nonspecific inflammatory diseases of the genital organs, including 83 men and 97 women **(Table 1).**

By age, the patients were distributed as follows: 18-28 years - 60, 29-39 years - 58 and 40-50 years - 44 patients.

Control and study groups are residents of the city (99%), most of them (86%) being engaged in intellectual and administrative activities. Financial status according to modern criteria is defined as an average 30% of the surveyed persons constantly or sporadically visit hairdressers, gyms and baths. The number of sexual partners in almost all subjects is 1-2. To investigate the state of platelet hemostasis, adhesion, adenosine diphosphate (ADP)-aggregation of platelets in platelet-rich plasma was studied **(Figure 7)**.

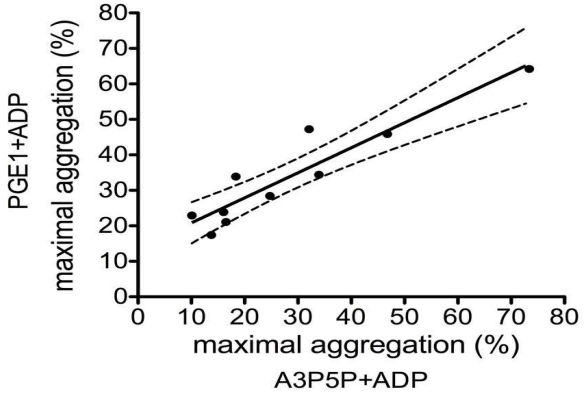

Figure 7. ADP-induced aggregation in platelet rich plasma.

Test persons were also divided into groups depending on the type of pathogen of inflammatory process of genital organs **(Table 2)**.

Platelets were counted using a Goryaev counting chamber. ADP aggregation time was also determined. We studied the degree of maximum aggregation (expressed as a percentage difference between the initial

platelet count, which was taken as 100%, and the platelet count 10 min after adding ADP solution to the sample); the degree of platelet adhesion (the difference between the initial platelet count and the platelet count after contact with glass under rotation on an electromagnetic stirrer for 5 min). In patients with chronic nonspecific inflammatory diseases of the genital organs, the content of von Willebrand factor contained in poor platelet plasma was also determined using formalized donor platelets by the method of Evans et Osten in the modification of O.A. Tsyguleva [11].

The principle of the method is to determine the effect of von Willebrand factor under study on the aggregation of washed and formalin - fixed platelets of healthy individuals under the influence of ristocetin.

Quantitative determination is carried out by the dilution curve of normal mixed platelet-free plasma.

The method is based on the fact that platelets treated with a weak solution of formalin retain the ability to ristocetin-aggregation (in the presence of von Willebrand factor in the medium), but do not undergo other types of aggregation (spontaneous, under the influence of ADP, adrenaline, thrombin, etc.).

Reagents:

1. 3.8 % sodium citrate solution;
2. Buffer solution (pH 7.6; 2 mol. KH_2PO_4; 8,02 mol. NaCl; 8,8 mol. Na_2HPO_4 dissolved in 1 L of distilled water);
3. Buffered EDTA (ethylenediaminotetraacetic acid) - formalin solution: 3mL 0.007 M (0.483%) EDTA, 5mL 4% formalin solution, 2mL buffer, 10mL distilled water;
4. EDTA- buffer solution: 0.77 M EDTA (1 part) with buffer solution (49 parts);
5. Ristocetin solution (10 mg per 1 mL of buffer).

Preparation of suspension of washed fixed platelets of healthy people: 9 parts of venous blood of donors are mixed with 1 part of EDTA - formalin solution; into which blood is injected directly from the puncture needle. Centrifuged for 5 min at 1500 rpm, rich platelet plasma is obtained, in which hemolysis can be expressed. Poor platelet plasma is obtained from this plasma by centrifugation for 20 min at 4000 rpm. Poor platelet plasma is removed, and the platelet precipitate is washed twice with EDTA - buffer solution (4-fold volume with centrifugation each time for 10 min at 4000 rpm). The buffer containing EDTA is removed by suction, and the platelet precipitate is diluted in buffer solution without EDTA so that 1 μL contains about 200,000 platelets. Concentration of normal platelets: normal formalized platelets can be preserved in order not to prepare them again each time. To do this, after washing with EDTA - buffer solution

(twice), they are placed in phosphate buffer (pH 7.4) with 0.01% sodium azide solution.

The suspension is packed in 3 mL in sterile vials, rolled up and stored in the freezer (at -10 -12 ºC) for 2-3 months. If necessary, the contents of the vials are thawed, platelets are washed twice from the preservative solution with buffer without EDTA and used in the test.

Preparation of platelet-free plasma of the subject. Blood is taken from a vein under siliconization conditions and mixed with 3.8% sodium citrate solution (9:1). Centrifuged for 7 min at 1500 rpm. The rich platelet plasma is removed and centrifuged for 20 min at 4000 rpm. Poor platelet plasma is transferred to another silicone or plastic tube and used in the test.

The course of the study.

Inject into 2 cuvettes for FEC (photoelectric colorimeter) with a working edge of 5.65 and a volume of 2.5 mL1 mL of suspended, washed normal platelets, 0.4 ml of platelet-free plasma from the subject and 0.4 mL of buffer without EDTA.

Add 0.6 mL buffer to the control cuvette. Both cuvettes are placed in the FEC (photoelectric colorimeter) and at $\lambda = 630$ nm the FEC (photoelectric colorimeter) arrow in the cuvette with the sample is set to "O", 0.2 mL ristocetin solution is injected, mixed and the stopwatch is switched on. After 2 minutes, the changes in optical density of the sample associated with platelet aggregation under the influence of ristocetin are recorded.

Construction of the dilution curve.

To quantify the presence of von Willebrand factor in the test plasma, a standard dilution curve obtained from a large group of healthy young people with normal platelet-free plasma is used. This plasma is diluted with buffer without ethylenediaminetetraacetic acid at a ratio of 1:2 to 1:32, after which washed normal platelets are injected into each sample according to the above methodology to determine ristocetin platelet aggregation. The calculation point is the dilution of plasma at which ristocetin no longer causes platelet aggregation. This point corresponds to a presence of 2 - 3 % of von Willebrand factor in the medium. The data obtained is plotted on logarithmic paper. If constructed correctly, the curve looks like a straight line in the bilogarithmic coordinate system. This curve is used to determine the presence of the von Willebrand factor in the test plasma. To achieve greater accuracy, the latter can also be examined in 2 - 3 dilutions.

To assess the state of local and systemic general reactivity of the body, a complete blood count was performed. The number of erythrocytes, leucocytes and platelets in the Goryaev counting chamber was counted. The concentration of haemoglobin in the blood and the colour index were determined. Morphological examination of

blood cells in smears stained by the Romanovsky-Giemsa method was performed. The leukogram was calculated according to a uniform method, and the erythrocyte sedimentation rate was determined.

To assess the nature of dyslipoproteinaemia in patients with chronic non-specific inflammatory diseases of the genital organs, changes in lipid metabolism were studied.

The content of total cholesterol was determined spectrophotometrically using reagent kits from "Filisit Diagnostics", Dnipropetrovs'k. The presence of chylomicrons and very low density cholesterol lipoproteins was determined by visualization of the sample after exposure of the blood plasma at a temperature of 0°-+4° C, the concentration of low density cholesterol lipoproteins according to the method of Burstein and Samai, the concentration of cholesterol of high density lipoproteins with a reagent kit of the company "Cormay", the triglycerides with a reagent kit of the company "Lahema", Czech Republic. The phenotype of dyslipoproteinaemia was checked in accordance with the guidelines for the diagnosis of cardiovascular diseases.

Results and discussion

The state of platelet adhesion and aggregation properties as a factor in increasing thrombosis propensity when assessing the state of platelet haemostasis in patients with chronic inflammation.

For the laboratory diagnosis of the activity of the inflammatory process and the prognosis of complications, the assessment of the functional state of the platelets is of great importance. The indicators for the adhesion and aggregation functions of platelet haemostasis were examined. In addition, the relative concentration of von Willebrand factor was determined, whose platelet component characterizes platelet aggregation, while the vascular component is considered a marker for endothelial damage. The study showed a 1.2-fold increase in platelet adhesion intensity **(Table 3)** in group 2 men ($p<0.05$) and in women of group 3 by 1.4 times ($p<0.05$). The time of onset of ADP - platelet aggregation was significantly reduced in men of the 1st and 2nd groups by 1.9 and 1.6 times ($p<0.05$), respectively, and in women of the 2nd and 3rd groups by 1.5 ($p<0.05$) and 1.6 ($p<0.05$) times compared to control.

The intensity of maximum platelet ADP aggregation significantly exceeded this in all patient groups. Thus, this index was increased 2.0-fold ($p<0.05$) in men of the 1st, 2nd and 3rd groups. In women of the 1st, 2nd and 3rd groups, the degree of maximum ADP platelet aggregation was increased 2.0-, 1.7- and 1.6-fold, respectively ($p<0.05$).

The relative concentration of von Willebrand factor was significantly reduced in

all patient groups and was only between 30 and 62 % of the control group (100 %). Taking into account that the vascular component of von Willebrand factor is a marker for the functional state of the vascular endothelium, it can be assumed that in patients with chronic non-specific inflammatory diseases of the genital organs there is damage to the endothelial cells, endothelial dysfunction with a decrease in the production of von Willebrand factor **(Figure 8)**.

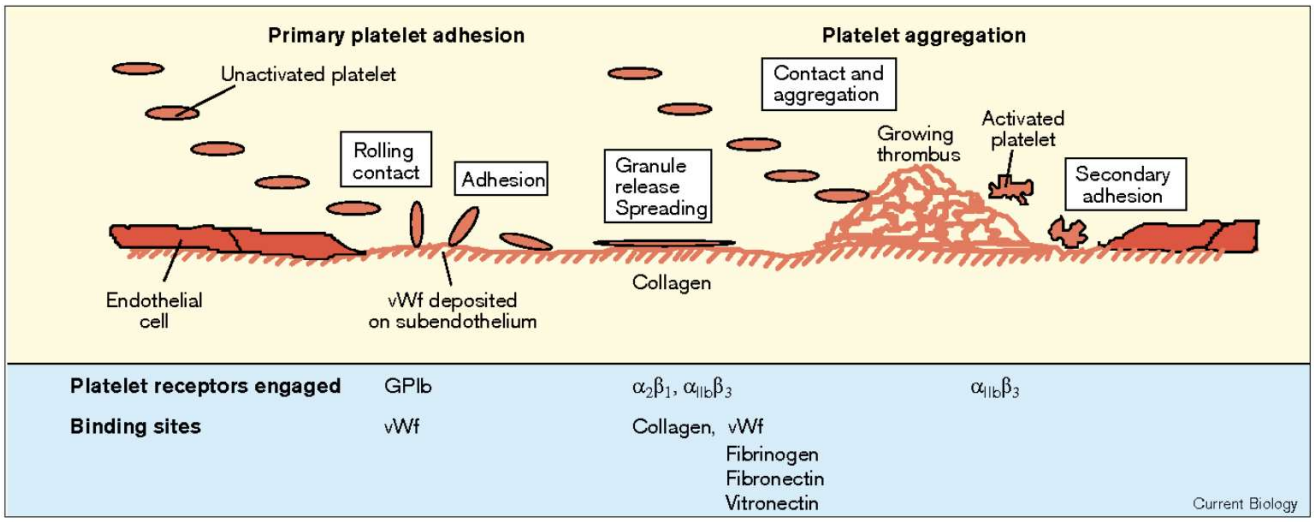

Figure 8. Platelet adhesion, activation and aggregation on exposed subendothelium

Analysis of the function of platelet parameters in patient groups depending on the type of inflammatory agent **(Table 4)** showed a significant increase in platelet adhesion in all groups, except the 5th group (viral infection) on average by 1.4-fold ($p<0.05$); decrease in aggregation time by 1.3-fold ($p<0.05$); increase in maximum aggregation by 1.9-2.2-fold ($p<0.05$). The relative concentration of von Willebrand factor in blood plasma decreased significantly by 2.4-3.2-fold in all groups of patients with various sexually transmitted infections. The decrease of this indicator in patients of group 4 with chlamydial infection was most significant compared to the control, 1-3 and 5-6 groups ($p<0.05$).

In general, violations of platelet adhesion and aggregation functions occurred in the direction of increased thrombogenic potential, while the relative level of von Willebrand factor decreased in group 4 patients with (chlamydial infection) von Willebrand factor ($p<0.05$).

This may lead to a disturbance in the regulation of the vascular haemostasis and platelet system, primarily in the direction of an increase with a possible subsequent decrease in primary haemostasis activity due to depletion of von Willebrand factor and consumption of the circulating platelet pool.

We have followed the relationship between shifts in lipid metabolism, platelet adhesion and aggregation function and the

relative concentration of von Willebrand factor in the blood plasma of patients with chronic non-specific inflammatory processes of the genital organs.

We have shown that the shift in low-density lipoprotein cholesterol concentration had a strong inverse relationship with the number of platelets per unit blood volume (r = -0.73) (**Table 5),** the time of onset of ADP platelet aggregation (r = -0.52) and the relative content of von Willebrand factor in blood plasma (r = -0.52) ($p < 0.05$). Changes in total cholesterol concentration were strongly inversely related to the number of platelets per unit blood volume (r= -061), the time of onset of ADP platelet aggregation (r= -0.74), the relative content of von Willebrand factor in blood plasma (r= -0.86), and a direct strong correlation with the intensity of maximal platelet aggregation (r= +0.89), ($p<0.05$).

Conclusions.

If endothelial dysfunction and impaired platelet function lead to restricted access of drugs to the lesion on the one hand and do not exclude complications from the blood coagulation system on the other hand, the question arises whether chronic non-specific inflammatory processes of the genital organs may play a role in the development of platelet disorders of haemostasis. In our study, an increase in the concentration of low-density lipoprotein cholesterol and total cholesterol concentration was associated with a decrease in the number of platelets per unit of blood volume, an acceleration and an increase in the intensity of platelet ADP aggregation and a decrease in the relative concentration of von Willebrand factor.

At the same time, the value of low-density lipoprotein cholesterol concentration showed a direct strong correlation with the number of platelets per unit of blood volume (r= +0.73), the time of onset of platelet ADP aggregation (r= +0, 51), the relative concentration of von Willebrand factor in blood plasma (r= +0.64) and strong inverse relationships (r= -0.63, $p<0.05$) with the intensity of maximum platelet ADP aggregation

This means that an increase in high-density lipoprotein cholesterol was associated with an increase in platelets per unit of blood volume, presumably due to a decrease in their consumption, a decrease in the rate and intensity of platelet aggregation and a normalization of von Willebrand factor levels in plasma.

From this, it can be generalized that careful monitoring of platelet adhesion and aggregation functions and relative von Willebrand factor levels is necessary to prevent thrombosis or haemorrhagic complications, to avoid the development of severe inflammatory processes and their complications in patients with chronic non-specific inflammatory diseases.

Table 1. Distribution of respondents by age and gender

Group	C1	C2	C3	1	2	3
Age (years)	18-28	29-39	40-50	18-28	29-39	40-50
Number of men	15	20	15	28	30	25
Number of women	15	15	15	36	30	29

Table 2. Test persons divided into groups depending on the type of pathogen of inflammatory process of genital organs

Indicator	C	1	2	3	4	5	6
Pathogen	non-specific. Bacteria Flora	Bacteria	Trichomonads	Mycosis	Chlamydo-monas	Viruses	Mixed flora
Average	35.3±7.2	31± 7.4	28.3± 6.8	34.3± 8.1	34.2± 8.8	31.3± 6.4	31.6± 7.1
Age (years)	45	36	26	30	28	19	41
Total number	24	16	11	13	14	9	20
Number of men.	21	20	15	17	14	10	21

Table 3. Indicators for platelet haemostasis and von Willebrand factor in patients with chronic non-specific inflammatory diseases of the genital organs

Group		Degree of adhesion, %	Time of ADP aggregation onset, s	Degree of maximum aggregation, %	Relative level of von Willebrand factor, %
C1	M	40.5±4.9	15.7±2.8	17.9±5.3	100
	W	38.9±4.1	14.9±3.6	20.2±4.9	100
C2	M	41.2±5.3	15.2±3.3	18.8±4.8	100
	W	40.0±3.8	14.3±5.3	21.1±7.2	100
C3	M	42.0±3.8	14.8±3.6	20.7±5.3	100
	W	40.7±4.7	14.0±2.8	23.4±5.5	100
1	M	42,8±2.3	8.38±3.3*	36.6±6.4*	44.3±39.1
	W	42.7±2.0	12.2±3.4	41.6±12.3*	42.1±27.4
2	M	50.0±6.0*	9.81±3.88*	38.3±6.8*	38.9±25.5
	W	40,4±2.3	10.2±2.3*	36.4±6.6*	34.8±22.0
3	M	39.6±2.3	12.5±5.3	39.4±7.9*	61.,8±46.1
	W	56.1±4.1*	8.75±3.2*	37.2±4.8*	29.7±21.8

Notes:

* - $p<0.05$; compared to the control.

Table 4. Indicators of platelet haemostasis and VWF content in the blood plasma of patients with different types of sexually transmitted infections

Indicator	C	1	2	3	4	5	6
Unit of measurement	40.6± 0.6	54.2± 1.2*	55± 1.2*	56.7± 1.3*	56.8± 1.4*	39± 1.2	57.2± 1.7*
Degree of adhesion, %	14.9± 0.4	9.7± 0.3*	9.1± 0.2*	9.2± 0.3*	9.4± 0.3*	11.3± 0.4*	11.4± 0.4*
Time of onset of ADP aggregation, s.	19.9± 1.1	40.1± 1.6*	38.3± 1.3*	38.6± 1.3*	43.4± 1.2*	37.6± 1.3*	40.5± 1.5*
Degree of max aggregation, %.	100	41.2± 3.6*	34.2± 2.9*	31.2± 2.4*	23.3± 1.9*^	38.8± 2.6*	36.7± 2.6*

Notes:

*- $p<0.05$, compared to the control group.

^ - $p<0.05$, compared to all other groups.

Table 5. Correlation coefficients (r) of lipid metabolism and platelet haemostasis and von Willebrand factor content in blood plasma in patients with chronic non-specific inflammatory diseases of the genital organs

Unit measurements	Platelet count, L^{-1}	Time of onset of ADP aggregation, s	Intensity of maximum aggregation of Tr, %	Relative level of Willebrand factor, %
Cholesterol level - low density lipoproteins, mmol L^{-1}	-0.73*	-0.52*	0.48	-0.52*
Cholesterol level, mmol L^{-1}	-0.61*	-0.74*	0.,89*	-0.86*
Cholesterol level - high density lipoproteins mmol L^{-1}	0.73*	0.51*	-0.63*	0.64*

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