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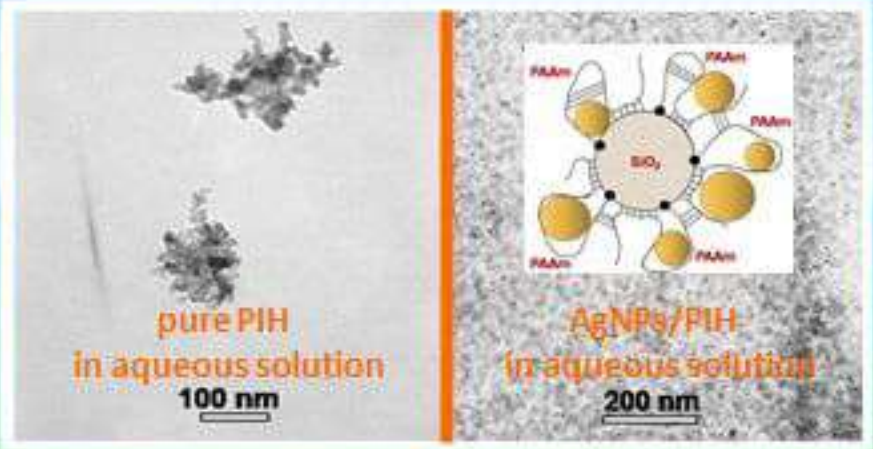

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Investigation of aspects of the interaction of the indicators of lipid exchange, trombocitarian block of hemostasis, total body reactivity and their influence on the psychosomatic harmonization of the man in chronic inflammatory processes

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For the first time on the basis of clinical and laboratory researches were revealed the correlation of indicators of lipid metabolism, platelet level of hemostasis and general reactivity in patients with chronic inflammatory processes of the genital system. The new pathogenetic aspects of the course of inflammatory diseases have been established. It has been shown that chronic inflammatory process is accompanied by disorders of lipid metabolism. The degree of severity of these changes depends on the severity of the inflammatory process, the reduction of phagocytic activity of polymorphonuclear leukocytes and the activation of macrophage and specific cellular mechanisms, accompanied by auto-intoxication. It is established that the frequency of atherogenic dyslipoproteinemias, as well as the intensity of lipid peroxidation increases in accordance with the increase age of the examined patients. Most atherogenic dyslipoproteinemias are found in patients with viral and chlamydial infections. The summarized data of the correlation analysis allow us to establish that the growth of atherogenic properties of blood plasma of patients with chronic inflammatory processes of the reproductive system occurs in accordance with the increase of adhesive-aggregation properties of platelets and damage of the vascular endothelium. These shifts occur in parallel with the predominance of the monocyte-macrophage linkage of phagocytosis against the background of reduced activity of neutrophils and cellular mechanisms of development of immunopathological reactions.

Introduction

Lipid metabolism plays an important role in the development of complications of chronic inflammatory processes [4]. It is known that phagocytes activate the increased release of reactive oxygen species (ROS). Its interaction with polyunsaturated fatty acids initiates lipid peroxidation (POL) during the inflammation. Often, oxidized components are low-density lipoprotein components [1]: unsaturated fatty acids with different amounts of double bonds, B-100 apolipoproteins, alcohol, cholesterol, uric acid, bilirubin, estrogens, etc. Reactivity mechanisms are provided by the antioxidant protection system (AOZ) - a set of enzymatic and non-enzymatic factors that protect the cell from free radicals formed [2]. (Figure 1)

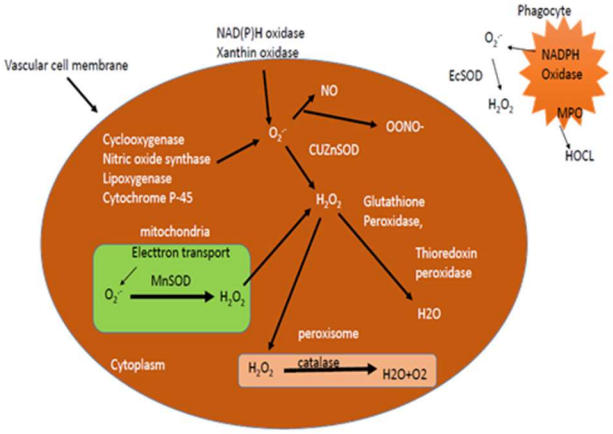

Figure 1. Outline of various sources of reactive oxygen species and action of antioxidant enzymes.

Antioxidant enzymes include superoxide dismutase, which catalyzes the dissociation of oxygen into hydrogen peroxide, glutathione reductase, glutathione peroxidase, ceruloplasmin, and catalase, which decomposes hydrogen peroxide into water and oxygen molecules. The non-enzymatic AOP system includes fat-soluble (α-tocopherol, ubiquinone, naphthoquinone, carotenoids, creatinoids, steroid hormones, including estrogens, etc) and water-soluble (sodium thiosulfate, glutathione, ascorbic acid and nicotinic acid. Also among the natural antioxidants are a group of proteins, which include thiol groups (cysteine, methionine, etc.). Antioxidants are able to inhibit free radical oxidation by binding free radicals and their transformation products.

In recent years, it has been proven that peroxide oxidation - the physiological stage of inflammation of oxygen forms is a stage of the systemic inflammatory response syndrome [7]. (Figure 2) Synthesis activationis the part of the biological function of maintaining the "purity" of the internal environment of a multicellular organism. The production and secretion of PCT cells by cell-activated antioxidant enzymes (superoxide dismutase, glutathione peroxidase, catalase) is the part of the syndrome of compensatory anti-inflammatory protection in which the neuroendocrine system is involved. There is a certain association between the state of immunity and lipid peroxidation rates and the activity of antioxidant defense enzymes in the patients with increased susceptibility to respiratory tract infections and bronchial asthma, pyelonephritis, prostatitis [14]. Quite clear changes in the activity of lipid peroxidation and

antioxidant protection system is determined in many infectious and inflammatory diseases.) and a decrease in the characteristics that characterize the antioxidant protection system (glutathione reductase activity and α-tocopherol content) [5]. In viral hepatitis A, B, C, D, E revealed activation of lipid peroxidation, which depends on the period and course of the disease. The highest concentrations of diene conjugate and malondialdehyde in serum and erythrocytes were observed in severely ill patients during hepatitis.

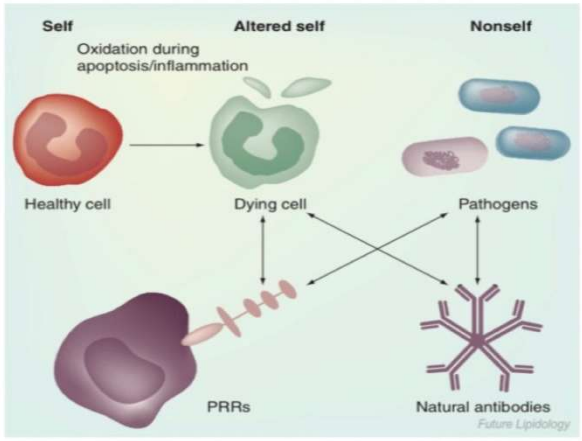

Figure 2. Oxidative stress.

The relationship between the state of immunity and indicators of lipid peroxidation and the activity of enzymes of the antioxidant defense system is also determined in patients with noncommunicable diseases: atherosclerosis, coronary heart disease, hypertension, obesity, diabetes mellitus, malignant diabetes, malignancy, diabetes [17]. (Figure 3)

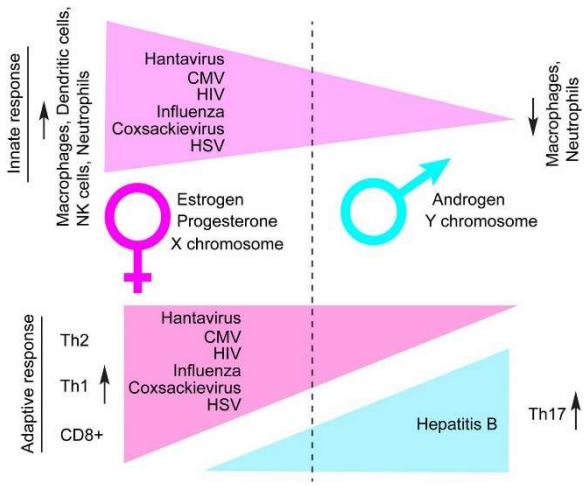

Figure 3. Innate response and Adaptive response.

Increased lipid peroxidation is accompanied by an increase in the formation of prostanids, leukotrienes, which leads to changes in vascular reactivity, impaired vascular wall permeability, increased platelet aggregation capacity, increased viscosity and ordering of lipid fibrillation, alteration of lipid electrocardiography phospholipids between two monolayers. It is also important in the development of many diseases [6]. There are disorders of the platelet level of hemostasis. In inflammatory diseases of the genital organs disturbances of microcirculation are also observed. Endothelial activation and dysregulation of endothelial and dendritic cell relationships have been shown to accelerate the development of atherosclerosis and cardiovascular disease, since dendritic cell adhesion and migration enhances atherogenesis [9]. Inhibition of nitric oxide synthesis by endothelial cells, hypoxia, oxidized low-dispersion lipids, tumor necrosis factor (TNF) in inflammation also increase the adhesion and

migration of dendritic cells. The marker of activation and / or damage to the endothelium is the increase in plasma levels of von Willebrand factor, which functions as a "bridge" between the subendothelial structures of the damaged vascular wall and platelets, as well as between individual platelets [8]. (Figure 4)

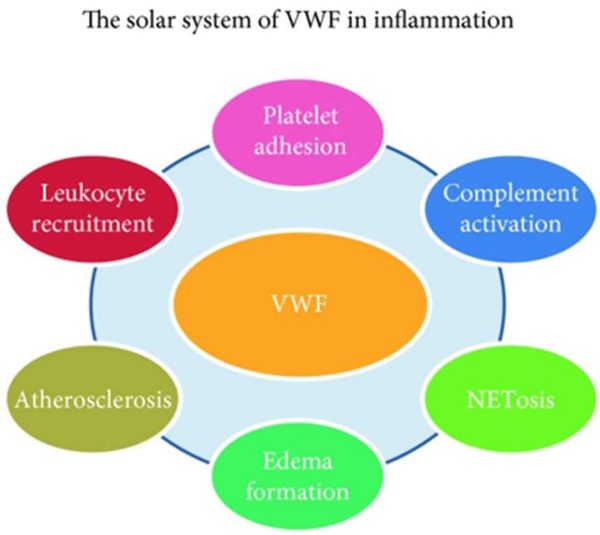

Figure 4. The “solar system” of VWF-mediated vascular inflammation.

VWF is central in the “solar system” of vascular inflammation, and many inflammatory pathways orbit in its “gravitational field.” VWF supports leukocyte and platelet recruitment in inflamed tissue, modulates vascular permeability and edema formation, may promote atherosclerotic plaque formation and inflammation, and provides an activating surface for complement activation and NETosis. All these mechanisms may contribute to tissue injury and organ failure in thromboinflammatory disorders.

Elevation of von Willebrand factor in blood plasma is observed in patients with hypertension, ischemic stroke, pulmonary hypertension, limb involvement in sepsis [10]. In addition, references in the literature indicate changes in the functioning of other units of hemostasis in inflammatory diseases (prostaglandins, prostacyclin, thromboxane A2 (ThA2), etc. It is known that the cyclic endoperoxides formed due to the activation of peroxide oxidation in the process of oxidation of peroxide oxidation, a substrate for the synthesis of thromboxane A2 in platelets and prostacyclin in the vascular endothelium.Tromboxane A2 is a potent activator of platelet aggregation and causes vascular spasm, whereas, on the contrary, inhibits aggregation. Changes is found in the balance between thromboxane A2 and prostacyclin towards prostacyclin cause activation of the clotting system and thrombosis, in particular, in chronic glomerulonephritis, a tendency to decrease the level of plasminogen activator and antigen content of fibrin. A link of platelet aggregation, which is in the patients with chronic nephritis, is found between an increase in platelet aggregation function and oxidative "stress" (an increase in diene levels of the conjugate and malonic dialdehyde in the blood). Deterioration of local microcirculation was detected in patients with vasomotor rhinitis. In lupus nephritis is a depletion of the fibrinolytic system, first of all, the local renal vascular tract, and then systemic, depend on the severity of the

disease [13]. Studies of the functions of microcirculatory hemostasis in patients with bronchial asthma have shown an increase in the number of platelets, their ability to respond to the action of aggregating agents, impaired content of thromboxane A2. In steroid-dependent bronchial asthma and chronic obstructive pulmonary diseases, the authors observed the activation of total fibrinolytic activity of blood plasma up to the development of disseminated intravascular coagulation syndrome [12]. 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 endothelial cells of inflamed vessels [11]. In psoriasis, there is an increase in the activity of the platelet level of hemostasis against the background of reduced fibrinolytic activity of the blood, and at the same time platelet factors are involved in the implementation of psoriatic inflammation. The authors have identified a correlation between endothelial activation and release of adhesion molecules, impaired hemostasis, immunity, and indicators that characterize the development of atherosclerosis in rheumatoid arthritis [3]. In hypertension, platelet endothelial dysfunction occurs with the involvement of proinflammatory cytokines, which indicates the immunoinflammatory nature of endothelial damage at elevated blood pressure. (Figure 5).

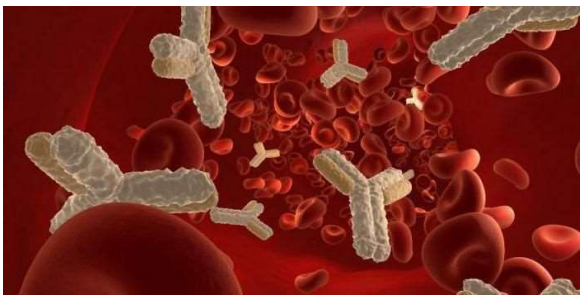

Figure 5. Vascular bed with red blood cells and ammune cells.

Increased rates of spontaneous platelet aggregation have been found in insulin-dependent diabetes mellitus. These processes are thought to depend on the deficiency of nitric oxide secretion by damaged endothelial cells. In the case of lesions, sexually transmitted infections that can cause inflammation of the genitals, there are also disorders of the hemostasis system and signs of endothelial damage. (Figure 6).

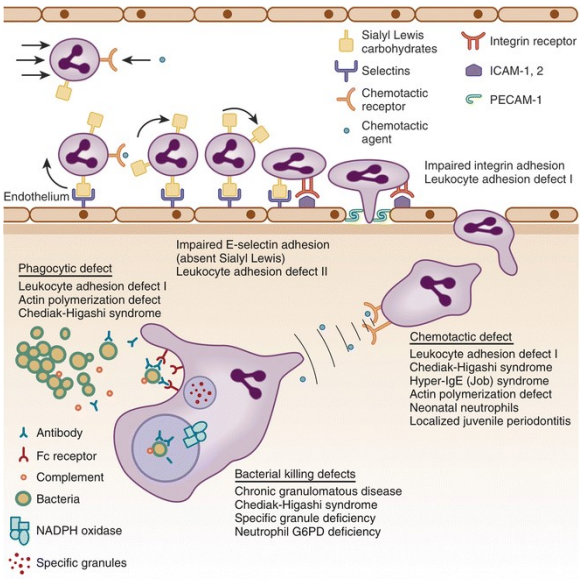

Figure 6. White blood cell chemotaxis through the vessel wall.

Thus, inflammation causes a cascade of reactions, which are, first, a factor, and secondly, a consequence of activation and / or damage to the vascular endothelium. This process is multifactorial. It involves circulating blood cells, endothelial cells, dendritic cells. Of the humoral factors, interleukin-1, interleukin-6, tumor necrosis factor (TNF), antibodies, platelet activation factor (PAF), lipid mediators, active oxygen radicals and products of lipoperoxidation, prostanoids, leukotrienes, factor, . Due to the activation and / or damage of the endothelium, dysregulation of endothelial cell function occurs, and the endothelium itself acts as a producer of pathogenic factors. The development of endothelial dysfunction, manifested by the imbalance of chemoattractant-1, adhesion molecules, enzymes of phagocytes, C-reactive protein, antiendothelial between factors that ensure normal homeostasis: between vascular relaxation and constriction factors, pro- and anti-hemostatic mediators, stimulants and growth inhibitors.

The state of the general reactivity and resistance of the body in inflammatory processes.

In the pathogenesis of chronic nonspecific inflammatory diseases of the genital organs and their complications play an important role disorders of the circulation in the genital organs, rheological properties of blood, hormonal background, activity of enzyme systems, peroxide oxidation of lipids, state of nonspecific and specific organism. blood, and in the lesion.(Figure 7)

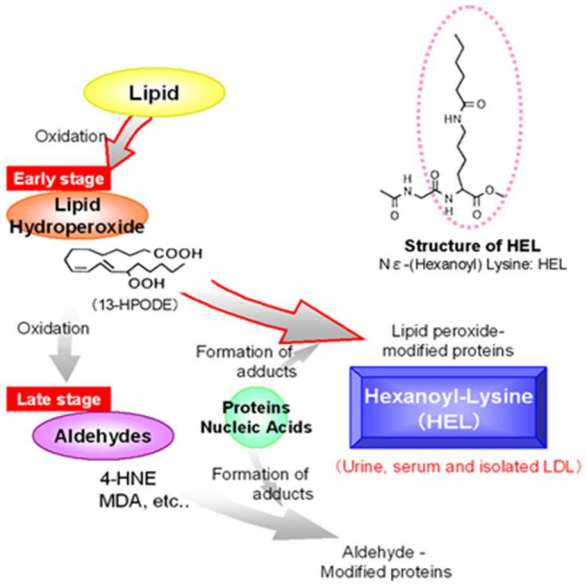

Figure 7. The lipid's metabolism.

Men with chronic nonspecific inflammatory diseases of the genital organs showed impaired phagocytic activity of circulating blood neutrophils: increased migration, decreased glycogen content, increased activity of acidic and alkaline phosphatase, decreased activity of myeloperoxidase (MP.1), 7. test with nitrosine tetrazolium (HCT test). (Figure 8).

Common Diseases and Disorders of the Male Reproductive System

Disease/Disorder	Description
Benign prostatic hypertrophy (BPH)	Nonmalignant enlargement of the prostate gland
Epididymitis	Inflammation of an epididymis; usually starts as an urinary tract infection
Impotence or erectile dysfunction (ED)	Disorder in which erection cannot be achieved or maintained; about 50% of males between 40 and 70 have some degree of ED

Figure 8. Common diseases and disorders of the male reproductive system.

In men with infectious inflammatory diseases of the genital organs, there was also a decrease in stimulated chemoluminescence of neutrophils, which is an indicator of oxygen-dependent mechanisms of bactericidal function of phagocytes, a decrease in opsonic activity of blood serum, which is a significant criterion in the factorizations. Polymorphonuclear leukocytes from the site of inflammation (urethra and prostate secretion) also revealed violations of phagocytosis: HCT test, which reflects the activity of oxygen-dependent mechanisms of phagocytosis, phagocytic number and phagocytic index. In patients with chronic nonspecific inflammatory diseases of the genital organs, shifts in the activity of the cellular level of specific protection were detected, both by cytochemical parameters and by rosette methods with ram erythrocytes and monoclonal antibodies. (Figure 9).

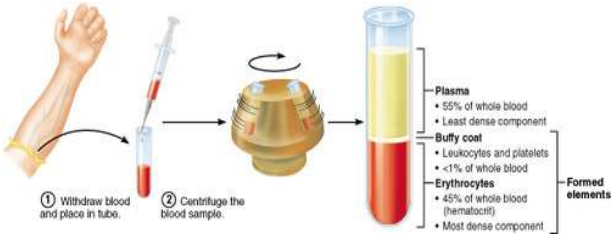

Figure 9. An example of a blood test by centrifugation.

These shifts were observed both in the circulatory system and in the biomaterial from the inflammation site. The T-helper / T-suppressor ratio was decreasing, the number of natural killer cells and B lymphocytes was increasing. Regarding the humoral linkage of specific protection, researchers have identified shifts in the levels of immunoglobulins of the major classes (A, G, M), but their data are mixed. (Figure 10)

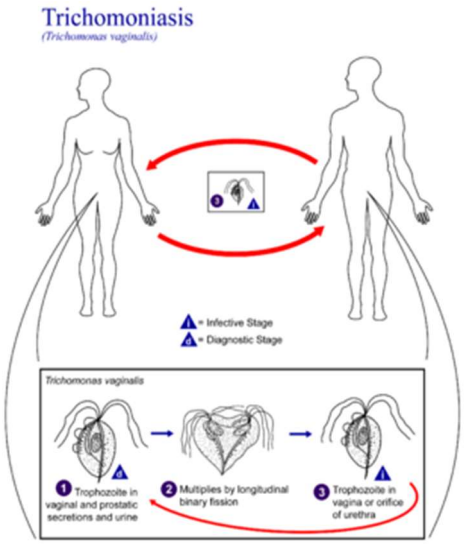

Figure 10. Morphology and transmission of Trichomonas vaginalis.

It was revealed that, in women with urogenital trichomoniasis, there was a decrease in the relative number of theophylline-resistant rosette-forming cells (E-RUKT, probably lymphocytes with T-helper activity)) and a sharp decrease in the E-RUCT / E-RUCT ratio . Concentrations of IgM, IgG and secretory IgA increased. In men with gonorrheal urethritis with active clinical features, some researchers have observed an increase in the average cytochemical coefficient of spontaneous HCT test in polymorphonuclear leukocytes of the urethral exudate. However, in polymorphonuclear leukocytes of the circulating blood of patients, the mean cytochemical coefficient of spontaneous HCT test did not differ significantly from that of control subjects, while the mean

cytochemical coefficient of stimulated HCT test significantly exceeded that in control. (Figure 11)

Figure 11. The main symptoms, routes of infection, methods of protection and treatment of Trichomonas vaginalis.

Chlamydial infections, including urogenital chlamydia, were also associated with impaired immune system status in 82% of women and 80% of men. These disturbances were characterized by ambiguity and variability .In the pathogenesis of chlamydiosis, endo- and exotoxins that can block phagocytosis play an important role. In the early stages of the disease, the pathogen binds to the cell receptor of cells of the superficial layer of the epithelium and enters it by endocytosis [15].

Endosomes of infected epithelial cells coalesce with formed cytoplasmic vacuoles, where chlamydia is protected from the effects of lysosomal enzymes. That is, such an important chain of natural immunity as phagocytosis does not work. This leads to the death of the epithelial cell. Infiltration of the site of destruction of monocytes and polymorphonuclear leukocytes begins. Some endotoxins are eliminated by neutrophils.

On the other hand, antibodies produced by plasma cells of the stroma and epithelium also do not play a significant role in protection against this intracellular pathogen. T-lymphocytes, located in the lesion, activate the oxidation processes, which can cause cell apoptosis and other structural and functional changes in immunocompetent cells and promote the persistence of chlamydial infection. There was no increase in the specific phagocytic index of peripheral blood phagocytes, but there was a decrease in the stimulated HCT test and myeloperoxidase activity of polymorphonuclear leukocytes, indicating a decrease in the activity of the oxygen-dependent mechanism of phagocytosis. (Figure 12).

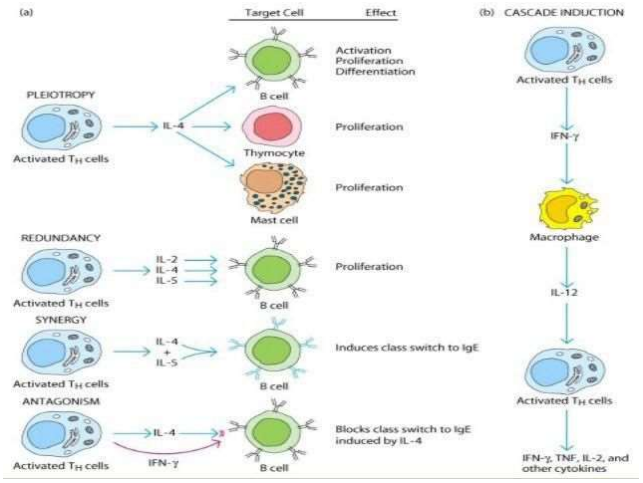

Figure 12. Immune cell activation.

Patients with chronic chlamydia found a predominance of Tx-2 type of response. An increase in the level of interleukin-6, which is secreted by type 2, indicates an exacerbation of

the chronic inflammatory process, and interleukin-4 a clear acute process. Suppression of the Tx-1 immune response link (decrease in interleukin-2 levels) causes long-term persistence of chlamydia in organs and systems of the body. A slight increase in the level of interleukin-3 indicates the presence of a mild allergic reaction. One of the known factors that induces chlamydia life cycle delay is interferon-γ. It is formed in TX-1. The influence of interferon-γ often causes the persistence of chlamydia, including in macrophages [16].It has been established that in patients with chronic course and complications of urethral chlamydia, changes in immunity are observed. In particular, there is a decrease in the total population of T lymphocytes (CD3), thromboxanes (CD4) and immunoregulatory index (CD4 / CD8) along with an increase in the number of Tc (CD8), NK cells and B lymphocytes. The level of IgM and IgG is increasing. Concerning the concentration of IgA in patients with urogenital chlamydia, the data of different authors are opposite. (Figure 13)

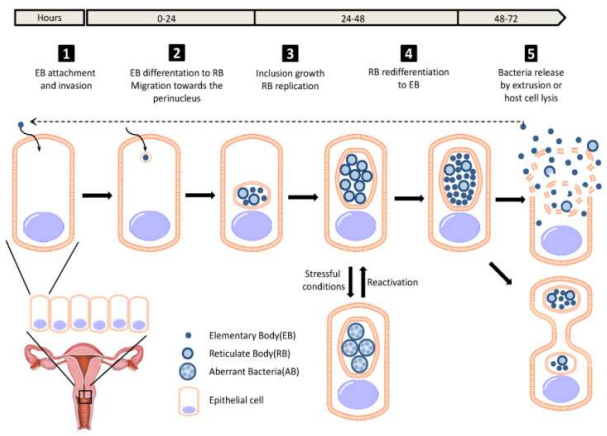

Figure 13. Description and image of hourly changes in vaginal epithelial cells.

Mycoplasma infection is characterized by the fact that it develops on the background of immunosuppression, accompanied by various immunopathological reactions, mycoplasmas can evade the immune surveillance of the host, which causes the generalization of infection, chronic course of damage, or prolonged persistence. Moreover, in vitro experiments have shown that mycoplasmas can cause apoptosis in leukemic cells of the lymphoid and myeloid rows (relative to normal cells of the blood system, data is not enough). (Figure 14).

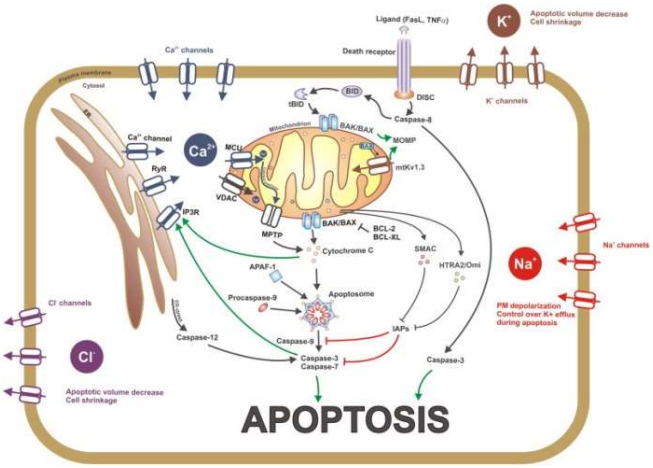

Figure 14. Apoptosis pattern.

It has also been proved that in patients with genital mixed infection (cytomegalovirus, chlamydia, ureaplasma), interferon synthesis disorders occur: increase in serum and spontaneous interferon production and decrease in interferon-γ and interferon-α. IO Heir and others. found that in patients with chronic herpetic infection there is a significant decrease in the phagocytic index of phagocytes, a decrease in the activity of the complement system, an increase in the level of medium and small

circulating immune complexes and an increase in the level of large immune complexes. In their research, the authors point to changes in superficial architectonics, functional activity and intracellular lymphocyte metabolism (increase in nonspecific esterase activity) of patients with genital herpes lesions, indicating the involvement of lymphocytes in infectious and / or process. Chronic herpetic - infection is accompanied by an imbalance in the production of Tx-1- and Tx-2-cytokines. In particular, the inhibition of Tx-1-cytokines is inhibited, moreover in the phase of relapse than in remission. (Figure 15).

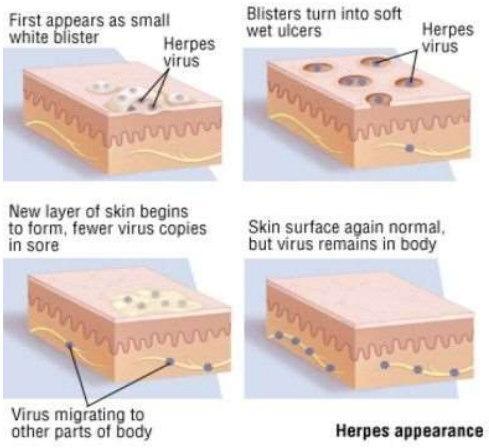

Figure 15. The interaction of the herpes virus with the skin.

Thus, it has been proved that patients with chronic nonspecific inflammatory diseases of the genital organs are affected by changes in the immune status, which depend on the pathogen, phase and level of damage.

Experimental part

Material and methods

Investigation of aspects of changes in lipid metabolism, functional status of platelets and reactivity of the body in patients with chronic non-specific inflammatory diseases of the genital organs.

In order to evaluate the type of dyslipoproteinemia 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 by spectrophotometry, using the sets of reagents of NNPP "Philitis Diagnostics", Dnipropetrovsk. The presence of chylomicrons and very low density lipoprotein cholesterol was determined by the method of visualization of the sample after exposure to blood plasma at 0 ° - + 4 ° C, low density cholesterol lipoprotein concentration by Burstein and Samai, high cholesterol concentration using lipoprotein reagent kit from Cormay, triglycerides using Lahema reagent kit, Czech Republic. Dyslipoproteinemia phenotypes were verified according to diagnostic guidelines cardiovascular diseases. (Figure 16) (Figure 17)

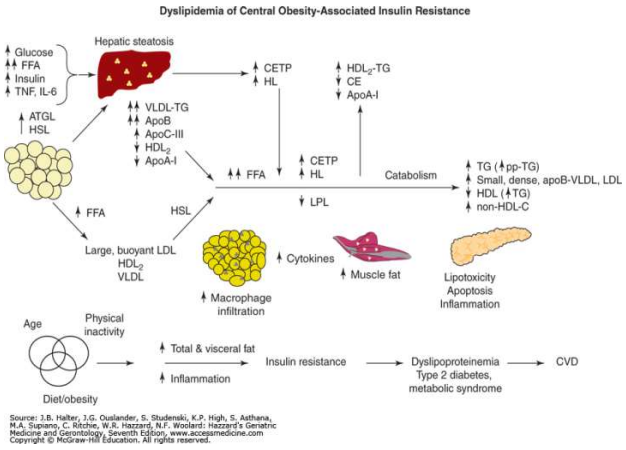

Figure 16. Changes in lipid metabolism in organs in patients with chronic nonspecific inflammatory diseases of the genital organs.

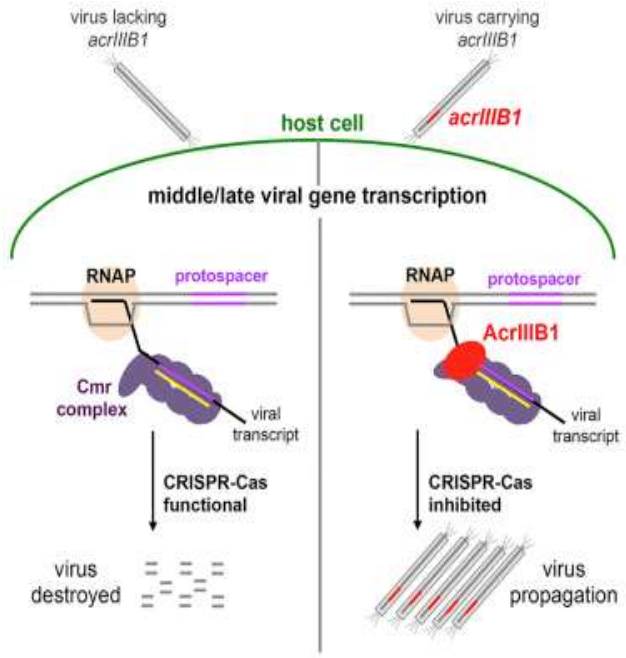

Figure 17. Middle/Late viral transcription in host`s cell.

The intensity of lipid peroxidation was judged by the concentration of malonic dialdehyde, which was determined by reaction with thiobarbituric acid. Adhesion, adenosine diphosphate (ADP) aggregation of platelet peripheral blood in platelet-rich plasma was investigated to study the status of the platelet link of hemostasis. Platelet counts were performed using a Goryaev counting chamber. The time of adenosine diphosphate aggregation was also determined. 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 minutes after the adenosine diphosphate solution) was investigated; degree of platelet adhesion (difference between baseline platelet count and platelet count after contact with glass under rotation on an electromagnetic stirrer for 5 min). (Figure 18, 19)

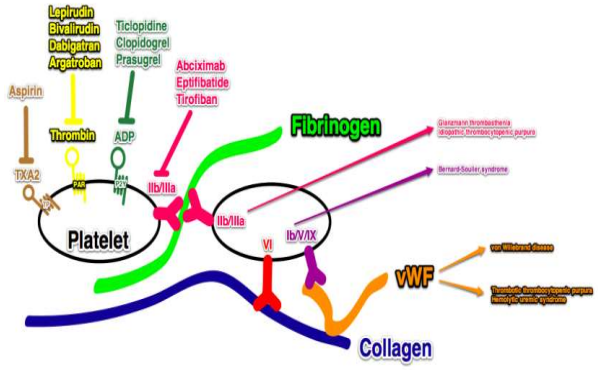

Figure 18. Platelet formation mechanism.

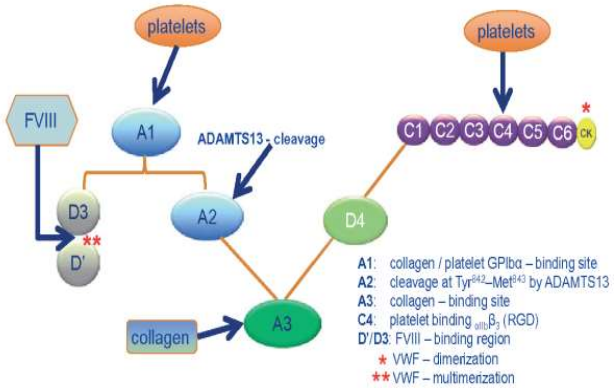

Figure 19. Collagen Sites Activation Mechanism.

Patients with chronic nonspecific inflammatory diseases of the genital organs also determined the content of von Willebrand factor contained in poor platelet plasma using

formalized donor platelets by the Evans et Osten method in the modification of A.A. Tsiguleva. The principle of the method is to determine the effect of the investigated von Willebrand factor on the aggregation of washed and formalin-fixed platelets of healthy individuals under the influence of ristocetin. Quantitative determination is carried out on the dilution curve of normal mixed platelet-free plasma. The method is based on the fact that platelets treated with a weak formalin solution retain the ability to ristocetin - aggregation (in the presence of von Willebrand factor factor), but not subject to other types of aggregation (spontaneous, under the influence of adenosine diphosphate, adrenaline, thrombin.)

Reagents.

1. 3.8% sodium citrate solution;

2. Buffer solution (pH 7.6; 2 = KH2 PO4; 8 02 NaCl, 8.8 = Na2HPO4 dissolved in 1 liter of distilled water);

3. Buffered EDTO (Ethylenediaminotetraacetic acid) - formalin solution: 3 ml of 0.007 M (0.483%) of ethylenediaminotetraacetic acid, 5 ml of 4% formalin solution, 2 ml of buffer, 10 ml of distilled water;

4. Ethylenediaminotetraacetic acid - buffer solution: 0.77 M ethylenediaminotetraacetic acid (1 part) with buffer solution (49 parts);

5. Ristocetin solution (10 mg per 1 ml of buffer). Preparation of washed washed fixed platelets of healthy people: 9 parts of venous blood of donors are mixed with 1 part of ethylenediaminotetraacetic acid - formalin solution; into which blood is injected directly from the puncture needle. Centrifuged for 5 min at 1500 rpm, get a rich platelet plasma, in which hemolysis can be expressed. Poor platelet plasma was obtained from this plasma by centrifugation for 20 min at 4000 rpm. The poor platelet plasma was removed and the platelet precipitate was washed twice with ethylenediaminotetraacetic acid - buffer solution (4 times volume with centrifugation each time for 10 min at 4000 rpm). The buffer containing ethylenediaminotetraacetic acid is removed by suction and the platelet precipitate is diluted in buffer solution without ethylenediaminotetraacetic acid so that 1 µl contains about 200,000 platelets. (Figure 20)

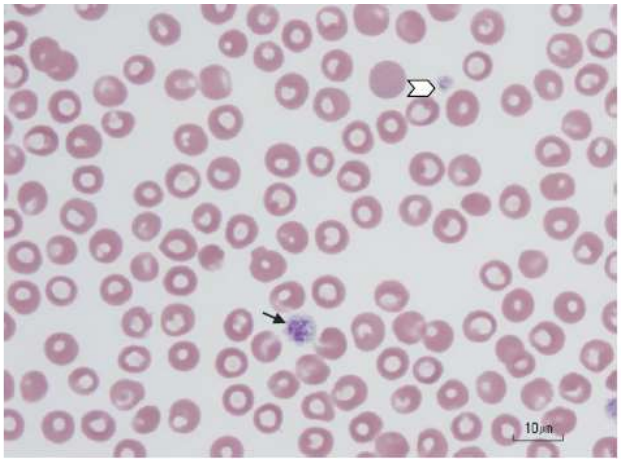

Figure 20. Blood smear from a 3-year-old CKCS demonstrating platelet size variation.

Normal Platelet Concentration: Normal formalized platelets can be preserved so that they are not cooked again each time. To do this, after

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

The suspension was packed in 3 ml in sterile vials, rolled and stored in freezers (at -10 -12 ° C) for 2-3 months. If necessary, the contents of the vials are thawed, platelets are washed twice from the preservative solution with buffer without ethylenediaminotetraacetic acid and used in the test. (Figure 21)

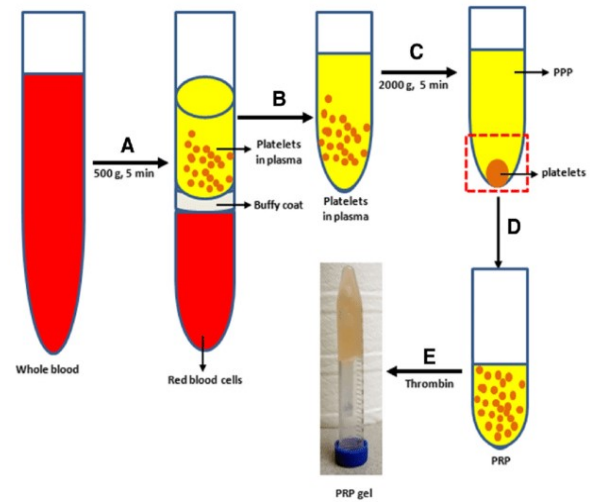

Figure 21. Preparation of platelet-free plasma of the test.

Preparation of platelet-free plasma under study. Blood is drawn from the vein under silicone conditions and mixed with 3.8% sodium citrate solution (9: 1). Centrifuged for 7 min at 1500 rpm. Rich platelet plasma was removed, which was centrifuged for 20 min at 4000 rpm. The poor platelet plasma is transferred to another silicone or plastic tube and used in the test.

Course of study.

In 2 FEC cells with a working face of 5.65 and a volume of 2.5 ml, 1 ml of washed normal platelets, 0.4 ml of platelet-free plasma under test and 0.4 ml of ethylenediaminotetraacetic acid buffer are injected. (Figure 22)

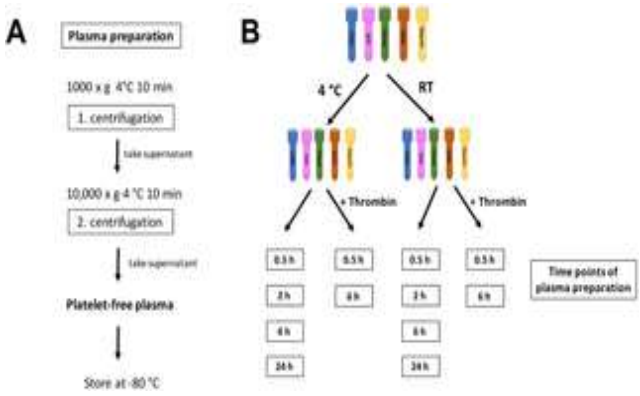

Figure 22. Platelet Aggregation Study Under the Effect of Ristocetin.

0.6 ml of buffer is injected into the control cuvette. Both cuvettes are placed in the FEC and at $\lambda = 630$ nm set the FEC arrow to "O" in the cell with the test sample, enter 0.2 ml of ristocetin solution, mix, turn on the stopwatch. After 2 minutes, changes in the optical density of the test sample, which are related to platelet aggregation under the influence of ristocetin, are recorded.

Construction of a dilution curve.

They use a standard dilution curve obtained from a large group of healthy young normal platelet-free plasma To quantify the presence of the von Willebrand factor in the test of plasma. This plasma is diluted with buffer without ethylenediaminotetraacetic acid from 1: 2 to 1:32, after which washed normal platelets are introduced into each sample according to the above method, rhistocetin is determined - platelet aggregation. The point of calculation is the dilution of plasma at which ristocetin no longer

causes platelet aggregation. This point corresponds to 2 - 3% presence in the environment of the factor Willebrand. The data obtained is plotted on logarithmic paper. With proper construction, the curve in the White-coordinate coordinate system looks like a straight line. Using this curve, determine the presence of von Willebrand factor in the study plasma. For greater accuracy, the latter can also be examined in 2 - 3 dilutions. (Figure 23)

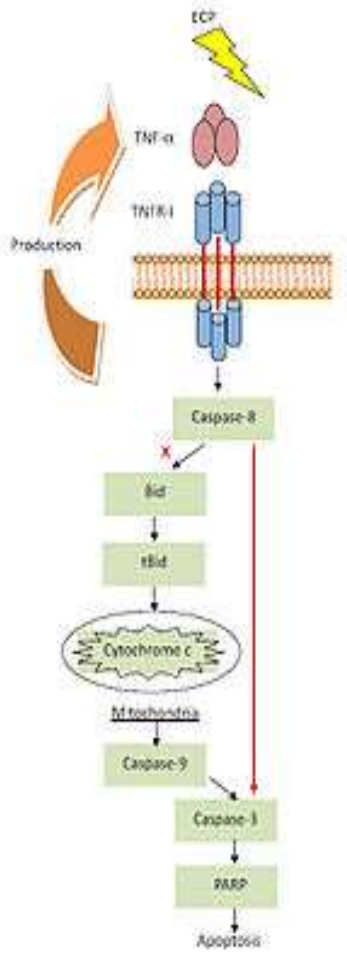

Figure 23. Cytochrome C activation pattern under the influence of an external stimulus.

A general clinical blood test was studied to assess the status of local and systemic general reactivity of the body. There were calculated the number of erythrocytes, leukocytes, and platelets in Goryaev's counting chamber. There were determined the concentration of hemoglobin in the blood and color index. They conducted a morphological study of blood cells in smears stained by the Romanovsky-Gims method. The leukogram was calculated by a unified method, the erythrocyte sedimentation rate was determined. Additionally, cytochemical parameters of leukocytes were examined in blood smears. The activity of myeloperoxidase polymorphonuclear leukocytes was studied by the Graham-Knoll method, the content of cationic proteins (KB) - by the VG method. Shubich, the average cytochemical coefficient was calculated. The activity of the enzyme naphthylacetatesterase was determined by the Leffler method to evaluate the activity of monocytes.

The percentage of positively responsive cells also was determined. The percentage of positively responsive cells of esterase-positive lymphocytes (probably T lymphocytes) in the total lymphocyte pool was also calculated.

The understanding of the status of systemic nonspecific reactivity of the organism can be obtained by analyzing quantitative and qualitative indicators of the composition of leukocytes and the rate of sedimentation of red blood cells. Integral hematologic indices may change already in the pre-pathological period, or in the early stages of the disease, when

preventive measures to regulate the protective reactions are most effective. Formalized integrative metrics can also change in a slow, chronic illness, when overall blood counts do not go far beyond the normal range. In addition, the use of design indicators allows, without complex additional surveys, to estimate the activity of different parts of the non-specific reactivity system. According to leukograms and peripheral blood erythrocyte sedimentation rates, integral indices were calculated using mathematical formulas. The calculation of integral formalized indices of peripheral blood leukograms was performed using a special computer program. (Figure 24)

1. Leukocyte offset index (ILL/IЗЛ):

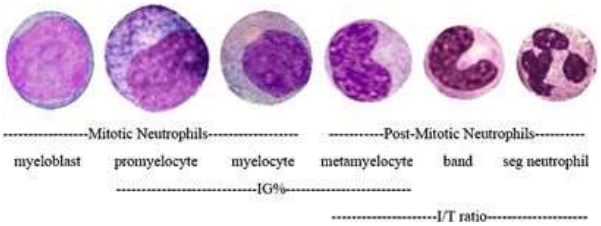

Figure 24. Microscopic photo of mitotic and post-mitotic neutrophils.

$$ІЗЛ = \frac{е + б + н}{Мо + Лі},$$

where

e-eosinophils;

b-basophils;

Li lymphocytes;

Mo-monocytes.

This figure does not depend on the total number of leukocytes in the peripheral blood. Its increase indicates an active inflammatory process and impaired immunological reactivity.

2. Leukocyte Ratio Index and Blood Sedimentation Rate (ELSE/ІЛШОЕ):

$$ІЛШОЕ = \frac{Лі \times ШОЕ}{100},$$ where

Li - lymphocytes;

ESR - the rate of sedimentation of erythrocytes.

Changes in this indicator indicate the presence of intoxication associated with an infectious (decrease) or autoimmune (increase) process. (Figure 25)

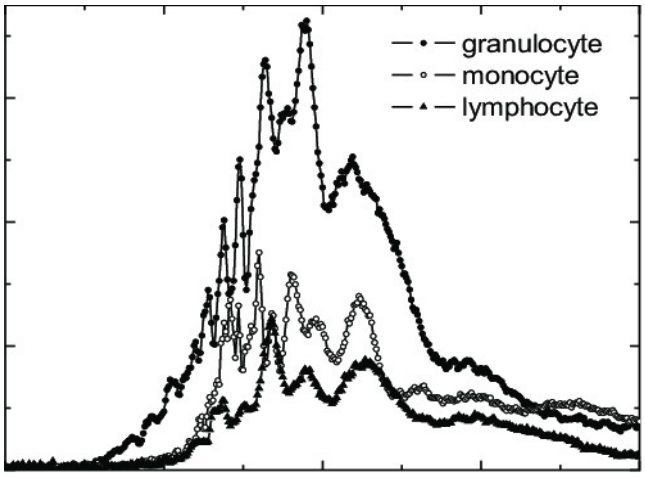

Figure 25. The graph of the ratio of granulocytes, monocytes and lymphocytes

$$ІЛГ = \frac{Лі \times 10}{мм + м + п + с + е + б},$$ where e-eosinophils;

b-basophils;

Li lymphocytes;

c-segmented nuclear neutrophils;

p-rod nuclear neutrophils;

m-myelocytes;

mm-metamyelocytes.

The indicator also allows to differentiate between auto-intoxication and infectious intoxication.

4. Common Index (CI):

$$ЗІ = ІЛШОЕ + ІЛГ.$$

This index allows to identify and distinguish between the nature of intoxication in the earlier stages, when the previous two indices are offset slightly.

5. Neutrophil-Lymphocyte Ratio Index (ICNL):

$$ІСНЛ = \frac{n + c}{Лі}.$$

Li lymphocytes;

c-segmented nuclear neutrophils;

p-rod nuclear neutrophils;

This indicator reflects the ratio of nonspecific and specific cell protection.

6. Neutrophil and monocyte ratio index (CCIM/ICHM):

$$ICHM = \frac{c + n}{Mo}.$$

Mo-monocytes.

c-segmented nuclear neutrophils;

p-rod nuclear neutrophils;

The index reflects the ratio of the components of the microphage-macrophage system.

7. Lymphocyte to Monocyte Ratio Index (ISLM/ICJIM).

$$ICJIM = \frac{Лі}{Mo}.$$

Li lymphocytes;

Mo-monocytes.

This indicator allows us to evaluate the relationship between the affective and effector units of the immune process.

8. Lymphocyte to eosinophil ratio index (ISLE/ICJIE).

$$ICJIE = \frac{Лі}{e}.$$

e-eosinophils;

Li lymphocytes;

The index allows us to estimate the relationship between delayed and immediate types of hypersensitivity reactions. The state of local nonspecific protection was evaluated in the study of smear scrapings of the genital mucosa of patients with chronic nonspecific inflammatory diseases of the genital organs. The average number of leukocytes in smears stained by the Romanovsky-Gims method and their percentage were calculated, cytochemical parameters were additionally determined: myeloperoxidase activity and cationic protein content of monomorphonuclear leukocytes, monophthylacetate acetate activity. (Figure 26)

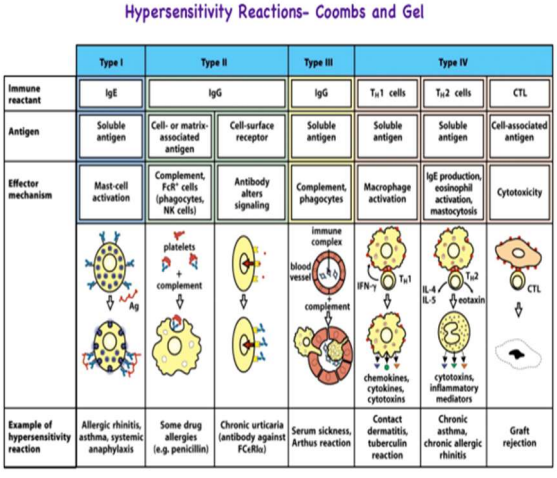

Figure 26. Herpesensitivity Reactions – Coombs and Gel

Results and discussion

The surveyed persons with persistence of various agents of sexually transmitted infections in the genital organs identified the likely strong feedbacks of the concentration of total cholesterol in the blood plasma and the time of onset of adenosine diphosphate - aggregation (r = -0,79) and the relative content of von Willebrand factor r = -0.96) ($p < 0.05$), as well as strong direct links with maximum platelet aggregation (r = +0.94) ($p < 0.05$) (Table 1).

That is, the level of total cholesterol is associated with an acceleration and increase in adenosine diphosphate - platelet aggregation and with a decrease in the relative level of von Willebrand factor in blood plasma. Similar associations were observed in the concentration of malondialdehyde in blood plasma. This indicator had strong feedbacks on the time of onset of adenosine diphosphate - platelet aggregation (r = -0.84) and relative von Willebrand factor level (r = -0.94), as well as strong direct links with the intensity of adenosine diphosphate - aggregation (r = -0.97).

Thus, it was found that an increase in the level of proatherogenic substances in blood plasma (total cholesterol, low-density cholesterol-lipoprotein, malondialdehyde) contributes to an increase in platelet aggregation activity and a decrease in von Willebrand factor level.

At the same time, an increase in anti-atrogenic substances (high-density lipoprotein cholesterol) decreases platelet aggregation and increases the level of von Willebrand factor in blood plasma.

Table 1. Correlation coefficients (r) of lipid metabolism and platelet counts of hemostasis and the content of Villebrand factor in the blood plasma of subjects with various infectious agents in the genital organs.

Indicator, unit of measure	Start time of Adenosine diphosphate aggregation, p	Intensity of maximal aggregation Tr,%	Relative level of FV,%
Concentration of HS, mmol/l^{-1}	-0,79*	0,94*	-0,96*
Concentration of MDA, mcmol/l^{-1}	-0,84*	0,97*	0,97*

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

Conclusions

Thus, it has been proved that in patients with chronic non-specific inflammatory diseases of the genital organs there are shifts in the immune status, which depend on the pathogen, phase and level of damage.

Summarizing the results of the correlation analysis of the relationship of platelet levels of hemostasis and the overall reactivity of the organism, we can conclude that the increase in thrombogenic potential of platelets is, as well as a decrease in the relative content of von Willebrand factor in blood plasma (reflecting the defeat of monotherapy endothelium) macrophage system in mechanisms of nonspecific protection, as well as the advantage of the cellular level of immunity. There was

endogenous intoxication, mainly of autoimmune origin.

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