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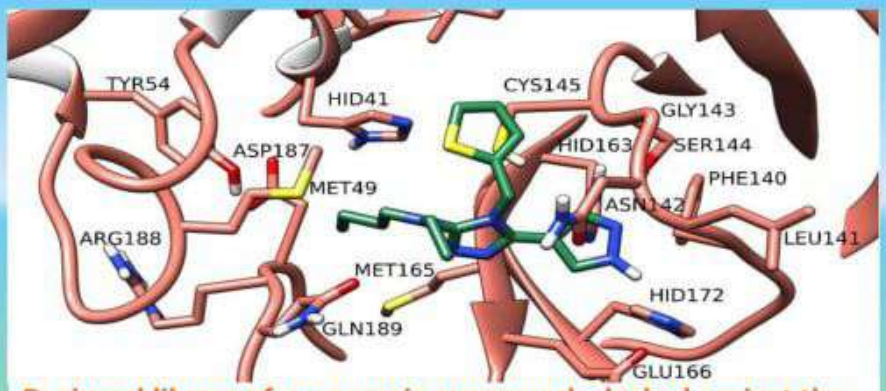

Designed library of congeneric compounds docked against the main protease (Mpro) of coronavirus SARS-CoV-2 (2019-nCoV)

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Features of Indicators of Blood General Clinical Analysis and the Summary Analysis of an Organism's General Reactivity at Chronic Inflammatory Process

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Inflammatory diseases cause health disorders which result in a reduction of the population. That is why this medical problem is considered to be a very important one. The human immune system is responsible for protecting the body from infections of various origins, while inducing chronic inflammation (characterized by a long, often invisible course) which can result in proneness to recurrence, complications and resistance to therapy. The authors of the article analyzed and proved that there are immune status shifts in patients with chronic nonspecific inflammatory processes depending on the pathogen, phase and level of damage.

Introduction

Nowadays, in Ukraine the state of people's health, especially reproductive health, is characterized by two main factors: decrease in birth rate and sterility. Each year about 300 thousand teenagers reach their reproductive age. Their harmonious development determines their reproductive potential. Especially for young girls, because the state of their somatic and reproductive health, determines to some extent their future lives, in both medical and social aspects.

An important indicator of the state of reproductive health is sterility. According to numerous researches, sterility in married couples obviously has the tendency to increase in most

European countries. The problem raised here is of both medico-biological and socio-economic value. The percentage of sterile married people of reproductive age fluctuates from 12-18% of all married couples. In 40-50% of the cases, the cause of a sterile marriage is a pathology of the reproductive system in one of the spouses, rarely in both. In Ukraine about 40,000 female cases of sterility and 11,000 male cases have been annually registered during the last years. Among them were 11,000 newly diagnosed cases in females and about 3,000 in males.

Among the illnesses that negatively influence reproductive health and factors that increase risk of ectopic pregnancy, infertility, menstruation disorders and appearance of new cancerous or benign growth, chronic inflammation has a ponderable importance.

The frequency of this pathology remains high, occurring in about 1,300 out of 10,000 women and is caused by various pathogens. In 2016, 173,8 out of a 100,000 cases of trichomoniasis among women were presented, 82,3 urogenital micoplasmosis and 52,1 chlamydia illnesses.

Chronic inflammation is a slow process, with a propensity to relapse and result in complications and resistance to therapy. Conversely, chronic diseases start with sharp inflammation, and end with destructive changes.

1. The state of general reactivity and immunity in chronic heterospecific inflammation is used for certain FIRES (Febrile Infection-related epilepsy syndrome) diseases of the sexual system.

In the pathogenesis of chronic non-specific inflammatory diseases of the genital organs and their complications, blood circulation in the genital organs, rheological properties of blood, hormonal background, activity of enzymatic systems and peroxide-mediated lipid oxidation (**Figure 1**), play a prominent role, together with the state of nonspecific and specific protection of the patient's body, at both the levels of the circulating system blood and the lesion core [1].

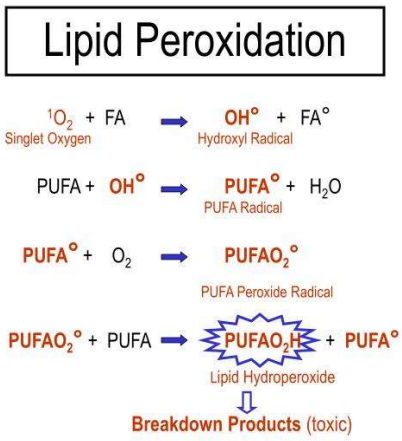

Figure 1. The lipid peroxidation. FA = fatty acid, PUFA = polyunsaturated fatty acids.

Men who have chronic non-specific inflammatory diseases of the genital organs have a violation of phagocytic activity of circulating blood neutrophils, increased migration, reduced glycogen content, increasing activity of acid and alkaline phosphatase and reduced activity of myeloperoxidase (MP). There was also a decrease in stimulated chemiluminescence of neutrophils in men with infectious inflammatory diseases of the genital organs, which is an

indicator of oxygen-dependent mechanisms of the bactericidal function of phagocytes. A decrease in opsonic blood serum activity is a significant criterion in assessing humoral factors of phagocytosis. In polymorphonuclear leukocytes from the inflammation center (urethra and prostate secretion) there was also a violation of phagocytosis indicators: NST test, which reflects the activity of oxygen-dependent mechanisms of phagocytosis, phagocytic number, and phagocytic index. In male patients, chronic non-specific inflammatory genital diseases of the genital organs have been detected by the changes in the activity of the cellular level of specific protection both by cytochemical parameters and by means of methods of development with ram erythrocytes and monoclonal antibodies. These shifts were observed in the system of circulating blood, and in the biomaterial from the center of inflammation. While the ratio T-helper/T-suppressors decreased, the number of natural killers and T-lymphocytes increased. Regarding the humoral link of specific protection, researchers have determined the shifts *in* levels of immunoglobulins of *the* basic classes (A, G, M), but their data *are* ambiguous [2].

It was revealed that, in female patients with genito-urinary trichomoniasis, there was a decrease in the relative amount of theophylline-resistant cells (E-RUCR, probably lymphocytes with T-helper activity), an increase in the number of theophylline sensitive cells (E-RULCH, probably, with suppressor activity) and a sharp decrease in the E-RUCR / E-RUPCH ratio [3]. Concentrations of IGM, IgG and secretory IgA were raised (**Figure 2**). In men with gonococcal urethritis with active clinical signs, some researchers observed an increase in the average cytochemical coefficient of spontaneous NST test *(Nitroblue tetrazolium reduction test - the NST-test reflects the bactericidal activity of phagocytes, i.e. ability to destroy microbial cells)* in polymorphonuclear leukocytes of the urethral exudate.

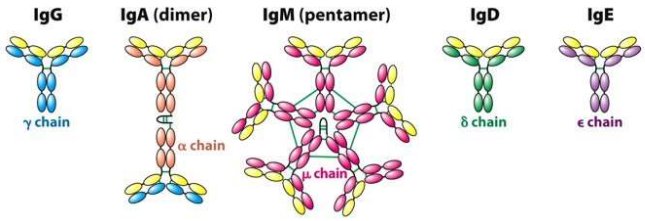

Figure 2. The different types of immunoglobulins

But in polymorphic leukocytes of circulating blood of patients, the average cytochemical coefficient of spontaneous NST test does not significantly differ from that of the control group, while the average cytochemical coefficient of stimulated NST-test significantly exceeds that of the control.

Chlamydial infections (**Figure 3**), including urogenital chlamydias, were also accompanied by violations of the immune system in 82% of women and 80% of men. These violations were characterized by ambiguity and variability [4].

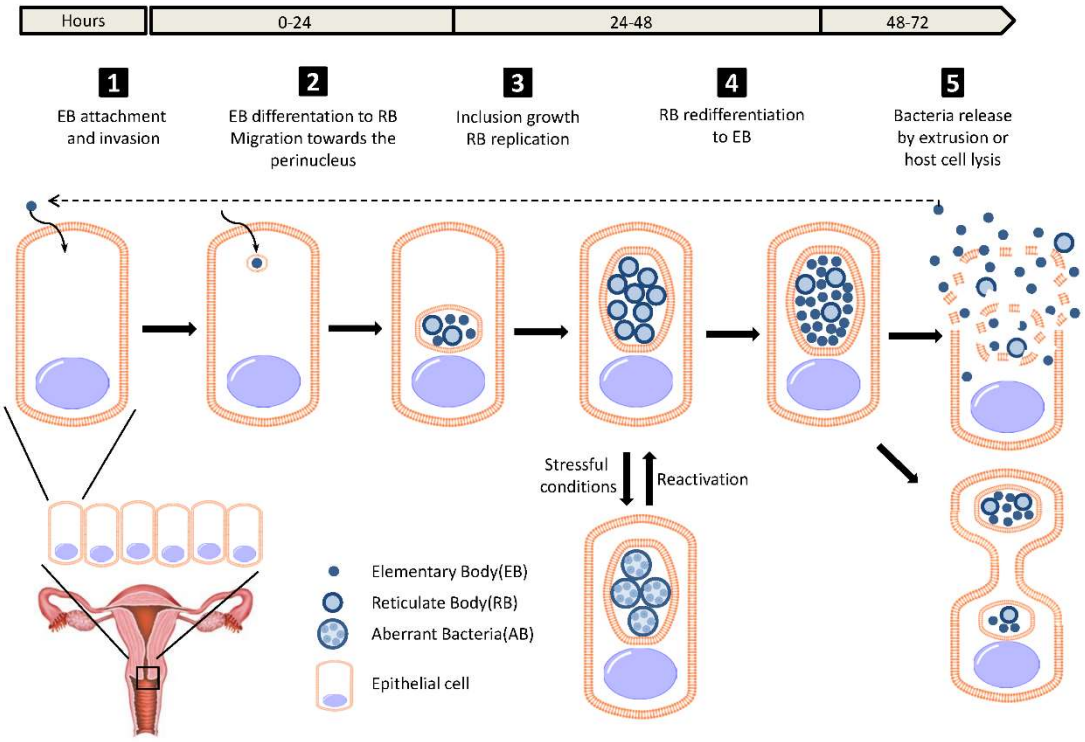

Figure 3. Life cycle of chlamydia.

In the pathogenesis of chlamydia, an important role is played by endo- and exotoxins that are capable of blocking phagocytosis (**Figure 4**).

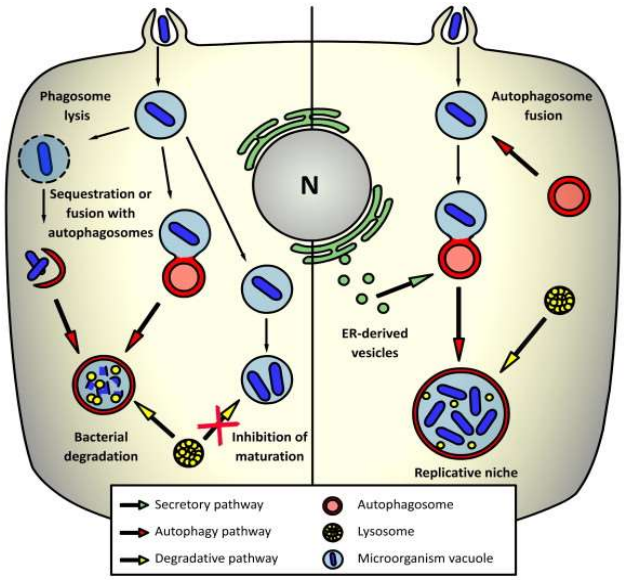

Figure 4. Autophagy in intracellular bacterial infection

In the early stages of the disease, the pathogen binds to the cellular receptor of the surface layer of the epithelium and penetrates into it by endocytosis.

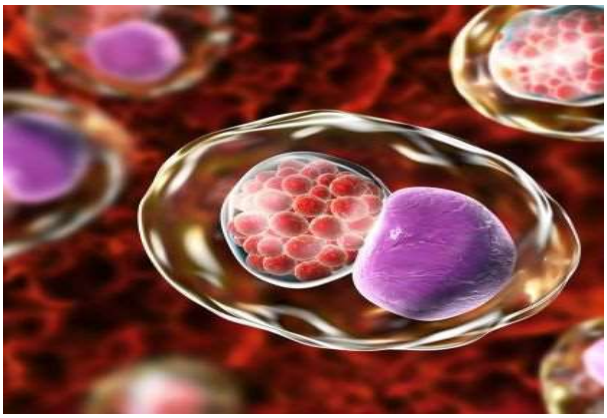

Figure 5. Chlamydia [Kateryna Kon / Shutterstock.com]

Endosomes of infected epithelial cells merge with formed cytoplasmic vacuoles, where chlamydia is protected from the influence of lysosomal enzymes **(Figure 5)**. That is, this important chain of natural immunity does not work as phagocytosis. This leads to the death of epithelial cells. Infiltration of the area of destruction of monocytes and

polymorphonuclear leukocytes begins. Some endotoxins are eliminated by neutrophils.

On the other hand, antibodies produced by plasma cells in stroma and epithelium also do not play a significant role in the protection against this intracellular pathogen.

In T-lymphocytes located in the lesion center, activation of oxidation processes may cause apoptosis of cells, other structural and functional changes in immunocompetent cells as well as contribute to persistence of chlamydial infection. An increase in the specific phagocytic index of phagocytes of peripheral blood was not determined, but there was a decrease in the indicators of a stimulated NST-test and the activity of myeloperoxidase polymorphic leukocytes (**Figure 6**), indicating a decrease in the activity of the oxygen-dependent mechanism of phagocytosis.

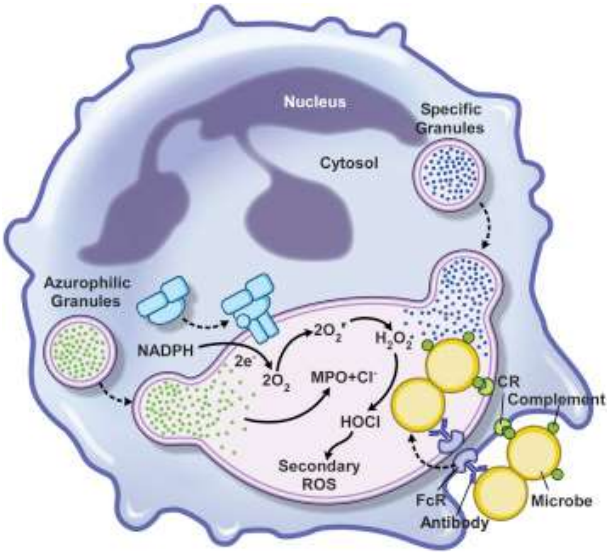

Figure 6. Myeloperoxidase action in polymorphic leukocytes.

In patients with chronic chlamydia, there is a predominance of T helper 2-type response. An increase in the level of interleukin-6 which secretes the T helper 2, indicates an aggravation *of the chronic* inflammatory process, and an increase in the level of interleukin-4 indicates a clear acute process. Inhibition of T helper-1 units of the immune response (decreasing the level of interleukin-2) causes a persistence of chlamydia in organs and organism systems. A slight increase in the level of interleukin-3 indicates the presence of a slightly expressed allergic reaction. One of the known factors that induces the delay of the life cycle of chlamydia is interferon-γ. It is formed in T helper-1 lymphocytes. Influence of interferon-γ often causes persistence of chlamydia, including in macrophages (**Figure 7**).

It is established that in patients with chronic disease and complications of urethral chlamydia, immunity changes are observed. In particular, there is a decrease in the number of total T-lymphocyte population **(Figure 8)** (CD3), thromboxanes (CD4) and immunoregulatory index (CD4 / CD8) along with the increase in the number of TC (CD8), NK cells and B-lymphocytes. IgM and IgG levels increase. Regarding the concentration of IgA in patients with urogenital chlamydia, data from different authors are opposite.

Mycoplasma infection is characterized by the fact that it develops on the background of immunosuppression, accompanied by various immunopathological reactions. Mycoplasma may evade the immune supervision of the owner, which causes the generalization of infection, chronic course of damage or long term stability

of a microorganism. Moreover, in vitro experiments, it is shown that mycoplasma can cause apoptosis in leukemic lymphoid and myeloid cells (relative to normal blood system cells, data is not enough).

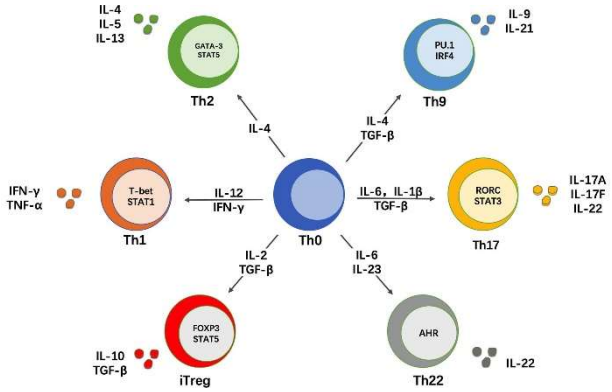

Figure 7. The activation mechanism of the immune response.

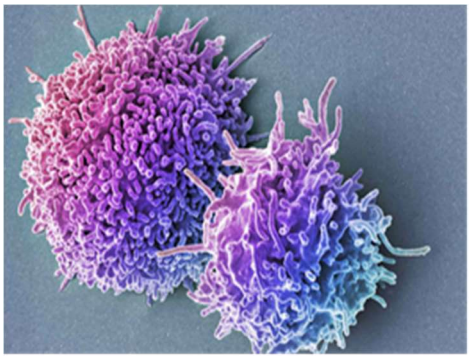

Figure 8. T-lymphocyte. [This is a colored scanning electron micrograph (SEM) of resting T lymphocytes from a human blood sample.]

It is also proved that in patients with micro-infection of genital organs (cytomegalovirus, chlamydia, ureaplasma), there are violations of the synthesis of interferon: increase of serum and spontaneous interferon products and reducing interferon-γ and interferon-α [5]. I. O. Nerladnikov and others [6, 7] found that, in patients with chronic herpetic infection there is a significant decrease in the phagocytic index of phagocytes, reduced function of complement system, increasing levels of medium and small circulating immune complexes, and increasing levels of large immune complexes.

Also, in their studies, the authors indicate changes in surface architectonics, functional activity and intracellular lymphocyte metabolism (increasing the activity of nonspecific esterases) in patients with herpetic lesions of genitals, indicating the participation of lymphocytes in an infectious and / or antiviral process.

Chronic herpes (**Figure 9**) - an infection, is accompanied by an imbalance in T helper -1- and T helper-2-cytokines products. There is inhibition of synthesis of T helper -1-cytokines in the phase of relapse of the disease to a greater degree than during the phase of remission.

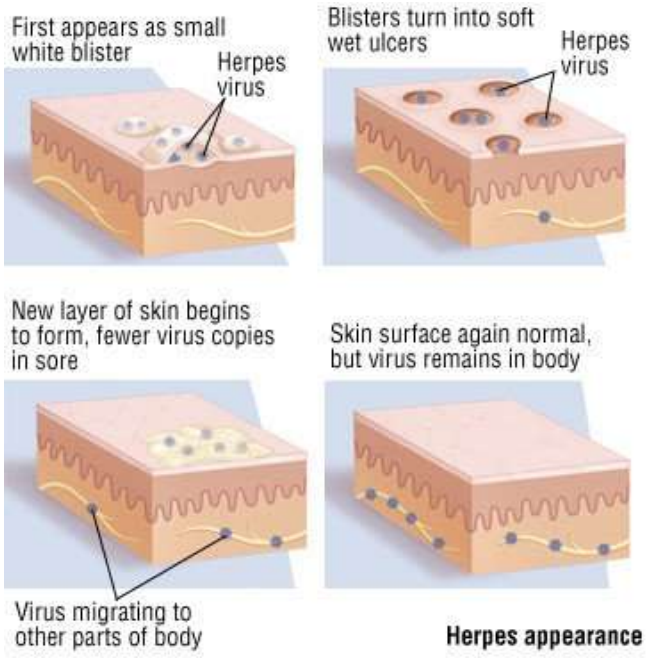

Figure 9. The interaction of the herpes virus with the skin.

Thus, it is proved that in patients with chronic non-specific inflammatory diseases of the genital organs, there are changes in the

immune status that depend on the pathogens of the disease, phase and level of defeat.

Experimental part

Material and methods

For biochemical, general clinical and cytological examination of blood and scraping from the mucous membrane of the urogenital tract were taken before the course of treatment. Blood was taken from the vein and stabilized with a 5% solution of sodium citrate. Scrapings from the mucous membrane of the genital were taken from men - from the middle part and lade-shaped mole of the urethra, women - from the urethra, the back vault of the vagina and the cervical canal [6, 7].

2. Clinical characteristics of examinations of patients. Subject to inspection, 95 clinically healthy persons (50 men and 45 women) and 180 patients with chronic non-specific inflammatory diseases of the genital organs were subject to the survey. The clinical condition of patients was evaluated on the basis of a survey, collecting complaints, anamnesis and examination of the skin of genital organs in women's vaginal mucosa with a gynecological mirror.

Clinical examination of patients and collection of biomaterials for laboratory survey was done with a dermatovenerologist of the city hospital №6 in Zaporozhye Lankina I.O.

The control group (K) examined 95 clinically healthy persons (non-donors), of which were 50 men and 45 women (**Table 2.1**). By age, the composition was as follows: 18-28 years - 30 people, 29-39 years old - 35 people, and 41-50 years - 30 people. Groups of investigated persons included 162 patients with chronic non-specific inflammatory diseases of the genital organs, including 83 men and 79 women. (**Table 2.1**). By age, patients were distributed as follows: 18-28 years - 60, 29-39 years - 58 and 40-50 years - 44 patients.

Table 2.1. Distribution of surveyed persons by age and sex.

Group	K1	K2	K3	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

Persons of control and investigated groups are inhabitants of the city (99%), most of them (86%) are engaged in intellectual and administrative activities. Material condition according to modern criteria is defined as an average 30% of surveyed persons permanently or sporadically visit hairdressers, sports halls and baths. The demographic and clinical characteristics of all groups of patients were approximately the same. According to the conditions of life, patients were distributed to homogeneous groups. Patients to be investigated excluded patients who had taken a systemic or local antimicrobial treatment in the last 3 months with a violation of the liver, kidney, gastrointestinal pathology, diabetic patients, pregnant and breastfeeding women. Patients with inflammatory diseases of the urogenital tract for 2 weeks before the antimicrobial examination and immunomodulatory drugs were disqualified.

The examined persons were also distributed into groups depending on the type of pathogen of the inflammatory process of the genital organs.

All patients performed compulsory examinations: a general blood test; general urine analysis; blood test on glucose; analysis of feces on helminths; fluorography. Glucose in urine was not determined in any patient; blood glucose levels were within normal limits. The results of the survey on helminths were negative. The results of fluorography were also normal. In the studied patients, the duration of inflammatory diseases of the reproductive system] was 2-20 years and was compared with age **(Table 2.2).**

Table 2.2. Distribution of examined persons by type of genital inflammation pathogen

Indicator	K	1	2	3	4	5	6
Causative agent	NBF	Bacteria	Trichomonas	Fungus	Chlamydia	Virus	Mixed flora
Middle age	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
Total number	45	36	26	30	28	19	41
Men	24	16	11	13	14	9	20
Women	21	20	15	17	14	10	21

(* nonspecific bacterial flora)

Thus, in patients of the 1st group the average duration of the disease was 2.0 years, in patients of the 2nd group, 5.5 years, and in the 3rd group, 13 years. All patients complained about the ineffectiveness of previous local or systemic antimicrobial treatment with short-term remission. Women with inflammatory diseases of the urogenital tract complained of severe discharge and itching. Examination revealed swelling and redness of the mucous membrane of the vulva and vagina. Some men with inflammation of the genitourinary tract also complained of itching and burning in the urethra.

Methods.

To assess the state of local and systemic general reactivity of the body studied a general clinical blood test (**Figure 10**) [8,9].

The number of erythrocytes, leukocytes, and platelets in the global chamber of Goryaev was counted. The concentration of hemoglobin in the blood and the color index was determined.

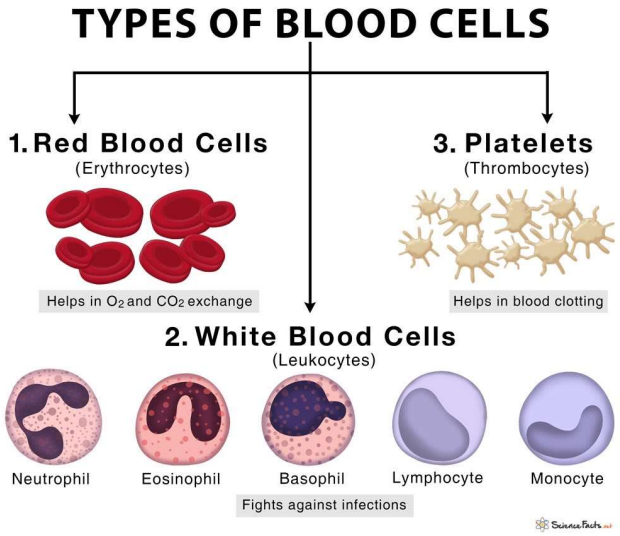

Figure 10. Types of blood cells.

The morphological examination of blood cells in smears painted by the Romanovsky - Himza method was carried out. Calculation of the leukogram with a unified method and determination of the rate of calibration of erythrocytes were done. In addition, cytochemical parameters of leukocytes were investigated in blood smears.

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The percentage of positively reacting cells was determined. The percentage of positively reacting cells of esterase-positive lymphocytes (probably T - lymphocytes) were calculated in the general pool of lymphocytes (**Figure 11**).

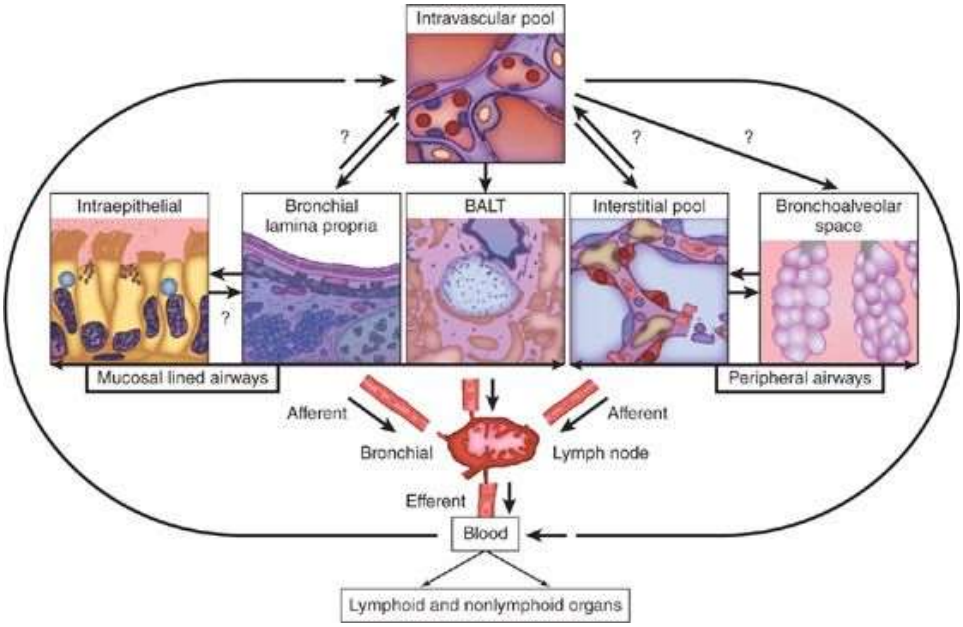


Figure 11. General pool of lymphocytes.

The state of system non-specific reactivity of the body can be obtained by analyzing quantitative-qualitative parameters of the composition of leukocytes and the rate of sedimentation of erythrocytes. Integral hematologic indicators may vary in the pathological period, or in the early stages of the disease, when prophylactic measures for regulating protective reactions are most effective. Also, formalized integrative indicators may vary with chronic course of illness, when the indicators of general blood analysis are not exceeded by the rather wide limits of normal values. In addition, the use of estimated indicators allows uncomplicated additional surveys to roughly evaluate the activity of various parts of the system of nonspecific reactivity.

According to the leukograms and the rate of precipitation of peripheral blood, integral indices using mathematical formulas [11,12,13,14] were calculated. The calculation of integral formalized indicators of peripheral blood leukograms was carried out using a commercial special computer program.

1. Index of leukocyte shift (ILS):

$$ILS = \frac{e + b + n}{Mo + Ly}$$

where

e-eosinophils;

b-basophils;

Ly-lymphocytes;

Mo-monocytes.

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

2. Index ratio of leukocytes and blood settlement (IRLBS):

$$\text{IRLBS} = \frac{Ly \times ESR}{100}$$

Ly - lymphocytes;

ESR is the sedimentation rate of erythrocytes.

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

3. Lymphocytic granulocyte index (ILG):

$$ILG = \frac{Ly \times 10}{mm + m + r + s + e + b}$$

where

e-eosinophils;

b-basophils;

Ly-lymphocytes;

s-segmental neutrophils;

r-rod nuclear neutrophils;

m-myelocytes;

mm-metamyelocytes.

The indicator also allows us to differentiate autointoxication and infectious intoxication.

4. General index (GI):

$$GI = ILG + IRLBS$$

This index allows us to detect and distinguish between the character of intoxication at an earlier stage, when the previous two indices are shifted slightly.

5. Index of neutrophil ratio and lymphocytes ratio (INLR):

$$\text{INLR} = \frac{s+r}{Ly}$$

This indicator reflects the ratio of non-specific and specific protection cells.

6. Index of neutrophil and monocytes ratio (INMR):

$$\text{INMR} = \frac{s+r}{Mo}$$

Mo-monocytes;

s-segmented neutrophils;

r-rod nuclear neutrophils.

7. Index of lymphocyte and monocytes ratio (ISLM).

$$\textbf{ISLM} = \frac{Li}{\text{Mo}}$$

Li-lymphocytes;

Mo-monocytes.

This indicator evaluates the relationship between the receptor and effector units of the immune process.

8. Index of lymphocyte and eosinophils ratio (ISLE).

$$\mathbf{ISLE} = \frac{\mathrm{Li}}{\mathrm{e}}$$

e-eosinophils;

Li-lymphocytes;

The index allows us to roughly evaluate the relationship between the hypersensitivity and immediate types of reactions. The state of local nonspecific protection was evaluated in the study of smears of frames of the mucous membranes of patients with chronic nonspecific inflammatory genital diseases. The average number of leukocytes in the smears painted by the Romanowsky - Giemsa **(Figure 12)** method and their percentage ratio were further determined by cytochemical parameters: the activity of myeloperoxidase and the content of cationic proteins of polymorphonuclear leukocytes, the activity of naphthyl acetate esterase mononuclear (monocytes and lymphocytes).

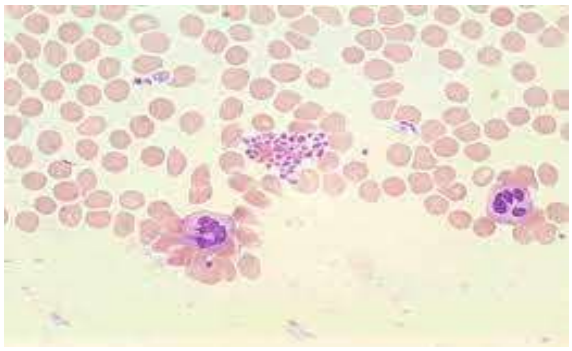


Figure 12. Coloring on Romanowsky-Giemsa. [Peripheral blood smear: high-power view (100x) of monocytes.]

Discussion

Features of indicators of general clinical analysis of blood in patients with chronic nonspecific inflammatory diseases of the genital organs of different age groups.

When studying red blood in patients with chronic non-specific inflammatory diseases of the genital organs, it was found that the average number of erythrocytes and the average concentration of hemoglobin per unit volume of blood in patients in all groups were within the limits of physiological oscillations and significantly differed from such clinically healthy individuals (**Table 3.1**). The color index of all surveyed was about 1. The average number of platelets in patients of all groups was within the normal range, but in women of the 3rd group it approached the lower limit of the norm. The rate of sedimentation of erythrocytes in patients also did not go beyond the limits of physiological fluctuations.

The number of leukocytes per unit blood volume was also within the limits of physiological fluctuations and significantly differed from such clinically healthy individuals. The percentage of eosinophils in leukocyte count in patients was within the limits of physiological fluctuations and also did not differ from such clinically healthy individuals. The percentage of rods of the nuclear neutrophils in patients in all groups exceeded twice ($p < 0.05$) the corresponding control indicator.

Table 3.1. Indicators of peripheral blood in patients with chronic nonspecific inflammatory genital diseases.

Indicator, unit of measurement	Group of subjects											
	K1		K2		K3		1		2		3	
	M	W	M	W	M	W	M	W	M	W	M	W
The number of erythrocytes, $10^{12}.l^{-1}$	4,53± 0,26	4,25± 0,25	4,49± 0,22	4,10± 0,17	4,50± 0,19	4,36± 0,27	4,17± 0,44	4,23± 0,48	3,96± 0,39	4,45± 0,37	4,45± 0,37	3,47± 0,56
Hemoglobin concentration, $g.l^{-1}$	148±11	141±9	145±10	138±8	147±12	145±13	136± 21	135± 12	140± 17	127± 12	142± 11	127± 17
Color indicator	0,98± 0,73	1,00± 0,03	0,97± 10,06	1,00± 0,11	0,98± 0,08	1,00± 0,07	0,98± 0,02	0,97± 0,03	0,97± 0,03	0,96± 0,03	0,97± 0,03	0,96± 0,04
Platelet count $10^9.l^{-1}$	249± 30	264±2 7	252± 28	270± 30	247± 26	263± 29	263± 60	224± 42	249± 56	242± 31	249± 56	199± 48
ESR, mm per hour	4,54± 3,77	6,24± 3,63	4,27± 2,98	5,98± 2,87	4,73± 3,45	7,00± 3,34	3,92± 2,08	6,28± 3,24	5,75± 3,59	7,07± 4,00	5,87± 3,39	8,96± 5,95
Number of leukocytes, $10^9. l^{-1}$	5,43± 0,73	8,57± 5,56	5,18± 0,87	7,96± 0,99	4,98± 0,78	8,18± 0,66	6,41± 2,12	6,62± 4,39	7,07± 1,51	7,06± 1,54	7,23± 1,00	6,85± 1,93
Number of eosinophils,%	2,21± 1,13	1,81± 0,98	2,17± 0,97	2,19± 1,00	2,24± 0,83	1,60± 1,10	2,04± 0,72	2,97± 1,02	2,56± 0,88	2,73± 0,82	2,71± 0,82	2,45± 0,88
The number of rod-shaped neutrophils,%	4,21± 1,04	4,19± 1,25	4,28± 1,01	4,24± 1,13	4,17± 1,07	4,20± 0,99	8,58± 2,70*	8,97± 4,01*	8,09± 2,37*	8,10± 2,86*	8,11± 1,35*	9,20± 2,31*
The number of segmental neutrophils,%,	58,8± 4,1	58,4± 6,9	5,77± 3,9	61,2± 5,7	60,7± 4,8	57,4± 6,3	48,5± 4,1*	49,9± 4,7	47,8± 5,5*	49,8± 4,8	50,1± 3,8	45,0± 6,5*
The number of lymphocytes, %	29,5± 3,4	31,3± 5,4	30,7± 4,1	27,3± 3,8	28,4± 4,3	32,5± 5,1	35,4± 3,0	33,7± 4,6	35,4± 4,7	34,8± 4,2	34,4± 3,2	38,2± 4,6
The number of monocytes, %	5,08± 1,26	4,24± 1,48	4,77± 1,05	4,62± 1,33	4,63± 0,99	4,03± 1,39	4,54± 1,45	4,85± 1,30	5,22± 1,48	4,40± 1,29	4,67± 1,24	4,54± 1,49

Note. * - $P < 0.05$ compared to the control group

At the same time, the percentage of segmental nuclear neutrophils, although it did not go beyond physiological fluctuations , was lower than the percentage in the control, with this difference in men of the 1st and 2nd groups (1.2 times) and in women 3 - group (1.3 times). The percentage of lymphocytes and monocytes were within normal limits and practically did not differ from such control. Similar shifts in the indicators of general blood analysis were observed in the distribution of patients with groups depending on the type of pathogen of chronic nonspecific inflammatory diseases of the genital organs. The number of erythrocytes, leukocytes, platelets per unit volume of blood, hemoglobin concentration, color index and ESR were not significantly different from the values in the control **(Table 3.2).**

The percentage of erythrocytes and monocytes was also at the level of control indicators. However, the percentage of the rods of the nuclear neutrophils was significantly elevated in all groups by 1.77 - 2.15 times, while the amount of segmental neutrophils was reduced by 1.2 times ($p < 0.05$).

Thus, patients with chronic non-specific inflammatory genital diseases of the genital organs observed a tendency to increase the sedimentation rate of erythrocytes, an increase in the percentage of the rods of the nuclear

neutrophils in the leukocyte formula and an increase in lymphocytes.

Table 3.2. Indicators of peripheral blood in patients with chronic nonspecific inflammatory diseases of the genital organs, depending on the type of inflammatory agent.

Indicator, unit of measurement	Group of subjects						
	K	1	2	3	4	5	6
The number of erythrocytes, $10^{12}.l^{-1}$	4,39± 0,14	4,08±0,54	4,3±0,48	4,15±0,43	3,98±0,6	4,07±0,44	4,2±0,38
Hemoglobin concentration, $g.l^{-1}$	145± 3,0	132±17	141±17	135±15	131±13	131±14	137±12
Color indicator	0,99± 0,01	0,98± 2,03	0,97±0,04	0,96±0,04	0,96±0,03	0,97±0,03	0,97± 0,03
The number of platelets, $10^{9}.l^{-1}$	256± 75	229± 61	211±50	239±53	239±46	228±41	245±52
ESR, mm per hour	5,39± 0,85	5,75±0,85	7,15±0,68	5,9±0,67	7,39±0,35	6,79±0,33	5,85±0,7
Indicator, unit of measurement	Group of subjects						
	K	1	2	3	4	5	6
Number of leukocytes, $10^{9}.l^{-1}$	7,00±1,57	6,76±1,82	6,52±1,59	7,46±1,62	6,41±1,54	7,04±1,79	7,62± 1,55
The number of eosinophils, %	2,02±0,2	2,39±0,91	2,35±1,09	3,17±1,26	2,14±0,68	2,89±0,75	2,56± 0,78
Number of rods of nuclear neutrophils,%	4,2±0,01	8,92±0,81*	7,73±0,63*	7,43±0,21*	9,04±1,22*	7,94±1,47*	8,39± 1,26*
Number of segmental neutrophils,%	58,6±0,2	48,2±4,2*	47,8±4,6*	48,6±5*	49,4±4*	49,5±4,7*	48,1± 3,9*
Number of lymphocytes,%	30,4±0,9*	35,8±2,6*	37,6±5,0*	33,7±5,6*	34,3±2,7*	35,1±2,3*	35,7± 3,1*
Number of monocytes,%	4,66±0,42	4,25±1,64	4,42±1,38	4,73±1,2	5±1,43	4,63±1,38	5±1,07

Note. * - $P < 0.05$ compared to the control group.

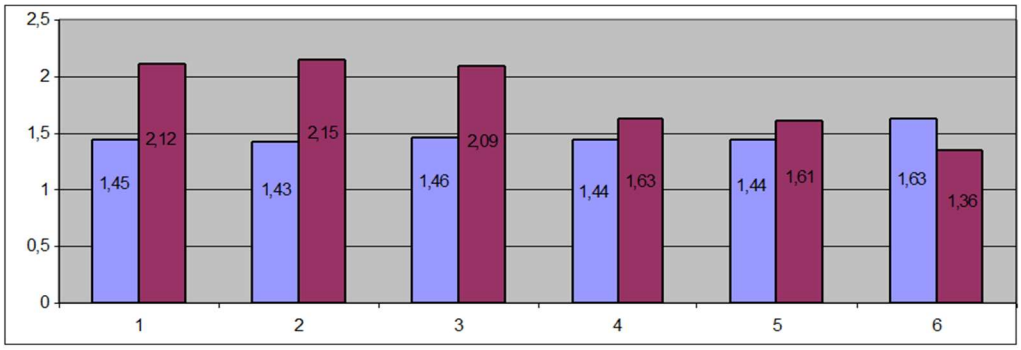
The shifts in these indicators corresponded to the presence of a weakly pronounced immune response. Significant differences in groups with different types of infections were not found.

Results

1. Analysis of shifts in general reactivity of the body of patients with chronic nonspecific genital diseases

Approximate assessment of the state of general reactivity of patients with chronic non-specific inflammatory diseases of the genital blood organs was carried out by calculating the integral indices of peripheral blood leukograms and ESR: index of leukocyte shift, index ratio of leukocytes and ESR, lymphocytic granulocytic index, general index, index of neutrophils and ESR: index of leukocyte shift, index ratio of leukocytes and ESR, lymphocytic granulocytic

index, general index, index of neutrophils and lymphocytes, index of ratio neutrophils and monocytes, index of lymphocyte and monocytes ratio, index of ratio of lymphocytes and eosinophils (**Figure 13**).



Notes:
1-3-men K1-K3;
1'-3 '.- Women K1-K3;
4-6-male 1st, 2nd, 3rd groups of patients;
4'-6 '.- Women 1st, 2nd, 3rd group of patients;
- mean square deviation from the average value

Figure 13. Index of shifts of leukocytes in patients with chronic nonspecific inflammatory diseases of genital organs.

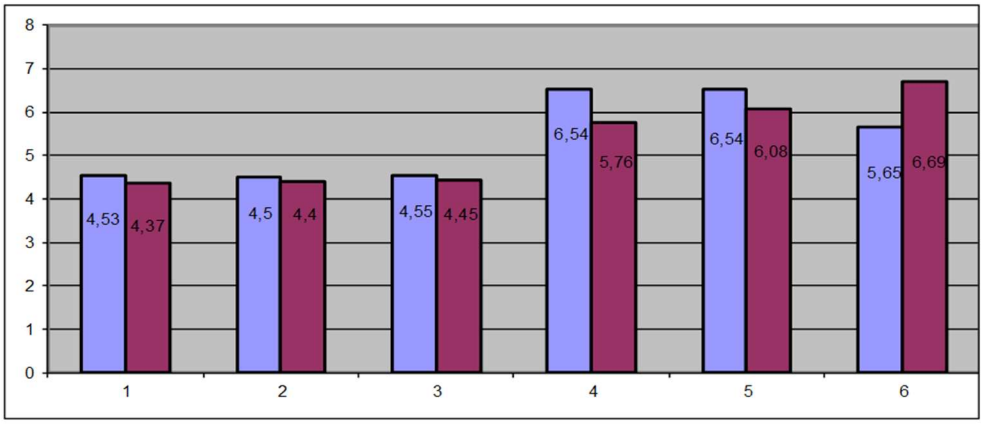
By conducting a total analysis of the shifts in these indicators, it is possible to assume the presence of autotoxication in patients, the advantages of a macro phagocytic link in the phagocytosis and an affective link in the mechanisms of immunity and also propensity to the reaction of hypersensitivity.

2. Analysis of integral formalized indicators of peripheral blood leukograms

The observed estimate of the state of the total reactivity of patients with chronic non-specific inflammatory diseases of the genital organs can be obtained by assessing the integral formalized indicators of peripheral blood leukograms and rates of red blood cells.

It is found that in clinically healthy people, the index of leukocyte shift significantly differed depending on sex and regardless of age. In men, this figure was 1.5 times ($p < 0.05$) less than in women. The index of leukocyte shift in patients with chronic nonspecific inflammatory diseases in men of all three groups did not significantly differ from those in the control (K) (**Figure 14**). At the same time, patients with chronic nonspecific inflammatory diseases of women 1st, 2nd and 3rd groups were 1.3; 1.3 and 1.6 times ($p < 0.05$), respectively, lower than the index of leukocyte shifts in the control K. The decrease in this indicator corresponds to an increase in the age of patients. This indicates a violation of nonspecific protective mechanisms in the examined patients. Indicator Lymphocytic - granulocyte index in examined clinically healthy men and women of all ages were at the same level. In the examined sick men and women of all three groups, the lymphocytic and granulocyte index increased significantly. In men of the 1st, 2nd and 3rd groups there was an increase of 1.4; 1.4 and 1,3 times ($p <0,05$) above the values in the control K. In women, the growth

of the lymphocytic - granulocytic index was corresponding to the middle age of patients in the group. In the first group, this indicator exceeded the control values by 1.3 times, and in the 2nd and 3rd group - 1.4 times ($p < 0.05$). In addition, the lymphocytic and granulocytic index in women of the 3rd group was 1.2 times more than in the control K ($p < 0.05$).



1-3-men K1-K3;
1'-3 '.- Women K1-K3;
4-6-male 1st, 2nd, 3rd groups of patients;
4'-6 '.- Women 1st, 2nd, 3rd group of patients;

Figure 14. Index of ratio of lymphocytes and granulocytes in patients with chronic nonspecific inflammatory diseases of genital organs.

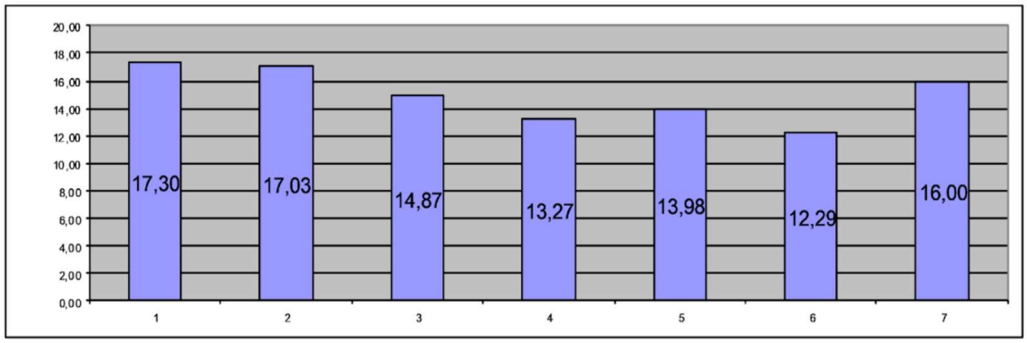


Figure 15. Index of ratio of neutrophils and lymphocytes in patients with chronic nonspecific inflammatory diseases of genital organs with different types of infections transmitted sexually.

3. Therefore, we can conclude that the violation of the integrative parameters of peripheral blood leuko form and erythrocyte sedimentation rate in patients with chronic nonspecific inflammatory diseases indicate a violation of nonspecific defense mechanisms and the predominance of macrophage component in the mechanisms of phagocytosis is most pronounced in patients with viral infections. The mechanisms of specific protection and predisposition to autointoxication is most pronounced in patients with chlamydial infection and with *Trichomonas* while immediate-type hypersensitivity reactions are more pronounced in patients with *Trichomonas* infection (**Figure 16).**

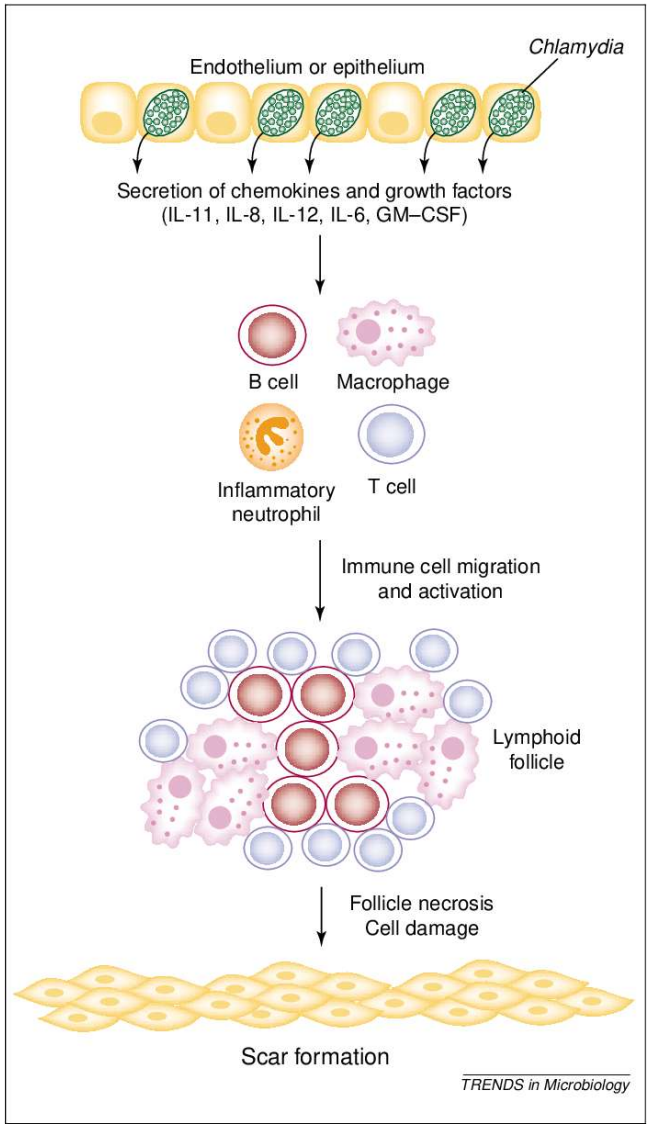


Figure 16. Pathogenesis of fallopian tube damage caused by *Chlamydia trachomatis* infection.

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