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# MODELS OF SHIFTS AND CORRELATION LINKS OF HEMATOLOGICAL AND IMMUNOLOGICAL PARAMETERS OF PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS

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**Abstract:**

The goal of this study is to examine and to evaluate hematological and immunological parameters of patients with chronic generalized periodontitis based on the models of shifts and correlations. At that, the assessment of carried-out modeling and correlations allows to identify the leading parameters of diagnostics and intrasystemic blood parameters and cell-mediated immunity.

**Key words:** Generalized periodontitis, Correlation, Local immunity.

## Introduction

Chronic generalized periodontitis (CGP) with people of working age is not only a medical, but also a social problem [1-5]. The disease holds a leading position among dental pathologies and is characterized by high prevalence and increasing frequency in recent years. Increasing CGP morbidity adversely affects the quality of life and causes significant shifts in regulatory systems in the organisms of the patients, including the immune system and peripheral, which to date remains poorly studied.

**Goal of the research**. Analysis and modeling of changes and correlations of hematological and immunological parameters of patients with CGP.

**Research technique**. The study includes 106 patients with CGP and 65 almost healthy persons as a control group. Patients of both groups received clinical and immunological examination.

Clinical examination included the analysis of the local objective symptoms and peripheral blood. The latter was analyzed with an automated hematology analyzer Quiktus (Sweden). The parameters of cellular immunity in peripheral blood were determined with the help of monoclonal antibodies and immunofluorescence method. The activity of blood neutrophils was studied by the reaction of recovery of nitroblue tetrazolium spontaneous (NBT sp.)

and nitroblue tetrazolium stimulated (NBT st.). Determination of shift parameters that allow to evaluate in normalized values the change of diagnostic indicators under investigation, having different modality. Correlation models were made based on the results of the correlation analysis carried out using the «Statistica 6.0» statistical software package.

**Body of the research.** CGP progression is accompanied by significant changes in peripheral blood parameters (Table 1).

**Table 1: Parameters of peripheral blood of patients with CGP and from the control group M±m.**

| Parameter name, unit of measure | Patients with CGP | Control |
|---|---|---|
| Leucocytes, $x10^9$/l | 8.9±0.7* | 6.6±0.8* |
| Lymphocytes, $x10^9$/l | 3.6±0.3* | 1.7±0.4* |
| Lymphocytes, % | 52.7±1.8* | 29.1±1.2* |
| Segmentonuclear neutrophils, % | 63.4±2.1* | 45.8±1.1* |
| Banded neutrophils, % | 6.1±0.2* | 1.4±0.2* |
| Monocytes, % | 3.8±0.2 | 4.1±0.2 |
| Basophils, % | 0.8±0.1 | 0.7±0.08 |
| Eosinophils, % | 2.5±0.2 | 2.3±0.3 |
| Hemoglobin, g/l | 117.5±2.2 | 122.4±1.9 |
| Red blood cells, $x10^{12}$/l=l | 4.1±0.4 | 4.4±0.3 |
| ESR, mm/h | 27.6±1.3* | 8.4±0.6* |

* Authentic differences from control

However, the increase of erythrocyte sedimentation rate and the relative number of lymphocytes was the most sizeable. Authentically patients with CGP have an increased absolute lymphocyte count. At the same time patients on admission have a significant increase in band neutrophils and segmented neutrophils. There are no obvious changes in the content of monocytes, basophils and eosinophils. Authentic differences compared with the control group in the parameters of hemoglobin and erythrocytes in the blood were not registered (P> 0.05). Pathological changes in the ratio of formed elements of patients with CGP quantitatively characterize the amounts of shift (Table 2).

**Table 2. The shift of hematological parameters in patients with CGP compared with the control group (%).**

| Parameter name, unit of measure | Amount of shift | Rank position |
|---|---|---|
| Leucocytes, $x10^9$/l | +34.8 | 6 |
| Lymphocytes, $x10^9$/l | +211.8 | 3 |
| Lymphocytes, % | +181.2 | 4 |
| Segmentonuclear neutrophils, % | +38.4 | 5 |
| Banded neutrophils, % | +435.8 | 1 |
| Monocytes, % | +7.3 | 9 |

| | | |
|---|---|---|
| Basophils, % | +14.3 | 7 |
| Eosinophils, % | +8.7 | 8 |
| Hemoglobin, g/l | +4.0 | 11 |
| Red blood cells, $x10^{12}$/l | +6.8 | 10 |
| ESR, mm/h | +328.6 | 2 |
| Total | +1235.5 | - |

Among the parameters of general blood analysis relative to the control group the amount of shift for banded neutrophils with a plus sign is maximal. Shift amount for ESR is set with a similar sign, but with less relative value.

The third rank position is the change in the absolute number of lymphocytes in peripheral blood by the development of inflammatory process in the periodontium. Shift parameters of other blood values of main group patients are significantly lower than previously indicated. Hemoglobin, red blood cells and monocytes have especially small amount of shift. Therefore, the mathematical evaluation of peripheral blood shows a high diagnostic value of band neutrophils, erythrocyte sedimentation rate and absolute number of lymphocytes. More pronounced changes of body temperature and erythrocyte sedimentation rate associated with CGP were observed in case of staphylococcal infection (37.68±0.38°C and 32.50±2.33 mm/h). By purulent inflammation caused by streptococcus, the average temperature and erythrocyte sedimentation rate reached 37.26±0.23°C and 31.73±12.99 mm/h, respectively [6]. In the process of study of white blood cell count more pronounced changes were observed at CGP caused by staphylococcus (8.32±1.72$x10^9$/l). By streptococcal infection white blood cell count was 7.83 ± 2.38 $x10^9$/l.

Banded neutrophils by streptococcal infection amounted to 1.6±0.6%, while by purulent inflammation caused by staphylococcus – 1.5 ± 0.5% [6]. Complete blood cell count of some patients remains generally normal except that the erythrocyte sedimentation rate is increased to 48 mm/h [7]. Model of pathological abnormalities in peripheral blood associated with CGP shows the extent of changes in the absolute number of lymphocytes, banded neutrophils and ESR (Fig. 1).

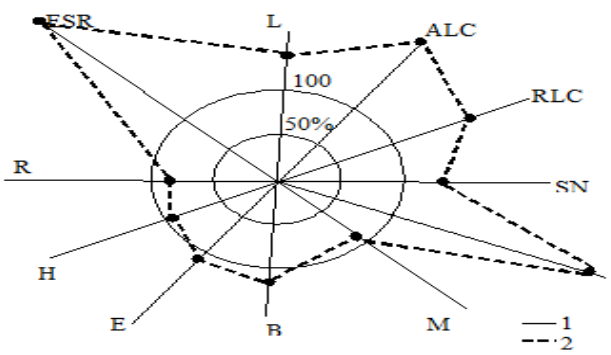


**Fig. 1. Model of changes in parameters of peripheral blood cellular composition of patients with CGP in relation to the control group (%).**

Fig. 1 contains the following legends: L - leucocytes, ALC - absolute lymphocyte count, RLC – relative lymphocyte count, SN - segmentonuclear neutrophils, BN – banded neutrophils, M – monocytes, B – basophils, E – eosinophils, H – hemoglobin, R - red blood cells, ESR - erythrocyte sedimentation rate.

1 – healthy adults, 2 – patients with CGP.

However, a significant part of blood corpuscle didn't reveal any significant abnormalities in CGP patients. This refers to the content of monocytes, basophils, erythrocytes, eosinophils, hemoglobin level. Deviation of other peripheral blood parameters showed an increase compared to the group of healthy adults.

Contingence of hematological parameters in the control group is significantly lower than of patients with CGP (Fig. 2).

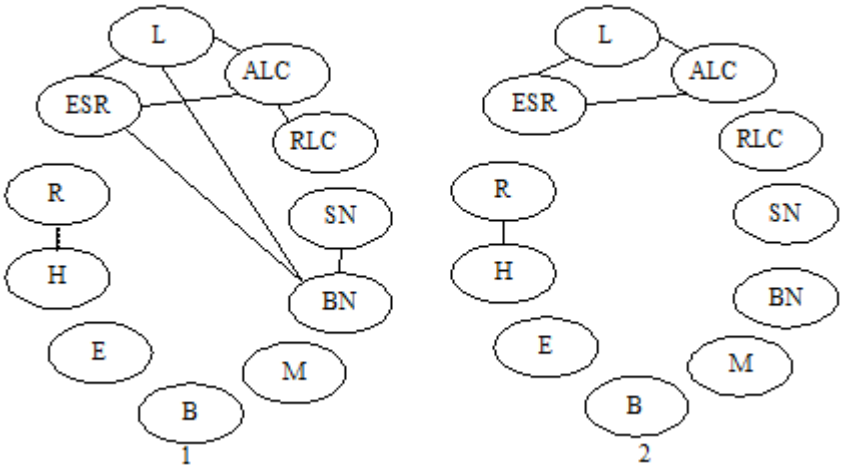


**Fig. 2. Model of correlation links of peripheral blood parameters of CGP patients (1) and healthy persons (2).**

Fig. 2 legends are the same as of fig. 2.

_____ direct authentic link

-------- reverse authentic link

…….. curvilinear authentic link

Four representative direct links were revealed between the peripheral blood parameters of healthy persons. They were noted between the content of white blood cells, absolute lymphocyte count and ESR. Direct correlation link is specific for the absolute lymphocyte count and erythrocyte sedimentation rate. The same direction of link is typical for the hemoglobin level and red blood cells count. The largest number of correlation links is typical for ESR, absolute lymphocyte count, white blood cells count and band neutrophils. Thus, band neutrophils have a direct link with the white blood cell count, erythrocyte sedimentation rate and the percentage of segmentonuclear neutrophils. ESR in turn has authentic contingency with band neutrophils, white blood cells and the absolute lymphocyte count.

The latter also has three direct authentic correlation links. The curvilinear link in the study group is set between the red blood cell count and hemoglobin level, i.e. it has changed compared to the control group. Diagnostic study of systemic immunity parameters of CGP patients allowed to detect T-lymphocyte hyperactivation and insufficiency of T-helpers, T-suppressors and of neutrophils activity in the test of nitroblue tetrazolium spontaneous and nitroblue tetrazolium stimulated (Table 3).

**Table 3. Immunological parameters at the system level of CGP patients and control group (M±m).**

| Parameter under study, unit of measure | Study group | Control group |
|---|---|---|
| CD3+, $x10^9$/l | 1.7±0.2* | 0.8±0.1* |
| CD3+,% | 58.3±0.6* | 47.6±0.7* |
| CD4+, $x10^9$/l | 0.3±0.05* | 0.8±0.06* |
| CD4+,% | 27.8±0,5* | 44.2±0.7* |
| CD8+, $x10^9$/l | 0.3±0.02* | 0.5±0.03* |
| CD8+,% | 18.1±1.0* | 29.7±0.9* |
| NBT-sp., c.u | 89.7±0.6* | 99.4±0.7* |
| NBT-st., c.u. | 118.5±3.2* | 176.8±2.9* |
| NBT-st./NBT-sp. | 1.3±0.2 | 1.8±0.3 |

* - authentic differences

Regardless of this, all changes in the immune system of the patients had a representative manner, except for the ratio of the parameters NBT-st. to NBT-sp. (P> 0.05). The inflammatory process in the bone tissue caused a significant increase in both absolute and relative T lymphocyte count. Change in T-helpers and T-suppressors was unidirectional and was accompanied by inhibition of the production of these clusters in absolute and relative terms. Average test value of NBT-st. and NBT-sp. of CGP patients statistically significantly decreased.

Previous study of cellular immunity parameters of CGP patients revealed a significant decrease in the content of T-lymphocytes ($p < 0.001$) in the peripheral blood of patients with CGP due to a decrease in count of both T-helper lymphocytes (CD4+ cells) and cytotoxic lymphocytes (CD8+ cells). The count of T-helper lymphocytes decreased 1.5 times ($p < 0.001$), and the relative count of cytotoxic T-lymphocytes - 1.4 times ($p < 0.05$) compared to that in control group [4].

Outcomes of previous studies of acute and chronic infectious processes in the oral cavity, as well as many other infection-caused inflammation processes show that in these forms of pathology the reduction of T-lymphocytes occurs mainly in lymphocytes of the helper subpopulation (CD4+ cells) and the reduction of cytotoxic T-

lymphocytes prevails only by atopic diseases [2, 3, 8]. Periodontitis-caused T-cell deficiency develops both in T-helper lymphocytes and cytotoxic T- lymphocytes [4].

The study of local immunity parameters based on the analysis of periodontal fluid, revealed an increase in anti-inflammatory cytokine IL-8, FNOα and reduction of anti-inflammatory cytokine IL-4 [7].

Mathematical evaluation of systemic immunity changes through shift indicator shows the most significant shift in absolute T-helper and T-lymphocyte count in the peripheral blood of CGP patients (tab. 4).

**Table 4: Amount of shift of systemic immunity parameters of CGP patients compared to the control group (%).**

| Parameter under study, unit of measure | Study group | Rank position |
|---|---|---|
| CD3+, $x10^9$/l | +212.5 | 2 |
| CD3+,% | +122.5 | 4 |
| CD4+, $x10^9$/l | -266.7 | 1 |
| CD4+,% | -62.9 | 8 |
| CD8+, $x10^9$/l | -166.7 | 3 |
| CD8+,% | -67.8 | 6 |
| NBT-sp., c.u. | -9.8 | 9 |
| NBT-st., c.u. | -67.0 | 7 |
| NBT-st./NST-sp. | -72.2 | 5 |
| Total | -378.1 | - |

Significant shift occurred in both absolute count of T-suppressors and relative count of T-lymphocytes. The amounts of shift regarding the number of T-suppressors, T-helpers, NBT-st. test and NBT-st./NBT-sp. ratio were almost equal in value and had the same sign. The lowest amount of shift of CGP patients was stated for NST-sp. test. The total amount of shift of systemic immunity parameters was 378.1 and had a negative sign.

Modeling of the exposed changes of the immune system parameters on the organismic level of CGP patients revealed in most cases unidirectionality of shifts (Fig. 3).

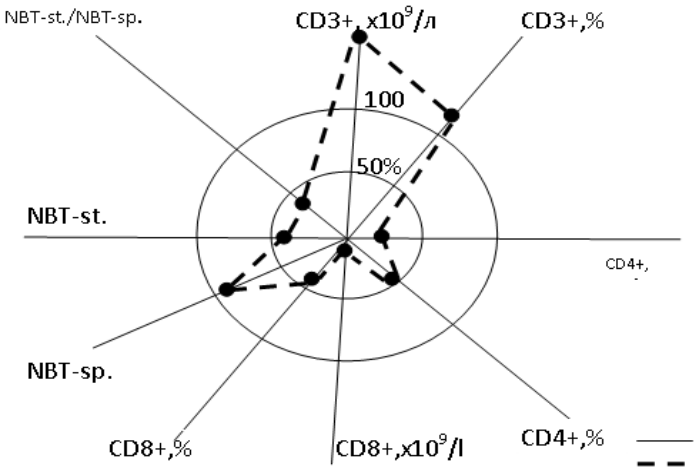


**Fig. 3. Model of changes of systemic immunity parameters of CGP patients compared to the control group (%).**

Fig. 3 contains the following legends: CD3+,x$10^9$/l – absolute T-lymphocyte count, CD3+,% - relative T-lymphocyte count, CD4+,x$10^9$/l – absolute T-helper count, CD4+,% - relative T-helper count, CD8+,x$10^9$/l – absolute T-suppressor count, CD8+,% - relative T-suppressor count, NBT-sp. – nitroblue tetrazolium spontaneous recovery test, NBT-st. - nitroblue tetrazolium stimulated recovery test, NBT-st./NBT-sp. – tests ratio.

The maximum deviation from the parameters of healthy persons is revealed for the absolute T-helper count, which is characterized by a pronounced suppression of this cluster of immune cells differentiation. A significant deviation is also typical for another T-lymphocytes subpopulation - the absolute T-suppressor count. Along with that, the opposite high value of deviations was observed for the absolute T-lymphocyte count. Less significant changes were observed for the relative T-helper and T-suppressor count and neutrophils activity in the NBT-st. test. Change in the relative T-lymphocytes count in peripheral blood occupies an intermediate position. Neutrophils activity in the NBT-sp. test remained almost unchanged. These changes should be considered in the diagnostics of the nosological form of CGP.

The ratio of immune cells in peripheral blood in study and control group represented in the form of graphic model differs both in quantity and direction of links (Fig. 4).

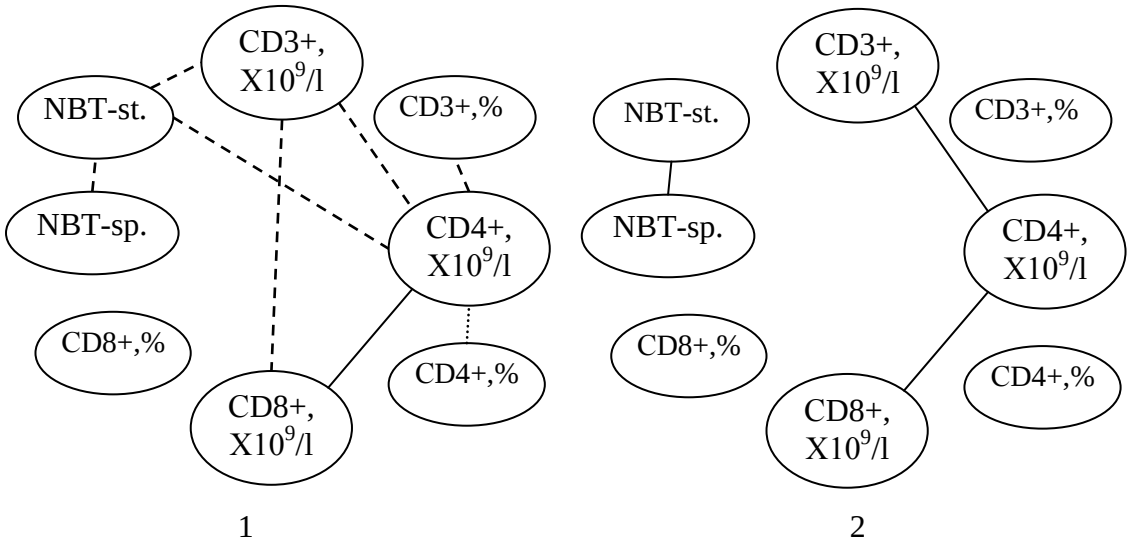


**Fig. 4. Model of correlation links of systemic immunity parameters of patients CGP patients (1) and healthy persons (2).**

Fig. 4 legends are the same as of fig. 3.

_____ direct authentic link

-------- reverse authentic link

…….. curvilinear authentic link

The highest number of authentic correlation link among CGP patients is typical for the absolute T-helper count, which in general have five links with other subpopulations of immune cells. The absolute T-helper count has three reverse representative links with absolute and relative T-lymphocyte count and NBT-st. test. Direct and curvilinear link exists between the absolute T-helper count and absolute T-suppressors count, respectively. The correlation model clearly reveals the absolute T-lymphocyte count at the systemic level, which is characterized by three reverse links – with absolute T-helper and T-suppressor count and NBT-st. test. The latter is in the reverse interrelation with NBT-sp. test. The contingence of immune system parameters in the comparison group is significantly lower. Three existing correlation links are direct; two of them are accrue to the T-helper differentiation cluster in absolute terms.

**Conclusion**

The conducted modeling of shifts and correlation links of hematological and immunological parameters of CGP patients T-cell cluster allowed to reveal the leading diagnostic parameters with quantitative evaluation and an increase of contingence of intrasystem links on the part of peripheral blood and cell-mediated immunity. This confirms the important role of changes and can be used for the diagnosis and evaluation of CGP therapy effectiveness.

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