of the smoking. 3 National congress for Baud. Saint Petersburg. 1992; 664. (In Russ)].

12. Величковский Б.Т, Коркина Л.Г, Черемисина З.П., Суслова Т.Б. Хемолюминесцентные методы в профилактической и клинической медицине: Методические рекомендации. М. 1990. [Velichkovskiy BT, Korkina LG, Cheremisina ZP, Suslov TB Chemoluminescent methods in preventive and clinical medicine. Systematic recommendations. M. 1990. (In Russ)].

13. Хронический обструктивный бронхит. Методические рекомендации Всероссийского общества пульмонологов для врачей. М. 2003; [Methodical recommendations regarding the use of a method of spirometry. Moscow. 2016;].

14. Чучалин А.Г., Сахарова Г.М. Болезни легких курящего человека. Хронические обструктивные болезни легких. 1998; 338-365. [Chuchalin AG, Sakharov GM. Diseases of the lungs of the smoking person. Hronicheskie-obstruktivnye-bolezni-legkih. 1998; 338-365. (In Russ)].

15. Шишкиш Г.С., Устюжанинова Н.В. Функциональные состояния внешнего дыхания здорового человека. Новосибирск: Изд-во СО РАН, 2012; 329. [Shishkish GS, Ustyuzhaninova NV. Functional states of the external respiration of healthy person. Novosibirsk: izd-vo SO RAN, 2012; 329. (In Russ)].

16. Brown CA, Crombie IK, Smith WC et al. Cigarette tar content and symptoms or chronic bronchitis: results of the Scottish Heart Health Study. *J. Epidemiol. Community Health*. 1991; 45(4): 287-290.

17. Buist AS. Risk factors for COPD. *Eur. Respir. Rev*. 1996; 6 (39): 253-258.

18. Chen Y., Horne SL, McDuffie HH, Dosman JA. Combined effect of grain farming and smoking on lung function and the prevalence of chronic bronchitis. *Int. J.-Epidemiol*. 1991; 20(2): 416-23.

19. Janus ED, Phillips NT, Carrell RW. Smoking, lung function and aKalra J., Chaudhary AK, Prasad K. Increased production of oxygen free radicals in cigarette smokers. Int. *J. Exp. Pathol*. 1991; 72: 1-7.

20. Leunberger Ph., Schwartz J, Ackermann-Leibrich U [et al]. Passive smoking exposure in adults and chronic respiratory symptoms (SAPALDIA study). *Am. J. Resp. Critic. Care Med*. 1994;150: 1221-122.

21. Pryor W.A. Biological effects of cigarette smoke, wood smoke and the smoke from plastics: The use of electron spin resonance. *Free radical Biol. and Med*. 1992; 659-676.

22. Repine JE, Bast A, Lankhorst I. Oxidative stress in chronic obstructive pulmonary disease. *Amer. J. Respir. Crit. Care Med*. 1997; 156:341-357.

23. Reznick A.Z., Cross C.E., Hu M. et al. Modification of plasma proteins by cigarette smoke as measured by protein carbonyl formation. *Biochem. J.* 1992; 286: 607-611.

24. Richards R. Cigarette smoke, metabolism and lung target cells. *The international monitor*. 1991; 2 (4): 103-107.

25. Simecek C. Reflection of passive exposure to smoking in the home on the prevalence of chronic bronchitis in non-smokers. *Czech Med*. 1980; 3(4): 308-10.

26. Uchiyama M., Michara M. Determination of malonaldehyd precursor in tissues by thiobarbituric acid test. *Anal. Biochem*. 1978; 86 (1): 271-278.

I.S. Pinelis, Yu.I. Pinelis, M.S. Malezhik, I.D. Ushnitsky

CONGENITAL AND ADAPTIVE IMMUNITY INDICATORS IN CHRONIC GENERALIZED PERIODONTITIS IN ELDERLY AND SENILE PATIENTS

DOI 10.25789/YMJ.2020.69.15

УДК 616.31-0:612.66

By 2055, the share of elderly people will be up to 40-55% of the total population of the country, which will require significant adjustments in medicine and social insurance of health care in Russia. At the same time, one of the important problems is still the disclosure of regulation mechanisms of dynamic constancy of internal environment of human oral cavity during different age periods. In this regard, the main purpose of the research was to carry out a complex of clinical and laboratory studies with the determination of the dynamics of cellular and humoral immunity indicators, the impact of basic therapy on their recovery in patients with chronic generalized periodontitis (CGP) of the elderly and senile age patients with cardiovascular diseases.

Material and methods.

During 2003-2011, 448 patients with chronic generalized periodontitis aged 60-89 years old were examined and admitted to the Veterans Hospital of War and Labour of Chita and the House of Veterans of Labor "Mercy" village Atamanovka of Transbaikal region for preventive treatment of ischemic heart disease. The criteria for inclusion in the studies were elderly (60 to 74 years old) and senile (75 to 89 years old) patients with moderate CGP and clinical manifestations of IHD (stable effort angina of the I-II functional class, chronic cardiac insufficiency of VA stage, hypertension of the 1-2 stage). Taking into account WHO recommendations, all patients were divided into 2 groups: the 1st group - 204 patients aged 60-74, who were assigned a complex of standard treatment of CGP; 2nd group - 190 people aged 75-89, who were assigned a complex of Standard Medical Treatment of CGP. The control group consisted of 25 practically healthy persons who did not have acute and chronic periodontal diseases, as well as somatic pathology at the time of the study.

All researches were carried out with participants' informed consent and was consistent with the ethical principles set by Law 24 of the Constitution of the Russian Federation, the Helsinki Declaration of the World Medical Association of Helsinki, 1964, 2000.

Results and discussion.

The overall hemolytic activity is reducing in patients of elderly people with CGP in blood and oral fluid. Meanwhile, the content of the C3a complement fragment in blood is increased to control rate up to 59 and 52%, respectively. In addition, there is a suppression of complementary activity, which leads to persistent and irreversible effects of periodontal pathology, in senile age more than in elderly age. To a greater extent, general and local immunity are violated in patients of senile age. Meanwhile, the correction of immunity is insufficient in patients with CGP of moderate severity of the elderly and senile age, under the influence of standard treatment. However, the continued high level of IgG indicates the continued activation of the humoral link of immunity. Changes in immunity after treatment indicated a high antigenic load of local and universal nature. In the oral fluid of patients, signs of hypercoagulation after baseline therapy were maintained. Such a situation was dangerous to the development of thrombogenic complications, and a relapse could easily occur against that background.

Conclusion. The recovery of immunity indicators takes place in insufficient volume in patients with CGP of elderly and senile age by basic therapy. The detected disorders in the immune response of this disease are basic, but not the only pathogenetic mechanism explaining the inflammatory process.

Keywords: periodontitis, oral fluid, elderly and senile age, immunity, hemostasis.

PINELIS Iosif Semenovich - Professor, Head of the Department of Surgical Dentistry of «Chita State Medical Academy," 39a, Gorkogo Str, 672000, Chita, Russia. Tel: 89145200178. E-mail: pinelis1@mail.ru. **PINELIS Yury Iosifovich** - Professor of the Department of surgical Dentistry of "Chita State Medical Academy," 672090, Chita, 39a, Gorky Str. tel. 7 (914) 461-59-08, e-mail: pinelisml@mail.ru, **MALEZHIK Margarita Sergeevna** − Assistant of the Department of Dentistry of Childhood of "Chita State Medical Academy" 672090, Chita, 39a Gorky Str, tel. 7 (924) 271-41-45, e-mail: ri-ta.malezhik@mail.ru, **USHNITSKY Innokentiy Dmitrievich** − MD, professor, head of the department of therapeutic, surgical, orthopedic dentistry and dentistry of children's age Medical institute " M.K. Ammosov North-Eastern federal university". 27, Oyunsky Str., 677013, Tel. 84112496961. E-mail: incadim@mail.ru.

The State Report of the Russian Federation [4] noted that by 2055 the proportion of old people will significantly increase - to 40-55 % of the total population of the country, which will require significant changes in health care and social security [1, 10, 12].

The ageing process of human undoubtedly affect the state of structures and tissues of the oral cavity [3, 5, 15, 17]. People over 60 years old, due to evolving age changes, develop a mild and prolonged period of dental diseases, often lead to chronic process and require longer treatment than in young and middle-aged patients [6, 9, 11, 13, 14]. In the elderly, these phenomena are exacerbated by a decrease of the re-generative and compensatory capacity of the oral mucosa [2, 7, 14].

In particular, one important problem is the disclosure of mechanisms for regulating the dynamic constancy of the internal environment of the human oral cavity in different age periods [12]. The main role of the local protection factors of the oral cavity is ensuring its normal functioning [8]. At the same time an important link in realization of these processes are the barrier all-organism nonspecific functions providing inclusion of one of protective mechanisms of homeostatic character in response to various pathological states [3, 5].

Purpose of the research. On the basis of complex clinical and laboratory research, the dynamics of cellular and humoral immunity indices, the effect of basic therapy on their recovery in patients with chronic generalized periodontitis (CGP) of the elderly and senile age with pathologies of cardiovascular system are determined.

Research materials and methods. During 2003-2011, CGP 448 patients aged 60-89 years old were examined, at Veterans Hospital of War and Labour of Chita and the House of Veterans of Labor "Mercy" village Atamanovka of Transbaikal region for preventive treatment of ischemic heart disease.

Inclusion criteria: elderly (60 to 74 years old) and senile (75 to 89 years old) patients with moderate CGP and clinical manifestations of IHD (stable effort angina of the I-II functional class, chronic cardiac insufficiency of VA stage, hypertension of the 1-2 stage).

Exclusion criteria: patients under 60 years old with moderate CGP, with acute diseases and exacerbation of chronic somatic diseases, periodontal diseases and exacerbating their severity, as well as endocrine pathology, diabetes mellitus, diseases of the cardiovascular system (except for those specified in the inclusion criteria).

All patients were divided into 2 groups, taking into account WHO recommendations:

- the 1st group - 204 persons at the age of 60-74 years old with a complex of standard CGP treatment;
- the 2nd group - 190 people at the age of 75-89 years old with a complex of standard CGP treatment;

The control group consisted of 25 almost healthy people who had no acute and chronic periodontal diseases, as well as somatic pathology. The values of the indicators obtained during their examination are taken as a norm. Study of innate and adaptive immunity, determination of immunoglobulin level, cytokine level, study of complement system and hemostasis was carried out.

Traditional CGP treatment of patients at the age of 60 – 89 years old included: oral hygiene training; Occupational hygiene and oral sanitation; Anti-septic treatment of periodontal tissues with Romazulan solution, 0.06% Chlorhexidine solution, 1% hydrogen peroxide solution; Applying a non-solidifying bandage comprising Dicain, Heparin, Prednisolon, Synthomycin for 20 minutes; closed curettage of infrabone pockets, mouth oralogy with "Rotocanum" solution - 3 times a day, auto-massage with "Metrogyl Denta" gel - 2 times a day for 5 days. At the same time, rational prosthetics or application of orthopedic splinted crowns were carried out. In addition, patients received anti-inflammatory, desensitizing and antibacterial preparations for 10-12 days.

Statistical processing of the results was performed by STATISTICA 6.0 (StatSoft Inc., USA) determining the statistical significance of the differences at $p < 0.05$. Non-variable methods were used in comparing quantitative values due to abnormal distribution of values in the variation series. The test parameters were presented as a median (Me [25th; 75th percentile]). The differences between groups was evaluated by Mann-Whitney test (U-test). The significance of the differences over baseline was assessed by Wilcoxon test.

Research was carried out with the informed consent of the participants and was consistent with the ethical principles of Law 24 of the Constitution of the Russian Federation and the Helsinki Declaration of the World Medical Association (World Medical Association Declaration of Helsinki, 1964, 2000 ed.), "Rules of clinical practice in the Russian Federation," approved by Order of the Ministry of Health of the Russian Federation No. 266 of 19.06.2003, and ethical standards of the Committee on Experiments, Clinical Research Standards GCP (GOST R 52379-2005).

Results and discussion. The overall hemolytic activity is reducing in patients of elderly people with CGP in blood and oral fluid. Meanwhile, the content of the C3a complement fragment in blood is increased to control rate up to 59 and 52%, respectively (Table 1).

However, while C3a increased by 27% in the oral fluid of elderly patients, it decreased by 30% in senile age. Its concentration increase indicates the activation of the complement system and accelerated cleavage of C3 component, which activity increases in the oral cavity with inflammation. The C3a fragment has the ability to induce macrophages with monokine isolation. Perhaps, through this mechanism, the complement system contributes to the increase in the level of anti-inflammatory cytokines in saliva and blood in inflammatory periodontal diseases (Table 2).

Table 1

Indicators dynamics of complement system parameters in patients' blood with chronic generalized periodontitis of elderly and senile age [Me (25–75 0/00)]

Indicator	Control (n = 20)	Elderly age (n = 60)		Senile age (n = 50)	
		before treatment	after treatment	before treatment	after treatment
Blood value complement, c.u	89.75 (89.40; 91.05)	80.40* (80.20; 80.88)	83.10*▲ (82.50; 83.40)	80.10* (78.50; 81.30)	84.20*▲ (81.80; 85.20)
C1- inhibitor, μg/ml	546.17 (536.3; 552.8)	369.70* (348.1; 370.6)	451.65*▲ (446.1; 461.9)	408.50* (402.2; 419.3)	441.70*▲ (437.2; 449.6)
C3a, ng/ml	408.25 (402.4; 415.03)	642.75* (640.1; 667.9)	589.20*▲ (584.3; 597.6)	626.90* (603.5; 643.2)	561.90*▲ (554.9; 572.5)
C5a, ng/ml	4.50 (4.50; 4.60)	5.20* (5.20; 5.30)	4.90*▲ (4.90; 5.10)	5.35* (4.90; 5.73)	4.75 (4.48; 5.10)

Notes. In the Tbl. 1-6 n - number of surveyed; * - distinctions of values in comparison with control (Mann-Whitney's test); ▲ - distinctions of values in comparison with the initial level (Wilcoxon's test); ■ - differences of values between groups.

The concentration of C1 inhibitor in oral fluid in periodontal inflammation in elderly and senile patients is reduced by almost 3 times, and in blood - by 48 and 42%, respectively. Such concentration may indicate a tense adjustment of its activation or insufficient synthesis.

Thus, there is a suppression of complemental activity, which leads to persistent and irreversible consequences of periodontal pathology, in elderly age in patients with CGP of both groups.

Pre-treatment suppression of complementary blood activity in elderly patients and after the course of basic therapy did not undergo major changes, therefore, the non-specific level of protection remained vulnerable. In particular, the overall complementary activity and the level of the C5a fragment of the complement remains low and the levels of the C1 inhibitor and the C3a fragment are elevated, and elderly patients have little or no change except a decrease in the C5a fragment of the complement (Table 1). The activity of complement components in oral fluid was substantially unchanged after standard treatment (Table 2).

Indicators of general and local immunity for CGP in elderly and senile patients are accompanied by a decrease in the number of cells carrying CD4 and CD8 markers, as well as CD4/CD8 and CD3/CD19 rates. At the same time, cell activity (increase in the number of cells CD4 CD25, T-dependent and T-independent NK) and humoral immunity with excessive synthesis of all basic classes of immunoglobulins in blood and oral fluid are observed. To a greater extent, general and local immunity indicators are damaged in senile patients.

Disorders detected in senile patients at different immune units did not undergo significant changes after standard treatment. Thus, the number of lymphocytes, monocytes, CD3/CD19 ratio increased and reached the norm. The number of CD4 increased slightly, decreased - CD3 CD19-, the concentration of IgG decreased, but all of them did not reach the control values (Table 3).

Indicators of cellular and humoral immunity of patients of senile age after treatment slightly differed from those of patients of old age. In private, the absolute number of lymphocytes has increased, and their percentage has exceeded the norm. The quantity of CD3 CD19-, CD4, CD8, CD3 HLA-DR, HLA-DR also became above, but did not reach norm. On the other hand, reduction of quantity of monocytes, granulocytes, CD3 CD16 CD56, CD3-CD16 CD56, CD4 CD25 and also concentration of IgG and IGM was noted. However, their values remained above normal. The ratio of CD3/CD19 to CD4/CD8 increased markedly, and the number of B cells continued to increase, while the IgA level remained unchanged (Table 3). Patients raised, but there was below norm a quantity of CD4, HLA-DR, a ratio of CD3/CD19 and CD4/CD8. Number of CD3 CD16 CD56, CD3-CD16 CD56 and CD4 CD25 - cages and also concentration of IGA, IgG and IGM decreased and got closer to values of norm. In addition, the concentration of IgA and IgG decreased by almost 30%, and the level IgM reached the norm in this group of patients (Table 3).

It has been established that content of IL-1α in plasma blood in the elderly and senile age patients exceeded the norm by almost 7, IL-4 - by 2.5 times, and IL-8 - by 1.5 and by 2 times accordingly. In elderly patients there was a decrease in IL-1α concentration by 2 times in blood plasma on the background of therapy. And even with such a sharp decrease, it exceeded the norm by 3times. IL-4 content continued to increase and exceeded the benchmark by almost 3 times. The concentration of IL-8 decreased slightly, but was also far from normal (Table 3).

The concentration of IL-1α decreased by 1.5 times in blood on the background of therapy in patients of senile age. And even with such a sharp decline, it remained 4 times higher than normal. IL-4 content continued to increase and exceeded the benchmark by almost 3 times. The concentration of IL-8 decreased slightly, but was also far from normal (Table 3).

The concentration of IgA increased by 2.5, IgG by 2, and IgM and sIgA by 3 times as compared to the control (Figure 4) in the oral fluid of patients. The IgM and IgA content in the oral cavity of elderly patients reached controlled values after baseline therapy, and concentrations of sIgA and IgG remained virtually unchanged. IL-4 level, although reduced, remained 9 times above control. IL-1α content was reduced by 2 times and reached reference values, the concentration of IL-8 remained virtually unchanged (Table 4). In senile patients, IgA content after baseline therapy reached a control value. Concentrations of sIgA, IgM and IgG remained high. IL-4 level, although reduced, was 10 times higher than the control. IL-1α fluid content in the oral cavity was reduced twice and reached the norm, the concentration of IL-8 was practically unchanged (Table 4).

Thus, in patients with CGP of moderate severity of elderly and senile age under the influence of standard treatment, the correction of immunity indicators is insufficient. In the oral fluid, the concentration of IgA decreased to normal, while the sIgA content remained high, indicating the need to synthesize the secretory component IgA the mouth mucosa. IgG level has not changed. No significant dynamics of immunity indices occurred in blood, but still decrease of IL-1α content and increase of IL-4 after treatment characterizes partial reduction of inflammatory process. However, the maintained high level of IgG indicates the continued activation of the humoral link of the immunity. Changes in immunity preserved after treatment indicate high antigenic load of local and universal nature.

The conducted researches of indicators of the general and local hemostasis at patients of old and senile age with a chronic generalized periodontal disease of moderate severity hyper coagulation (Tab. 5) is observed that testifies to aPTT shortening and thrombin clotting time, and thrombin clotting time is stronger reduced and extended fibrinolysis in group of patients of senile age. Induced clotting is accompanied by the rise of fibrinogen level, fibrinolysis suppression and high co-centralization of SFC, which are markers of thrombinemia.

Table 2

Values dynamics of complement system in oral fluid of patients with chronic generalized periodontitis of elderly and senile age [Me (25–75 0/00)]

Indicator	Control (n = 10)	Elderly age (n = 60)		Senile age (n = 50)	
		before treatment	after treatment	before treatment	after treatment
Blood value complement, c.u.	6.07 (5.86; 6.20)	3.12* (2.90; 3.12)	4.72*▲ (4.57; 5.23)	3.52* (3.51; 3.52)	3.98*▲ (3.77; 4.28)
C1- inhibitor, μg/ml	32.93 (32.77; 33.16)	12.40* (11.8; 14.85)	22.36*▲ (19.43; 23.25)	13.70* (12.13; 16.73)	23.53*▲ (22.36; 26.12)
C3a, ng/ml	49.14 (49.03; 49.40)	62.09* (60.07; 63.82)	65.80*▲ (64.90; 68.40)	33.60*▪ (30.83; 34.80)	36.50*▲ (35.80; 38.55)
C5a, ng/ml	6.30 (5.33; 6.58)	3.30* (2.90; 3.55)	4.60*▲ (3.80; 4.85)	3.35* (2.90; 4.00)	4.05*▲ (3.80; 5.28)

After standard treatment in blood of elderly patients, hypercoagulation decreased, INR reached a reference value, and frequent thrombin clotting time remained accelerated. The latter indicates that the external clotting activation pathway due to tissue fragments remains initiated. The lysis time of the fibrin clot remained elongated, and the concentration of fibrinogen and pro-ducts of its degradation was high. The dynamics of the hemostasis system in the senile patients after treatment had changes similar to those in the elderly patients, except INR, which remained at the baseline (Table 5).

It has been found out that procoagulant acivity of saliva is higher than in elderly and senile patients than in healthy people (shortened prothrombin and thrombin clotting time, aPTT). No significant differences between age groups were found (Table 6).

The ability of oral fluid to influence fibrinolysis is suppressed with age. This may be due to a decrease in the overall protease activity of saliva and an increase in the concentration of fibrinolysis inhibitors. In oral fluid of patients, hypercoagulation signs after basic therapy were preserved. In particular, the procoagulant potential decreased somewhat and its fibrinolytic activity remained still inhibited (Table 6). Positive dynamics of procoagulant potential of oral fluid is connected not only with reduction of hypercoagulation in blood flow, but also with action of local therapy.

The research results of the hemostasis system show that hypercoagulation is observed in the blood of patients with chronic generalized periodontitis of moderate severity over 60 years of age. The concentration of the compounds having procoagulantive activity in the oral fluid is higher than in healthy individuals, and fibrinolytic activity is suppressed. Such a situation was dangerous to the development of thrombogenic complications, and a recurrence of inflammation could easily occur on that background.

Conclusions. In patients with CGP of elderly and senile age under the influence of basic therapy, the recovery of immunity indicators takes place in insufficient volume. In case of chronic generalized periodontitis of moderate severity in patients of elderly and senile age there is observed systemic polyclonal B-cell activating factor. The reason for this may be bacterial endotoxemia and autoimmune processes. The immunopathology is expressed by imbalance in the system of a complement, malfunction of T-lymphocytes, decrease in intensity cellular and strengthening of humoral immunity, polyclonal activation of V-lymphocytes.

Table 3

Values dynamics of cellular and humoral immunity indices in patients with chronic generalized periodontitis of elderly and senile age [Me (25–75 0/00)]

Indicator	Control (n = 25)	Elderly age (n = 70)		Senile age (n = 80)	
		before treatment	after treatment	before treatment	after treatment
Lymphocytes,%	34.0 (34.0; 35.0)	31.50 (27.0; 34.75)	34.50 (32.0; 37.75)	34.00 (32.00; 34.0)	36.00* (35.0; 38.0)
Lymphocytes, abs./μl	2380.00 (2333.5; 2395)	1723.0* (1575.0; 1847.0)	1878.0▲ (1764; 1998)	2075.50* (2031.8; 2140.0)	2217.00*▲ (2193.8; 2238.3)
Monocytes,%	7.00 (6.0; 7.0)	6.00 (4.00; 7.00)	7.0 (5.00; 8.00)	7.00 (7.00; 8.00)	7.00 (6.00; 7.00)
Monocytes, abs/μl	444.00 (405.5; 460.0)	371.0 (292.5; 410.0)	412.0▲ (342.5; 456.5)	469.00* (454.0; 481.0)	407.50*▲ (396.0; 425.3)
Granulocytes,%	54.00 (51.0; 56.5)	68.0* (64.25; 71.0)	68.0* (62.25; 71.0)	65.00* (63.0; 66.0)	61.00* (59.0; 65.0)
Granulocytes, abs./μl	4270.00 (4205; 4362.5)	3248.0* (2983.0; 3482.0)	3465.0* (3170; 3597)	5124.0* (4985.0; 5245.0)	4652.00*▲ (4532.5; 4748.0)
CD3+CD19-, %	79.40 (78.85; 79.90)	80.10 (76.20; 82.15)	74.85▲ (72.40; 77.80)	70.30* (68.5; 70.9)	70.60*▲ (70.50; 71.25)
CD3+CD19-, PLT./ mql	1832.00 (1785.5; 1932)	1683.5* (1468.3; 1775.5)	1568.0*▲ (1446.0; 1668.0)	1486.00* (1446.0; 1490.0)	1623.50*▲ (1560.3; 1686.0)
CD4+, %	48.20 (47.65; 48.35)	39.75* (37.7; 44.15)	43.8*▲ (41.35; 45.8)	39.10* (38.40; 39.55)	40.40*▲ (39.58; 40.8)
CD4+, PLT./ mql	1117.00 (1080.5; 1135)	859.0* (768.0; 902.5)	964.0*▲ (879.0; 987.0)	822.50* (815.5; 834.0)	909.00* (897.0; 919.0)
CD8+, %	30.10 (29.20; 30.35)	21.20* (18.9; 24.6)	23.75* (22.33; 26.05)	18.45*▪ (16.65; 19.83)	33.75*▲ (32.83; 34.28)
CD4+, PLT./ mql	686.00 (666.0; 714.0)	279.0* (263.5; 315.5)	324.5*▲ (289.0; 346.5)	251.0*▪ (234.0; 289.0)	434.00*▲ (419.5; 453.0)
CD4+/CD8+	1.70 (1.70; 1.80)	3.09* (2.30; 2.80)	2.98*▲ (2.03; 2.40)	3.27 (2.96; 3.58)	2.1 (1.89; 2.24)
CD3+CD16+CD56+, %	4.60 (4.25; 4.80)	6.85* (6.23; 7.63)	6.95* (6.20; 7.28)	9.60* (9.15; 10.4)	8.70*▲ (7.9; 8.9)
CD3+CD16+CD56+, PLT./ mql	110.00 (106.0; 115.0)	170.0* (159.0; 183.25)	168.5* (163.0; 174.75)	197.50* (190.0; 207.25)	161.00*▲ (153.0; 168.0)
CD3-CD16+CD56+, %	10.60 (10.4; 11.0)	10.90 (9.10; 12.30)	11.25 (9.95; 12.80)	21.20* (18.4; 21.7)	14.80*▲ (13.1; 15.7)
CD3-CD16+CD56+, PLT./ mql	252.00 (233.0; 267.5)	223.50 (210.0; 244.50)	231.0 (210.0; 250.25)	513.00* (501.0; 524.0)	435.50*▲ (412.0; 446.0)
CD3-19+, %	8.50 (8.25; 8.7)	6.80* (5.90; 7.70)	7.25* (6.43; 7.60)	12.50* (11.7; 12.8)	11.80* (10.9; 12.4)
CD3-19+, PLT./ mql	210.00 (199.5; 216.5)	102.0* (90.5; 156.5)	116.0* (96.0; 163.0)	226.00* (217.0; 228.0)	234.00* (221.0; 240.0)
CD3+HLA-DR+, %	4.20 (4.10; 4.55)	5.80* (5.00; 6.55)	5.20* (4.65; 6.05)	2.40* (2.10; 2.70)	3.20*▲ (2.60; 3.40)
CD3+HLA-DR+, PLT./ mql	92.00 (88.5; 97.0)	109.50* (95.5; 127.5)	106.0* (93.75; 120.0)	81.00* (81.0; 83.0)	83.00* (82.0; 84.0)
CD4+CD25+, %	8.10 (7.8; 8.45)	19.95* (17.3; 21.35)	16.3*▲ (15.2; 17.1)	21.10* (19.4; 21.9)	18.50*▲ (18.1; 19.28)
CD4+CD25+, PLT./ mql	187.00 (182.0; 193.0)	347.0* (298.75; 366.5)	318.0* (308.0; 329.0)	391.00* (373.0; 398.0)	356.00*▲ (350.0; 371.3)
HLA-DR+, %	80.30 (79.8; 80.65)	74.70* (72.93; 76.40)	76.3* (72.1; 78.9)	63.00* (60.6; 65.4)	67.80*▲ (65.85; 70.85)
HLA-DR+, PLT./ mql		297.00 (288.3; 311.8)	308.0 (293.0; 319.0)	259.00 (237.0; 286.0)	299.00▲ (283.5; 315.5)
CD3+/CD19+	10.70 (10.4; 11.0)	15.40* (14.25; 16.68)	11.6*▲ (11.0; 12.3)	8.40* (7.95; 8.9)	9.30*▲ (8.90; 9.7)
IgA, mg/mL	1.80 (1.70; 1.88)	3.00* (2.90; 3.20)	2.80 (2.6; 3.0)	2.90* (2.80; 3.03)	2.80* (2.80; 3.00)
IgM, mg/mL	1.85 (1.65; 2.05)	2.90* (2.80; 3.15)	2.80▲ (2.55; 2.80)	2.80* (2.6; 2.8)	2.40*▲ (2.2; 2.6)
IgG, mg/mL	12.60 (12.3; 12.7)	21.60* (21.25; 22.10)	16.90*▲ (15.4; 18.1)	21.45* (20.8; 21.8)	16.45*▲ (16.2; 17.2)
IL-1α, pcg/ml	23.50 (23.0; 26.25)	147.00* (142.5; 149.0)	74.6*▲ (72.5; 79.0)	149.00* (140.0; 151.0)	96.6*▲ (94.2; 99.0)
IL-4, pcg/ml	12.00 (10.0; 13.5)	27.90* (27.8; 27.9)	32.4* (31.5; 34.0)	27.0* (26.0; 28.0)	34.1* (32.5; 34.9)
IL-8, pcg/ml	16.50 (16.0; 17.0)	26.30* (25.41; 26.7)	23.4* (22.3; 24.2)	30.0*▪ (29.0; 31.0)	26.5* (24.5; 27.9)

Table 4

Dynamics of the content of immunoglobulins and interleukins in oral fluid in patients with chronic generalized periodontitis of elderly and senile age [(Me (25-750/00)]

Indicator	Control (n = 15)	Elderly age (n = 35)		Senile age (n = 25)	
		before treatment	after treatment	before treatment	after treatment
IgG, mg/mL	0.20 (0.13; 0.21)	0.39* (0.38; 0.41)	0.40* (0.38; 0.42)	0.40* (0.37; 0.41)	0.40* (0.38; 0.42)
IgM, mg/mL	0.026 (0.022; 0.026)	0.072* (0.068; 0.074)	0.032▲ (0.029; 0.037)	0.074* (0.068; 0.078)	0.036*▲ (0.031; 0.037)
IgA, mg/mL	0.040 (0.04; 0.04)	0.099* (0.098; 0.101)	0.047▲ (0.042; 0.052)	0.100* (0.098; 0.102)	0.047▲ (0.044; 0.052)
sIgA, mg/mL	10.98 (10.73; 12.44)	34.50* (33.47; 34.73)	26.80*▲ (26.49; 28.1)	34.96* (33.78; 36.25)	27.15*▲ (26.5; 28.19)
IL-1α, pcg/ml	8.90 (8.15; 9.58)	13.48* (13.48; 14.32)	7.08*▲ (6.6; 7.45)	13.56*	7.08▲ (6.6; 7.35)
IL-4, pcg/ml	20.45 (20.25; 21.4)	320.30* (301.5; 329.45)	182.20*▲ (172.2; 231.8)	327.20* (313.4; 331.8)	216.5*▲ (192.2; 231.8)
IL-8, pcg/ml	15.92 (14.18; 17.14)	26.30* (25.41; 26.7)	23.60*▲ (23.2; 23.9)	28.73* (27.94; 29.55)	26.55* (25.42; 28.8)

Table 5

Dynamics of hemostasis system indicators in patients with chronic generalized periodontitis of old and senile age [Me (25-75 0/00)]

Indicator	Control (n = 15)	Elderly age (n = 30)		Senile age (n = 25)	
		before treatment	after treatment	before treatment	after treatment
INR	1.05 (1.0; 1.10)	1.20* (1.20; 1.20)	1.10 (0.96; 1.26)	1.20* (1.13; 1.20)	1.20* (1.11; 1.21)
aPTT, s	43.10 (40.5; 44.9)	32.90* (29.80; 35.0)	39.00*▲ (38.0; 39.5)	32.50* (28.15; 34.25)	37.60*▲ (36.43; 38.65)
thrombin clotting time, s	17.20 (17.2; 17.3)	15.20* (14.60; 15.6)	15.90*▲ (15.8; 16.5)	14.50*▪ (14.13; 14.60)	15.40*▲ (14.98; 15.58)
fibrinogen, g/l	2.75 (2.3; 3.0)	6.30* (5.9; 6.5)	5.55*▲ (5.5; 5.8)	6.40* (5.83; 6.65)	5.90* (5.80; 6.08)
SFC,mg/100 mL	3.00 (2.9; 3.0)	8.15* (8.00; 9.00)	6.30*▲ (6.00; 6.5)	8.20* (8.00; 8.60)	6.40*▲ (6.13; 6.70)
fibrinolysis, min	141.0 (138.0; 147.0)	191.50* (188.0; 200.0)	178.00*▲ (176.0; 179.0)	195.00* (193.0; 199.5)	177.00*▲ (175.0; 180.0)

Table 6

Effect of oral fluid of patients with chronic generalized periodontitis of elderly and senile age on blood clotting and fibrinolysis after treatment [Me (25-75 0/00)]

Indicator	Control (n = 15)	Elderly age (n = 30)		Senile age (n = 20)	
		before treatment	after treatment	before treatment	after treatment
prothrombin, %	75.80 (74.63;78.6)	61.10* (59.0; 63.0)	65.90*▲ (62.1; 69.5)	59.00* (58.0; 61.35)	67.10*▲ (64.4; 67.9)
aPTT, %	80.10 (79.8;81.80)	60.20* (58.3; 61.0)	70.10*▲ (67.95;70.8)	60.00* (57.2; 60.35)	69.20*▲ (67.3; 70.75)
thrombin clotting time, %	80.28 (78.8;82.81)	63.40* (62.2; 65.3)	68.30*▲ (65.6;70.65)	63.30* (62.2; 63.85)	68.50*▲ (65.7; 70.65)
fibrinolysis, %	73.50 (73.0;75.75)	87.0* (84.0; 89.0)	83.00*▲ (82.0; 83.5)	88.00* (85.0; 89.0)	83.00*▲ (82.0; 84.0)

The findings of the immune response in this disease are fundamental, but not the only, pathogenetic mechanism that explains the course of the inflammatory process.

References

1. Блашкова С.Л. Разработка критериев качества патогенетической терапии хронического генерализованного пародонтита: автореф. дис. … д-ра. мед. наук. Казань. 2010; 38. [Blashkova S L. Development of quality criteria of pathogenetic therapy of chronic generalized periodontitis: thesis…doctor of medical sciences. Kazan. 2010; 38. (In Russ.).]
2. Голдобин Д.Д., Быстрова Н.А., Евсегнеева И.В. Нарушения на системном и локальном уровнях при хроническом пародонтите, взаимосвязь с оксидантными изменениями. *Иммунология.* 2017; 38 (1):47-51. [Goldobin D D., Bystrova N A., Evsegneeva I V. Disorders at the systemic and local levels in chronic periodontitis, the link with oxidative changes. *Immunology*. 2017; 38(1): 47-51. (In Russ.).]
3. Денисов А.Б. Механизмы патологических и приспособительных процессов при заболеваниях слюнных желез: экспериментальное исследование: дис. … д-ра мед. наук. Москва, 2007; 38. [Denisov A B. Mechanisms of pathologic and adaptive processes with the diseases of the salivary glands: the experimental study: thesis doctor of medical sciences. *Moscow*. 2007; 38. (In Russ.).]
4. Здравоохранение в России. 2017 г. Статистический сборник. Москва. 2017; 48. [Public health in Russia. 2017. *Statisticheskij sbornik*. Moscow. 2017; 48. (In Russ.).]
5. Кузник Б.И., Цыбиков Н.Н., Давыдов С.О., Харинцева С.В., Пинелис И.С. Пинелис Ю.И. Изучение пептидных биорегуляторов в клинике. *Успехи геронтологии.* 2017; 6. 38-9. [Kuznik B I., Tsybikov N N., Davydov S O., Kharintsev S V., Pinelis I S. , Pinelis . I. Study of peptide bioregulators in clinic. *Uspexi gerontologii*. 2017; 6: 38-9. (In Russ.).]
6. Ушницкий И.Д., Иванов А.В., Иванова А.А., Юркевич А.В., Сейдалова Е.М., Новогодин А.А. Клинико-эпидемиологическая характеристика патологических процессов тканей пародонта воспалительно-деструктивного характера. *Якутский медицинский журнал.* 2018; 1(61): 83-86. [Ushnitsky I D., Ivanov A V., Ivanova A A., Yurkevich A V., Seydalova E M., Novogodin A A. Clinical and epidemiological characteristics of pathological processes of periodontal tissues of an inflammatory and destructive nature. *Yakutskij medicinskij zhurnal*. 2018; 1(61): 83-86. (In Russ.).]
7. Пинелис Ю.И. Адаптационные возможности защитных систем организма при хроническом генерализованном пародонтите у людей пожилого возраста. *Академический журнал Западной Сибири.* 2011; 2:36-7. [Pinelis, Y I. Adaptation possibilities of protective systems of organism at chronic generalized periodontitis in the elderly patients. *Akademicheskii zhurnal Zapadnoi Sibiri*. 2011; 2: 36-7. (In Russ.).]
8. Пинелис Ю.И. Резистентность полости рта у людей пожилого и старческого возраста [Электронный ресурс]. *Забайкальский медицинский вестник.* 2014; 2:153–161. Режим доступа: http://chitgma.ru/zmv2/journal/2014/2/28. Pinelis Yu.I. Resistance of the oral cavity of elderly and senile age people. *Zabaikalskii medicinskii vestnik*. 2014; 2:153–161. http://chitgma.ru/zmv2/journal/2014/2/28. (In Russ.).]

9. Попков В.Л., Леонтьев В.К., Фаустов Л.А. Патоморфологическая характеристика лечебного эффекта «Мексидол» у больных с хроническим генерализованным пародонтитом на фоне сахарного диабета второго типа. *Пародонтология*. 2007; 1: 20–25. [Popkov V L., Leontiev V K., Faustov L A. Pathomorphological characteristic of the therapeutic effect «Mexidol» in patients with chronic generalized periodontitis on the background of second type diabetes mellitus. *Parodontologia*. 2007; 1: 20–25. (In Russ.).]

10. Сувырина М.Б., Ушницкий И.Д., Юркевич А.В., Кобец А.Р., Иванова А.А., Иванов А.В. Частота и структура патологических процессов тканей пародонта воспалительно-деструктивного характера у населения Дальневосточного региона. *Якутский медицинский журнал.* 2018; 3(63): 71-74. [Suvyrina M B., Ushnitsky I D., Yurkevich A V., Kobets A R., Ivanova A A., Ivanov A V. The frequency and structure of the pathological processes of periodontal tissues of an inflammatory and destructive nature in the population of the Far Eastern region. *Yakutskij medicinskij zhurnal*. 2018; 3(63): 71-74. (In Russ.).]

11. Теблоева Л.М., Гуревич К.Г. Остеоиммунология и пародонтит. *Патологическая физиология и экспериментальная терапия.* 2014; 58 (3): 67-72. [Tebloeva L M., Gurevich K G. Osteoimmunologiya parodontit. Pathologic physiology and experimental therapy. *Patologicheskaya fiziologiya i eksperimentalnaya terapiya*. 2014; 58(3):67-72. (In Russ.).]

12. Туровская Е.В. Здоровье лиц пенсионного возраста как медико-социальная проблема : втореф. дис. … канд. мед. наук. Волгоград, 2012; 24. [Turovskaya E V. Health of the pension age patients as medical-social problem: thesis… candidate of medical sciences. *Volgograd*, 2012; 24. (In Russ.).]

13. Ушницкий И.Д., Зеновский В.П., Вилова Т.В. Стоматологические заболевания и их профилактика у жителей Севера. Москва: Наука; 2008; 172. [Ushnitsky ID, Zenovsky VP, Vilova TV. Dental diseases and their prevention among inhabitants of the North. Moscow: Science; 2008; 172. (In Russ.).]

14. Хавинсон В.Х. Молекулярные основы пептидергической регуляции старения. Санкт-Петербург. Наука. 2015; 170 [Khavinson V Kh., Molecular basis of the peptidergic regulation of ageing. *Saint-Petersburg*: «Science». 2015; 170 (In Russ.).]

15. Kuznik B., Davydov S., Tsybikov N., Kharintseva S., Pinelis I., Pinelis Yu. Clinical use of peptide bioregulators. International Symposium of Experts. *Effective current approaches in anti-aging medicine and gerontology*. Stockholm, Sweden, 2018; 53-6.

16. Molecular changes in the gingival epithelium associated with necrotizing ulcerative periodontitis: a case report. B. Dannewitz [et al.]. *J. Periodontol. Restorat. Dent.* 2006; 26 (2):191–196.

17. Revazova Z, L Tebloeva, I Bobr. Comparative evaluation of the clinical efficacy of non-surgical treatment of periodontal disease. Europerio 8, London. 2015; 103.