The introduction of new treatment methods into periodontology, based on the modulating role of cytokines in the regulation of organism immune response [9].

The aim of the study – to determine the pathogenetic role of cytokinogenesis for early stages of the experimental bacterial-immune periodontitis development.

MATERIALS AND METHODS The investigations was performed with use of white, non-breeding, clinically healthy male rats 150–200 g of weight in conditions of vivarium. Experimental animals were randomly selected and divided into two experimental groups: the group 1 – intact animals, control; the group 2 – animals with an experimental periodontitis on the 7th day. Experimental bacterial-immune periodontitis in experimental animals was caused by introducing into the tissue of the periodontal complex a mixture of microorganisms diluted with egg protein [10]. In order to strengthen the immune response, an injection into the rat’s foot of the full Freund’s adjuvant was performed at the same time. For further research the blood serum was selected, in that was determined the content of tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-4 (IL-4), interleukin-10 (IL-10).

Conclusion. Formation of experimental periodonitis is accompanied by a complex of pathological changes characterized by reliable progressive increase of proinflammatory cytokines for the early stage of inflammatory reaction development, that prove participation of TNF-α and IL-1β in the periodontal diseases pathogenesis.

Key words: bacterial-immune periodontitis; immune system; inflammation; inflammatory cytokines; anti-inflammatory cytokines.

INTRODUCTION According to the WHO, periodontal pathology occupied the second place in the structure of dental diseases and is the main cause of premature teeth loss [1]. Generalized periodontitis develops under the influence of local and general factors, but bacterial is considered the leading [2]. The periodontal pathogens triggers a number of protective reactions, which lead to the development of inflammation [3, 4]. Recent studies have shown the leading role of pro- and anti-inflammatory cytokines in regulation of the immune-inflammatory response. Progressive destruction of bone tissue in patients with periodontal disease is associated with a combination of cytokines IL-1β, IL-6, TNF-α and prostaglandins E2. These cytokines can activate osteoclastogenesis and bone resorption by osteoclasts. Strengthened migration of macrophages under the influence of cytokines and their constant presence in tissues enhances destructive processes in periodontium [5]. In this case, the degree of resorption of the alveolar bone depends on the severity of the organism immune response to bacterial invasion.

However, the relationship between clinical morphological parameters and mediators of the inflammatory-destructive process in periodontium is insufficiently studied. In the last two decades, progress in the study of factors contributing to the periodontal diseases development has led to a deeper understanding of the complex interaction of various mechanisms of organism immune defense, including both innate and acquired adaptive immunity [6]. Research in this direction has revealed several proinflammatory cytokines that have been identified as key molecules that contribute to the destruction of periodontal tissues. This is interleukin-1 (IL-1), tumor necrosis factor alfa (TNF-α), interferon gamma (IFN-γ), interleukin 6 (IL-6) [7]. Unlike proinflammatory cytokines, which play an important role in the primary development of inflammatory response in periodontal tissues, anti-inflammatory cytokines inhibit osteoporosis and inhibit macrophage activity, contributing to the relief of inflammatory response in the periodontal complex [8].

The progress in the study of the pathogenetic mechanisms of inflammation development in the periodontal complex will be promote better imagine the interconnection between inflammation and immune system, and also allow the introduction of new treatment methods into periodontology, based on the modulating role of cytokines in the regulation of organism immune response [9].
was determined with the normal distribution by criterion U-criterion Mann-Whitney [13].

**RESULTS AND DISCUSSION** In a result of our research there was found that content of inflammatory cytokines IL-1β, TNF-α in the rat’s blood serum with experimental generalized periodontitis was increased significantly as compared with control (Table).

IL-1β belongs to the proinflammatory cytokines of the first line and it is an activator of T-cells, NK-cells, NKT-cells, stimulates the formation of T-cell by cytokines.

In the animals with experimental bacterial-immune periodontitis during the acute phase of the inflammatory process, namely on the 7th day of the study, were found a significant increase in blood serum (by 86.31 %; p<0.01) of interleukin-1β relative to the control groups (Figure 1).

The TNF-α concentration was higher by 66.55 % (p<0.01) in the rat's blood serum on the 7th day of the experiment as compared to the control group of animals (Figure 1). This cytokine as a stimulator of leukocyte activity, production of cells IL-1β, IL-6 exerts a destructive effect to tissues.

The obtained data as a result of the experiment indicate that changes of proinflammatory cytokines concentration in the rat’s blood serum for the early stage of bacterial-immune periodontitis suggests in respect of immune mechanisms restructuring of oral defense in response to the action of pathogens, since the hyperproduction of TNF-α and IL-1β contributes to the enhancement of inflammatory process, damaging the periodontal tissue [14].

As for changes of the proinflammatory cytokines, which included IL-10 and IL-4, then maintenance their in the animal blood in these conditions simulated inflammation is changed in the opposite direction (Table).

In particular, IL-10 belongs to the group of anti-inflammatory cytokines, is an important endogenous regulator of immune and inflammatory processes, which can suppress the activation and function of T-cells, NK-cells, macrophages, and their proinflammatory cytokines [15]. Thus, the content of this interleukin on the 7th day was decreased in the rat's serum blood by 70.24 % (p<0.01) relative to intact animals (Figure 2).

In regard to changes in the content of another anti-inflammatory cytokine IL-4 in the blood serum of experimental animals with periodontitis, it should be noted that on the 7th day of the experiment, its indices were significantly lower (by 40.05 %, p<0.01) compared to those that were obtained in animals of the control group (Figure 2).

As a result of decrease in the content of anti-inflammatory and an increase in the content of proinflammatory cytokines in the blood serum of experimental animals, cytokine imbalance arose, as evidenced by a violation of their ratio (IL-1β / IL-10).

As compared the ratio of IL-1β / IL-10 in blood serum of experimental animals, it was found that it was significantly prevalent in rats with experimental bacterial-immune inflammation in the periodontal complex on the 7th day (by 550.00 %; p<0.01), compared to the control group (Figure 3).

Thus, our experimental data indicate to implication of proinflammatory and anti-inflammatory cytokines in the pathogenesis of inflammatory reaction in the periodontal complex.

**CONCLUSIONS** 1. Formation of experimental periodontitis is accompanied by a complex of pathological changes

| The form of the experiment | Control, intact animals | White rats with experimental periodontitis |
|----------------------------|-------------------------|------------------------------------------|
| Experiment duration (days) | 7                       | 7                                        |
| Number of the animals      | 10                      | 8                                        |
| IL-1β, ng / l              | 8.40±0.51               | 15.65±0.50 (p<0.01)                      |
| TNF-α, ng / l              | 25.80±0.51              | 42.97±0.70 (p<0.01)                      |
| IL-10, ng / l              | 71.06±2.96              | 21.52±2.11 (p<0.01)                      |
| IL-4, ng / l               | 20.05±1.04              | 12.02±0.60 (p<0.01)                      |
| IL-1β / IL-10              | 0.12±0.01               | 0.78±0.06 (p<0.01)                       |

Notes: p – significant of differences in relation to intact animals.

Figure 1. Dynamics of proinflammatory cytokines content in blood serum of white rats with experimental periodontitis (times, relative to control). Notes: * – significant of differences in relation to the intact animals (p<0.01).
characterized by reliable progressive increase of proinflammatory cytokines for the early stage of inflammatory reaction development, that prove participation of TNF-α and IL-1β in the periodontal diseases pathogenesis.

2. For the experimental bacterial-immune periodontitis (on the 7th day of the research) the level of anti-inflammatory cytokines in the animal serum blood, in particular IL-10 and IL-4, decreases, indicating their insufficiency in the regulation of the immune-inflammatory response in this modeled pathology.

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Figure 2. Dynamics of the anti-inflammatory cytokines content in the rat’s blood serum with experimental periodontitis (times, relative to control).
Notes: * – significant of differences in relation to the intact animals (p<0.01).

Figure 3. Dynamics of proinflammatory and anti-inflammatory cytokines ratio in the rats with experimental periodontitis (times, relative to control).
Notes: * – significant of differences in relation to the intact animals (p<0.01).
ЦИТОКИНОВЫЕ МЕХАНИЗМЫ В РАННІМ ПЕРИОДІ РОЗВИТКУ ЕКСПЕРИМЕНТАЛЬНОГО БАКТЕРИАЛЬНО-ІММУНОГО ПАРОДОНТИТУ

Резюме. У статьї наведено результати досліджень показників цитокінового профілю як посередника імунного захисту, що визначали за рівнем прозапальних та протизапальних цитокінів у сироватці крові інтактних тварин та на 7-му діб розвитку експериментального бактеріально-імунного пародонтиту. Звертають увагу на характерну зміну показників цитокінової ланки у наведеному експериментальному патологічному процесі. Зокрема, у період гострих проявів запального реакції на 7-му діб відмічалося підвищення у сироватці крові концентрації IL-1β та THF-α, а вміст IL-10, IL-4 за даних умов зменшувався. При цьому співвідношення про- та протизапальних цитокінів (IL-1β/IL-10), як важливий показник імунної реакції, значно підвищувалося. На підставі цих результатів було здійснено дослідження, що подтверджує роль цитокінового комплексу у регуляції імунно-воспалільного відділення при даному патологічному процесі.

Матеріали і методи. Дослідження проводили з використанням білих клінічно здорових щурів-самців масою тіла 150–200 г в умовах віварію. Експериментальних тварин відбирали та поділяли на дві експериментальні групи: перша група – здорові тварини, контроль; друга група – тварини з експериментальним пародонтитом на 7-й день.

Результати досліджень та їх обговорення. Експериментальний бактеріально-імунний пародонтит у досліджуваних тварин виникав введенням у тканину комплексу пародонта суміші мікроорганізмів, розбавлених яєчним білком. Таким чином цитокінова реакція, однією з провідних шляхів в регуляції імунно-воспалільного відділення при даному патологічному процесі, проводиться через зміни в генерації і секретії цитокінів. Статистичне аналіз зміни концентрації цитокінів у сироватці крові на 7-му діб оцінювали методом множинного регресійного аналізу. В результаті було здійснено вивчення зміни концентрацій цитокінів IL-1β та THF-α, а також зміни концентрації IL-10, IL-4 в сироватці крові на 7-му діб у відповідності до наведеного експериментального патологічного пародонтиту.

Висновки. Формування експериментального пародонтиту супроводжується змінами цитокінового звена, що характеризується надійним градієнтом зростання прозапальних цитокінів та зменшенням протизапальних цитокінів. Експериментальний пародонтит супроводжується зменшенням концентрації IL-10 та збільшенням концентрації IL-1β та THF-α, що вказує на активування прозапальних шляхів.

Ключові слова: бактеріально-імунний пародонтит; імунна система; запалення; запальні цитокіни; протизапальні цитокіни.