**ТАШКЕНТСКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ**

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# MODERN APPROACHES TO THE DIAGNOSIS AND TREATMENT OF PERIODONTITIS IN PATIENTS WITH PEMPHIGUS

**(Monograph)**

**Tashkent 2026**

**UDC: 616.314.18-002.66(616.527)-07-08**
**BBK: 56.6**

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In this monograph, the author analyzes and systematizes contemporary world literature, as well as the results of her own research in the field of diagnosis, treatment, and prevention of inflammatory periodontal diseases in patients with pemphigus. Analysis of the data obtained showed that inflammatory-destructive processes in the periodontium against the background of pemphigus have their own characteristics. The developed principle of comprehensive diagnosis and treatment of periodontitis occurring in combination with pemphigus was aimed at correcting the common pathogenetic mechanisms of both pathologies and was introduced into practical dentistry.

The monograph is intended for researchers, doctoral students, graduate students, teachers of dental departments, students, masters, and residents of dental faculties of higher educational institutions.

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**ISBN:**

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## List of symbols and terms

| | | |
|---|---|---|
| AOS | — | antioxidant system |
| VSMA | — | substances of medium molecular weight |
| GP | _ | generalized periodontitis |
| GP | _ | glutathione peroxidase |
| GPLS | _ | mild generalized periodontitis |
| GPLS | _ | generalized moderate periodontitis |
| GPT | _ | Severe generalized periodontitis |
| OHI-S | _ | Hygiene and plaque index |
| PI | _ | periodontal index |
| PMA | _ | periodontal marginal alveolar index |
| POL | _ | lipid peroxidation |
| SOPR | _ | oral mucosa |
| TRCF | _ | tartrate-resistant acid phosphatase |
| ALP | _ | alkaline phosphatase |
| EI | _ | endogenous intoxication |

# INTRODUCTION

Inflammatory and destructive periodontal diseases are widespread throughout the world and affect 90% of the population. Today, they are characterized by an increase in the incidence and severity of periodontal damage. "...Modern social and medical studies conducted by scientists in Uzbekistan over the past decade have shown that the standard of living (50%), the environment (20%), population genotype (20%), and level of medical care (10%) play an important role in the development of diseases, as these are factors that determine the health of the population..." Currently, treatment of chronic generalized periodontitis observed against the background of internal organ diseases does not cause positive changes in periodontal tissues, nor does it lead to complete remission.

Currently, in the Republic of Uzbekistan, special attention is paid to the development of the medical sector, in particular, the prevention of chronic diseases among the population, including reducing the negative effects of periodontitis on overall health in the case of such a dangerous dermatosis as pemphigus. To address these issues, based on the Strategy for Action in Five Priority Areas of Development of the Republic of Uzbekistan for 2017-2021, tasks have been set to "...improve the efficiency and quality of specialized medical care, maternal and child health care, and the promotion of a healthy lifestyle...". In order to implement these tasks, a set of measures has been developed to improve the medical services provided to patients, and great attention is also being paid to the development of modern methods of treatment based on the use of innovative technologies in the diagnosis of periodontitis and the provision of high-quality medical services.

In dermatological practice, pemphigus accounts for only 0.6–1% of cases, but the problem of early diagnosis and optimization of the treatment system for the disease, as well as the prevention of complications, is a pressing issue today. Information provided in scientific literature sources shows that pemphigus is a complex multifactorial disease. As a result of the development of pemphigus, a concept has been formed demonstrating the connection between stereotypical reactions of a local and systemic nature, which is associated with the development

and intensification of the process of endogenous intoxication, demonstrating an increase in medium-molecular peptides and oligopeptides in the blood, activation of proteolytic processes, POL, a decrease in AOS, and an increase in oxidized protein modifications (Latycheva S.V., 2004; Libik, 2010; Mavlonova Z.Sh., 2010; Fumie H., Kazutoshi H., Noriko A., 2011; Feldman R.J., Christen W.G., Ahmad A.R., 2012). Some scientists have noted that prolonged use of glucocorticosteroids leads to mineral imbalance, reduced bone remodeling, and the development of osteoporosis (Panteleeva G.A., Suzdaltseva I.V., 2009; Nizamova A.V., 2010; Bleiker T.O., Derby U.K., 2010; Di Zenzo G., Della Torre R., Zambruno G., Borrandori L., 2012).

In Uzbekistan, a number of scientists have conducted studies on the treatment of various clinical symptoms of periodontitis (Mavlonova Z.Sh., 2010; Kamilov H.P., 2017; Alimova D.A., 2018). The lack of a comprehensive approach to the systemic treatment of periodontitis in patients with pemphigus can be explained by the lack of clinical cooperation between dentists and dermatologists. The relevance of the problem and the lack of data on local and systemic metabolic disorders that occur during the development of generalized periodontitis in patients with pemphigus against the background of glucocorticoid therapy serve as the basis for determining the goals and objectives of our scientific research. Despite a number of studies reporting the exacerbation of inflammatory and destructive processes in the periodontium of patients with skin diseases, there are no studies on the combined course of pemphigus and periodontitis. To date, the systemic pathogenetic mechanisms of periodontitis in patients with pemphigus have not been studied.

In order to optimize the diagnosis, treatment, and prevention of periodontitis in patients with pemphigus, the authors conducted a series of scientific studies. The main subject of the study was to examine the clinical features of inflammatory and inflammatory-destructive periodontal diseases in patients with pemphigus, depending on the localization of pathological elements and the duration of the disease, indicators of mineral metabolism in blood serum, gingival blood, etc. The method of complex treatment of periodontitis aggravated by pemphigus is aimed at

changing the level of endotoxicosis, affecting the pathogenetic links of alveolar ridge atrophy in systemic osteoporosis resulting from glucocorticoid therapy. The following are of great importance: assessing the effectiveness of treatment, reducing the consequences of the disease, and improving preventive measures.

Thus, analysis of available literature sources and the results of our own research on the problem under consideration shows that pemphigus causes aggravation of dental pathology, in particular, an increase in the incidence of periodontal disease, a significant decrease in the body's immunobiological and allergic reactions, and on this basis, the development of targeted, differentiated comprehensive treatment and prevention programs for this pathology is one of the pressing tasks of modern medicine.

# CHAPTER I.

# CURRENT ASPECTS OF THE ETIOLOGY, PATHOGENESIS, AND TREATMENT OF PUPILLARY DISEASE

True pemphigus is a typical autoimmune disease belonging to the group of bullous dermatoses, the main pathomorphological feature of which is acantholysis [2].

In terms of the number of complications and fatalities, pemphigus remains one of the most serious diseases, and its treatment is one of the most difficult tasks in modern dermatology [60; 36].

Pemphigus accounts for 12.2% of the causes of disability due to skin disease in adults [57].

In the Republic of Uzbekistan, there has been an increase in the number of young patients with a torpid clinical course and ineffective treatment [41].

The etiology of pemphigus vulgaris remains unclear. The pathogenesis of the disease involves the development of autoaggression directed against the intercellular substance, desmosome proteins, cells of the spinous layer of the epidermis, and the multilayered squamous epithelium of mucous membranes in various locations.

The pathogenesis of pemphigus is based on autoimmune processes, the essence of which is the formation of autoantibodies to the cementing intercellular substance and the membranes of the cells of the spinous layer under the influence of changes in their antigenic structure, presumably induced, in turn, by altered cell nucleus DNA. They are called "pemphigus-like" antibodies and belong to immunoglobulin G (IgG). Pemphigus-like antibodies are detected in direct immunofluorescence reactions as fixed antigen-antibody complexes at the sites of blister formation; and can be detected in the epidermis of apparently intact skin. They are responsible for the development of acantholysis, the leading link in the morphogenesis of pemphigus; under their influence, the intercellular substance dissolves, desmosomes are destroyed, and epidermal cells lose their ability to reproduce.

One of the concepts of the origin of pemphigus is the damage theory, based on the disruption of DNA-dependent RNA synthesis in keratinocytes under the influence of some factor (retrovirus) on the genetic apparatus of the cell, which leads to the production of pemphigus-like antibodies. Thus, the formation of "pemphigus-like" antibodies and acantholysis is the final stage of morphogenesis, not its beginning.

Among the variety of etiological factors leading to the development of AP, hereditary, metabolic, viral, and infectious theories are discussed [2].

The most promising theory appears to be that of the inducing effect of retroviruses on the cell genome, in the presence of genetic determinism (carriage of the DR/DRN6 gene).

The role of the immune mechanism, primary or secondary immunodeficiency, as one of the leading factors in the pathogenesis of acantholytic pemphigus has been demonstrated [61].

A comprehensive examination, including immunological data, is undoubtedly important and decisive in the diagnosis of bullous dermatosis. In pemphigus, band-like IgG formations or IAиC3 concretions are found in the basement membrane zone [17].

The detection of biospecific IgG antibodies to keratinocyte antigens in the blood serum of patients with vulgar pemphigus also indicates autoimmune damage [64].

Immunohistochemical studies have established that Langerhans cells play a special role in the morphogenesis of vulgar pemphigus... During exacerbations, their number changes dramatically, with degenerative forms predominating [28].

The presence of fibrinous exudate in the tissues of patients with autoimmune bullous dermatoses indicates profound, serious disturbances in the hemostatic system, leading to the development of life-threatening complications such as sepsis and disseminated intravascular coagulation [43].

Patients with oral pemphigus experience a decrease in overall resistance and local defense factors, impaired colonial resistance, and the development of oral

fibrosis. At the same time, conventional therapy does not lead to positive dynamics in the identified disorders [63].

Pemphigus is a malignant disease that clinically manifests itself in the formation of blisters on intact skin and mucous membranes, which develop as a result of acantholysis and spread to the entire skin without adequate treatment.

There are several clinical forms of pemphigus: vulgaris, vegetans, foliaceus, and seborrheic (erythematosus). The mucous membranes are most often affected in pemphigus vulgaris (in 75% of patients), which is why it is of greatest interest to dentists. Vulgar pemphigus almost always begins with damage to the mucous membrane of the oral cavity or larynx, and then spreads to the skin. Even if the disease begins with the skin, damage to the mucous membrane of the mouth is almost always detected later.

A retrospective analysis of medical records from the Research Institute of Dermatology and Venereology of the Republic of Uzbekistan for 2002-2007 showed that the highest incidence (78.78%-76.70%) was for vulgar pemphigus [41, 63].

Clinical picture (peruphigus vulgaris). Vulgar or common pemphigus occurs more often than other forms. Men and women over 35 years of age suffer from this disease, children very rarely.

Lesions of the mucous membrane of the mouth and lips in pemphigus are characterized by the formation of blisters with serous or hemorrhagic contents, which have a very thin covering. Due to constant maceration in the oral cavity, the blisters burst very quickly, so it is extremely rare to see them in the oral cavity. Large or oval erosions that do not heal for a long time form in place of the blisters. The bright red erosions are located on the background of an unchanged or slightly inflamed mucous membrane. The size of erosions in pemphigus varies from small abrasions to extensive areas of congested red color. Initially, there is usually no coating on the surface of the erosions, or there may be a thin layer of light fibrous coating. Most often, erosions are localized on the mucous membrane of the tongue (especially in the retromolar region), the lower surface of the tongue, the palate, and the floor of the mouth.

Without treatment, new erosions appear, which merge together to form extensive erosive surfaces without a tendency to fester. Erosions become infected quickly, especially in an unsanitary oral cavity. The addition of coccal and fungal flora and fusospirochetosis aggravate the patient's condition, causing a specific odor from the mouth and increased salivation. First, the corners of the mouth macerate, and painful cracks appear. Bubbles and erosions covered with hemorrhagic crusts may also appear on the red border of the lips and in the corners of the mouth. Sometimes hoarseness occurs, indicating damage to the larynx. Blisters form on the skin, mainly in areas of friction with clothing, pressure maceration (abdomen, back, groin areas), and are very painful after opening.

Pemphigus is characterized by a wave-like course, with periods of exacerbation followed by periods of remission, which often occur spontaneously, more often under the influence of treatment. If the process began on the mucous membrane, then in the absence of appropriate treatment, it spreads to the skin of the trunk, face, and extremities within 1-6 months. At the same time, the general condition of the patient deteriorates sharply, intoxication increases, cachexia develops, and 1-2 years after the onset of the disease, without treatment with corticosteroids, patients die.

Diagnosis. An important diagnostic sign of vulgar pemphigus is Nikolsky's symptom, which is very easily induced on the mucous membrane: if the cover of the blister is pierced with tweezers, the epithelial film peels off on the apparently unchanged mucous membrane; When rubbing the apparently unchanged mucous membrane, as well as areas located far from the affected area, rapid formation of blisters and erosions immediately occurs.

Cytological examination. The presence of acantholytic cells in scrapings from the bottom of the erosions is essential for the diagnosis of pemphigus. Acantholytic cells, or Tzank cells, are altered cells of the spinous layer. They are rounded in shape and smaller in size than normal spinous layer cells. The nucleus is large relative to the entire cell, with a diameter of 1/3 to 1/2 or more of the cell diameter, stained dark blue, often with 1 to 6 or more light nucleoli. The cytoplasm of the cells is

heterogeneously stained. Giant multinucleated cells and "monsters" are found. At the height of the disease, the number of acantholytic cells increases sharply, merging into a continuous conglomerate of polymorphic cells. During remission and during treatment with corticosteroids, the number of acantholytic cells decreases [8].

Unlike other bullous dermatoses, direct immunofluorescence (IFM) in pemphigus allows the detection of immune complexes containing IgG in the area of the spinous layer membrane and the cementing substance between them, or more precisely, IgG antibodies in the blood serum (Bormann).

From a clinical point of view, pemphigus is a complex multifactorial disease [2].

The main biochemical and physiological reactions of the body occur at the level of the extracellular environment of cells, cell receptors of organ membranes (liver, kidneys) and systems (nervous, immune, connective tissue, skin, and mucous membranes). At the same time, changes in the skin and mucous membranes, which are multifunctional systems, are of particular importance. Currently, a concept has been formulated according to which the development of dermatoses is caused by stereotypical reactions of both a local and general nature and is associated with the formation and persistence of the process of endogenous intoxication, which manifests itself in a significant increase in the blood of medium-weight molecules and oligopeptides. This is characterized by the activation of proteolytic processes and lipid peroxidation (LPO) [80]. As a result of damage, when the barrier, protective, and regulatory functions of the mucous membranes and skin are disrupted, they become a focus for the formation of toxic metabolites. Overcoming intercellular and intertissue barriers and entering the body's metabolism, endotoxins lead to an imbalance in homeostatic processes and contribute to the aggravation of negative changes in the body.

As a result of acantholysis, massive cell destruction develops at the epidermal level, and a large amount of cell degradation products and under-oxidized metabolites of a protein, carbohydrate, and lipid nature enter the intercellular space and bloodstream. These substances, possessing the properties of endogenous toxins

and antigens, have an adverse effect on the vascular wall and the rheological properties of blood, disrupt the regulation of microcirculation in the focus, with the subsequent development of tissue hypoxia, further stimulating the production of autoantibodies and inflammatory mediators.

As a result of the pathogenetic synergy of the effects of hypoxia and endotoxemia, antioxidant defense is weakened and subsequent accumulation of highly reactive substances of various nature, destroying the cytoplasmic membranes of intact cells, gets out of control. A vicious circle of mutually stimulating pathophysiological processes is created, leading to the development of endogenous intoxication and creating conditions for the torpid course of true pemphigus.

The role of the activation of LPO processes, suppression of the antioxidant system (AOS), oxidative modification of proteins, pathological proteolysis, endogenous intoxication of medium-weight molecules and oligopeptides in the progression and recurrence of dermatosis has been established [3].

Treatment remains pathogenetic, aimed at suppressing the synthesis of autoantibodies to desmoidal proteins of spinous cells. None of the currently available drugs have a morbidostatic effect comparable to that of GCs and cannot be used as monotherapy. These methods do not prevent disease recurrence or deterioration in the general condition and quality of life of patients and have their own side effects [52].

Local treatment is not crucial for pemphigus. Rinsing with various disinfectants and deodorants is prescribed. Lubrication of erosions with solutions of aniline dyes, including Castellani's liquid, regenerating ointments – solcoseryl, dental adhesive paste. Oral cavity sanitation is very important for epithelialization. When the red border of the lips is affected, ointments containing corticosteroids and antibiotics (borgeksin) are prescribed.

The basic drugs for the treatment of pemphigus are corticosteroid hormones at doses of 1,500 mg/kg per day (in terms of prednisolone). The dose of prednisolone is selected taking into account the prevalence of rashes; in particularly severe cases, prednisolone is prescribed at doses of up to 2000 mg/day and above [35].

Treatment of AP patients with glucocorticosteroids at doses of 100-1600 mg/day (in terms of prednisolone) is accompanied by a significant negative shift in cellular and humoral immunity, the endogenous system, causes a deepening of immunodeficiency, and leads to the formation of serious side effects and complications. Serious complications of corticosteroid therapy, such as gastric and duodenal ulcer disease, Ischenko- -Cushing syndrome, diabetes mellitus, bacterial, viral, and fungal infections, osteoporosis, and osteomalacia, leading to the development of pathological fractures [111].

Combined methods of treating patients with acantholytic pemphigus, based on a combination of high doses of glucocorticosteroids and immunosuppressive drugs, significantly increase the risk of complications and side effects, which are the main causes of fatalities from the therapy. Thus, the mortality rate when using these drugs ranges from 6 to 15% [52, 60, 72].

At the same time, treatment of patients with adaptive (60-90 mg/day) doses of corticosteroids has a moderate immunomodulatory effect, leads to less suppression of endocrinological parameters, and reduces the risk of infectious complications. When conducting systemic and long-term therapy with corticosteroids, it seems justified to prescribe immunomodulators to compensate for immunological shifts and the development of infectious complications [52, 61].

Thus, the use of glucocorticosteroids (prednisolone) at a dose of 80 mg/day and polyoxidonium at 6 mg twice a week accelerated the process of epithelialization of erosions, reduced the development of candidal lesions of the oral cavity and purulent-septic complications [60].

A method for treating acantholytic pemphigus has been proposed, based on a combination of glucocorticosteroids and immunomodulators, in which Invertal is used as an immunomodulator in the form of 1 IU injections every other day for a course of 10 injections with simultaneous administration of prednisolone at a dose of 1 mg/day for 10-15 days, followed by a reduction in dose to 2.5 mg for 3 days. Under the influence of invertal, the immunoaggressive action of

glucocorticosteroids is reduced, which is important in the treatment of patients with acantholytic pemphigus [37].

The treatment of acantholytic pemphigus is a very complex therapeutic problem that requires a balanced approach both from the point of view of the clinical efficacy of modern drugs and from the point of view of assessing the clinical efficacy of the risk of developing possible complications and the risk of immunosuppression against the background of its use. It should be emphasized that the use of aggressive treatment technologies does not improve the overall prognosis of the disease or the patient's quality of life. In this regard, it is recommended to use gentle medical technologies, including the use of adjuvant immunotropic drugs, which allow reducing the duration of high-dose corticosteroid therapy and the patient's hospital stay, as well as preventing further relapses of the disease.

The choice of treatment depends on the activity of the autoimmune process. In the malignant course of the disease, the immune response shifts towards immunosuppression, accompanied by a decrease in the level of CIK and immunoglobulins of all classes. Therefore, effective methods of therapy in combination with immunosuppressants are indicated, and measures aimed at correcting disturbances in water-electrolyte and protein homeostasis are required [56].

Once remission is achieved, therapy consists of a daily dose of 30 mg of prednisolone and is characterized by a low level of progression of acantholytic pemphigus, taking into account the broad spectrum of immunomodulatory and antibacterial activity of the drugs. For autoimmune pathology, Viferon is prescribed 3-2 times a day in 5-10 equal cycles with an interval of three months. This will achieve a lasting effect, the possibility of reducing the dose of corticosteroids, and a shorter hospital stay [16].

In complex therapy of patients with pemphigus based on the use of systemic GCs, high levels of LPO activity, pathological proteolysis, and complex formation were recorded after treatment, and phospholipid metabolism disorders were observed. The use of high doses of GCs suppresses AOS [52].

It has been established that traditional therapy does not lead to normalization of endotoxemia levels, and the use of cytostatic drugs (methotrexate) exacerbates the processes of endogenous intoxication. The use of enterosorbents significantly reduces endogenous intoxication, reduces the toxic effects of cytostatic drugs, and contributes to clinical improvement [29].

To increase the activity of antioxidant systems in patients with pemphigus, the use of the antioxidant Reamberin 1.5% solution at a dose of 400 ml per day intravenously No. 10 is indicated, which contributed to a reduction in treatment time by 13 days and an increase in the total antioxidant activity of blood plasma [52].

Long-term use of glucocorticoids creates the conditions for the development of glucocorticoid osteoporosis.

At doses used in the treatment of pemphigus, glucocorticoids inhibit the development of lymphoid and connective tissues, including the reticuloendothelium, reduce the number of labrocytes, thereby reducing the production of hyaluronic acid, suppressing the activity of hyaluronidase and contributing to a decrease in capillary permeability. Glucocorticoids inhibit protein synthesis and accelerate protein breakdown. The production of glucocorticoids by the adrenal cortex is regulated by adrenocorticotropic hormone (ACTH). Glucocorticoids, in turn, affect the pituitary gland, reducing ACTH production and adrenal gland function. Therefore, long-term treatment with corticosteroids leads to adrenal cortex atrophy and suppression of ACTH and thyroid-stimulating hormone production in the pituitary gland.

In glucocorticoid-induced osteoporosis, changes in mineral metabolism can vary, but hypocalcemia and hypophosphatemia, increased calcium and phosphorus excretion in the urine, and decreased reabsorption are more commonly observed.

Anti-osteoporotic treatment (calcium preparations, vitamin D, and bisphosphonates) leads to significantly less pronounced disturbances in mineral metabolism and bone metabolism. It has been shown that the prevention of osteoporosis in patients with pemphigus should be started simultaneously with glucocorticoid therapy, in which case the metabolic disorders leading to the development of OP may be reversible [81].

The main causes of pemphigus recurrence were insufficient maintenance doses of hormones, as well as independent discontinuation of medication, surgical interventions, and exacerbation of other chronic somatic diseases [69].

# CHAPTER 2.
# PATHOGENETIC MECHANISMS OF PERIODONTITIS ASSOCIATED WITH SYSTEMIC DISEASES

The generally accepted pathogenesis of periodontal diseases is inflammatory-destructive changes in the periodontal complex in response to microbial invasion.

However, it is known that the degree of pathological changes in the periodontal complex is dysbacteriosis, which varies even with an identical spectrum of bacterial responses. This leads to the emergence of the concept of the balance between bacterial aggression factors and reserve capabilities, the degree of reserve capabilities, and determines the severity of pathological processes in the periodontium.

The presence of somatic pathology, which weakens the body's defenses, creates conditions for the periodontium to be affected by both the microflora present in the oral cavity and endogenous periodontal pathogenic factors. They contribute to autosensitization and the development of immunopathological mechanisms. Thus, inflammatory periodontal diseases are rightly classified as diseases with systemic factors of etiology and pathogenesis.

Many autoimmune and immune-dependent diseases affecting the skin and mucous membranes can lead to damage to the tissues of the oral cavity. Moreover, most of them can affect periodontal tissues or exacerbate its clinical manifestations.

The prevalence of periodontal disease among people with skin pathology increases with age, reaching a minimum at the age of 20-29 (41.3±1.41%) and a maximum at the age of 60 (92.63±2.58%). At the same time, gingival bleeding was noted in 1.92±0.12 segments, and gingival pockets 4-5 mm and >6 mm deep were found in 28.26 and 9.48% of cases, respectively [42].

The pathogenetic features of lichen planus of the oral mucosa suggest frequent involvement of the periodontal complex with the development of specific LPL-associated periodontal diseases requiring timely diagnosis, special approaches to systematization, and treatment [40].

A feature of inflammatory periodontal diseases is the appearance in its structural formations of a nonspecific inflammatory degenerative process in response to a wide variety of changes in various organ systems.

The lack of accurate understanding of the etiology and pathogenesis of periodontitis prompts researchers to seek a solution to the problem by deciphering it at the cellular level. Major advances in medicine in recent years have made it possible to establish universal mechanisms underlying cell apoptosis and cell alveolation of various origins. These are mediated by systemic reactions of free radical oxidation and immunological imbalance [67].

It is these common mechanisms that explain the pathogenesis of many diseases and their association with numerous risk factors. They are also involved in the development of inflammatory periodontal lesions.

Changes in immunoglobulins A and G in the blood, reflecting a decrease in the body's antiviral, antitoxic, and antibacterial defenses, are pathogenetically significant in the formation of more pronounced distinctive features of inflammatory-destructive processes in periodontal tissues. A characteristic increase in class A and G antibodies to transmutase, which stabilizes connective tissue, indicates its damage, which may serve as a secondary factor in inflammatory and destructive periodontal diseases.

A metabolic imbalance in the oral cavity has been established in the form of a decrease in calcium and phosphorus and an increase in amylase activity (Burduuli). New signs of inflammatory-destructive periodontal diseases have been identified: an increase in the pH of oral fluid, an increase in the level of cholesterol, serolipids, urea, and medium-weight molecules, the appearance of substances in the spectral range of 230-240 nm, characteristic of low molecular weight changes and catabolism, as well as an increase in the amplitude of proteins in the range of 280-290 nm, which is characteristic of protein compounds entering the oral fluid from the blood [77].

Analysis of the parameters of the POL revealed that in GP, endotoxemia syndrome develops with an increase in lipointoxication processes and a decrease in

antioxidant status; the most pronounced changes are found in patients with combined pathology [9].

In the pathogenesis of GP, disorders of periodontal trophism (metabolism and morphology), imbalance of nervous and hormonal regulation, and immune-competent and barrier systems are considered important [74]. As a result, hypoxia of the periodontal tissues occurs, leading to the activation of free radical oxidation, which results in the formation of active forms of osteoporosis (superoxide, hydroxyl radical). The generation of active oxygen forms normally induces the synthesis of protective systems (antioxidants). However, due to aggravating factors, the antioxidant defense system becomes unable to respond adequately by synthesizing sufficient amounts of antioxidant substances. As a result of the imbalance between ROS and AOS, the balance shifts towards the former, free radical oxidation in the periodontium develops rapidly, the level of ROS increases with the destruction and death of periodontal cells, and endogenous toxins are released. Cell division is disrupted, and products of peroxide destruction of lipids and proteins accumulate [79].

Today, systemic bone damage—osteoporosis—is also considered to be of considerable importance in the pathogenesis of GP.

In the presence of osteoporosis, periodontal tissue damage is practically independent of the degree of bone mineral density loss; at the same time, in patients without osteoporosis, the severity of periodontal damage is proportional to the degree of alveolar bone mineral density loss.

The alveolar ridge, as part of the skeletal system, reacts to exogenous and endogenous factors affecting the human body. Dystrophic-destructive processes in periodontal tissues and metabolic processes in the bone tissue of the alveolar ridge are interrelated with the structural and functional state of the skeletal system, as well as with the intensity of metabolic processes and the intensity of internal restructuring (remodeling) of the bones of the skeleton. Therefore, in the complex of general therapeutic measures for patients with GP, in order to reduce destructive-resorptive

processes, it is necessary to include drugs that regulate protein-mineral metabolism in combination with antiresorptives and stimulants of bone tissue formation.

Among mineral metabolism disorders, changes caused by corticosteroid therapy are particularly noteworthy, as these disorders are accompanied not only by systemic osteoporosis of the body's bone structures, but also by local osteoporosis in the alveolar bone, which is determined by the presence of osteoporosis foci in the interdental alveolar septa [45].

With progressive osteoporosis, changes in the skeleton are also progressive. As a result of a systemic shift in metabolism caused by impaired calcium absorption from the gastrointestinal tract and the suppressive effect of corticosteroid therapy on the proliferation and functional activity of osteoblasts, changes occur, including in the jaw bones. Local therapy alone is insufficient in somatically compromised patients [48].

A decrease in bone mineral density is the result of impaired mineralization, accompanied by changes in the microelement profile and morphological picture [121].

Pharmacological correction of bone remodeling disorders should be an integral part of a complex of therapeutic and preventive measures. Persistent remission of the underlying (somatic) disease is a prerequisite for anti-osteopathic therapy.

Analysis of the literature data proves the unity of systemic pathogenetic mechanisms in the combination of systemic diseases and periodontitis. The presented evidence of the pathogenetic role of systemic endotoxemia (processes of free radical oxidation of lipids, increase in toxic protein breakdown products); imbalance of mineral metabolism and disruption of alveolar tissue remodeling processes in systemic osteoporosis; metabolic disorders and homeostatic shifts characterize metabolic processes and alteration of cellular structures in various organs and tissues in systemic intoxication.

# CHAPTER 3.
# TREATMENT OF PERIODONTAL DISEASES IN PATIENTS WITH SOMATIC PATHOLOGY

Traditional treatment of generalized periodontitis boils down to eliminating inflammation in the periodontium by removing local irritants and using local and general antimicrobial therapy, antimicrobial, anti-inflammatory, desensitizing, immunomodulatory, vitamin preparations, and, much less frequently, it is supplemented with agents that stimulate metabolic processes in the alveolar tissues.

Clinical studies show that such treatment is not effective in all cases.

The multifactorial nature of the pathogenetic unity of various diseases of internal organs associated with generalized periodontitis is regarded as negative comorbidity, predisposing to the formation of a periodontal continuum with progressive damage to periodontal tissues, which necessitates the search for approaches to the specific treatment of these patients through systemic correction of pathogenetically significant factors [14].

It has been established that complex therapy aimed at key links in the pathogenesis that unites diseases of the internal organs and periodontium (antioxidants, vitamins E, A, C, mineral-containing preparations) causes a synergistic normalization of various factors of altered homeostasis [14].

The primary goal of periodontal treatment in patients with skin diseases is not only clinical stabilization of the process, but also subjective improvement in dental health and relief of skin pathology manifestations, as determined by specific quality of life criteria [40].

The use of calcineurin inhibitors as a means of pathogenetic therapy for CPD-associated periodontal diseases allows for an increase in the effectiveness of periodontal treatment and the quality of life of patients. The use of 1% pimecrolimus-based preparations in their original form, adapted to the specifics of periodontal pathology, provides high clinical efficacy comparable to that of toxic steroids [40].

Timely oral sanitation in patients with chronic dermatoses prevents recurrence of skin disease, prolongs the period of remission, and promotes the transition from widespread forms to localized ones. The combination of therapy for dermatological and dental diseases with simultaneous treatment of concomitant pathology improves the quality of life of patients [49].

The absence of noticeable complaints and a decrease in quality of life in the early stages of periodontitis means that a significant proportion of patients seek help only when tissue destruction has reached a significant extent. In this regard, surgical methods come to the fore in complex treatment as the only way to ensure the regeneration of the structural and functional complex of periodontal tissues [38,42]. Modern osteoplastic drugs allow for significant success in the restoration of bone defects [44,70, 107, 112]. However, studies have shown that the prognosis for treatment outcomes, especially AFP, is not always favorable [47,66]. This fact testifies to the relevance of the search for new pharmacological drugs capable not only of restoring lost tissues, but also of inducing a sustained remission of the disease.

The search for effective means of regulating bone metabolism in periodontal disease has led dentists to turn their attention to anti-osteoporotic drugs. There is no doubt that the use of osteotropic drugs will increase the effectiveness of surgical treatment of periodontitis [53,55,80,88]. This issue needs to be discussed in more detail.

Osteotropic drugs have been used in periodontology for a relatively short time. However, even limited experience with the use of antiresorptive agents for the treatment of periodontal disease, which regulate bone metabolism, has shown the ability of these drugs to normalize metabolic processes in periodontal tissues, reduce the rate of remodeling of interdental and interradicular bone septa by decreasing the activity of resorption processes and stimulating osteogenesis in the alveolar bone and in the body as a whole. The use of osteotropic drugs allows effective results to be achieved in the treatment of patients with generalized periodontal diseases, to

stop the progressive loss of the alveolar ridge, and to stimulate reparative regeneration processes [64].

Pharmacological drugs that regulate bone metabolism can be divided into three groups:

1- drugs that regulate calcium homeostasis, promoting a positive balance of CT remodeling;

2- drugs that inhibit CT resorption processes - antiresorptives;

3) drugs that stimulate osteogenesis processes.

Of the drugs in the first group, *calcitonin* (thyrocalcitonin) is of greatest interest. It is a peptide hormone whose physiological function is to regulate the metabolism of calcium (Ca) and phosphorus (P). Interest in this hormone is primarily due to its role in maintaining relatively constant calcium levels (2.1-3 mmol/L in blood plasma; 0.7-0.95 mmol/L in erythrocytes; 1.05-1.5 mmol/L ionized Ca).

The last decade of research into the structure of calcitonin has made it possible to synthesize this hormone and use it as a therapeutic agent. It slows down the decrease in bone mineral density, primarily in the lumbar spine in osteoporosis, and acts not only as a therapeutic but also as a prophylactic agent [69, 105].

The main factor affecting the thyroid gland and activating the synthesis and secretion of calcitonin is the concentration of calcium in the blood serum. An increase in Ca levels, especially in ionized form, in the blood increases calcitonin secretion, while a decrease reduces it. A decrease in calcium levels in the gastrointestinal tract increases gastrin secretion, which in turn leads to increased synthesis and secretion of calcitonin by the thyroid gland.

The primary site of action of calcitonin (its target organ) is bone. The main effect of calcitonin is manifested by hypocalcemia and hypophosphatemia, and its production is stimulated by hypercalcemia. The biological action of the hormone consists in inhibiting bone resorption.

Calcitonin inhibits not only spontaneous bone resorption, but also osteolysis, which can be stimulated by parathyroid hormone, vitamin D, and other factors, and promotes bone tissue repair in fractures [69].

Today, synthetic salmon calcitonin, Miacalcine (Novartis, Switzerland), is the most effective and popular drug in clinical practice worldwide. Miacalcine is available in a dosage form for parenteral administration and as an aerosol for intranasal use [127]. Its use in the form of rectal suppositories is considered an alternative [77, 129]. Hypercalcemia of any origin may be an indication for treatment with this drug, especially those hypercalcemic conditions caused by increased osteolysis [102,115]. In addition to its ability to slow bone resorption, it is also a powerful analgesic. The drug is widely used to treat osteoporosis, Paget's disease, hypercalcemia, and bone pain [118].

In general, most researchers note that during menopause, Miakaltsik aerosol is less effective than other antiresorptive drugs in terms of MPC, but in terms of reducing the risk and number of fractures, the drug successfully competes with other drugs [97]. It has no serious side effects and is non-toxic. Intranasal administration of 200 ME of Miakaltsik every day is much easier than regimens for bisphosphonates and cyclic hormones. It has a powerful analgesic effect and is better tolerated by patients than other drugs used in the treatment of osteoporosis. All this makes the use of intranasal Miakaltsik the treatment of choice for those suffering from severe and chronic pain, as well as for patients who cannot adhere to complex drug regimens.

The use of calcitonin in the complex treatment of periodontitis has been studied much less extensively, although it is pathogenetically justified. Thus, T.V. Nikitina (2005) conducted studies on the use of thyrocalcitonin in 160 patients with periodontal diseases [80; pp. 588-590]. The drug was prescribed at a dose of 40-50 IU subcutaneously daily. The results of treatment showed that on the 8th-10th day, pus discharge, tooth mobility, hyperemia, and gum swelling decreased; the duration of remission was 1-2.5 years.

In recent years, many researchers have noted the leading role of dystrophic bone tissue disorders in pathogenesis. However, clinical observations on the use of Miakaltsik in the complex treatment of periodontitis are few and far between. In the work of I.P. Mazur (2003), an unequal effect of Miakaltsin therapy on the mineral

density of bone tissue in various parts of the skeleton was noted [64]. The structural and functional state of the supporting skeleton, according to ultrasound densitometry indicators, remained unchanged, since the doses of the drug used are insufficient to increase the mineral density of the bones of the skeleton.

Alveolar bone responded better and faster to antiresorptive therapy with Miakaltsik nasal spray than skeletal bone tissue. The author notes that the antiresorptive effect of Miakaltsik is achieved through the suppression of osteoclast function by directly acting on their receptors.

In addition, Miakaltsik therapy blocks the inflammatory component of the pathogenesis of pathological processes in periodontal tissues.

It is recommended to use Miakaltsik in the form of a nasal spray for patients with thyrotoxicosis and bone metabolism disorders before dental surgery (implantation) [53]. After correction of thyroid status by an endocrinologist, endonasal calcitonin spray should be prescribed at a dose of 200 ME once a day in combination with alfacalcidol and calcemin.

Given the limited amount of research on the use of nasal spray in the treatment of CGD, further study of various aspects of the use of Miakaltsik in dentistry is needed. The role of calcium and vitamin D deficiency in the development of metabolic osteopathy is now beyond doubt [116]. To build a strong and healthy skeleton, it is necessary to consume the recommended amount of calcium and engage in physical exercise from childhood and adolescence onwards for both sexes. However, the most important thing is that simply consuming calcium in food or calcium supplements is not enough to treat osteoporosis, and it should not be an alternative or substitute for other medications prescribed for osteoporosis. Moreover, in the first few years after menopause, rapid bone loss can occur even with calcium supplements [87]. Vitamin D is necessary for adequate calcium absorption and normal bone metabolism. With aging, the level of 1,25-hydroxyvitamin D decreases, kidney function weakens, the amount of time spent in the sun decreases, and the ability of the skin to synthesize vitamin D decreases. Vitamin D deficiency can lead

to secondary hyperparathyroidism, which in turn causes increased bone turnover [32].

In dentistry, calcium and vitamin D preparations are used for various diseases of the dentoalveolar system. However, the main indication for their use is pathology of hard tooth tissues [32]. There are data in the literature on the results of using Calcium-Active. After traditional dental treatment, the prescription of this drug reduces the formation of new carious cavities [69]. E.V. Venskel (2007) recommends the use of Alfakatsidol, which contains calcium and active forms of vitamin D, to reduce retention time and optimize the processes of remodeling in periodontal tissues [17]. Studies have also been conducted on the effectiveness of Calcium-DZ Nikomed in various dental pathologies, proving the possibility of using this drug for osseointegration in jawbone fractures [46,96].

Despite the obvious positive effect on bone remodeling of drugs that affect calcium homeostasis, many researchers acknowledge their low effectiveness compared to other types of treatment [95]. Among the drugs of the second group, which are promising for the treatment of calcium-phosphorus metabolism disorders, bisphosphonates are of interest. In recent years, clinical experience has been accumulated on the use of bisphosphonates in the treatment of osteoporosis [130]. All representatives of this group of drugs are capable of significantly slowing down bone remodeling. At the same time, the latest generation of drugs have a significant effect on bone resorption. *Fosamax* (sodium alendronate, MSD trademark) is an amine bisphosphonate that acts as a potent specific inhibitor of osteoclast-induced bone resorption and thus normalizes the rate of bone remodeling, which allows this drug to be classified as a pathogenetic antiresorptive agent ( ). The greatest effect was observed in the spine [100]. In addition, in a study investigating the effect of the drug on the prevention of osteoporotic fractures (FIT), Fosamax reduced the incidence of hip fractures by 51%, new compression fractures of the vertebrae by 47%, and multiple (2 or more) vertebral fractures by 90% [117].

The logic of clinical thinking suggests the use of this drug to prevent osteoporotic, osteodestructive, and osteolytic processes in the bone tissue of the

alveolar process in patients with generalized periodontitis. However, we were only able to find data from a study conducted by a group of Ukrainian specialists [88]. For complex treatment, they used drugs with a pronounced antiresorptive effect (Fosamax, Osteochin). The authors demonstrated that the maximum effect of inhibiting osteoclastic resorption is achieved on average one month after taking the drugs. At the same time, it is emphasized that during the period of exacerbation of periodontitis, the activity of destructive processes in the alveolar process is so high that the therapeutic effect of antiresorptive agents in the first 3 weeks of drug administration does not compensate for the loss of bone tissue. In addition, in most cases, suppression of osteoclast activity by antiresorptive agents such as bisphosphonates, calcitonin, vitamin D, and calcium leads to secondary suppression of osteoblast activity through a coupling mechanism [95].

This phenomenon may underlie the recently discussed jaw necrosis observed in patients after bisphosphonate use [79, 119, 124, 128]. In an analytical review, A. Cheng et al. (2009) conducted a comparative assessment of the condition of the axial skeleton and jaw bones after the use of bisphosphonates. The authors note that bisphosphonate-associated osteonecrosis of the jaw (ONJ) primarily manifests itself in the alveolar part. e necrotic changes can occur either spontaneously or after surgical interventions on the alveolar bone, such as tooth extraction or periodontal surgery [40]. However, the mechanism of such disorders has not yet been established. In this regard, the development of preventive measures to combat the side effects of bisphosphonate use is a pressing issue for dentists [128].

Considering the negative aspects of using drugs from the first and second groups, the necessity and validity of using osteotropic agents in the complex treatment of CGP, it is necessary to continue the search for optimal pharmacotherapy based on new data on the etiology and pathogenesis of chronic generalized periodontitis, including aggressive forms. The prerequisites for such research already exist in the scientific literature. For example, in the works of M. Bellido et al. (2010) and M. S. Lutfioglu et al. (2010), the leading role in the development of alveolar bone resorption is attributed to parathyroid hormone [113, 114].. The

studies are experimental in nature, but their results open up new clinical perspectives for the pharmacocorrection of bone remodeling disorders in CGD.

The anabolic effect of PTH has a direct effect on cells by binding to membrane receptors and causes an increase in intracellular cAMP, phosphoinositol metabolites, and cytolytic Ca, and through these mechanisms, it can affect cell proliferation and differentiation [68]. At the cellular level, PTH increases the formation of new osteoclasts and osteoblasts and their activity. The effect of parathyroid hormone on osteoclasts is mediated through osteoblasts [129]. Indirect stimulation of local synthesis of growth factors and cytokines also plays an important role. However, it is still unknown which parts of the skeleton are attacked by PTH and why. In this regard, the data obtained by G. Di Bernardo et al. (2010), who studied the effect of PTH on mesenchymal stem cells (MSCs), are interesting. Unlike the stem cell s of hematopoietic origin, which also receive signaling regulation from PTH, MSCs were much more "responsive" to the hormone, as evidenced by a decrease in the rate of apoptosis [100].

In recent years, marked by the search for drugs that affect the body's systems as a whole, there has been a risk of upsetting the balance of other systems that are interrelated in their functions. At the same time, the lowest risk of undesirable consequences is associated with the use of antihomotoxic therapy. In dental practice, complex drugs such as Traumeel C, Osteohel C, and Calcohel have found application. Traumeel C has received the widest application as an anti-inflammatory drug. Calcohel, which improves metabolism and helps normalize calcium homeostasis, and Osteohel, which affects the metabolism of bone and connective tissue, are also promising for use. In this regard, it is relevant to study the feasibility of their use in cases of bone metabolism disorders associated with hormonal imbalance. There are few publications devoted to this problem [8,71].

Thus, the results of the literature review indicate the need to improve the provision of periodontal care in the system of comprehensive treatment of patients with diseases of the skin and mucous membranes of the oral cavity, improving the professional competence and interdisciplinary activity of dentists and dermatologists

in the diagnosis and treatment of periodontitis, which is often combined with skin and mucous membrane lesions, as well as systemic pathology.

## CHAPTER 4.

## CHARACTERISTICS OF CLINICAL MATERIAL AND RESEARCH METHODS

The work is based on the results of a survey of 49 patients aged 30 to 50 years. The majority of them were women, as it is at this age that they pay the most attention to the condition of their oral cavity. The work was carried out in 2015-2017 and was conducted at the Tashkent State Dental Institute at the Department of Hospital Therapeutic Dentistry and the Republican Dermatological and Venereological Clinical Hospital. The study mainly included patients with chronic generalized periodontitis against a background of pemphigus and 20 people with intact periodontium.

To implement the first direction, 49 patients with vulgar pemphigus undergoing inpatient treatment were examined.

**Table 1**

**Distribution of pemphigus patients in comparison groups when studying the characteristics of the clinical course periodontal diseases**

| Groups by age, years | Pemphigus, duration of disease, years | | | | | | | | | Pemphigus in general | | | Control | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | More than 1 year | | | More than 2 years | | | More than 3 years | | | | | | | | |
| | Total | Male | Female | Total | Male | Female | Total | Male | Female | Total | Male | Female | Total | Male | Female |
| 31-40 | 1 | - | 1 | 2 | 1 | 1 | 2 | 1 | 1 | 5 | 2 | 3 | 15 | 5 | 10 |
| 41-50 | 2 | 1 | 1 | 5 | 2 | 3 | 4 | 2 | 2 | 11 | 5 | 6 | 32 | 10 | 22 |
| 51-60 | 4 | 2 | 2 | 6 | 2 | 4 | 8 | 2 | 6 | 18 | 6 | 12 | 49 | 12 | 37 |
| Over 60 | 4 | 1 | 3 | 5 | 1 | 4 | 6 | 2 | 4 | 15 | 4 | 11 | 39 | 9 | 30 |
| Total | 11 | 4 | 7 | 18 | 12 | 12 | 20 | 7 | 13 | 49 | 17 | 32 | 120 | 36 | 99 |

All patients were admitted to the hospital during an exacerbation of their underlying disease and were therefore prescribed standard glucocorticosteroid therapy.

Table 2.1.1 shows the distribution of patients with pemphigus in the study groups according to gender, age, and duration of the underlying disease—pemphigus. As can be seen from Table 1, pemphigus mainly affects women aged 40 and older (65.31%), with men accounting for 34.69%.

As a control group, the adult population of Tashkent was examined, with the ratio of men to women and age groups corresponding to those of patients with pemphigus. The criteria for inclusion in the study were the absence of skin pathology and exacerbation of systemic disease.

**Table 2**

**Distribution of patients in groups in the study of local pathogenetic mechanisms of periodontitis development in patients with pemphigus**

| Age groups, years | Control | | | Patients with GP without pemphigus | | | Patients with GP and pemphigus | | |
|---|---|---|---|---|---|---|---|---|---|
| | Total | Men | Women | Total | Men | Women | Total | Men | Women |
| 31-40 | | | | | | | | | |
| 41 | 3 | 1 | 2 | 4 | 2 | 2 | 3 | 2 | 1 |
| 51-60 | 10 | 3 | 7 | 13 | 3 | 10 | 12 | 4 | 8 |
| Over 60 | 7 | 2 | 5 | 9 | 2 | 7 | 10 | 3 | 7 |
| Total | 20 | 6 | 14 | 26 | 7 | 19 | 25 | 8 | 17 |
| GPLS | - | - | - | 3 | 1 | 2 | 2 | - | 2 |
| GPST | - | - | - | 6 | 3 | 3 | 5 | 3 | 2 |
| GPT | - | - | - | 17 | 3 | 14 | 18 | 8 | 10 |

The study of the pathogenetic mechanisms of periodontitis development was carried out in patients with pemphigus; as a comparison group, the indicators of

patients with GP of the corresponding severity in patients without pemphigus were studied, and the indicators of healthy patients (without periodontitis and pemphigus) were taken as control indicators (Table 2).

As can be seen from Table 3, the gender and age distribution of the subjects and the severity of periodontitis were identical in the compared groups, which made it possible to compare the results and draw reasonable conclusions**.**

**Table 3**

**Distribution of patients by groups in the treatment of periodontitis in patients with pemphigus**

| Age groups, years | Test | | | Basic | | |
|---|---|---|---|---|---|---|
| | Total | Men | Women | Total | Men | women |
| 31-40 | 1 | 0 | 1 | 2 | 1 | 1 |
| 41-50 | 5 | 1 | 4 | 4 | 1 | 3 |
| 51-60 | 6 | 2 | 4 | 6 | 2 | 4 |
| 61 and older | 2 | 1 | 1 | 2 | 1 | 1 |
| Total | 14 | 4 | 10 | 15 | 5 | 10 |
| GPP | 1 | - | 1 | 1 | - | 1 |
| GPST | 3 | 1 | 2 | 4 | 1 | 3 |
| GPT | 10 | 3 | 7 | 10 | 4 | 6 |

Two groups of patients with pemphigus were selected to implement the third approach. Patients in the control group received standard treatment for periodontitis, while the main group received a pathogenetically justified comprehensive treatment method (Table 3).

As can be seen from Table 3, the distribution of patients with pemphigus by gender and age in the groups, as well as their distribution by severity of GP, ensures the representativeness of the studies and allows for comparison of treatment results.

All patients with periodontitis against the background of pemphigus underwent a standard treatment regimen for periodontitis, including oral sanitation, removal of supragingival and subgingival dental deposits, and elimination of traumatic factors. Training in oral hygiene rules using soft toothbrushes and toothpastes without abrasive components. Periodontal pockets were rinsed with disinfectant (3 mg/l) ozone concentrations and an application of Metrogil-Denta ointment under a protective fixing bandage.

At this stage of treatment, patients were divided into two groups. Patients in the control group continued treatment according to the above-described regimen, while patients in the main group received additional complex treatment, including:

Group 1: patients with GPD had 10 g of Metrogil-Denta gel applied to the periodontal pockets under a bandage for 5-7 days;

Group 2: patients were treated with 10 g of Enterosgel gel applied to the surface of the gums and 1 tablespoon taken orally once a day for 5-7 days;

Osteotropic therapy aimed at normalizing mineral homeostasis, regulating calcium and phosphorus metabolism, and increasing bone mineral density. For this purpose, patients took Bonviva 1 capsule once a day in long courses, for more than 6 months.

Study of medical history, duration of the underlying disease (pemphigus) and periodontitis. The condition of the oral cavity, the presence of carious teeth, traumatic occlusion, and bite pathology were assessed.

The prevalence and intensity of periodontal disease was assessed using the PI periodontal index according to ARussel (1956);

The degree of gum inflammation was assessed using the gingivitis index (PMA) according to Parma (1960).

The level of oral hygiene was assessed using the OHI-I hygiene and tartar index (J. Green, J. Verruillion, 1969).

the degree of gum bleeding was assessed using the bleeding index (H.P.Muhleman, S. Son, 1971).

The following criteria were taken into account when assessing the clinical effectiveness of treatment for patients with acantholytic pemphigus:

1. Changes in subjective sensations (reduction or disappearance of pain, itching, burning);

2. General condition (temperature, blood pressure, pulse, clinical blood and urine tests, including biochemical and immunological blood tests);

3. Dynamics of objective clinical manifestations (change in color, reduction in size and depth of erosions). At the same time, the following were considered positive dynamics of the pathological process:

-absence of fresh elements in the oral cavity;

-the onset of sluggish epithelialization of erosions;

-active epithelialization of erosions;

-absence of Nikolsky's symptom;

-normalization of laboratory parameters.

For analysis, blood was collected in Vacuette R vacuum tubes without anticoagulant on an empty stomach. Blood was collected with minimal vein compression and without muscle strain.

The levels of parathyroid hormone (PTH, g/ml) and calcitonin (CT, ng/ml) were determined by immunoenzymatic assay using a special kit from BioChemMac.

Biochemical markers of bone remodeling—osteocalcin (ng/mL), a non-collagenous protein that binds collagen to form hydroxyapatite—were determined by immunoenzymatic analysis using a kit from BioChemMac (Russia).

The bone resorption marker (β-CrossLaps (ng/ml), which shows the amount of bone resynthesis based on the amount of type I collagen degradation products in blood serum, was determined using a kit from ROSH on an Elecsys 1010 autoanalyzer (ROCHE, Switzerland).

Calcium concentration was determined by a standardized colorimetric method based on a color reaction with cresolphthalein complexone and expressed in mmol/L; phosphorus concentration was determined by a standardized method based

on the reduction of phosphomolybdenum heteropolyacid and expressed in mmol/L [49].

Alkaline phosphatase activity was determined using a standardized method based on the hydrolysis of H-netrophosphate and expressed in ME [49]; resistant acid phosphatase was determined based on the hydrolysis of P-nitrophenylphosphate and expressed in ME [49].

The level of lipid peroxidation and the activity of the antioxidant system were assessed by the level of malondialdehyde (MDA) and the activity of superoxide dismutase (SOD), determined by spectrophotometric methods [2,24,25]. The MDA/SOD•1000 ratio was used to assess the state of free radical oxidation and antioxidant protection. The anti-peroxide activity (APA) of the biological fluids studied was determined by chemiluminescence.

All patients with periodontitis against the background of pemphigus underwent a standard periodontitis treatment regimen, including oral sanitation, removal of supragingival and subgingival dental deposits, and elimination of traumatic factors. Training in oral hygiene rules using soft toothbrushes and toothpastes without abrasive components. Periodontal pockets were rinsed with disinfectant (3 mg/l) concentrations of ozone and an application of Metrogil-Denta ointment under a protective fixing bandage.

At that stage of treatment, patients were divided into two groups. Patients in the control group continued treatment according to the above-described regimen, while patients in the main group received additional complex treatment, including:

- systemic antioxidant therapy in the form of infusion of 400.0 ml of ozonated physiological solution at a concentration of 1.5 mg/ml, No. 5;

- systemic inactivation of endotoxemia with Reosorbilat 500.0 ml IV every other day, No. 5;

- osteotropic therapy aimed at normalizing mineral homeostasis, regulating calcium and phosphorus metabolism, and increasing bone mineral density.

For this purpose, patients took calcium D3 Nikomed, 1 tablet twice a day for long courses of more than 6 months.

# CHAPTER 5.

# CLINICAL FEATURES OF THE COURSE OF PERIODONTITIS IN PATIENTS WITH PUSTULOSIS

## 5.1. Results of a retrospective analysis of pemphigus incidence from 2014 to 2018.

According to a retrospective analysis of the incidence of pemphigus in the Republic of Uzbekistan for 2014-2018, we identified 135 patients, of whom 19 patients (14.1% of the total number of cases) were in 2014, there were 21 patients (15.6%), in 2016 there were 30 patients (22.2%), in 2017 there were 35 patients (25.9%), and in 2018 there were 30 patients (22.2%) (Fig. 1).

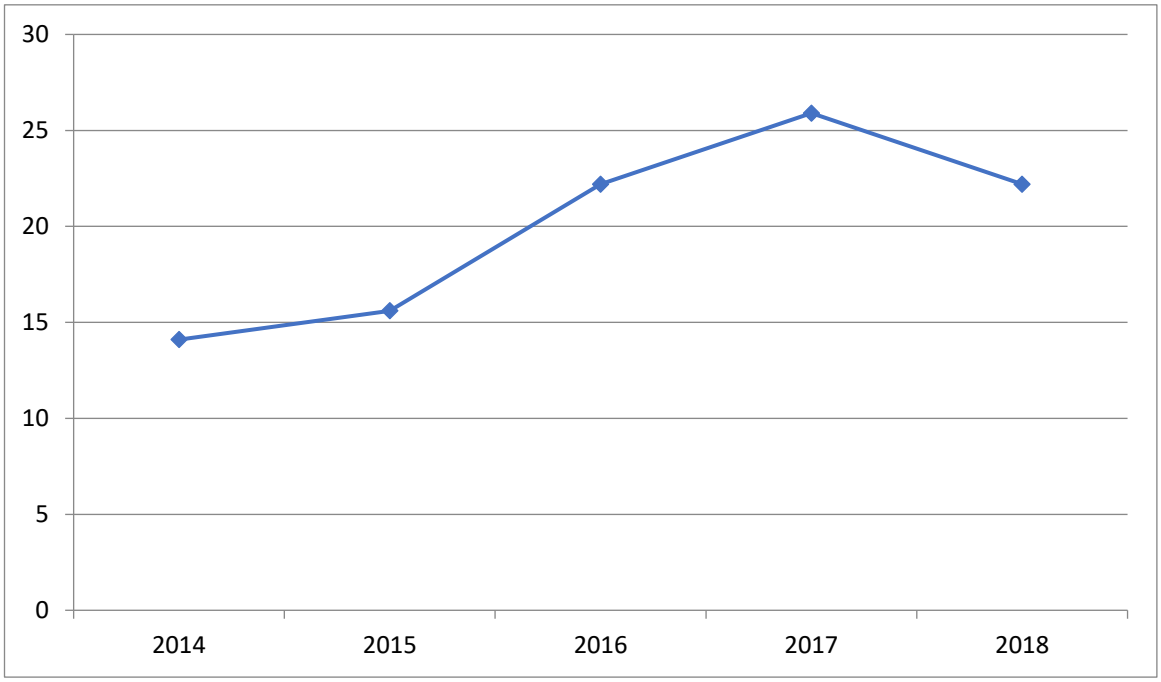



**Fig. 1. Results of a retrospective analysis of pemphigus incidence from 2014 to 2018.**

When studying the age of patients (135 people) with pemphigus, it was determined that there were four patients (2.96%) aged 18 to 29, and eight patients (5.93%) in each of the 30-39 and 40-49 age groups. The highest number of people with this pathology was noted in the 50-59 age group – 56 people (41.5%), and in the 60+ age group – 59 patients (43.7%).

A correlation was found between the age of patients and the number of patients with pemphigus ($\rho=0.925$, $p>0.05$).

As a result of the analysis, we found that women were most often affected – 97 people (71.9%), while men were affected much less frequently – 38 people (28.1%).

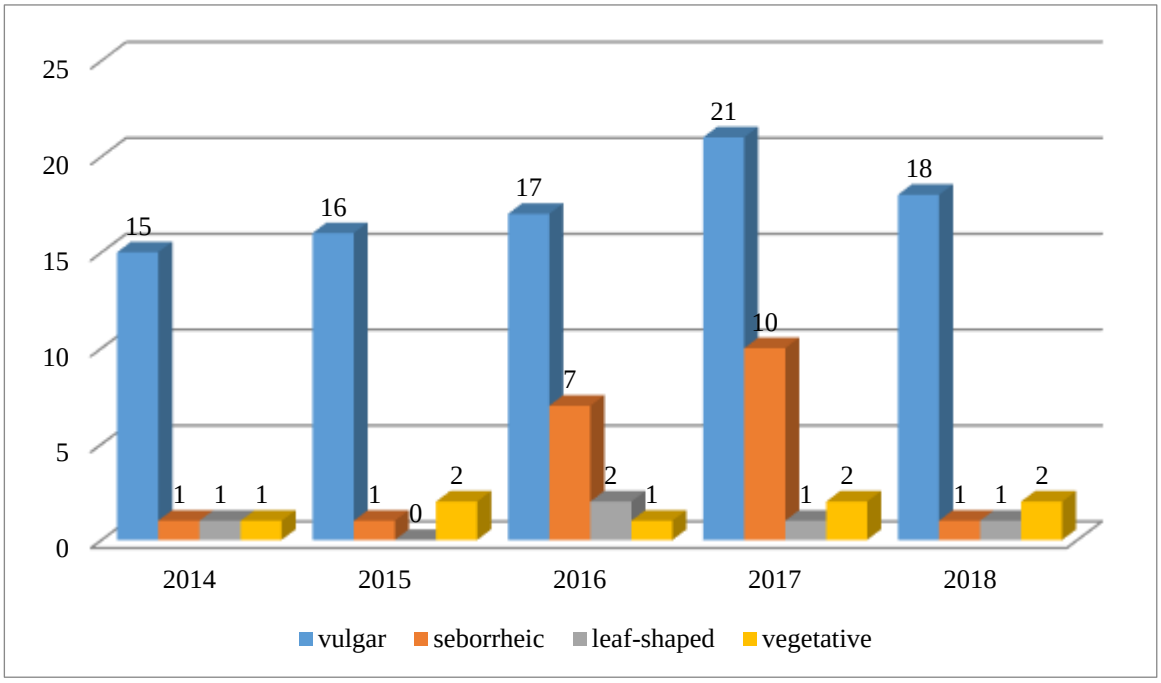



**Fig. 2. Frequency of detection of forms of pemphigus from 2014 to 2018**

Analyzing the prevalence of various forms of pemphigus in 135 patients, we found that vulgar pemphigus was more common in 98 (71.1%) patients. The clinical manifestations of this form consisted of the appearance of a primary lesion in the form of a sluggish blister occurring on apparently healthy skin and the mucous membrane of the mouth. Seborrheic (erythematous) pemphigus was observed in 22 (16.5%) patients. Foliate pemphigus was diagnosed in only 6 (4.44%) patients. Blisters appeared on the scalp and trunk. The blisters were located in the superficial layers of the epithelium, so when the blisters were opened, the exudate dried into thin crusts resembling sheets of puff pastry. Vegetative pemphigus was detected in 10 (7.4%) patients. Vegetative pemphigus manifested as small growths (vegetations) at the bottom of the erosion after the blister was opened. Blisters appeared in skin folds (between the buttocks, in the armpits, in the groin folds, under the mammary glands, behind the ears).

## 5.2. Clinical and immunological characteristics of the oral mucosa in patients with pemphigus

As a result of a comprehensive dental examination of 96 patients, 61 of them had vulgar pemphigus with manifestations on the skin and oral mucosa, complaining of lesions of the oral mucosa in the form of ulcers with uneven contours and pronounced redness of the gums. Complaints included sharply painful erosions, bad breath, bleeding when eating or touching, limited food choices, and inability to smile and talk easily and openly. Complaints included inability to eat properly, hunger, weakness, poor sleep, and sticky saliva.

During external examination of patients with pemphigus, regional lymph nodes (parotid, buccal, submandibular anterior, submandibular middle, submandibular posterior, submental, retroauricular, lateral neck, mentum, and retroauricular) were not enlarged. Seventeen patients had crunching in the TMJ. The color of the lips was congested with hyperemia and isolated erosive lesions.

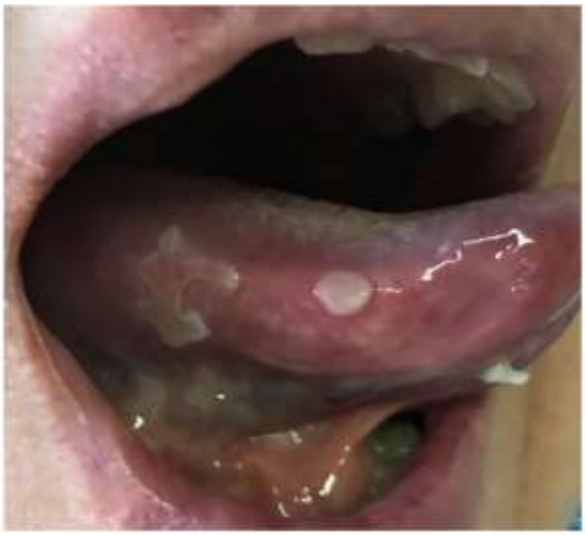


**Fig. 3. Clinical manifestations of vulgar pemphigus in the form of blisters on the lateral surface of the tongue**.

Of all four forms of pemphigus (vulgar, vegetative, erythematous, leaf-like), lesions of the oral mucosa were observed only in the vulgar form (Fig. 3). We determined that in 61 patients with pemphigus, lesions on the oral mucosa were found in the following areas: pharynx - 8 people (13.1%), cheek mucosa - 15 people (24.5%), soft palate - 7 people (11.4%), hard palate - 6 people (9.8%), tongue - 13 people (21.3%), lips - 12 people (19.9%) (Fig. 4).

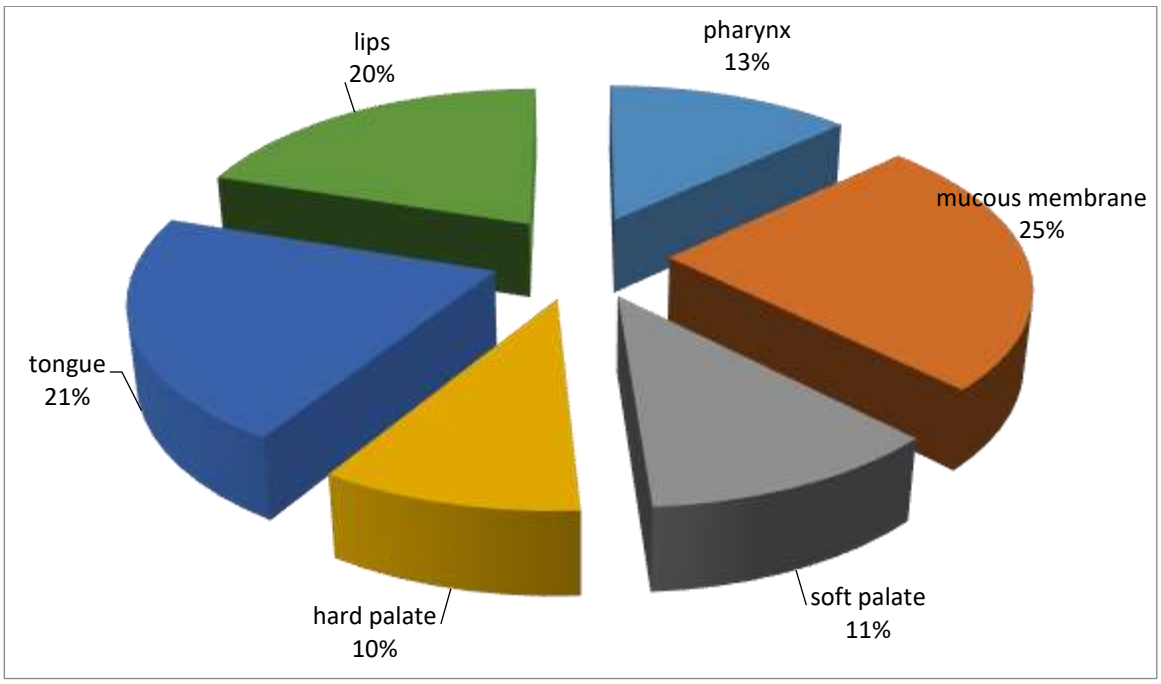



**Fig. 4. Localization of lesions in pemphigus on the oral mucosa.**

During examination of the oral cavity, irregularly rounded and oval erosions (3-5 elements) were noted on the unchanged mucosa in various locations. On palpation, they were painful, soft in consistency, and ranged in size from 0.5 mm to 2 cm or more. Fragments of blister membranes were visible around the periphery of the erosions, and Nikolsky's sign was observed when pulling on them.

During examination of the erosions, no signs of hyperkeratosis characteristic of KPL and leukoplakia and systemic lupus erythematosus were found, which was confirmed by luminescent diagnostics (Wood's lamp).

A detailed examination of dental status revealed malocclusion: deep in 29 patients (47%) and straight in 5 patients (24%).

During a comprehensive dental examination, 61 patients had a 100% prevalence of caries; the CPO index was 19+7.25, with a predominance of the "U" component (11.26%+7.54), which is associated with age-related changes. Four patients had fixed prostheses, and 57 patients required orthopedic prosthetics (40 of them had partial removable prostheses and 17 had fixed prostheses). Rational prosthetics in patients with pemphigus was constantly postponed due to relapses of the disease. Twenty-three patients (37%) needed tooth extraction. Partial tooth loss was observed in 37 patients (29%).

When examining the periodontal tissues of patients with pemphigus, chronic gingivitis was detected in 5 patients (8.3%) - mild degree, in 12 patients (19.6%) - moderate degree, and in 44 patients (72.1%) - severe degree according to the PMA index (Fig. 5).

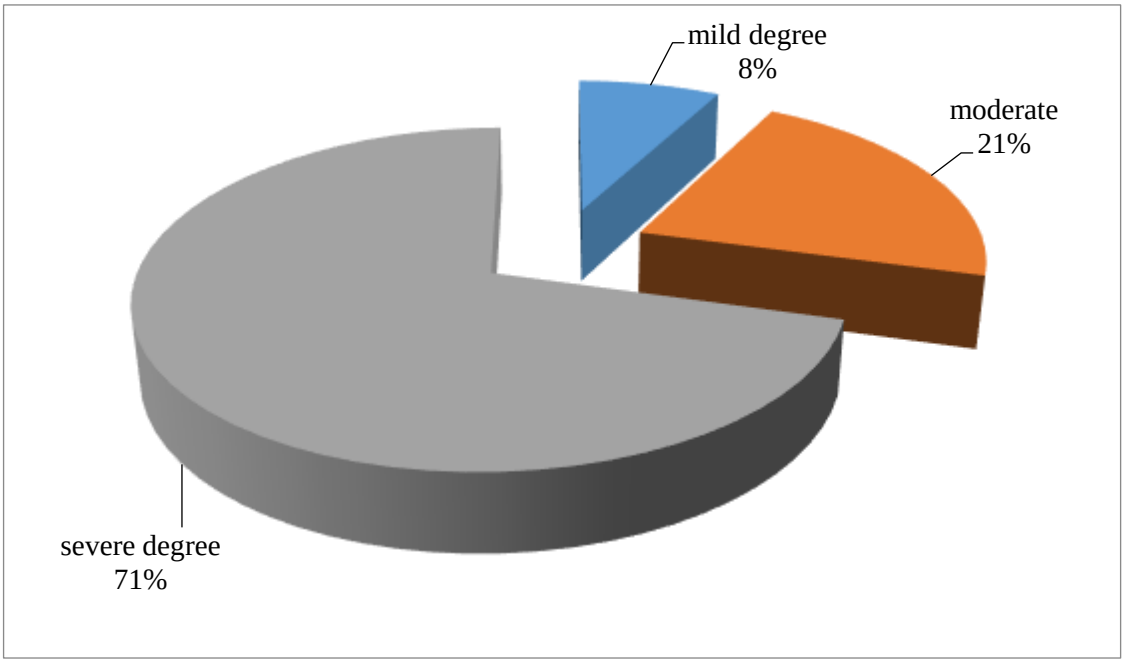



**Fig. 5. Severity of chronic gingivitis in patients with pemphigus.**

According to the SPITN index, all patients required professional oral hygiene and comprehensive treatment of periodontal tissues.

We found that oral hygiene was unsatisfactory in patients with pemphigus. The simplified oral hygiene index (OHI-S) was 3.38± 0.87, which corresponds to poor hygiene. The components of the hygiene index in patients indicated a significant amount of dental plaque and tartar—the dental plaque component was 1.47± 0.34, and the tartar component was 1.8±0.54.

**Subjective and objective condition of patients with pemphigus.** During the examination of the study group, the complaints most often characterized by increased pain syndrome during eating, chewing food – 61 people (100%); taste disturbance – 46 people (75%). Clinical manifestations in the oral cavity were assessed according to the following criteria: presence of painful erosions – 61 people (100%); halitosis – 61 people (100%); impaired tongue relief – 44 people (71%);

presence of dental plaque – 61 people (100%). The data of subjective and objective criteria are presented in Figure 6.

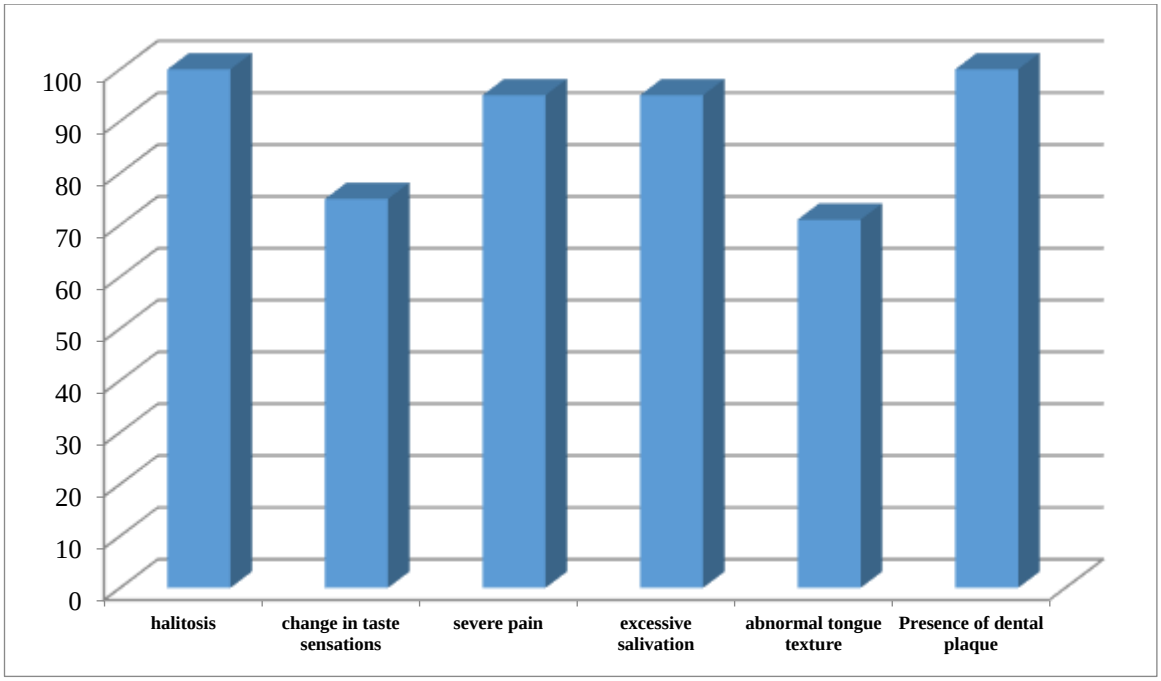



**Fig. 6. Structure of objective and subjective signs in patients with pemphigus before treatment.**

### 5.3. Results of the study of local humoral immunity of the oral cavity in patients with pemphigus.

In our studies of the results of immunological examination of 61 patients with isolated acantholytic pemphigus of the oral cavity before treatment in patients without negative dynamics of the process and with subsequent transformation of the process into a severe variant of the course (progression and dissemination of the lesion) showed significantly lower concentrations of IL-6 (1.9 pg/ml and below) and IL-1β (87 pg/ml and below) and higher concentrations of IL-4 (46 pg/ml and above) in the oral fluid of the latter. These results may indicate a depletion of the ability of the immune system of patients with pemphigus to produce pro-inflammatory cytokines (IL-6 and IL-1β), which leads to exacerbation of the chronic process and unfavorable course, as well as activation of the production of the immunomediator IL-4 (which ensures the course of the humoral immune response) during prolonged exposure to antigenic stimulation.

**Table 5**

**Content of cytokines IL-4, IL-1, IL-6 in oral fluid in patients with pemphigus**

| | IL-4, pg/ml | IL-6, pg/ml | IL-1β, pg/mL |
|---|---|---|---|
| Patients with pemphigus | 45.12+1.64 | 1.95+0.16 | 86.91+10.3 |
| Healthy individuals | 42.32+4.68 | 2.29+0.17 | 93.45+12.65 |

Note:* - the difference is statistically significant at $p \leq 0.05$.

## 5.4. Clinical and topographical features of pemphigus of the oral mucosa

Despite the success of domestic and foreign studies in clarifying the mechanisms of pathogenesis and improving methods of treating patients with true pemphigus, the problem of pemphigus remains relevant and is due to the severity of the disease, its incurability, and potential lethality.

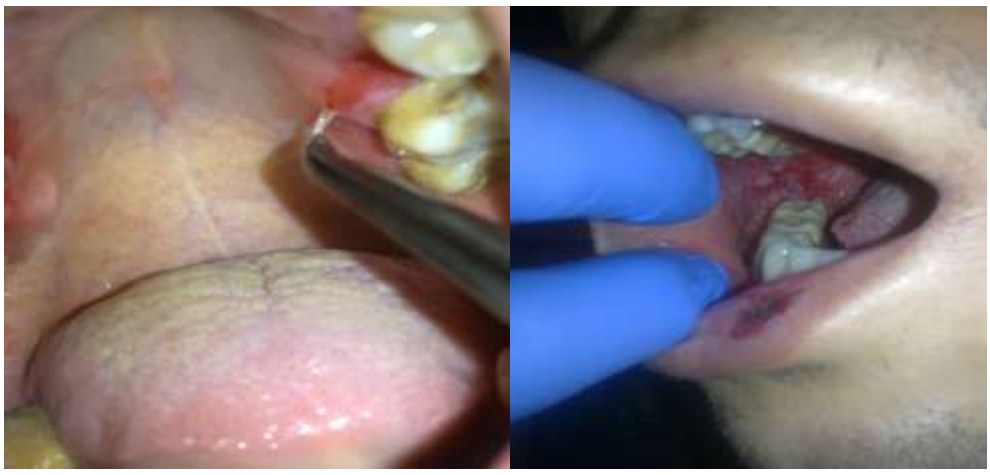


**Fig. 7. Research methods according to Nikolsky (Patient A.A. Diagnosis: vulgar pemphigus).**

Clinical experience shows that dentists often assess the condition of the oral cavity symbolically, without thorough visual examination. However, in order to assess the clinical condition of the dental status based on examination parameters, it is important to evaluate and identify the symptoms of the lesion in each specific case.

As is known, the microstructure of the tissues of the oral mucosa differs in topographic zones, which serve as key links in visual examination.

The literature available to us lacks data on the condition of the oral cavity and an in-depth clinical and topographical characterization of its gingival manifestations of pemphigus [41,42].

All of the above determined the purpose of the study: to investigate the frequency of gum complex lesions, risk factors, and the clinical infrastructure of periodontal diseases in patients with vulgar pemphigus.

Forty-nine patients with vulgar pemphigus receiving corticosteroid therapy and in the stages of clinical exacerbation were examined. Multiple erosions, often merging with each other, were recorded in patients with unchanged oral mucosa.

The affected areas had an extensive erosive surface of bright red color, often with a bluish tint, covered with a grayish-white fibrinous coating.

The bright red erosions were located against the background of unchanged mucosa. Fragments of blisters were found around the periphery of the erosions, and Nikolsky's symptom was elicited when pulling on the edges. Some of the erosions were covered with a grayish-white, easily removable coating.

A survey of patients with pemphigus showed that 10% of those examined complained of pain in the oral cavity, while 19 (38.77%) of those surveyed experienced discomfort in the oral cavity; 24 (48.98%) complained of pain when talking and chewing food, and 6 (12.24%) refused to talk and eat because of the pain. Thirty-one (63.26%) patients complained of excessive salivation, and 39 (79.6%) complained of bad breath (Table 3).

All patients had complaints related to general intoxication of the body. Thus, 68 (36.73%) patients complained of decreased appetite, and 33 (67.38%) of insomnia. Thirty-seven (75.5%) patients experienced symptoms of intoxication such as nausea, dizziness, and weakness, while 35 (71.43%) had elevated body temperature; 29 (59.18%) had a history of frequent diarrhea; 42 (85.71%) suffered from frequent acute respiratory infections, and 19 (38.78%) had pneumonia.

Studies have shown that patients with pemphigus receiving corticosteroid therapy of varying duration differed significantly: the intensity of complaints of general intoxication and the frequency of background somatic pathology increased significantly with the duration of the disease.

**Table 3**

**Complaints made by patients with pemphigus**

| Complaints | Duration of disease, scales | | | |
|---|---|---|---|---|
| | Up to 1 year | 1-3 years | More 3 years | Total |
| 1. Pain:<br>1.1. Discomfort in the oral cavity | 5/45.45 | 6/33.33 | 4/20 | 19/38.7 |
| 1.2. Pain when talking and eating | 4/36.36 | 10 | 14 | 24 |
| 1.3. Refusal to talk or eat due to pain | 2/18 | 2 | 2 | 6/12 |
| 2. Excessive salivation | 5/45.45 | 10/55.5 | 16 | 31 |
| 3. Bad breath | 6/54.55 | 13/72.22 | 18/90.0 | 39/79.60 |
| 4. Decreased appetite | 4 | 7/38.89 | 11 | 18 |
| 5. Insomnia | 5/45.45 | 12/66.67 | 16 | 33/67.35 |
| 6. Symptoms of intoxication (nausea, dizziness, weakness) | 7/63.64 | 12 | 18 | 37/75.51 |
| 7. Elevated temperature | 6/54.55 | 12 | 17 | 35/71.43 |
| 8. Diarrhea | 5/45.45 | 10 | 14 | 29/59.18 |
| 9. Frequent OPZ | 8/72.73 | 16/88.89 | 18 | 42/85.71 |
| 10. Pneumonia | 3/27.27 | 6 | 10 | 19 |
| 11. Total number of patients | 11/100 | 18 | 20 | 49 |

Note: the numerator shows the absolute number of patients, the denominator shows the percentage of the number in the group.

A detailed analysis of the anatomical and topographical location of the lesions (Table 5) showed that the highest frequency of their location was on the mucous membrane of the cheeks – 21 (47.86%) patients; the second most frequent location

was the back of the tongue and the floor of the mouth – 18 (36.13%) patients; isolated lesions of the gums ranked third among other topographical areas of the oral cavity in terms of frequency of involvement in patients with pemphigus – 16 (32.65%). The frequency of detection of gingival localization of lesions is 16 (32.65%).

**Table 4**

**Anatomical and topographical location of lesions in pemphigus of the oral mucosa**

| Topographic zone of the SOPR | Up to 1 year | 1-3 | Over 3 years | Total |
|---|---|---|---|---|
| 1. Isolated lesion of the gums and alveolar papillae | 2/18 | 6/33 | 8/40.01 | 16/32.65 |
| 2. Lips, excluding the oral surface | 3/27.27 | 4/22.22 | 5/25 | 12 |
| 3. Cheeks (right, left) | 2/18.18 | 8/44.4 | 11 | 21/42.861 |
| 4. Soft palate | 1/9.09 | 3/16.67 | 5/25 | 9/18.37 |
| 5. Hard palate | 2/18.18 | 4/22.22 | 7/35.0 | 13/26.53 |
| 6. Back of the tongue, bottom of the mouth | 3/27.27 | 6/33.3 | 9 | 18/36.73 |
| 7. Transitional fold of the vestibule of the oral cavity | 1/9.09 | 3/16.67 | 5/25.0 | 9/18.37 |
| 8. Retromolar region | 2/18.18 | 3/16.67 | 6 | 11/22.49 |
| 9. Total number of patients | 11/100.0 | 18 | 20 | 49 |

Other locations of lesions account for 12 (24.49%) (lips, excluding the oral surface) and 11 (22.44%) (retromolar region) (Table 5).

It should be noted that Table 5 shows the frequency of lesion localization in individual areas of the SOPR. As can be seen from the data presented, the frequency of occurrence of individual anatomical and topographical localizations increases with the duration of the underlying disease.

It should be noted that in pemphigus, combined lesions of the SOPR involving 2-3 or more areas are common.

As can be seen from Table 5, lesions of the alveolar gingiva and alveolar papillae account for 77.54% of all localizations of lesions in pemphigus of the oral

mucosa, while isolated localization of the alveolar ridge accounted for 32.56% and combined lesions involving other topographic areas of the periodontium accounted for 44.89%.

The periodontal aspects of pemphigus vulgaris are poorly understood, although its autoimmune origin suggests the involvement of the periodontium, the most important morphofunctional complex of the oral cavity.

Table 5

**Frequency of involvement of the alveolar gingiva in the pathological process in patients with pemphigus**

| Localization variant: | up to 1 year | 1-3 years | >3 years | Total |
|---|---|---|---|---|
| 1. Isolated lesion of the gums and alveolar papillae | 2/18 | 6/33 | 8/40 | 16 |
| 2. Combined lesion involving other topographic areas of the SOPR | 3/27.27 | 8 | 11 | 22 |
| 3. Without alveolar gingival involvement | 6/54.55 | 4/22.2 | 1 | 11/22.45 |
| Total | 11/100.0 | 18/100.0 | 20/100.0 | 49 |

Note: the numerator is the absolute number of patients; the denominator is the percentage of patients in the group.

Inflammatory periodontal diseases occupy one of the leading places in the structure of dental pathology and currently show no tendency to decline.

Periodontal disease has a negative impact on the condition of all organs and systems of the body, worsens human health indicators and quality of life, and impairs the treatment and prognosis of combined systemic pathology.

In this regard, it is important to note the increase in the frequency of isolated and combined periodontal lesions with an increase in the duration of pemphigus that we have discovered.

Given the insufficient study of the problem as a whole, it is relevant to conduct a full-scale clinical study devoted to the study of the clinical features of inflammatory periodontal diseases when combined with pemphigus.

### 5.5. Clinical features of inflammatory periodontal diseases in patients with pemphigus

A study of periodontal status in patients with pemphigus showed that generalized periodontitis occurs in 100.0% of cases. Its structure was dominated by **GPTs –** 62.27±6.89% versus 5.0±3.45% in the comparison group; GPT – 22.44±5.45% versus 25.0±6.85% and GPLS – 14.29±5.0% versus 37.5±7.65% (Table 6).

**Table 6**

**Clinical forms of inflammatory periodontal diseases (%) depending on the duration of pemphigus**

| Group, years, index | Gingivitis | Generalized periodontitis, degree | | |
|---|---|---|---|---|
| | | light | moderate | severe |
| Control n=20 | $\frac{13}{32,5 \pm 7,41}$ | $\frac{15}{37,5 \pm 7,65}$ | $\frac{10}{25,0 \pm 6,85}$ | $\frac{2}{5,0 \pm 3,45}$ |
| | Patients with pemphigus n=49 | | | |
| Up to 1 year n=11 | – | $\frac{5}{21,81 \pm 12,84}$ | $\frac{6}{28,57 \pm 13,62}$ | $\frac{10}{47,62 \pm 15,06}$ |
| 1-3 years n=25 | – | $\frac{2}{10,0 \pm 7,07}$ | $\frac{4}{20,0 \pm 9,43}$ | $\frac{14}{70,0 \pm 10,80}$ |
| >3 years n=20 | – | – | $\frac{1}{5,55 \pm 5,12}$ | $\frac{17}{94,44 \pm 51,12}$ |
| Total | $\frac{49}{100}$ | $\frac{7}{14,29 \pm 5,0}$ | $\frac{11}{22,44 \pm 5,95}$ | $\frac{31}{63,27 \pm 6,88}$ |

Note: the numerator is the number of patients; the denominator is the percentage of patients in the group.

Thus, the frequency of GPTs exceeds the corresponding values of the comparison group with a high degree of certainty. At the same time, the frequency

of GPTs progressively increases with the duration of pemphigus: with a disease duration of up to 1 year, its frequency was 47.62±5.06%; with a duration of 1-3 years, it was 70.0±10.8%; and with a duration of more than 3 years, it was 94.44±5.12%. Against this background, there is a decrease in the prevalence of GPT and GPLS, the frequency of which was 23.81±12.84% - 28.57±13.62% for diseases lasting up to 1 year; 1-3 years – 10.0±7.01% - 20.0±9.43% and more than 3 years – 0.0 – 5.55±5.12% (Table 7).

**Table 7**

**Clinical forms of inflammatory periodontal diseases depending on the localization of pemphigus**

| Localization variant | Gingivitis | Generalized periodontitis, degree | | |
|---|---|---|---|---|
| | | Mild | Moderate | Severe |
| **Control, n=40** | 13 / 32,5 | 15 / 37,5 | 10 / 25,0 | 2 / 5,0 |
| **Patients with pemphigus, n=49** | | | | |
| Isolated lesions of the gums and alveolar ridges, n=11 | - | 2 / 18,18 | 1 / 5,55 | 8 / 72,73 |
| Combined lesion with involvement of other topographic areas, n=18 | - | 2 / 11,11 | 5 / 27,28 | 11 / 66,67 |
| No involvement of the alveolar zone, n=20 | - | 3 / 15,0 | 5 / 25,0 | 12 / 60,0 |
| Total | 49 / 100 | 7 / 14,29 | 11 / 22,44 | 31 / 63,27 |

Note: the numerator is the number of patients; the denominator is the percentage of patients in the group.

From a clinical point of view, it is important to assess the condition of the periodontium depending on the location of the lesions in order to evaluate their pathogenetic significance in the formation of inflammatory-destructive periodontal lesions (Table 7).

The studies did not reveal any significant differences in the prevalence of periodontitis depending on the location of the lesions. Thus, the frequency of GTP in isolated lesions of the gums and alveolar ridges was 72.73±13.92%; in combined lesions, it was 66.67±11.11%, and in isolated lesions, it was 60.0±0.95%; intergroup differences in all cases are not significant (120.05%). The frequency of GTST was 5.55±6.9%; 27.78±10.55% and 25.0±9.68%. GPLS – 18.18±11.6%; 11.11±7.4% and 15.0±7.98%, respectively, in isolated, combined gum lesions and without alveolar zone lesions (Table 9).

It can be assumed that the leading factors in the initiation of inflammatory-destructive periodontal lesions are not the localization of the lesions, but systemic autoimmune disorders that determine the activity of aggressive factors and deplete the body's compensatory capabilities.

It should be noted that a distinctive feature of periodontal damage in pemphigus is the generalized nature of the damage, severe inflammatory-destructive disorders, and a persistent progressive course with frequent exacerbations that coincide with periods of pemphigus exacerbation.

The index assessment of the condition of the periodontium was carried out taking into account the duration of pemphigus (Table 10) and the anatomical and topographical localization of the lesions (Table 11).

The degree of periodontal destruction (PI index) in patients with pemphigus as a whole exceeded the corresponding value in the control group by 154.2% (P<0.01); the gingivitis index (GMA) – by 91.91% (P<0.01); oral hygiene ( -OHI-S) by 67.9% (P<0.01), and gingival bleeding (Müller index) by 116.9% (P<0.01).

**Table 8**

**Indices of inflammation, destruction, hygiene, and bleeding of the periodontium depending on the duration of pemphigus**

| Group, duration of corticosteroid use, years | DI, points | PMA, % | OHI-S, score | Bleeding, score |
|---|---|---|---|---|
| **Control**, n=40 | 2.65±0.15 | 35.25±1.66 | 2.87±0.14 | 1.42±0.10 |

| Patients with pemphigus, n=49 | | | | |
|---|---|---|---|---|
| Up to 1 year n=11 | 5.28±0.22 | 50.24±2.32 | 3.62±0.15 | 2.65±0.11 |
| 1-3 years n=18 | 6.44±0.31°,Δ | 66.31±3.11 | 4.88±0.21° | 3.00±0.14° |
| >3 years n=20 | 7.62±0.42°,Δ,X | 78.45±3.62°,Δ,X | 5.81±0.27°,Δ,X | 9.52±0.17°,Δ,X |
| Total n=49 | 6.66±0.22° | 67.65±23° | 4.82±0.22° | 3.08±0.11 |

Note: ° - P<0.05 relative to control;
Δ - P<0.01 relative to up to 1 year; X - P<0.01 relative to 1-3 years.

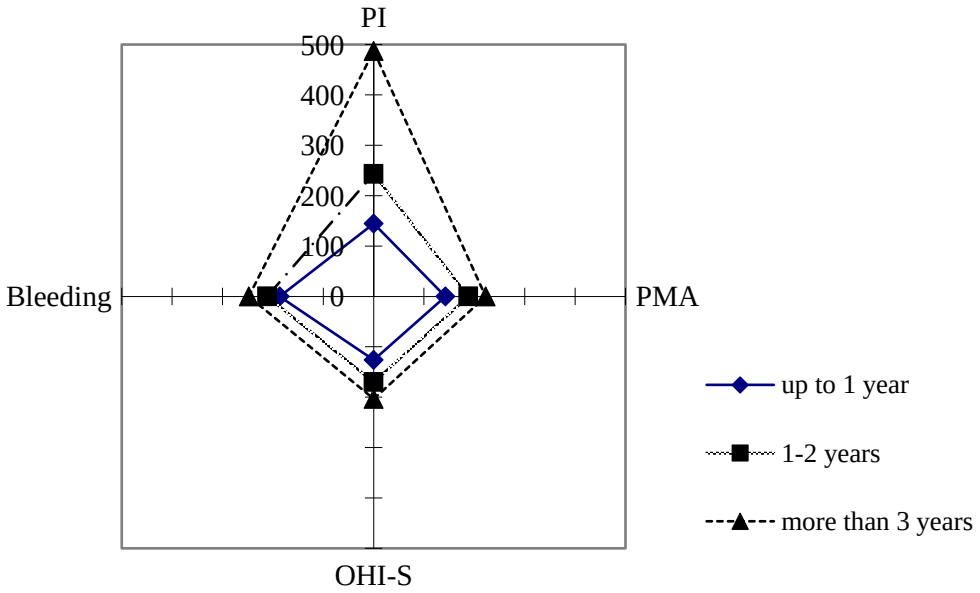



**Fig. 7. Dynamics of hygiene, inflammation, destruction, and bleeding indices of the periodontium in patients with pemphigus depending on the duration of the disease (relative to the control).**

Thus, the PI index value in patients with pemphigus exceeded the corresponding values of the control group with a disease duration of up to 1 year by 99.25% (P<0.01); 1-3 years by 143.02% (P<0.01) and more than 3 years by 187.55% (P<0.01); the corresponding dynamics for the PMA index was 42.52% (P<0.01); 88.11% (P<0.01) and 122.55% (P<0.01); the OSU-Sindex oral hygiene index – 26.13% (P<0.01); 70.03% (P<0.01)

Progressive deep inflammatory-destructive periodontal damage with an increase in the duration of pemphigus was established.

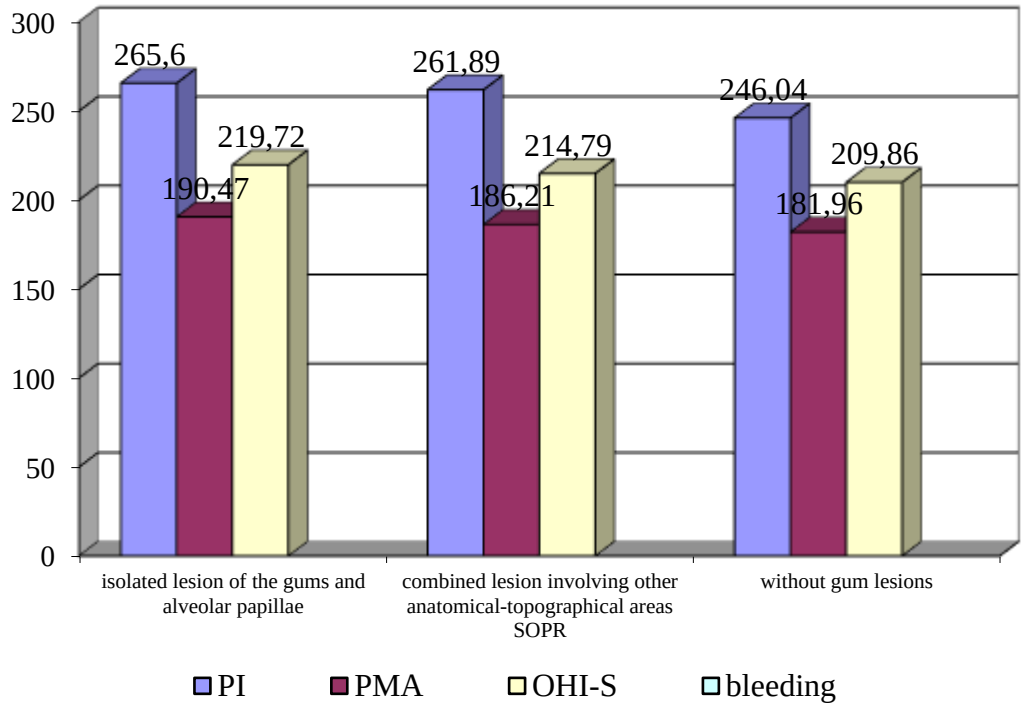



**Fig. 8. Dynamics of periodontal hygiene, inflammation, and destruction indices depending on the localization of lesions (in % relative to the control).**

Thus, in isolated periodontal lesions, the PI index exceeded the control values by 165.66% (P<0.01); in combined lesions, it exceeded the control values by 161.89% (P<0.01), and in the absence of alveolar gingival lesions, it exceeded the control values by 146.04% (P<0.01); the corresponding dynamics for the PMA index were 90.77% (P<0.01); 86.21% (P<0.01) and 81.96% (P<0.01); for the OHI-S index by 69.69% (P<0.01); 70.38% (P<0.01) and 60.98 (P<0.01); bleeding index - 119.42% (P<0.01); 114.79% (P<0.01) and 109.86% (P<0.01) (Table 9, Fig. 8).

The clinical features of periodontitis associated with pemphigus are erosive (destructive) lesions, high bleeding tendency, increased destruction of the periodontal complex, and poor oral hygiene, indicating a high risk of systemic infection and an urgent need for specialized periodontal care.

**Table 9**

**Indices of inflammation, destruction, hygiene, and bleeding of the periodontium depending on the location of pemphigus**

| Localization variant | PI, points | PMA, % | OHI-S, points | Bleeding, points |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| Control n=40 | 2.65±0.15 | 35.25±1.66 | 2.87±0.14 | 1.42±0.10 |
| | Patients with pemphigus, n=49 | | | |
| Isolated lesions of the gums and alveolar papillae | 7.04±0.32 | 67.15±3.01 | 4.87±0.24 | 3.12±0.14 |
| Combined lesion involving other topographic areas of the SOPR | 6.94±0.30 | 65.64±2.87 | 4.89±10.23 | 3.05±0.15 |
| No alveolar zone involvement | 6.52±0.29 | 64.14±2.65 | 4.62±0.22 | 2.98±0.13 |
| Total | 6.66±0.22 | 67.52±2.32 | 4.82±0.22° | 3.08±0.11° |

Note: ° - P<0.05 relative to control; $^{\Delta-}$ P<0.05 relative to isolated lesion; $^{X-}$ P<0.05 relative to combined lesion.

It has been established that, in addition to systemic factors in the genesis of periodontitis, local risk factors (irritating effects of toothpastes, restorations, orthopedic structures, tobacco smoking) play an important role.

**Table 10**

**Risk factors that aggravate periodontal disease in patients with pemphigus**

| Risk factors | GPLS | | GST | | GPT | | Total | |
|---|---|---|---|---|---|---|---|---|
| | K | P | K | P | K | P | K | P |
| 1. Irritating, traumatic, and other effects of toothpastes | 1/ 6.66 | 5/ 71.43 | 1/ 10.0 | 9/ 81.82 | 1/ 50.0 | 27 87.10 | 3 11.11±6.00 | 41 83.37±5.32 |
| 2. Gum injury caused by restoration | 1 6.66 | 3 | 2 20.0 | 6/ 54.55 | - | 17/ | 3 11.11±6.00 | 26 53.06±7.13 |
| 3. Injury to the gums caused by orthopedic structures | 2 13.3 | 4 57.14 | 2 20.0 | 5 45.45 | - | 12 | 4/ 14.81±6.90 | 21/ 42.29±7.06 |
| 4. Tobacco smoking | 2 13.13 | 5 71.43 | 3 | 7/ | 1/ 50 | 18/ | 6/ 22.22±8.0 | 30/ 61.22±6.96 |
| 5. Use of corticosteroids and cytostatics | - | 7/ 100.0 | - | 11/ 100.0 | - | 31/ 100.0 | 0/ 0 | 44/ 100.0 |
| 6. Polysystemic pathology | 5/ 33.33 | 7/ 100.0 | 7 70.0 | 11 100.0 | 2 100.0 | 31 100.0 | 27 100.0 | 49 100.0 |
| Total number of patients | 15 100.0 | 7 100.0 | 10 100.0 | 11 100.0 | 2 | 31 | 27 100.0 | 49 100.0 |

Note: C – control group; P – patients with pemphigus;
the numerator is the absolute number; the denominator is the percentage of patients in the group.

In the pathogenesis of periodontal disease in patients with pemphigus, along with general risk factors (polysystemic pathology, use of corticosteroids and cytostatics), the following local risk factors play a major role: the irritating and desquamating effect of toothpastes containing abrasive components, the frequency of which in patients with pemphigus was 83.27±5.32% versus 11.11±6.0% in the control group (P<0.05); the corresponding ratio of this local risk factor
risk factor, such as gum trauma caused by restoration, was 53.06±7.12% versus 11.11±6.0 (P<0.05); gum trauma caused by orthopedic structures was 42.29±7.06% versus 14.81±6.9% (P<0.05); tobacco-induced SOPR reactions in patients with pemphigus were recorded in 61.22±6.96% of cases versus 22.22±8.06% (P<0.05) in the control group (Table 10).

Periodontal complex disorders in pemphigus are associated with its resistance and, obviously, can determine the severity of the clinical course, the effectiveness of treatment, and the prognosis of the disease.

The results of clinical studies of periodontal diseases indicate a recurrent and progressive course of combined pathology and determine the involvement of dentists and dermatologists in their treatment.

### 5.6. Features of mineral exchange and bone metabolism

With the introduction of corticosteroids, the results of preventive and supportive therapy for pemphigus have improved significantly, and their use in dermatological practice has restored the ability to work for most patients. However, the effect of these drugs on the oral cavity in patients with pemphigus remains poorly studied, and there is no information on mineral and bone metabolism in various biological environments in patients with periodontitis against the background of pemphigus.

The alveolar ridge, as an integral part of the skeletal system of the supporting apparatus, reacts to exogenous and endogenous factors affecting the human body (Polozhenikov, 2003).

Systemic bone tissue damage, or osteoporosis, plays a significant role in the pathogenesis of generalized periodontitis. Scientific studies have demonstrated clinical and pathogenetic relationships between GP and osteoporotic changes in the skeleton (Kutusheva D.R., 2010).

However, in everyday dental care for patients with periodontitis, the presence of systemic osteoporosis and systemic bone loss in the periodontal complex is not taken into account.

Therefore, we conducted a comprehensive assessment of biochemical markers of bone resorption and formation in patients with periodontitis against the background of pemphigus.

The results obtained in a comparative study of bone tissue element profiles indicate mineral metabolism disorders in patients with periodontitis.

The direction and intensity of mineral metabolism disorders were determined by the nature of the background pathology.

In patients with GP without pemphigus, statistically significant differences were noted in the indicators of mineral homeostasis in gingival and peripheral blood, with more pronounced changes in gingival blood. Thus, the protein concentration in gingival blood was reduced relative to the control by 23.55% ($P<0.01$); in the periphery, it was reduced by 5.45% ($P>0.05$).

In patients with pemphigus, more significant changes in protein concentration were found, with no significant differences in gingival and peripheral blood parameters ($P>0.05$); The protein level was reduced relative to the control in gingival blood by 32.27% ($P<0.01$) and in peripheral blood by 22.49% ($P<0.01$) (Table 13, Fig. 6).

The total protein level reflects the activity of calcium in the blood serum, since half of it is bound to proteins and albumins.

All patients with periodontitis had a significant decrease in calcium content, which was especially pronounced in patients with pemphigus. These phenomena can be explained by the effect of glucocorticosteroid therapy, since corticosteroids stimulate calcium leaching. In patients without pemphigus, a significantly more

pronounced decrease in calcium was found in gingival blood (by 17.96%, $P<0.05$) and a less significant decrease in the periphery (by 9.8%, $P>0.05$).

In patients with pemphigus, no significant differences in calcium concentration were found in gingival blood and in the periphery; the active concentration was 29.8% ($P<0.01$) and 26.53% ($P<0.01$), respectively.

Serum calcium is one of the main mineral components of bone. The total calcium content in serum reflects the dynamic balance of hormonal calcium-regulated effects. A decrease in calcium content triggers calcium-regulating mechanisms. Activation of calcium-regulating mechanisms is usually accompanied by an increase in phosphorus concentration.

Thus, in patients with periodontitis without pemphigus, the concentration of phosphorus in gingival blood was increased by 13.88% ($P<0.05$); in the periphery, it was increased by 3.45% ($P>0.05$). Shifts in phosphorus content in steroid osteoporosis were characterized by hypophosphatemia, with its concentration in gingival blood reduced by 23.28% ($P<0.01$) and in the periphery by 20.69% ($P<0.01$).

It is evident that a significant role in the development of osteoporosis in patients with pemphigus and hypophosphatemia and hypocalcemia is played by a decrease in resorption and increased loss of trace elements in the urine caused by prolonged use of corticosteroids. At the same time, all patients with periodontitis showed an increase in the bone resorption marker TRP and a decrease in the bone remodeling marker ALP. More significant changes were observed in patients with pemphigus.

Table 11

**Mineral metabolism and bone metabolism indicators in patients with periodontitis and pemphigus**

| Indicators | Control group | | Patients with GP without pemphigus | | Patients with periodontitis and pemphigus | |
|---|---|---|---|---|---|---|
| | Gums | Periphery | Gums | Periphery | Gums | Periphery |
| Protein, g | 88.32±2.11 | 87.81±13.22 | 67.52±2.69▪ | 83.51±2.33 | 59.82±2.44°ˣ | 60.31±2.55°ˣ |
| Calcium, mol/L | 2.45±0.11 | 2.46±0.10 | 2.01▪±0.06 | 2.20±0.08 | 1.72±0.06°ˣ | 1.80±0.06°ˣ |
| Phosphorus, mol/L | 1.16±0.05 | 1.18±0.04 | 1.32▪±0.05 | 1.20±0.05 | 0.89±0.04°ˣ | 0.92±0.04°ˣ |
| Tartrate-resistant acid phosphatase, ME | 18.52±0.32 | 18.71±0.36 | 23.15▪±1.03 | 19.62±0.08 | 27.82±1.25°ˣ | 26.91±0.12°ˣ |
| Acid phosphatase, ME | 72.3±2.55 | 71.3±2.62 | 52.07▪±2.44 | 68.03±2.44 | 42.31±2.03°ˣ | 44.52±2.05°ˣ |

Note: ▪ - P<0.05 relative to control; ° -P<0.05 relative to gingiva; × -P<0.05 relative to patients without pemphigus.

Thus, in patients with GP without pemphigus, TRK activity in gingival blood was increased by 25.0% (P<0.01); in the periphery - by 4.80% (P>0.05). The corresponding dynamics in patients with pemphigus was 50.25% (P<0.01) and 43.32% (P<0.01).

Alkaline phosphatase activity in patients with GP without pemphigus was reduced in gingival blood by 27.98% and in the periphery by 4.60% (P>0.05). Similar dynamics in patients with pemphigus were 41.48% (P<0.01) and 37.56% (P<0.01) (Fig. 3.5.1).

The use of modern biochemical markers of bone remodeling allows us to assess the state of bone tissue metabolism, determine the rate of metabolic processes occurring in it, the rate of bone loss leading to the development of osteoporosis, as well as select adequate treatment and evaluate its effectiveness.

Currently, scientists are increasingly interested in the onset and development of metabolic disorders in young and middle-aged people who are reaching peak bone mass. Calcium plays an important role in bone mineralization, and its physiological level is maintained by calcium-regulating hormones. In turn, the production of parathyroid hormone is strictly regulated by the concentration of ionized calcium in the serum. This feedback system is one of the most important homeostatic mechanisms affecting bone mineral density (BMD).

Equally important for explaining the results of the study is the selective effect of PTH on different types of bone tissue. The works of M. Parisien et al. (2002) and P. Cristiansen et al. (2013) show that a slight increase in PTH levels is associated with a decrease in trabecular bone mineral density in experiments [82,110].

No explanation for this phenomenon has yet been found, but when comparing the condition of the MPC in patients with CGD, whose PTH levels significantly exceeded the control levels.

To compare the mineral metabolism in patients with periodontitis against a background of pemphigus, a dispersion analysis was performed. Studies have shown that patients with pemphigus receiving corticosteroid therapy of varying duration differed significantly in terms of the intensity of complaints of general intoxication

and the frequency of background somatic pathology increased significantly with the duration of the disease and the corresponding indicators.

Since it is known that the level of calcium absorption decreases with age, high serum calcium levels may be associated with increased osteoclastic resorption as a result of metabolic osteopathy, as in the case of glucocorticoid therapy in patients with pemphigus.

High levels of ionized calcium in patients with GP against the background of pemphigus can be explained by accelerated bone metabolism in the presence of a local inflammatory process—chronic generalized periodontitis of moderate to severe severity and, as a result, active resorption of the alveolar bone.

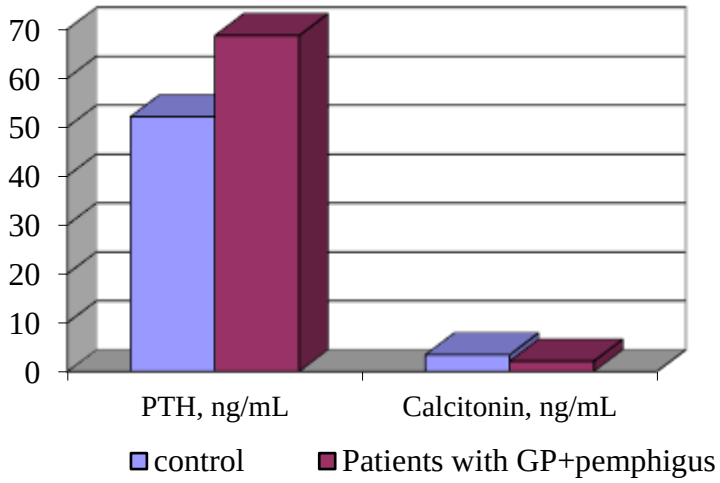



**Fig. 9. Levels of calcium-regulating hormones in the blood serum of patients with generalized periodontitis and pemphigus.**

Another important factor determining the level of calcium homeostasis is the change in the level of calcium-regulating hormones ( , PTH, and CT). In our study, we also conducted a corresponding analysis of PTH and CT indicators in patients with GP and performed a comparative assessment with similar data obtained from individuals in the control group (Fig. 7).

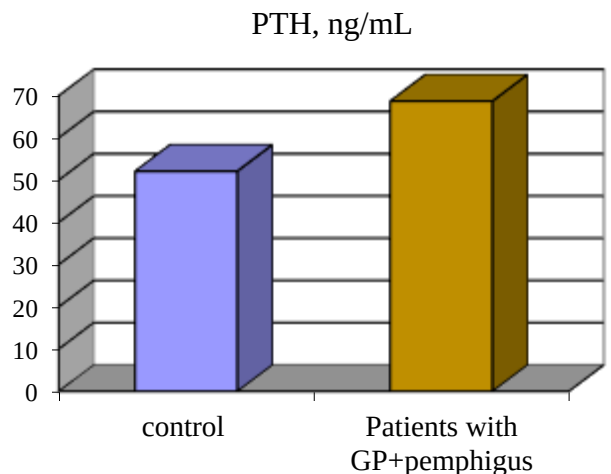
A comparative analysis of the data showed that high PTH levels in patients with generalized periodontitis associated with pemphigus differed significantly from those in the control group. At the same time, among patients suffering from GPD associated with pemphigus, its level was 68.7±4.38 ng/ml, but the role of another

calcium-regulating hormone, calcitonin, in the regulation of bone metabolism processes has not been definitively determined. At the cellular level, calcitonin is a potent inhibitor of osteoclastic resorption, but many authors claim that its blood levels have no significant effect on calcium homeostasis or MPC.

Therefore, it is quite difficult to determine its role in the development of periodontal pathology, since a decrease in its level relative to control values was obtained in the studied group. At the same time, low CT levels among the studied groups were found in patients with GPP+pemphigus (2.11±0.34 ng/L), which differed significantly from the control values (3.42±0.29 ng/mL). It is possible that the role of calcitonin in the development of metabolic osteopathies has yet to be established.

To decide whether to include osteotropic drugs in the comprehensive treatment of any bone pathology, it is necessary to determine the nature and rate of bone metabolism. In our study, the bone formation marker osteocalcin and the bone resorption marker P-CrossLaps were used for this purpose. A comparative analysis of the data obtained in the main groups showed (Table 14) that the level of osteocalcin in patients with GR+pemphigus was 43.2% higher and averaged 0.484±0.05 ng/ml. The decrease in osteocalcin levels in the examined patients is quite understandable given the increased PTH levels and its effect on the metabolic activity of osteoblasts. The result of this effect is a decrease in bone formation, which was shown in the results of our study (Fig. 8).

Thus, when characterizing the features of mineral and bone metabolism in patients with GPP with OP pemphigus, it should be noted that patients have the following characteristic signs of bone metabolism disorders, which probably lead to the development of periodontal pathology.



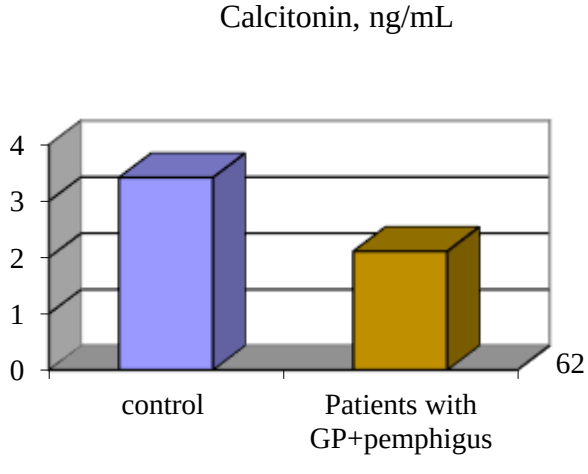



**Fig. 10. Bone metabolism indicators in patients with generalized periodontitis with pemphigus.**

Disruption in the calcium-regulating hormone system, determined by an increase in PTH levels against a background of a decrease in CT, leads to suppression of osteoblastic activity (a decrease in the bone formation marker osteocalcin) against a background of preserved bone resorption, which in turn leads to a disruption of the remodeling cycle with a shift towards bone resorption.

Elevated levels of ionized calcium are observed in patients with GP associated with pemphigus, indicating a disturbance in calcium homeostasis caused by low CT levels. In addition, according to, literature data show that patients with osteopenia have low levels of T3sv and T4sv relative to control values, which, according to a number of authors [89], may also affect bone metabolism by increasing irreversible collagen degradation. However, further research is needed to answer the question of the effect of low-normal levels of thyroid hormones on the development and course of periodontal pathology.

## 5.7. Radiographic and densitometric assessment of the alveolar process of the jaw

As part of the skeletal support system, the alveolar ridge reacts to exogenous and endogenous factors affecting the human body.

Systemic bone damage, or osteoporosis, plays a significant role in the pathogenesis of periodontitis.

The manifestations of systemic osteoporosis include the intensification of osteodystrophic processes in the jaws [57].

In progressive osteoporosis, changes in the skeleton are widespread. As a result of a systemic shift in metabolism caused by impaired calcium absorption from

the gastrointestinal tract and the suppressive effect of glucocorticosteroid hormones on the proliferation and functional activity of osteoblasts, changes occur in the bones of the skeleton, including the jawbones [48].

Modern comprehensive diagnosis of periodontal lesions that have developed against the background of systemic osteoporosis is a pressing issue in clinical dentistry.

X-ray examination is an informative method for diagnosing generalized periodontitis. Densitometric evaluation of diagnostic X-ray images has been proposed for assessing the mineral saturation of the jaws.

The use of densitometric studies allows for the assessment of the qualitative parameters of jawbone tissue and provides a quantitative characterization, from the actual structures of the jawbones to the characteristics of their density at various points [11, 79, 73, 113, 88, 117].

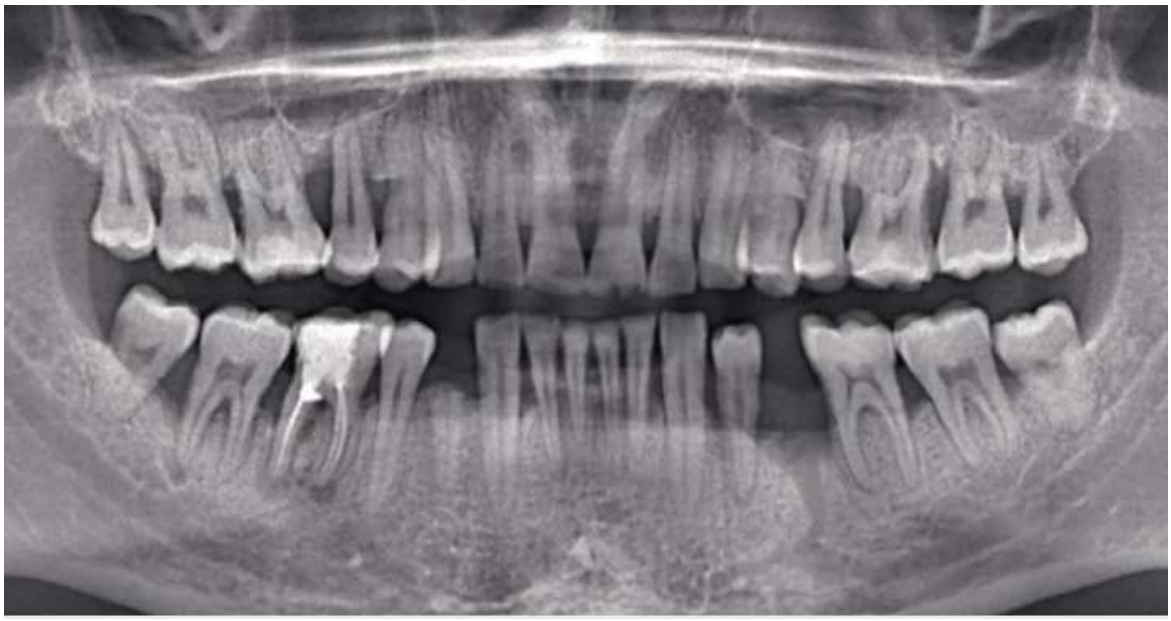


**Fig. 10. X-ray of patient R. Diagnosis: periodontitis.**

In this regard, we conducted a special study to provide radiographic characteristics and evaluate the radiographic densitometric profile of alveolar bone tissue in patients with periodontitis against the background of pemphigus.

To assess the condition of periodontal bone tissue, we used orthopantomography of the lower third of the facial skull. Orthopantomographic images were subjected to densitometric processing using indirect radiodensitometry.

When studying orthopantomograms in patients with pemphigus, a uniform change in bone density in the horizontal plane, a decrease in the amount of cancellous bone, thickness, and the presence of cortical plate on the vestibular and oral surfaces of the alveolar bone were noted. Such changes in bone tissue indicate uneven resorption and the presence of osteoporosis.

In some patients, there is virtually no dentate bone on the vestibular surface of the root, and the compact plate is significantly depleted. In the absence of alveolar bone tissue on the vestibular surface, the minimum thickness of the spongy layer on the lingual side is detected. In patients with generalized periodontitis without pemphigus, the radiographic symptoms corresponded to moderate-severe periodontitis - a decrease in the height of the alveolar ridge by more than 43.5 root length, foci of bone tissue rarefaction, and a decrease in the clarity of the boundaries of bone beams and trabecular spaces.

**Table 12**

**Mineral density of alveolar jaw tissue (in %) light absorption of orthopantomograms in patients with periodontitis depending on the presence or absence of pemphigus**

| Examined | Lower jaw | | Upper jaw | |
|---|---|---|---|---|
| | Molars | premolars | Molars | Premolars |
| **Control** | 87.81±3.22 | 83.92±3.61 | 88.01±2.92 | 84.12±3.11 |
| **Patients with periodontitis** | | | | |
| Without pemphigus | 73.62±3.21 | 71.22±3.11 | 73.82±2.81▪ | 71.33,3.05▪ |
| With pemphigus | 62.312.66 | 60.82±2.81 | 61.92±2.65° | 59.81±2.45 |

Note:▪ - (P<0.05) relative to the control group; ° - (P<0.05) relative to patients without pemphigus.

Analysis of orthopantomograms of patients diagnosed with chronic periodontitis showed a significant decrease in bone mineral density. In patients with pemphigus, the bone density in all sections of the dentoalveolar system was lower (P<0.05) than the corresponding values in patients without pemphigus, which indicates the presence of a long-term pathological process in patients in this group.

Thus, in patients with periodontitis without pemphigus, the mineral density of the lower jaw bone tissue in the molar projection area was reduced by 16.16% (P<0.05); and in patients with pemphigus, by 29.04% (P<0.01); the decrease in the premolar region was 18.13% (P<0.05) and 27.52% (P<0.01); The corresponding dynamics in the upper jaw were as follows: molars – by 16.17% (P<0.05) and 29.64% (P<0.01) and premolars – by 15.2% (P<0.05) and 28.9% (P<0.01) (Table 12).

Densitometric examination of orthopantomograms allows assessing the decrease in optical density of bone tissue, which is pathogenetically associated with the development of local inflammation in the periodontium and systemic bone mineralization disorders.

The level of mineralization of the jawbone tissue reflects the condition of the body's bone tissue as a whole and does not depend on the type, severity, or orientation of the bone beams. Quantitative assessment of this indicator can serve as a diagnostic and prognostic criterion for bone metabolism [80; pp. 588-590].

The data obtained on the progressive decrease in the mineral density of the alveolar bone in patients with pemphigus indicates a pathogenetic link between changes in the mucous membrane, periodontal bone tissue, and systemic osteoporosis. It is evident that these changes occur simultaneously and determine the need for systemic and local osteotropic therapy.

# CHAPTER VI.
# CLINICAL AND LABORATORY EVALUATION OF THE EFFECTIVENESS OF TREATMENT OF INFLAMMATORY PERIODONTAL DISEASES IN PATIENTS WITH PLEUROPHTHYMA

## 6.1. Clinical condition of the periodontium and SOPR during treatment

The studies showed that the treatment had a positive effect on the clinical condition of the periodontium. The number of complaints decreased significantly when studying the general well-being of patients. An objective study also demonstrated an improvement in the clinical condition of the periodontium, with normalization of the color of the gingival margin mucosa, tightening of the gingival papillae, and a significant reduction in bleeding during probing.

Analysis of clinical indices showed that a higher clinical effect was obtained in the main group. Thus, the degree of inflammatory-destructive periodontal damage decreased in the control group by 27.45% ($P<0.01$); in the main group – by 51.56% ($P<0.01$); the corresponding reductions in the intensity of periodontal inflammation (PMA index) were 46.18% ($P<0.01$) and 83.97% ($P<0.01$); oral hygiene (OHI-S index) – 45.55% ($P<0.01$) and 80.91% ($P<0.01$) and bleeding index – 34.52% ($P<0.01$) and 55.88% ($P<0.01$) (Table 15).

It should be noted that the studied indicators of periodontal status in the main group were lower than the corresponding values in the comparison group with high statistical significance ($P<0.01$) (Table 15).

Comparing the clinical data obtained with the changes in orthopantomograms, it should be noted that after 3 months, no noticeable radiographic changes were observed in patients in the main and comparison groups.

**Table 13**

**Indicators of hygiene, inflammation, destruction, and bleeding of the periodontium during treatment**

| Groups | PI, points | PMA, % | ONI-S, score | Bleeding, score |
|---|---|---|---|---|
| Comparison group: Before treatment | 6.63±2.65 | 67.35±2.64 | 4.82±2.03 | 3.10±0.12 |
| After treatment | 4.81±0.15 | 36.25±0.80 | 2.63▪±0.75 | 2.03▪±0.06 |
| Main group: before treatment | 6.71±2.83 | 67.443.01 | 4.82±2.11 | 3.06±0.14 |
| After treatment | 3.25±0.14▪,° | 10.81±0.25▪,° | 0.92±0.05▪,° | 1.35±0.06▪,° |

Note: ▪ - P<0.05 in relation to the value before treatment; ° - P<0.05 in relation to the comparison group.

However, in patients in the main group receiving the developed pathogenetically justified treatment complex in parallel with clinical stabilization, no progression of destruction (resorption) was noted on orthopantomograms.

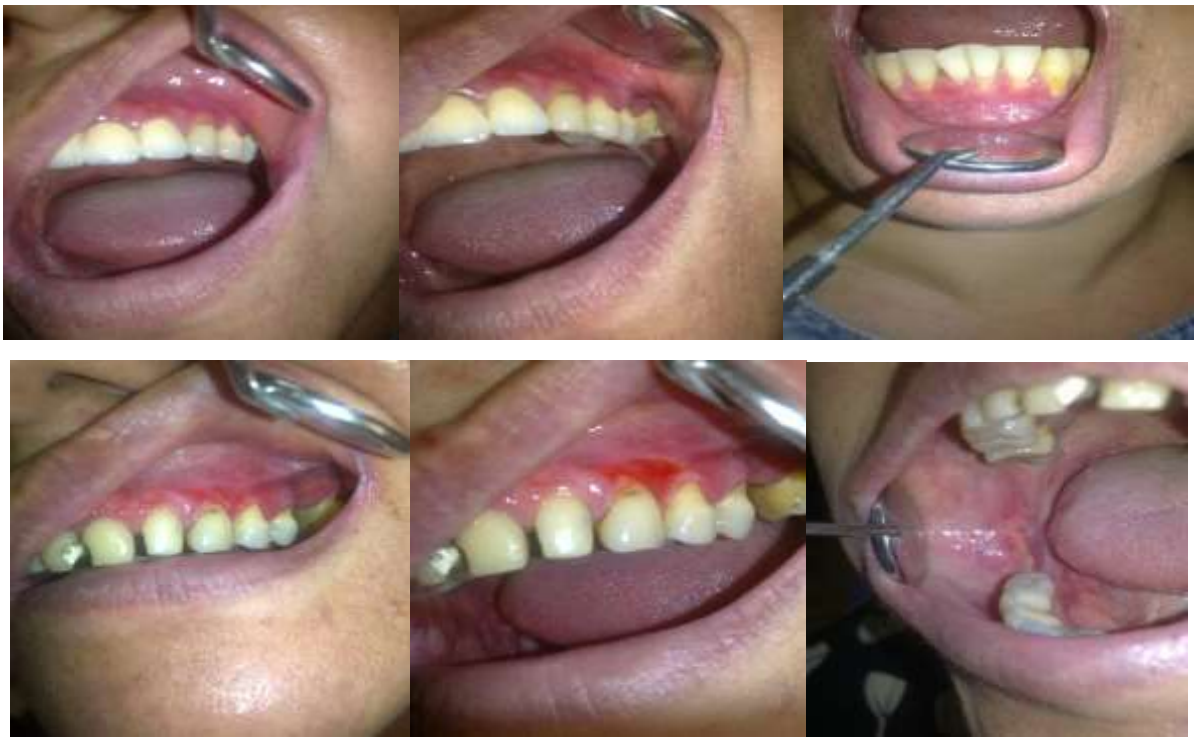


**Fig. 10. Patient S. S. Diagnosis: vulgar pemphigus.**

On orthopantomograms of patients in the comparison group, progressive resorption was noted at the specified time periods, in which the vertical type of

resorption was combined with active foci of osteoporosis and the absence of clear contours of the tops of the interdental alveolar septa.

Before treatment, the eruptions on the mucous membrane of the SOPR were represented by erosions located on the mucous membrane of the cheeks and the red border of the lips. The erosions had uneven edges, a diameter of up to 1.5 cm, a pink color, a white coating, fragments of epidermis along the edge zone, and a halo of hyperemia around the element. During examination, acantholytic cells were found in smears from the erosions, and Nikolsky's sign was positive. Table 16 shows the differences in quantitative indicators of clinical efficacy when using different methods of treating acantholytic pemphigus.

**Table 14**

**Clinical efficacy of treatment of patients with pemphigus**

| Indicator | Group Comparison | Main group |
|---|---|---|
| Absence of fresh cavity elements, days | 6.25±0.65 | 4.11±0.44▪ |
| Sluggish epithelialization of erosions, days | 8.62±0.91 | 6.11±0.32▪ |
| Active epithelialization of erosions, days | 12.11±0.31 | 10.00±0.44▪ |
| Absence of Nikolsky's sign, days | 9.81±0.66 | 6.81±0.32▪ |
| Normalization of laboratory parameters, days | 22.31±0.81 | 14.31±0.85▪ |
| Duration of maximum daily hormone intake, days | 18.22±0.62 | 14.20±0.92▪ |
| Duration of inpatient treatment, days | 45.61±2.81 | 30.11±1.80▪ |
| Complications from treatment, % | 12.13 | 13.13±8.72▪ |

Note: ▪ - $P<0.05$ relative to control.

Treatment did not lead to progression of the disease in any patient with acantholytic pemphigus. Clinical improvement was observed in all patients.

In the main group, a statistically significant ($P<0.05$) faster clinical effect was observed for all clinical parameters studied, and side effects of glucocorticosteroid

therapy (development of Cushing's syndrome, osteoneurotic syndrome, arterial hypertension) were observed significantly less frequently in the main group.

The high clinical efficacy of systemic therapy made it possible to reduce the duration of maximum glucocorticosteroid administration by more than 4 days.

The higher efficacy of periodontitis therapy in patients in the main group was also established when comparing the duration of treatment and the duration of remission. Thus, in patients in the main group, the average duration of treatment was 18.5±0.5 days (P<0.01). The average duration of periodontitis remission in the main group was 6.3±0.22 months; in the control group, it was 3.6±0.18 months (P<0.01).

A comparative analysis showed that the average total effectiveness of complex treatment on the clinical condition of the periodontium in the main group exceeded that of the control group by more than 27.79% (Table 17).

One of the pressing problems in modern dentistry is improving the effectiveness of treatment for periodontal diseases occurring against a background of chronic diseases, in particular pemphigus. This combination of pathologies due to metabolic disorders, increasing endogenous intoxication and lipid peroxidation, and progressive osteoporosis against the background of glucocorticosteroid use exacerbates the clinical course of periodontal disease and worsens the quality of life of patients.

**Table 15**

**Comparative analysis of the effectiveness (intravenous) of treatment on the clinical condition of periodontitis**

| Indicators | Effectiveness compared to: | Groups | |
|---|---|---|---|
| | | comparison | main |
| PI, score | Before treatment | 27.45 | >51.56 |
| | With control | | 30.52 |
| PMA, % | Before treatment | 46.18 | 83.97 |
| | With control | | >29.01 |

| | | | |
|---|---|---|---|
| ONI-S, score | Before treatment | 45.55 | 80.91 |
| | With control | | >27.96 |
| Bleeding, score | Before treatment | 34.52 | 55.88 |
| | With control | | >23.63 |
| Σ mean | | | >27.79 |
| Place | | 2 | 1 |

Thus, clinical studies have established the high efficacy of complex systemic therapy for periodontitis in patients with pemphigus, which allows its use to be recommended in the complex therapy of periodontitis in this category of patients.

One of the mechanisms of periodontitis development against the background of pemphigus is pronounced local and systemic endogenous intoxication, accumulation of under-oxidized products and VSMM, creating pathogenetic prerequisites for the aggravation of local inflammatory-destructive periodontal lesions. In this regard, studies of the POL-AOS processes and the content of VSMM against the background of the developed comprehensive treatment method were carried out.

## 6.2. Results of studying the POL-AOS system in the dynamics of treatment

Clinical and biochemical studies have revealed the high effectiveness of the developed treatment regimen on the POL-AOS processes in gingival and peripheral blood. At the same time, for all studied indicators, a higher effect ($P<0.05$) was established in patients of the main group (Table 16). It should be noted that complex (systemic and local periodontal therapy) contributed to positive dynamics of the studied indicators not only in gingival blood, but also in systemic blood flow. Thus,

in the comparison group of patients, the intensity of HL and the level of MDA in gingival blood after treatment exceeded the corresponding control values by 45.12% ($p<0.01$) and 35.75% ($p<0.01$), respectively; while the activity of SOD, CT, and GP remained lower than the corresponding control values by 28.57% ($p<0.01$); 31.39% ($p<0.01$) and 39.11% ($p<0.01$); similar dynamics in the main group were 18.13% ($p<0.05$); 15.03% ($p<0.05$); 8.37% ($p>0.05$); 13.56% ($p<0.05$) and 11.1% ($p>0.05$).

An even more significant difference was observed in peripheral blood. Thus, in the comparison group of patients, the intensity of HL exceeded the control values by 37.08% ($p<0.01$); the MDA level by 50.25% ($p<0.01$); SOD, CT, and GP activity was reduced by 22.58% ($p<0.01$); 18.5% ($p<0.01$) and 37.54% ($p<0.01$), respectively. During this study period, the intensity of HP in patients in the main group exceeded the control value by 5.07% ($p>0.05$); MDA levels by 19.21% ($p<0.01$); SOD, CT, and GP activity was lower by 6.45% ($p>0.05$); 7.35% ($p>0.05$), and 8.11% ($p>0.05$), respectively (Table 19).

At the same time, the total clinical effectiveness of normalizing the POL-AOS processes in the main group exceeded the corresponding dynamics of the comparison group in gingival blood by >31.65%; in peripheral blood by >36.46% (Table 16).

Table 16

**Indicators of lipid peroxidation and antioxidant activity in blood in the dynamics periodontitis treatment**

| Indicators | Control, healthy periodontium | Group: | | | |
|---|---|---|---|---|---|
| | | Comparison | | main | |
| | | Before treatment | After treatment | Before treatment | After treatment |
| | | gums | | | |
| HL, imp/sec | 24.81±1.11 | 42.01±1.65· | 36.02·,x ±1.25 | 41.90·±2.00 | 29.32·,x, °±1.11 |
| MDA, nmol/L | 1.93±0.07 | 3.09±0.11 | 2.62·,x ±0.11 | 3.11·±0.14 | 2.22·,x, °±0.10 |
| SOD UE ml | 2.51±0.12 | 1.20±0.06 | 1.80·,x ±0.08 | 1.24·±0.05 | 2.30·,x, °±0.09 |
| KG, mkat/min/ml | 22.33±1.06 | 10.59±0.45· | 15.32·,x ±0.66 | 10.64·±0.48 | 19.31·,x, °±0.92 |
| GP, nmol/min/ml | 157.85±7.32 | 78.01±3.22 | 110.31·,x ±4.32 | 76.32·±3.22 | 140.32·,x, °±6.81 |
| | | periphery | | | |
| HL, imp/sec | 25.03±1.03 | 41.62±2.03 | 34.31±1.24·,x | 41.83 ± 1.62 | 26.30·,x, °±1.03 |
| MDA, nmol/L | 2.03±0.06 | 3.05·±0.14 | 2.72±0.10·,x | 3.07 ± 0.11 | 2.42·,x, °±0.11 |
| SOD, U/ml | 2.48±0.11 | 1.50±0.06 | 1.92±0.08·,x | 1.46±0.06 | 2.32·,x, °±0.08 |
| CT, mkat/min/ml | 21.62±0.95 | 14.09±0.65 | 17.62±0.65·,x | 14.14 ± 0.65 | 20.03·,x, °±1.00 |
| GP, nmol/min/ml | 163.8±8.03 | 81.00±3.22 | 102.31±4.83·,x | 80.32 ± 3.65 | 150.42·,x, °±6.21 |

Note: · - P<0.05 relative to control;

x - P<0.05 in relation to the value before treatment;

° - P<0.05 in relation to the control group.

Table 17

**Comparative analysis of treatment effectiveness (%) based on POL-AOS indicators**

| Indicators | Effectiveness compared to | Group | |
|---|---|---|---|
| | | comparison | Main |
| **Gingival blood** | | | |
| HL, imp/sec | Before treatment | 14.26 | 30.02 |
| | With control | | >35.61 |
| MDA, nmol/L | Before treatment | 15.21 | 28.62 |
| | With control | | >30.60 |
| SOD, IU/ml | Before treatment | 50.0 | 91.67 |
| | With control | | >29.41 |
| CT, mkat/min/ml | Before treatment | 44.64 | 81.48 |
| | With control | | >29.41 |
| HR, bpm/min/ml | Before treatment | 41.40 | 83.86 |
| | With control | | >33.42 |
| On average | | | 31.65 |
| Total: | | 3 | 1 |
| **Periphery:** | | | |
| HL, imp/sec | Before treatment | 17.56 | 37.13 |
| | With control | | >35.78 |
| MDA, nmol/L | Before treatment | 10.82 | 21.17 |
| | With control | | >32.35 |
| SOD, IU/ml | Before treatment | 28.0 | 58.40 |
| | With control | | >35.56 |
| CT, mkat/min/ml | Before treatment | 25.05 | 41.65 |
| | With control | | >24.89 |
| KG, mkat/min/ml | Before treatment | 26.31 | 87.41 |
| | With control | | >53.73 |
| On average | | | >36.46 |
| Total: | | 2 | 1 |

Analysis of POL-AOS indicators clearly shows that the dynamics of these indicators during the treatment of periodontitis in patients with pemphigus in the systemic bloodstream is more effective. The higher level of normalization of POL-AOS indicators in the main group is determined by the characteristics of the therapy, in which local treatment was combined with systemic antioxidant therapy.

### 6.3. Results of the VSMA study in the dynamics of treatment

In recent years, the study of endogenous intoxication syndrome has been given a major role. It has been proven that endotoxemia develops in all pathological conditions associated with increased catabolism or blockade of the body's detoxification systems.

Practically any pathology and any stressful effect on the body activates the processes of free radical oxidation, which leads to the accumulation of toxic substances associated with endotoxicosis.

A decrease in the serum and peripheral blood content of POL products and an increase in the activity of enzymes that detoxify active forms of oxygen in patients with pemphigus was accompanied by a synchronous decrease in the amount of toxic substances classified as endotoxins.

In the comparison group and the main group, the amount of VSMM in the studied fractions was statistically significantly reduced compared to the corresponding values before treatment ($p<0.05$) (Table 21). At the same time, the level of all VSMM fractions in the main group was statistically significantly lower than the corresponding indicators in the comparison group.

When studying the concentration of VSMM after treatment in gingival blood and systemic blood flow, significant intergroup differences were found. Thus, in the comparison group, the value of 20 nm fractions in gingival blood decreased by 9.37% ($p<0.05$); and at the periphery, this decrease no longer had statistically significant differences from the pre-treatment value – 4.93% ($p>0.05$); the corresponding ratios for the 254 nm fractions were 7.0% ($p>0.05$) and 6.21% ($p>0.05$); for the 260 nm fractions, 11.76% ($p>0.05$) and 8.85% % ($p>0.05$); the 280

nm fractions were 6.54% (p>0.05) and 4.61% (p>0.05). Thus, the dynamics of the decrease in VSMM in gingival blood significantly outpaced systemic blood flow.

**Table 18**

**VSMM indicators in the dynamics of treatment**

| Indicators | Control, healthy periodontium | Group: | | | |
|---|---|---|---|---|---|
| | | Comparison | | main | |
| | | Before treatment | After treatment | Before treatment | After treatment |
| | | gums | | | |
| E 220 nm | 0.216±0.095 | 0.33±0.01· | 0.300±0.005 | 0.329±0.01˙ | 0.246± 0.01˙,x, ∘ |
| E 254 nm | 0.222±0.01 | 0.314±0.005· | 0.292 ±0.01° | 0.316·±0.01˙ | 0.252± 0.01˙,x, ∘ |
| E 260 nm | 0.231±0.01 | 0.442±0.01 | 0.390 ±0.01 | 0.438±0.005˙ | 0.251±0.05˙,x, ∘ |
| E 280 nm | 0.224±0.01 | 0.321±0.01 | 0.300 ±0.01 | 0.319±0.01˙ | 0.246± 0.01˙,x, ∘ |
| periphery | | | | | |
| E 220 nm | 0.220±0.01 | 0.284±0.005 | 0.270±0.005° | 0.288±0.005˙ | 0.236± 0.01˙,x, ∘ |
| E 254 nm | 0.219±0.01 | 0.290±0.01 | 0.272±0.01 | 0.292±0.01˙ | 0.240± 0.01˙,x, ∘ |
| E 260 nm | 0.228±0.005 | 0.418±0.01 | 0.381±0.01° | 0.422±0.01˙ | 0.234± 0.01˙,x, ∘ |
| E 280 nm | 0.226±0.01 | 0.304±0.01 | 0.290±0.01 | 0.308 ± 0.05 | 0.241± 0.01˙,x, ∘ |

Note: · - P<0.05 relative to control; o - P<0.05 relative to pre-treatment; x - P<0.05 relative to comparison group.

In patients of the main group, a significantly different dynamics of endotoxicosis indicators was established, which consisted in a synchronous decrease in VSMM in gingival blood and at the periphery. At the same time, the dynamics of all studied indicators had statistically significant differences in values before

treatment. Thus, the amount of VSMA fraction 220 nm decreased in gingival blood by 25.23% % % ($p<0.01$); in the periphery - by 18.06% ($p<0.01$); the 254 nm fraction decreased by 20.25% ($p<0.01$) and 17.84% ($p<0.01$), respectively; the 260 nm fraction decreased by 42.71% ($p<0.01$) and 44.55% ($p<0.01$); 280 nm fractions – by 22.83% ($p<0.01$) and 21.75% ($p<0.01$) (Table 21).

It should be noted that the concentrations of VSMM in the comparison groups did not decrease to control levels (patients without pemphigus).

**Table 19**

**Comparative analysis of treatment efficacy (in %) based on VSMM indicators**

| **VSMA, cond. units** | Effectiveness compared to | Group: | |
|---|---|---|---|
| | | comparison | main |
| **Gingival blood** | | | |
| E 220 nm | Before treatment | 9.37 | 25.23 |
| | Control | | >45.84 |
| E 254 nm | Before treatment | 7.00 | 20.25 |
| | Control | | >48.62 |
| E 260 nm | Before treatment | 11.76 | 42.70 |
| | Control | | >56.81 |
| E 280 nm | Before treatment | 6.54 | 22.88 |
| | Control | | >55.54 |
| On average | | | >51.70 |
| Total: | | 2 | 1 |
| **Periphery:** | | | |
| E 220 nm | Before treatment | 4.93 | 18.06 |
| | Control | | >57.11 |
| E 254 nm | control | 6.21 | 17.81 |
| | control | | >48.29 |
| E 260 nm | Before treatment | 8.85 | 44.55 |
| | control | | >66.85 |
| E 280 nm | Before treatment | 4.61 | 21.75 |
| | Control | | >65.02 |
| On average | | | >59.32 |

| | | | |
|---|---|---|---|
| Total: | | 2 | 1 |

## 6.4. Changes in mineral metabolism and bone metabolism indicators during treatment

When examining blood parameters (Table 23) after treatment, a tendency toward normalization of mineral homeostasis, bone metabolism, and collagen metabolism was observed: protein, phosphorus, and calcium levels increased, TRK activity decreased, and ALP activity increased. A decrease in OP and OPfree against the background of an increase in OPsv indicated positive dynamics of bone remodeling.

The severity of these processes in gingival blood and peripheral blood was statistically more significant in patients in the main group (Table 23).

At the same time, the dynamics of the studied indicators in the control group in gingival blood significantly exceeded the indicators of systemic blood flow. Thus, the protein concentration in gingival blood increased by 17.16%, and in peripheral blood by 10.13%; the corresponding ratios of calcium concentration dynamics were 11.11% - 2.79%; phosphorus - 15.55% - 7.52%; TRCF 10.63%–9.50%; CF 30.25%–13.0% (Table 4.4.1).

In patients in the main group, the positive dynamics of the studied indicators of gingival blood satisfactorily coincided with the corresponding dynamics of blood flow.

Thus, the protein concentration increased in gingival blood by 33.88%; in the periphery – by 33.08%; the corresponding dynamics of calcium and phosphorus were 32.95% - 24.86% and 21.59% - 25.27%; the decrease in TRK activity and the increase in ALP activity were 27.23%–28.29% and 56.03%–49.03%, respectively.

After treatment, the values of mineral metabolism and collagen metabolism did not reach the control values.

**Table 20**

**Indicators of mineral metabolism and bone metabolism in the dynamics of periodontal treatment**

| Indicators | Control, healthy periodontium | Group: | | | |
|---|---|---|---|---|---|
| | | Comparisons | | Main | |
| | | Before treatment | After treatment | Before treatment | After treatment |
| **Gums:** | | | | | |
| 1. Protein g/l | 88.32±2.11 | 60.02±2.45▪ | 70.32±2.65▪,° | 59.03±2.63▪ | 79.03±3.4°,x |
| 2. Calcium mmol/L | 2.45±0.11 | 1.71±0.05▪ | 1.90±0.06▪,° | 1.73±0.04▪ | 2.30±0.10°,x |
| 3. Phosphorus mmol/L | 1.16±0.05 | 0.90±0.01▪ | 1.04±0.04▪,° | 0.88±0.03▪ | 1.07±0.04°,x |
| 4. TRKF, ME | 18.52±0.32 | 28.01±0.12▪ | 25.03±1.03▪,° | 27.91±1.11▪ | 20.31±0.45°,x |
| 5.SHF, ME | 72.3±2.5 | 41.62±2.03▪ | 54.21±2.61▪,° | 42.44±2.03▪ | 66.22±2.48°,x |
| **Periphery:** | | | | | |
| 1. Protein g/L | 87.81±2.33 | 60.22±2.51▪ | 66.32±2.66▪ | 60.28±2.71▪ | 80.22±9.85°,x |
| 2. Calcium mmol/L | 2.46±0.10 | 1.79±0.06▪ | 1.83±0.05▪ | 1.83±0.06▪ | 2.26±0.09 |
| 3. Phosphorus mmol/L | 1.18±0.04 | 0.43±0.03▪ | 1.00±0.03▪ | 0.91±0.03▪ | 1.14±0.05°,x |
| 4.TRKF, ME | 18.71±0.36 | 26.87±1.23▪ | 24.32±1.08▪ | 26.93±1.10▪ | 19.31±0.65°,x |
| 5.SF, ME | 71.30±2.62 | 44.54±2.07▪ | 50.33±2.39▪ | 44.50±2.05▪ | 66.32±3.03°,x |

Note:▪P<0.05 relative to control;° - P<0.05 relative to pre-treatment value;
x - P<0.05 relative to the comparison group.

**Table 21**

**Comparative analysis of treatment effectiveness (%) based on mineral exchange and bone metabolism indicators in gingival blood**

| Indicators | Effectiveness compared | Group | |
|---|---|---|---|
| | | Comparisons | Main |
| 1. Protein | Before treatment | 17.11 | 33.88 |
| | After treatment | | >32.76 |
| 2. Calcium | Before treatment | 11.11 | 32.95 |
| | After treatment | | >49.57 |
| 3. Phosphorus | Before treatment | 15.55 | 21.59 |
| | After treatment | | >16.26 |
| 4.TRKF | Before treatment | 1063 | 27.23 |
| | After treatment | | >43.85 |
| 5. | Before treatment | 30.25 | 56.03 |
| | After treatment | | >29.88 |
| = average | | | >35.66 |
| Location | | 2 | 1 |

A comparative analysis showed higher effectiveness of mineral and bone metabolism normalization in the main group.

Thus, the effectiveness of increasing protein concentration in gingival blood exceeded that of the control group by >32.76%; in the periphery by >51.11; the corresponding excess of Ca was >49.57% and 79.82%; phosphorus - >16.26% and >54.13%; TRKF - >43.85% and 54.01%; SHF - >29.88% and >58.08%; OP ob - >27.13% and >55.70%; OP svyaz - >66.84% and 28.48%; Free OP - >14.03% and >43.64%. The average total effectiveness of normalizing mineral exchange and bone metabolism in the gingival blood of the main group exceeded the dynamics of the control group by >35.66%; and in the systemic blood flow by >53.12% (Table 25).

**Table 22**

**Comparative analysis of treatment effectiveness (%) based on mineral metabolism and bone metabolism indicators in peripheral blood**

| Indicators | Effectiveness compared | Group | |
|---|---|---|---|
| | | Control | Main |
| 1. Protein | Before treatment | 10.13 | 33.88 |
| | After treatment | | >51.11 |
| 2. Calcium | Before treatment | 2.79 | 24.86 |
| | After treatment | | >79.82 |
| 3. Phosphorus | Before treatment | 7.52 | 25.27 |
| | After treatment | | >54.13 |
| 4.TRKF | Before treatment | 9.50 | 28.29 |
| | After treatment | | >54.01 |
| 5. | Before treatment | 13.00 | 49.03 |
| | After treatment | | >58.08 |
| = average | | | >53.12 |
| Location | | 2 | 1 |

Thus, in the treatment of generalized periodontitis in patients with pemphigus, systemic osteotropic therapy has the most pronounced effect.

Given the high prevalence and severity of periodontal disease in patients with pemphigus, marked destruction and reduction in alveolar bone mineral density, mineral metabolism disorders, and reduced bone remodeling processes, it is advisable to use osteotropic drugs to stabilize the destructive process in the treatment of generalized periodontitis. The inclusion of biophosphonates in complex therapy normalizes osteoporotic processes in the alveolar bone and periphery, prevents the progression of degenerative processes, provides conditions for bone tissue regeneration, and clinical and radiographic stabilization of the disease.

When comparing the clinical data obtained with the orthopantomogram data in patients in the main group and the control group after 3 months, no improvement in radiographic indicators was observed.

Orthopantomograms of patients in the control group showed progressive resorption, with vertical resorption observed and no clear contour of the alveolar ridge margins between the foci of active osteoporosis and the teeth.

However, in patients in the main group who received the developed pathogenetic treatment, along with clinical improvement, there was no progression of the destruction observed on orthopantomograms.

Thus, in none of the patients with pemphigus did the treatment procedures lead to the development of the process. All patients showed clinical recovery.

As revealed by the analyses, in the main group, the overall effectiveness of complex treatment on the clinical condition of the periodontium in relation to the control group indicators exceeded 27.79%.

Improving the effectiveness of treatment for periodontal diseases, mainly chronic diseases, and especially periodontitis occurring against the background of pemphigus, is one of the important problems of modern dentistry. Such a combined course of diseases leads to metabolic disorders, increased endogenous intoxication, the development of osteoporosis against the background of glucocorticoid use, and worsening of the clinical course of periodontitis.

# CONCLUSION

Inflammatory and destructive periodontal diseases are one of the most intensively studied problems in modern dentistry. Despite significant progress in the study of pathogenesis and the development of new methods for the diagnosis and treatment of generalized periodontitis, its prevalence and severity continue to increase steadily. According to the literature, the incidence of periodontitis among the adult population reaches 90.0-100.0% [73].

Most authors attribute the leading role in the pathology of inflammatory periodontitis to bacterial colonization. Currently, the prevailing view is that microbial invasion is only a trigger for the destruction of tissues that are part of the periodontal complex. The effect of such an impact depends on the state of the body's defenses, which can either limit or promote the development of destructive processes in the periodontium. Studying the influence of various factors on the mechanism of local tissue reaction is a pressing issue in modern dentistry [7].

Clinical studies confirm the mutually aggravating effect of systemic somatic pathology and inflammatory-destructive periodontal lesions, with the prognosis being determined not by the nature of local treatment, but by complex therapy aimed at the common pathogenetic mechanisms that determine the course of periodontitis and background somatic pathology [13].

The pathogenesis of periodontitis is dominated by an increase in LPO processes and a deficiency of antioxidant resources [31].

A close relationship has been proven between the development of systemic osteoporosis and dystrophic resorptive processes in the alveolar bone [14, 82].

Pemphigus, bullous dermatosis, an integral feature of which is acantholysis, leading to the formation of intradermal blisters. The course of all forms of the disease is chronic, which, despite treatment, before the introduction of corticosteroids, ended in the death of the patient within 6 months to 1.5-2 years.

The pathogenesis of pemphigus is based on autoimmune processes, the essence of which is the formation of autoantibodies to the cementing intercellular substance and the membranes of the spiny layer cells [99].

The main drugs used are corticosteroid hormones (prednisolone), the use of which has radically changed the prognosis for pemphigus and significantly prolonged remission periods [28].

Currently, there is a concept that the development of pemphigus is caused by local and systemic stereotypical reactions characterized by endogenous intoxication: activation of POL, entry of large numbers of medium-weight molecules into the blood, activation of proteolytic processes, and suppression of the antioxidant system [52].

Corticosteroid therapy, which lasts for years, is inevitably accompanied by various complications, has an immunosuppressive effect, enhances LPO processes and pathological proteolysis, suppresses antioxidant protection, exacerbates endogenous intoxication processes, delays protein synthesis and accelerates protein breakdown, inhibits the development of lymphoid and connective tissue, and leads to the development of glucocorticoid-induced osteoporosis [81].

All of the above determines the relevance of studying the local and systemic mechanisms of periodontitis development in patients with pemphigus. The choice of modern treatment methods and the specifics of clinical procedures for combined pathology are relevant for practical medicine.

It is obvious that the question of choosing a treatment strategy and the possible prognosis of destructive changes in the periodontium must be decided from the standpoint of the impact on the universal mechanisms of the pathogenesis of periodontal disease and pemphigus, in collaboration between a dentist and a dermatologist.

Based on the above, the aim of the study was to investigate the pathogenetic features of periodontitis in patients with pemphigus and to develop a comprehensive method for its treatment.

The periodontal aspects of pemphigus are among the least studied, although its autoimmune genesis suggests the involvement of the most important morphofunctional complex of the oral cavity – the periodontium.

During the examination of 100.0% of patients with pemphigus, generalized periodontitis was detected, predominantly GPTs, with a frequency of 63.27±6.88% compared to 5.0±3.45% in the comparison group; GPT – 20.44±5.45% versus 25.0±6.85 and GPLS – 14.29±5% versus 37.5±7.6%.

The clinical features of periodontitis associated with pemphigus are the erosive nature of the lesion, high bleeding and destruction of the periodontal complex, and poor oral hygiene. Thus, the PI index value exceeded the corresponding indicator of the comparison group by 2.5 times ($P<0.01$); the PMA was 1.92 times higher ($P<0.01$); the ON1-S index was 1.6 times higher ($P<0.01$), and the bleeding index was 2.17 times higher ($P<0.01$).

A progressive worsening of inflammatory-destructive periodontal lesions was observed with an increase in the duration of pemphigus.

During examination of SOPR in patients with pemphigus, multiple erosions were found on the unchanged oral mucosa, often merging with each other. The microstructure of the oral mucosa differs in terms of topographical data, which serve as key links in visual examination. Alveolar gingival lesions accounted for 77.54% of all localized lesions in pemphigus SOPR. At the same time, isolated periodontal lesions accounted for 32.65% and combined lesions involving other topographic areas accounted for 44.89%.

From a clinical point of view, it is important to assess the condition of the periodontium depending on the localization of the elements of pemphigus lesions in order to evaluate their pathogenetic significance in the formation of inflammatory-destructive lesions of the periodontium. No significant differences ($P<0.05$) were found in the prevalence and intensity of periodontal lesions; indices of destruction, inflammation, hygiene, and bleeding. Depending on the localization of the lesions, it can be assumed that the leading factors in the initiation of inflammatory-destructive lesions of the periodontal complex in patients with pemphigus are not the localization of the lesions, but systemic disorders that determine the activity of aggressive factors and deplete the compensatory capabilities of the body.

The generalized nature of periodontitis in patients with pemphigus with severe inflammatory-destructive lesions, a persistent progressive course with frequent exacerbations coinciding with periods of exacerbation of pemphigus, determine the involvement of a dentist and dermatovenerologist in the treatment of this combined pathology.

Currently, it is widely accepted that the disorganization of cell membranes is one of the key mechanisms in the pathogenesis of pemphigus, the severity of which determines the severity of disorders, the level of internal metabolism in tissues and in the body as a whole [90].

However, the problem of the relationship between local changes and shifts at the systemic level in the development of periodontitis in patients with pemphigus remains virtually unexplored.

The dynamics of biochemical shifts in POL-AOS in patients with periodontitis was assessed as the activation of POL processes and suppression of AOS. In patients with GP without pemphigus, statistically significant shifts in the studied indicators were recorded in the area of the inflammatory-destructive focus ($P<0.01$), while in the systemic bloodstream, their values did not differ from those in the comparison group ($P<0.01$).The results confirm the opinion that as periodontitis develops, a histohematological barrier forms, , as a result, changes in peripheral blood are less pronounced than in gingival blood [67].

In patients with pemphigus, a clear trend was established in the studied indicators in gingival blood and systemic blood flow, and their levels differed significantly ($P<0.05$) in an unfavorable direction from those in patients with GP without pemphigus ($P<0.05$).

Thus, the intensity of HL in patients with pemphigus was increased relative to the control in gingival blood by 70.55% ($P<0.01$); in systemic blood flow by 67.08% ($P<0.01$); MDA levels were increased by 61.17% ($P<0.01$) and 51.72% ($P<0.01$), respectively; SOD levels were decreased by 51.39% ($P<0.01$) and 40.73% ($P<0.01$); CT and GP activity decreased by 52.44% ($P<0.01$) and 34.74% and 51.21% ($P<0.01$) and 51.07% ($P<0.01$), respectively.

It is evident that disruption of the histohematological barrier reduces isolation and more effective destruction of microorganisms in the focus of inflammation, the concentration (localization) of changes in the body to suppress inflammation and stimulate reparative processes, and reduces the body's defense against the spread of the inflammatory process.

Unidirectional disturbances in the POL-AOS system in gingival blood and systemic blood flow may be one of the pathogenetic mechanisms determining the severity of GP in patients with pemphigus.

The study of POL-AOS has shown the need for systemic antioxidant therapy in the treatment of SP in patients with pemphigus.

In the last decade, the important role of endogenous intoxication syndrome in the mechanisms of development of most diseases has been recognized. The role of endogenous intoxication in the progression and recurrence of pemphigus has been proven. At the same time, the state of endogenous intoxication is characterized by a close relationship between the activity of peroxide processes and the rate of generation of the main markers of endogenous intoxication – VSMM [70].

A study of VSMM concentrations showed that in patients with pemphigus, the amount of VSMM in gingival blood and systemic blood flow statistically ly significantly exceeded the corresponding values in patients with GP without pemphigus ($P<0.01$). It was noted that the concentration of VSMM substances in the 260 nm fraction was the highest and exceeded the corresponding values in the control group in gingival blood by 84.21% ($P<0.01$); the corresponding dynamics of the 220 nm fraction were 52.75% ($P<0.01$) and 30.0% ($P<0.01$); the 254 nm fraction was 41.89% and 32.42% ($P<0.01$), and the 280 nm fraction was 0 42.86 ($P<0.01$). And 35.40% ($P<0.01$). At the same time, it was found that the values of VSMM in gingival blood and systemic blood flow did not have statistically significant differences ($P>0.05$). An increase in the concentration of VSMM fractions 260 nm indirectly reflects the predominant breakdown of structural tissues – collagen, elastin, myosin.

It is evident that high levels of endotoxicosis necessitate the inclusion of systemic detoxifiers in complex therapy.

Systemic bone damage, or osteoporosis, is considered to be of considerable importance in the pathogenesis of generalized periodontitis. Recent studies have demonstrated clinical and pathogenetic relationships between GP and osteoporotic processes in the skeleton [49].

The use of corticosteroids in dermatological practice has restored the ability to work in most patients. Glucocorticoid-induced osteoporosis is considered one of the most characteristic and potentially serious consequences of glucocorticosteroid therapy.

In this regard, we conducted a comprehensive assessment of mineral metabolism and biochemical markers of bone remodeling in periodontitis against the background of pemphigus. A single pathogenetic mechanism of alveolar bone resorption and the development of systemic osteoporosis in pemphigus was established, which was recorded by the absence of statistically significant differences in the indicators of mineral homeostasis and bone metabolism in gingival blood and systemic blood flow. Thus, in patients with periodontitis and pemphigus, the concentration of protein in gingival blood relative to the control group was positive by 92.27% ($P<0.01$); in the systemic bloodstream by 22.49% ($P<0.05$); the corresponding dynamics of calcium was 29.8% ($P<0.01$) and 26.53% ($P<0.01$); phosphorus – 23.28% ($P<0.01$) and 29.8% ($P<0.01$). An increase in bone resorption was evidenced by an increase in tartrate-resistant bone phosphatase activity by 50.22% ($P<0.01$) and 43.83% ($P<0.01$); and a decrease in remodeling was evidenced by a decrease in alkaline phosphatase activity by 41.48% ($P<0.01$) and 97.56% ($P<0.01$).

Impaired collagen metabolism and active degradation of connective tissue in patients with periodontitis against the background of pemphigus manifested itself in an increase in total OP by 24.76% ($P<0.0\%$) in gingival blood and by 21.42% ($P<0.05$) in systemic blood flow; a decrease in the concentration of bound OP by 14.68% ($P<0.05$) and 14.49% ($P<0.05$), respectively; an increase in the free fraction

of OP by 172.25% (P<0.05) and 227.07% (P<0.05), reflecting the predominance of the breakdown of this protein over its synthesis.

The level of mineralization of the jawbone tissue reflects the condition of the body's bone tissue as a whole. A quantitative assessment of this indicator serves as a diagnostic criterion for bone system metabolism [79; pp. 76-81]. Densitometric studies of orthopantomograms revealed a decrease in the optical density of the bone tissue of the alveolar processes of the jaw. At the same time, in patients with GP without pemphigus, the density of the jaw bone tissue was reduced relative to the control by 15.2% (P<0.05)- 16.16% (P<0.05); and in patients with GP against the background of pemphigus, by 27.53% (P<0.05) – 29.64% (P<0.05). The data obtained on the progressive decrease in the mineral density of the alveolar process of the jaw in patients with pemphigus reflect the pathogenetic relationship between the development of local inflammatory-destructive periodontal lesions and glucose-induced osteoporosis. It is evident that these processes aggravate each other and determine the need for systemic osteotropic therapy.

The identified mechanisms of systemic homeostasis disorders in patients with periodontitis against the background of pemphigus determined the need for systemic antioxidant, sorption, and anti-osteoporotic therapy in the treatment of periodontitis in this category of patients.

To evaluate the effectiveness of standard and systemic therapy, patients with pemphigus were divided into two groups that were homogeneous in terms of age, gender, duration of pemphigus, and severity of periodontitis.

All patients with periodontitis against the background of pemphigus underwent the standard treatment regimen for periodontitis: oral sanitation, removal of supragingival and subgingival dental deposits, elimination of traumatic factors, and training in oral hygiene rules using soft toothbrushes and toothpastes without abrasive components. Periodontal pockets were rinsed with disinfecting (3 mg/l) concentrations of ozone in saline solution, and Metrogel-Denta ointment was applied to the affected pockets under a protective filter dressing.

Patients in the control group (14 people) received long-term treatment according to the described regimen.

Patients in the main group (15 people) received additional complex treatment, including:

- systemic antioxidant therapy in the form of infusion of regenerative concentrations (1.5 mg/l) 400.0 ml of ozonated physiological solution No. 5 every other day;

- systemic inactivation of endotoxemia with Reosorbilact 500.0 ml intravenously every other day;

- osteotropic therapy with Calcium D3 Nikomed AO 1 tablet twice a day for up to 6 months.

Before the start of treatment, there were no statistically significant differences in the clinical condition of the periodontium and the indices of destruction, inflammation, hygiene, and bleeding of the periodontium in the compared groups ($P>0.05$).

Clinical studies have shown positive dynamics in the clinical condition of the periodontium in both groups. The number of complaints decreased significantly, and the general well-being of patients improved. The color of the gums was restored, the gingival papillae became firmer, and bleeding decreased. A significant decrease in clinical indices assessing the condition of the periodontium was noted.

It should be noted that all the studied index indicators of periodontal condition in the main group after treatment were significantly lower ($P<0.01$) than the corresponding values in the control group. The average total clinical effectiveness of periodontal treatment in the main group exceeded the effectiveness of treatment in the control group by more than 27.79%. At the same time, the duration of treatment in the main group was 18.5±0.5 days; in the control group, it was 23.6±0.62 days, and the duration of remission was 6.3±0.22 and 3.60±0.18 ($P<0.01$) months, respectively.

One of the mechanisms of periodontitis development in patients with pemphigus is local and systemic endogenous intoxication, accumulation of under-

oxidized products and MSM, creating pathogenetic prerequisites for the aggravation of local inflammatory-destructive periodontal lesions.

A study of the dynamics of POL-AOS processes and MSM concentration using the developed comprehensive treatment method demonstrated its high effectiveness on local (gingival blood) and positive effect on pathological shifts in systemic blood flow. At the same time, the average total effectiveness of restoring the imbalance of POL-AOS indicators in the main group exceeded that of the control groups in gingival blood by 51.7%; in systemic blood flow by 57.32%; the corresponding dynamics of MSM was 51.70–59.32%.

It has been established that the inclusion of Calcium D3 Nikomed in the complex therapy of periodontitis in patients with pemphigus normalizes local and systemic osteoporotic processes, provides conditions for bone tissue regeneration and radiographic stabilization of the disease.

The average total effectiveness of the restoration of mineral exchange and bone metabolism in the main group exceeded the corresponding dynamics of control in gingival blood by more than 35.66%; in the systemic bloodstream >53.12%.

The results of the studies can be used to monitor patients with inflammatory periodontal diseases and pemphigus for joint care of this contingent by a dentist and dermatovenerologist for the treatment and prevention of pathology.

The study proved the interconnection of the pathogenetic mechanisms of complex homeostatic disorders at the local and systemic levels, which determine the severity of periodontitis and pemphigus. The need for systemic treatment of combined pathology has been proven.

The use of the developed method of complex treatment of patients with periodontitis against the background of pemphigus is justified from the point of view of treatment and prevention of both diseases. The components of complex treatment have a universal systemic antioxidant, detoxifying, and anti-osteoporotic effect, which reduces clinical manifestations and achieves a longer remission of periodontal disease and pemphigus.

Simultaneous treatment of pemphigus and periodontitis determines the effectiveness of treatment for such patients.

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