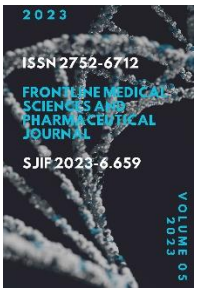
FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals



Journal Website: https://frontlinejournals.org/journals/index.php/fmspj

Research Article

ETIOPATHOGENETIC MECHANISMS OF INFLAMMATORY-DESTRUCTIVE PROCESSES IN PERIODONTAL TISSUES DEVELOPMENT(REVIEW)

Submission Date: February 01, 2024, **Accepted Date:** February 06, 2024,
Published Date: February 11, 2024
Crossref doi: https://doi.org/10.37547/medical-fmspj-04-02-03

K.Z. Adilov
Researcher, Tashkent State Dental Institute, Uzbekistan

ABSTRACT

According to the World Health Organization, inflammatory diseases are aggressive and practically untreatable, and their prevalence, according to various authors, varies from 35% to 95%. Along with this, the problem is exacerbated by the increase in morbidity due to problems of early diagnosis, difficulties in achieving stable remission, as well as the relationship between late presentation and ambiguity of approaches to treatment. In addition, the issue of the primacy of etiopathogenesis still remains controversial. Knowledge of the etiopathogenetic mechanisms of development is necessary for early diagnosis, drawing up an adequate treatment protocol, prevention and control of inflammatory periodontal diseases.

KEYWORDS

Periodontitis, prevention, etiopathogenetic mechanisms of development.

INTRODUCTION

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

Inflammatory periodontal diseases remain a pressing problem in dentistry [6,20] despite the improvement and introduction into practice of new surgical, therapeutic and orthopedic treatment methods. According to the World Health Organization, these diseases are aggressive and practically untreatable, and their prevalence, according to different authors, varies from 35% to 95% [8,13,18,22,25]

Along with this, the problem is exacerbated by the increase in morbidity due to problems of early diagnosis, difficulties in achieving stable remission, as well as the relationship between late presentation and ambiguity of approaches to treatment. [23]. In addition, the issue of the primacy of etiopathogenesis still remains controversial. [3,]. Researchers are increasingly paying attention to the study of endogenous and exogenous causes of periodontitis, but this issue still remains controversial among doctors and scientists [19,22,25,30].

Today, the generally accepted opinion is that under the influence of exogenous or endogenous factors, the activation of viruses and bacteria in dental plaque occurs and the attachment of other microorganisms to them [14,15,27,31,36,38]. Changes in the body's defenses, local changes in acid-base balance, hypoxia and other unfavorable factors make the environment convenient for the proliferation of pathogenic microorganisms, which causes an increase in the activity of opportunistic infection and the occurrence of inflammatory-destructive periodontal diseases [1,6,41].

The scientific literature on periodontology has proposed many concepts of the etiology and pathogenesis of inflammatory periodontal diseases.

Historical analysis of the etiopathogenetic causes of the development of inflammatory-destructive periodontal diseases for each time period has its own characteristics.

At the end of the 30s of the last century, thanks to the scientific research of A.I. Evdokimov, the vascular theory was considered the fundamental etiopathogenetic factor in the development of inflammatory periodontal diseases. By the beginning of the 70s of the last century, the leading role began to be assigned to occlusal trauma. The most popular concept over the past few decades is based on the role of microorganisms and associated inflammatory processes.

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

Changes in the body's defenses, local changes in acid-base balance, hypoxia and other unfavorable factors make the environment convenient for the proliferation of pathogenic microorganisms, which causes

- increased activity of opportunistic infection and attachment
- inflammatory and destructive periodontal diseases [14,43,45,49].

It is generally accepted that the leading role in the formation of the inflammatory process in periodontal tissues belongs to the anaerobic flora, namely endotoxins of periodontal pathogenic microorganisms [27.31]. At the present stage of development of dentistry, data have been obtained on the role of anaerobic and mixed bacterial flora in the development of periodontal diseases, which made it possible to identify a group of so-called periodontal pathogenic bacteria that produce necrotizing enzymes (collagenase, elastase, fibrinolysin, hyaluronidase, etc.), exotoxins leading to damage to the integrity of the epithelial tissues, contributing to the active destruction of periodontal tissues, which plays a fundamental role in the genesis of periodontitis. It is worth noting that periodontal pathogens have an anaerobic type of respiration and are characterized by high adhesive, invasive and toxic properties in relation to periodontal tissues.

Specific periodontal pathogens have a wide variety of virulent properties and the ability to colonize. The microflora of the periodontal pocket may differ both in different parts of the oral cavity and in a separate periodontal pocket. At the same time, not one, but several microorganisms play a role in the formation and progression of periodontitis, which distinguish several complexes - associations of microbes associated with periodontal diseases:

1. Porphyromonas gingivalis, Bacteroidies forsihus, Treponema denticola.

2. Streptococcus sanguinis, Streptococcus mitis, Streptococcus oralis, etc.

3. Actinomyces odontolyticus, Actinomyces naeslundii, Veillonella parvulla.

4. Prevotella intermedia, Fusobacterium nucleatum, Campilobacter rectus [33].

It has been established that Herpesviruses are involved in the pathogenesis of at least several inflammatory periodontal diseases, which can change the immune control over the quantitative

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

and qualitative composition of resident microorganisms and participate in several stages of the pathogenesis of inflammatory periodontal diseases: activation of persistent viruses, activation of periodontopathogenic microflora, development of immune reactions of the host organism [34].

Currently, the vast majority of researchers recognize that the immune system is one of the key links in the pathogenesis of the chronic inflammatory process in the periodontium [12,16].

Lymphocytes and macrophages, constantly making excursions to the surface of the gums, are able to quickly respond to the slightest changes in the external environment, quickly turning on protective mechanisms. The inclusion of a link of specific immune defense in the mechanism of pathogenesis of inflammatory periodontal diseases is evidenced by the high frequency of detection of positive skin tests for gingival antigen in patients with periodontitis [21]. Many microbial products (exo- and endotoxins) have been identified as activators of the indirect pathway of action on the macroorganism. In the literature of recent years, such microbial substances have been given the name "modulins" [29].

In the modern interpretation, bacterial plaque is called a biofilm, which is a specialized bacterial ecosystem that ensures the viability, preservation of its constituent microorganisms and an increase in the overall population. It is considered as a single entity, and not as the coexistence of different strains of bacteria [27,30]. It was noted [35] that strains of microorganisms with good ability to form biofilms are characterized by multiple resistance to widely used antibiotics. As part of a biofilm, bacteria persist for a long time in the host's body and become resistant not only to antibacterial drugs, but also to the action of factors of the humoral and cellular immunity of the macroorganism. Therefore, attempts to "cure a chronic infection" with antibiotics are doomed to failure, since antibiotics in such a situation provoke the survival of particularly resistant microorganisms, forcing them to cluster together.

Refractory (unresponsive) periodontitis develops in patients, even after proper therapy, has a complex course and has a huge number of complications. Despite the fact that normal oral hygiene is maintained, regular conservative treatment is carried out and local factors are

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

eliminated, the loss of supporting tissues continues in most cases in several areas of the periodontium. The affected areas are infected with periodontal pathogenic microorganisms. Today it can be stated that the immunological response to periodontal pathogens plays a key role in the pathogenesis of refractory periodontitis. In these patients, the relapse rate is extremely high. A characteristic feature is that initially there is a massive loss of supporting tissues, and then the loss of teeth. Research has shown that 17% of periodontal patients are "very difficult to treat" [48]. Refractory periodontitis is often caused by saprophytic subgingival microorganisms and is probably due to the weakened state of the macroorganism, while in this category of patients it is not possible to cope with the activity of the process, there is a continuing loss of periodontal attachment, despite carefully carried out traditional mechanical therapy, which, of course, is an indication for antibacterial therapy.

It should be noted that to date, no biological markers have been created that can identify individuals who are likely to experience periodontal destruction in the future. No single microorganism has been identified as pathognomonic for the transformation of gingivitis into periodontitis in adults. Some authors believe that some "dental plaque" microorganisms have a pronounced pathogenicity against periodontal tissues [13]. Others believe that in individuals with intact periodontium, the influence of the accumulation of "dental plaque" alone for periodontal inflammation is insufficient [37]. In periodontal disease, many potentially pathogenic microbes are constantly found in both healthy and affected areas.

In most cases, the microflora of dental plaque is not able to penetrate the gingival epithelium and underlying connective tissue [47]. At the same time, "intracellular" bacteria (microbial cells that persist in the cytoplasm of the host cells) serve as a source for maintaining chronic, low-grade inflammatory diseases of periodontitis.

Thus, after analyzing the available literature, we can draw a conclusion about the infectious-allergic nature of inflammatory periodontal diseases with the mechanism of implementation through associations of periodontopathogenic microflora of the periodontal complex [20,35].

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

Difficulties in treating inflammatory processes in the periodontium are also associated with the long-term persistence of pathogenic microorganisms, which inevitably leads to changes in the immune status of the body. In the complex treatment of periodontitis, taking into account the role of the microbial factor in the pathogenesis of the disease, it is recommended to use antimicrobial agents, the use of which, especially without clear indications, can contribute to the formation of dysbiosis of the oral cavity, primarily due to opportunistic microorganisms, including fungi, causing, in its turn, turn, exacerbation of comorbid conditions and concomitant diseases [3,16].

Dysbiosis is currently considered as a key condition for the development of a pathological process in the oral cavity, and periodontitis is considered by many to be a mixed infection, in which "concomitant microflora" in the form of an association of viral-microbial infections often plays a leading role in the progression of the pathological process and refractoriness to therapy [33,44]. At present, the role of H. pylori in the etiology of inflammatory processes in the periodontium has not been sufficiently established, while the persistence of H. pylori in the periodontal pocket is 16-25%; these are, as a rule, pathogenic strains that persist after eradication therapy [34 ,43]. The specific properties of Helicobacter are such that the immune response caused by it, in addition to limiting the pathogen itself through the mechanism of necrosis and apoptosis, causes the death of its own cells, which disrupts the course of the proliferative phase of inflammation and the processes of reparative regeneration of the mucous membrane [35]. At the present stage of development of dentistry, the mechanisms of synergism or antagonism, clinical features and approaches to the treatment of infectious lesions of the oral cavity caused by an association of pathogens have not been sufficiently studied.

In practical medicine, certain successes have been achieved in developing the principles of complex therapy of periodontitis. It is proposed to use antibacterial drugs, immunomodulatory agents, general detoxification and vitamin therapy, as well as local use of antiseptic substances, and the prescription of various physiotherapeutic procedures [7,12,29]. However, as is known, the use of the above methods of therapy is not always effective for chronic refractory periodontitis, which requires

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

further optimization of the complex treatment of the disease. It is now obvious that reducing the infectious load in the periodontal complex is only the first step in sanitizing the entire oral cavity and oropharynx from pathogenic flora, including fungi and viruses.

Free radical processes (FRP) play an important role in the pathogenesis of periodontitis as an inflammatory-destructive disease. However, studies devoted to the study of FRP in patients with periodontal diseases are few, and their results are contradictory [9,19,32,35].

The permeability of the epithelium of the gingival sulcus increases due to the action of antigens and toxins of the dental plaque, which, in turn, leads to increased secretion of sulcular fluid. Under its influence, bacteria together with leukotoxins (a polypeptide isolated from exudate that can activate the antigen-antibody complex) increase capillary permeability, promoting the release of phagocytes into the connective tissue of the gums and gingival fluid. As a result of their damage, lysosomal enzymes are released - starting sites for inflammation [28,36,39]. In periodontitis, hyperactivation of leukocytes, macrophages and platelets is observed [40]. The process of accumulation of hyperactivated leukocytes and platelets in foci of inflammation is the basis for the development of tissue destruction. Leukocytes carry out the process of phagocytosis of bacteria, tissue breakdown products and destroy them with their lysosomal enzymes (such as proteases, peptidases, oxidases, deoxyribonucleases and lipases). Arachidonic acid released from leukocyte membranes produces leukotrienes, thromboxanes, prostaglandins, which play an important role in the occurrence of inflammation [23,40]. Along with the above, it is worth noting that activated leukocytes begin to actively release ROS, which, in turn, cause periodontal damage both directly and through the initiation of SPOL [42]. As a result of changes in the acidity of the environment, the maturation of osteoblasts is disrupted and the formation of osteoclasts is activated [18,33]. Another pathogenic factor of periodontitis is traumatic occlusion. Traumatic occlusion further damages the inflamed periodontium. The synergy of these two components is more destructive than each of these factors separately [11,24]. Damage to periodontal tissue leads to disruption of the functioning of receptors and nerve conductors. In turn, this reduces their sensitivity, resulting in the formation of “denervation”, a kind of structural and functional removal of the damaged

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

periodontal area from nervous influences [44,48]. Thus, disruption of the periodontal-muscular reflex may occur. As a result, the force of muscle contractions will be significantly higher than the reserve forces of the periodontium, i.e., chewing and swallowing turn from physiological processes into destructive ones [6]. It should be said that dysfunction of the salivary glands (hyposalivation, xerostomia) also leads to periodontitis. At the same time, there is a decrease in the mechanical removal of food debris. This, in turn, can contribute to the formation of conditions for the proliferation of microorganisms [47]. In addition, the formation and secretion of immunoglobulin A, which prevents the attachment of bacteria to the tooth surface, may decrease due to an increase in saliva viscosity and a decrease in the rate and speed of its secretion [45]. The development of periodontitis can also be influenced by factors such as age, nervous strain, genetics (Chediak-Higashi syndrome, cyclic neutropenia, increased IL-1 reactivity), endocrinopathy (diabetes mellitus, pregnancy, gonadal dysfunction), smoking, autoimmune diseases, AIDS , sickle cell anemia, malabsorption syndrome (hypoand vitamin deficiencies), gastric and duodenal ulcers, dermatological diseases, etc. [2,11,17,26]

Modern innovative and priority directions in periodontology are associated with experimental and clinical studies of the etiology and pathogenesis of inflammatory periodontal diseases. Their results significantly expanded and deepened the existing understanding of the pathogenetic mechanisms of diseases, and although the role of local factors in the development of inflammatory periodontal diseases is quite obvious, the more subtle mechanisms of action of most of them remain unclear. Today, more and more evidence is emerging that the trigger for the occurrence of pathological changes in periodontal tissues are hormonal disturbances in regulatory processes, which entail secondary inflammatory changes in the soft tissues and bone tissue of the periodontium. Clinical manifestations of periodontitis must be considered at the level of the whole organism, taking into account neurohumoral-autocrine interactions [4]. The systemic nature of chronic generalized periodontitis (CGP), involving the main links in the regulation of homeostasis (hormones - growth factors - cytokines - signaling molecules - metabolic pool of cell membranes), allows us to consider this disease as a local manifestation of a generalized metabolic disease of functional

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

cellular homeostasis [1,17]. Currently, hormonal regulation is of great importance in these processes, but this aspect of the etiopathogenesis of CGP has been practically not studied. There are only separate, scattered, unsystematized works. And again the question arises, what comes first: local pathology in periodontal tissues or a systemic pathological process. The human body is characterized by a single pathogenetic mechanism of cellular damage, which is responsible for the development and course of general somatic processes in general and inflammatory diseases of the oral cavity in particular. An important role in the occurrence of changes is played by disturbances in the hormonal regulation of the process of osteogenesis. Summarizing the literature data, we can talk about the connection between the patient's hormonal background and pathological conditions in periodontal tissues. Thus, in diseases associated with hormonal imbalances, chronic and long-term stress, diseases of the gastrointestinal tract, diabetes mellitus, cystic fibrosis, an increased incidence of all nosological diseases of the oral cavity was registered.

Disorders of metabolic processes in bone tissue are an important link in the development of chronic periodontal inflammation in somatic pathology, contributing to the negative impact of the microflora present in the oral cavity, the further development of periodontal diseases and changes in the oral mucosa.

Bone tissue undergoes constant remodeling and renewal of its constituent substances, as well as adaptive rearrangements to changing operating conditions. These processes involve calcium and phosphorus, the level of which depends on the hormones that regulate their metabolism.

Factors responsible for bone remodeling can be divided into four groups:

1) hormones that regulate calcium metabolism (parathyroid hormone, calcitonin, vitamin D and its metabolites);

2) systemic hormones (sex hormones, glucocorticoids, insulin, thyroxine, somatotropin);

3) growth factors in the blood and bone tissue (protein factors of plasma, platelets and bone tissue (tumor necrosis factor, insulin-like growth factor 1, interleukins 1,4,6, macrophage colony-stimulating factor, RANK-ligand, etc.);

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

4) local factors produced in osteoclasts and osteoblasts (prostaglandins E, cAMP, cGMP, osteonectin, proteoglycans, glycosaminoglycans, etc.) [5, 28].

Hormones are specific regulatory molecules that determine all processes of human life. They are responsible for physiological and pathological changes in all types of tissues of the body. In periodontal tissues, receptors were found not only for parathyroid hormone and calcitonin, but also for all sex hormones. Consequently, systemic imbalance of the endocrine system plays an important role in the development of periodontal diseases [10,46].

Among patients with osteoporosis, 80% are women, as they are more likely to experience hormonal imbalances throughout their lives. Fluctuations in hormones during the menstrual cycle, periods of pregnancy, breastfeeding, taking oral contraceptives, menopause - all this directly affects periodontal tissue, contributing to the development of osteoporosis throughout the skeleton, including the bone tissue of the jaws. A decrease in bone density in women depends on the concentration of hormones, and not on the increased susceptibility of periodontal tissues to them, since it has been proven that the number of receptors for sex hormones does not depend on gender. [4,33,39].

Any increase in the concentration of glucocorticoids (Itsenko-Cushing syndrome and disease, treatment with glucocorticoids, regardless of the route of administration) causes the development of osteoporosis. There are no “skeletal safe” doses of corticosteroids. Fractures of the vertebrae and femur also occur with daily use of prednisolone at a dose of 2.5 mg, and with a dose of 7.5 mg per day the risk increases 5 times. Those who took prednisolone 10 mg for more than 3 months had a 17-fold increase in risk! [3,5,48].

CONCLUSIONS

The direct effect of hormones on periodontal tissue was proven after the discovery of specific receptors in osteoblasts, osteoclasts, fibroblasts, and vascular endothelial cells. This allows us to consider the periodontium as a target organ for the action of systemic and sex hormones. At different periods of a person’s life, the influence of each hormonal factor is different. For example, sex steroids have the greatest effect during puberty and reproductive age, and during

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

menopause their role and participation in the processes of bone tissue remodeling decreases.

Knowledge of the etiopathogenetic mechanisms of development is necessary for early diagnosis, drawing up an adequate treatment protocol, prevention and control of inflammatory periodontal diseases. In medicine, there is a direction that is called predictive medicine. Its main objectives are to identify and monitor individuals at high risk of pathology before they develop pronounced clinical symptoms. For preventive, therapeutic and diagnostic purposes, it has become possible to use fundamentally new predictors at the molecular level and the capabilities of so-called high dimensional biology with assessment of the genome, proteome, transcriptome, metabolome, and microbiome. Primary prevention of inflammatory periodontal diseases should be especially relevant in individuals who have risk factors for their occurrence. If pathological changes are detected at the preclinical stages of the disease, it is necessary to take measures to eliminate them in a timely manner in order to prevent the transformation, for example, of generalized gingivitis into generalized periodontitis

In foreign and domestic literature, when considering the etiology and pathogenesis of generalized periodontitis, the emphasis is on microflora as the dominant factor in the development of this disease. At the same time, it is recognized that the condition of oral tissues depends on many components that must be considered as a single regulatory mechanism.

REFERENCES

1. Antidze M.K. Evaluation of complex treatment of patients with chronic generalized periodontitis based on clinical and laboratory parameters: author. dis. ...cand. of Medical Science. 2013. 119 p.

2. Belskikh O. A. Features of the clinical course and treatment of dental diseases in chronic kidney disease: special. 01/14/14 “Dentistry”: dis. ...cand. honey. Sciences / Belskikh Olga Andreevna; Military Medical Academy named after. S. M. Kirov. – St. Petersburg, 2016. – Place of defense: First St. Petersburg State. University named after acad. I. P. Pavlov.

3. Bulkina N. V. Comorbidity of periodontal diseases and somatic pathology // Medical Bulletin of the North Caucasus. – 2012. – No. 3. –

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

URL: http://cyberleninka.ru/article/n/komorbidnost zabolev (access date: 02/19/2017).

4. Vishnyak G.N. Generalized periodontal diseases (periodontal disease, periodontitis). Kyiv, 1999. 216 p.

5. Vavilova T.P., Pashkova G.S., Grinin V.M. Studies of soluble osteoclast-activating factor and osteoprotegerin in mixed saliva of patients with periodontitis // Russian Dental Journal. 2010. No. 2. pp. 11–13.

6. Grigorovich E. Sh. Chronic generalized periodontitis: clinical morphological and molecular genetic basis of the heterogeneity of the disease, justification of prognosis and personification of therapy: abstract. dis. ...Dr. med. Sciences / Grigorovich Elmira Shadidovna. – Moscow, 2016. – 48 p.

7. Inina L.I., Luchkin R.L., Trigolos N.N. Hygienic condition and quality of oral sanitation in patients with moderate and severe type 2 diabetes mellitus [Electronic resource] // Dental South. 2012. No. 6. URL

8. Karachunova A. I. Inflammatory periodontal diseases as an urgent problem of modern dentistry / A. I. Karachunova // Science, education, society: trends and development prospects: collection of materials VII International. scientific-practical conf. (Cheboksary, September 24, 2017).– Cheboksary, 2017. – pp. 40–43

9. Katkhanova L.S., Akulova E.V., Lysov A.V., Mogila A.P. The influence of hormonal regulation on the condition of periodontal tissues // Bulletin of the medical Internet conference. 2014. V. 4, no. 12. pp. 77–79.

10.. Nizov A. A. Periodontitis and diabetes: two-way communication / A. A. Nizov, T. A. Ogannisyan // Central Scientific Bulletin. – 2018. – V. 3, No. 9 (50). -WITH. 32–33

11. Oganyan A.V. Clinical and morphological changes in the dental system in experimental hypothyroidism // Dental South. 2010. No. 12. P. 3–12.

12. Vasilyeva N. A., Bulgakova A. I., Imelbaeva E. A. [etc.] Assessment of local immunity of the oral cavity in traditional therapy of inflammatory periodontal diseases / // Problems of Dentistry. – 2018.T. 14, No. 3. – pp. 11–16

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL (ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

13. Atrushkevich V.G., Dmitrieva L.A., Zoryan E.V., Mkrtumyan A.M. Pat. 2415426 RF. A method for diagnosing chronic generalized periodontitis with an aggressive course /; applicant and patent holder Moscow State. Medical and Dental University N 2008147047/15; application 01.12.2008; publ. 10.06. 2010, Bull. N 9.

14. Perebeinos O. P., Ostrovsky P. Yu., Boytsanyuk S. I. The role of bacteria in periodontal diseases // Young people. – 2015. –No. 2–6 (17). – pp. 648–651

15. Mitronin A.V., Dashkova O.P., Galieva D.T. [et al.] Composition of the microflora of root canals and periodontal pockets in patients diagnosed with severe periodontitis // Dentistry - science and practice, development prospects: materials scientific-practical conference dedicated to the 90th anniversary of the birth of L.P. Ivanov (within the framework of the All-Russian Student Olympiad with international participation "Dentistry of the South-2017"). – 2017. – pp. 112–113.

16. Maslyakov V.V., Erokina N.L., Ilyukhin A.V. [et al.] State of immunity in chronic generalized periodontitis // Vestn. honey. Institute "REAVIZ": rehabilitation, doctor and health. – 2019. – No. 2 (38). – pp. 105–109

17. Sutaeva T.R. Periodontitis and its course in patients with functional disorders of the thyroid gland // Dental Yug. 2011. No. 12. pp. 10–14.

18. Tebloeva L. M. Osteoimmunology and periodontitis / L. M. Tebloeva, K. G. Gurevich // Pathological physiology and experimental therapy. –2014. – V. 58, No. 3. – P. 67–72.

19. Trukhan D.I. Periodontitis and cardiovascular diseases: in parallel or in one ligament? / D. I. Trukhan, L. Yu. Trukhan // Consilium Medicum. – 2015. – V. 17, No. 5. – P. 73–79.

20. Ulitovsky S. B. Problems of periodontology and modern ways to solve them / S. B. Ulitovsky, E. S. Alekseeva, A. A Vasyanina //Periodontology. – 2015. – V. 20, No. 3 (76). – pp. 33–36

21. Speranskaya E. M. (Nikolaeva), Golubtsova N. N., Mukhamedzhanova L. R. Chronic generalized periodontitis: proliferative activity of multilayer squamous epithelium of the gums // Morphology in theory and practice: materials of the All-Russian Federation. scientific-practical conf. with international participation dedicated to the 95th

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL (ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

anniversary of the birth of Dr. med. sciences, prof. D. S. Gordon. – 2017. –S. 227–231.

22. Tsepov L. M., Nikolaev A. I., Nesterova M. M. [et al.] Chronic generalized catarrhal gingivitis and chronic generalized periodontitis: common origins, sequential transition? (discussion) // Vestn. Smolensk State honey. academy. – 2018. – V. 17, No. 3. – P. 198–205.

23. Tsepov L.M., Tsepova E.L. Predictive periodontology (literature review) // Dental South. 2013. No. 8. pp. 13–15.

24. Yanushevich O.O., Sirbu O.N. The role of sex hormones in the pathogenesis of chronic generalized periodontitis (literature review) // Russian Dentistry. 2014. No. 7. pp. 3–7.

25. Tsepov L. M. Periodontitis: a local focus of serious problems (literature review) / L. M. Tsepov, E. L. Tsepova, A.L. Tsepov // Periodontology. – 2014. – T. 19, No. 3 (72). – P. 3–6.

26. Shilov A. M. Relationships between dysbiosis of the digestive tract (periodontitis, enterocolitis), atherogenic dyslipidemia and carbohydrate metabolism disorders in the early stages of metabolic syndrome // Attending physician. – 2016. – No. 2. – P. 7.

27 Abdrakhmanov A.K., Mamaeva E.V., Yakovleva G.Yu.. Juvenile periodontitis - species of isolated microorganisms [and others] // Pediatric dentistry and prevention. – 2016. – T. 15. – No. 3 (58). – pp. 4–9

28. Yarmoshuk I. R. Biochemical changes under the influence of surgical treatment of patients with generalized periodontitis with osteopenia // Current scientific research in the modern world. – 2016. – No. 10–4 (18). – pp. 64–69.29. Wei, X. Xiao, J. Li Activation of the STAT1 Pathway Accelerates Periodontitis in Nos3-/- Mice /W. // Journal of Dental Research. – 2019. – Vol. 98 (9). – P. 1027–1036

30. Shetty M. S., Jain S., Prabhu U. M.Assessment of Periodontal Disease Among the Dental Prosthetic and Nonprosthetic Wearers in an Adult Rural Population in Mangalore Taluk, South India / // Journal of Pharmacy & Bioallied Sciences. – 2019. – Vol. 11 (2). – S175–S179

31. Joshi V. M., Bhat K. G., Kugaji M. S. Characterization and serotype distribution of Aggregatibacter actinomycetemcomitans: Relationship of serotypes to herpesvirus and

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL
(ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

periodontal status in Indian subjects // Microbial Pathogenesis. – 2017. – Vol. 110. – P. 189–195.

32. Chapple L., Brock G. R., Milward M. R., Ling N., Matthews J. B. Compromised GCF total antioxidant capacity in periodontitis: cause or effect? / // The Journal of Clinical Periodontology. – 2007. – Vol. 34. – P. 103–110

33. Darveau R. P. Periodontitis: a polymicrobial disruption of host homeostasis /R. P. Darveau // Nature Reviews Microbiology. – 2010. – Vol. 8. – P. 481–490

34. White P., Cooper P., Milward M. [et al.] Differential activation of neutrophil extracellular traps by specific periodontal bacteria / // Free Radical Biology and Medicine. – 2014. – Vol. 75, Iss. 1. – P. 53

35. Chowdhry R., Singh N., Sahu D. K. [et al.]. Dysbiosis and Variation in Predicted Functions of the Granulation Tissue

Microbiome in HPV Positive and Negative Severe Chronic Periodontitis – BioMed Research International. –2019. – Vol. 14. – 2019. – URL: hhttps://bit.ly/2lVenu4

36. Passariello C., Gigola P., Testarelli L. Evaluation of microbiota associated with Herpesviruses in active sites of generalized aggressive periodontitis // Ann Stomatol (Roma). – 2017. – Vol. 8 (2). – P. 59–70

37. Global epidemiology of dental caries and severe periodontitis – a comprehensive review / J. E. Frencken, P. Sharma, L. Stenhouse [et al.] // Journal of Clinical Periodontology. – 2017. – Vol. 44 (18). – P. 94–105

38 Murakami M., Suzuki J.-I., Yamazaki S. High incidence of Aggregatibacter actinomycetemcomitan sinfection in patients with cerebral infarction and diabetic renal failure: a cross-sectional study // BioMed Central Infectious Diseases. – 2013. – Vol. 13(1). – P. 557.

39. Tonetti M. S., Jepsen S., Jin L. Impact of the global burden of periodontal diseases on health, nutrition and wellbeing of mankind: A call for global action / // Journal of Clinical Periodontology. – 2017. – Vol. 44 (5). – P. 456–462

40. Canakci C. F., Cicek Y., Yildirim A., Sezer U., Canakci V. Increased levels of 8-hydroxydeoxyguanosine and malondialdehyde and its relationship with antioxidant enzymes in saliva of periodontitis patients // European

FRONTLINE MEDICAL SCIENCES AND PHARMACEUTICAL JOURNAL (ISSN – 2752-6712)
VOLUME 04 ISSUE 02 Pages: 18-33
SJIF IMPACT FACTOR (2021: 5.14) (2022: 5.605) (2023: 6.659)
OCLC – 1272874727
Publisher: Frontline Journals

Journal Of Dental Education. – 2005. – Vol. 3. – P. 100–106.

41. Xing Y., Zhang Y., Jia L. [et al.] Lipopolysaccharide from Escherichia coli stimulates osteogenic differentiation of human periodontal ligament stem cells through Wnt/β-catenin-induced TAZ elevation // Molecular Oral Microbiology. – 2019. – Vol. 34 (1). – URL: https://bit.ly/2lYReqL

42. NADPH oxidase (CYBA) and FcgammaR polymorphisms as risk factors for aggressive periodontitis: a case-control association study // Journal of Clinical Periodontology. – 2006. – Vol. 33. –P. 529–539

43. Periodontal Status of Chinese Adolescents: Findings from the 4th National Oral Health Survey / X. Chen, W. Ye, J. Y. Zhan // The Chinese Journal of Dental Research. – 2018. – Vol. 21 (3). – P. 195–220.

44. Eke P. I., Thornton-Evans G. O., Wei L. Periodontitis in US Adults: National Health and Nutrition Examination Survey2009–2014 / // Journal of the American Dental Association. – 2018. – Vol. 149(7). – P. 576–588.

45. Salivary biomarkers: relationship between oxidative stress and alveolar bone loss in chronic periodontitis / D. Miricescu, A. Totan, B. Calenic, B. Mocanu // Acta Odontologica Scandinavica. – 2014. – Vol. 72. – P. 42–47.

46. Nguyen T. T., Ngo L. Q., Promsudthi A., Surarit R. Salivary oxidative stress biomarkers in chronic periodontitis and acute coronary syndrome // Clin Oral Investig. – 2017. – Vol. 21(7). – P. 2345–2353.

47. Scher J. U. Periodontal disease and subgingival microbiota as contributors for rheumatoid arthritis pathogenesis: modifiable risk factors? / J. U. Scher, W. A. Bretz, S. B. Abramson // Current opinion in rheumatology. – 2014. –Vol. 26. – P. 424–429

48. Stabholz A. Genetic and environmental risk factors for chronic periodontitis and aggressive periodontitis / A. Stabholz, W. A. Soskolne, L. Shapira // Journal of Periodontology. – 2010. – Vol. 53. – P. 138–153.

49. The role of bacteriophages in periodontal health and disease / G. Pinto, M. D. Silva, M. Peddey // Future Microbiology. – 2016. – Vol. 11. –P. 1359–1369