International Journal of Biomedicine 15(4) (2025) 634-638
http://dx.doi.org/10.21103/Article15(4)_RA2

REVIEW ARTICLE

INTERNATIONAL JOURNAL OF BIOMEDICINE

Oxidative Stress and Oral Microbiota in Periodontitis (Brief-Review)

Marina A. Darenskaya[1*], Ivan S. Goncharov[1,2], Natalya A. Yuzvak[1], Sergey I. Kolesnikov[1], Natalya E. Bolshedvorskaya[2], Lyubov I. Kolesnikova[1]

[1]*Scientific Centre for Family Health and Human Reproduction Problems, Irkutsk, Russian Federation*
[2]*Irkutsk State Medical University, Irkutsk, Russian Federation*

Abstract

The investigation of periodontitis pathogenesis is critically important due to its global prevalence. It has been established that periodontitis is associated with chronic periodontal inflammation, alveolar bone loss, the development of oxidative stress, and oral microbiota dysbiosis. Oxidative stress biomarkers (e.g., malondialdehyde, 8-OHdG) and genetic factors (CXCR4, SELL, ITGAL) exacerbate tissue damage and osteoclastogenesis. The oral microbiota plays a significant role in the development and progression of periodontitis through complex interactions with host immune responses, mediated by pathogenic bacteria like Porphyromonas gingivalis and their metabolic byproducts. Emerging therapies targeting OS (e.g., resveratrol, curcumin) and microbial balance highlight the need for integrated treatment strategies. In this context, it is particularly relevant to investigate the interplay between oxidative stress and microbial dysbiosis to develop targeted therapeutic strategies for the prevention and treatment of periodontitis and its systemic complications. (**International Journal of Biomedicine. 2025;15(4):634-638.**)

Keywords: periodontitis • pathogenesis • oxidative stress • inflammation • oral microbiome • systemic links

For citation: Darenskaya MA, Goncharov IS, Yuzvak NA, Kolesnikov SI, Bolshedvorskaya NE, Kolesnikova LI. Oxidative Stress and Oral Microbiota in Periodontitis (Brief-Review). International Journal of Biomedicine. 2025;15(4):634-638. doi:10.21103/Article15(4)_RA2

Abbreviations

8-OhdG, 8-hydroxy-2-deoxyguanosine; **AH**, arterial hypertension; **AOD**, antioxidant defense; **CAT**, catalase; **GPx**, glutathione peroxidase; **GR**, glutathione reductase; **GSH**, reduced glutathione; **LPO**, lipid peroxidation; **NO**, nitric oxide; **OS**, oxidative stress; **ROS**, reactive oxygen species; **SOD**, superoxide dismutase; **TBARs**, thiobarbituric acid reactants; **WHO**, World Health Organization.

Relevance of Studying Periodontitis

Periodontitis is one of the most common diseases, affecting between 50% and 90% of individuals in developing countries and between 4% and 76% in developed countries [1] According to the World Health Organization (WHO). intact periodontitis occurs only in 2-10% of cases, while inflammatory periodontal diseases are detected in 90-95% of the adult population.[2]

Periodontitis is characterized by prolonged periodontal inflammation, including the gum, periodontal ligament, and alveolar bone, with loss of the latter.[3] The main cause, as a rule, is pathogenic microorganisms contained in plaque.[4] The decisive predisposing factors are the fact of smoking, poor oral hygiene, genetic component, gastrointestinal disorders, etc.[5] At a young age, traumatic effects, bleeding gums, partial dentition, low bone mineral density, and obesity are added.[6] It was also noted that disorders in the immune system, local changes in acid-base balance, hypoxia, and other adverse factors contribute to the proliferation of pathogenic microorganisms, an increase in the activity of opportunistic infection, and the progression of inflammatory and destructive periodontal diseases.[7] In recent years, it has been proven that periodontitis, as an inflammatory process, can be epidemiologically related to other chronic diseases, which include cardiovascular, neurodegenerative, autoimmune, oncological, and others.[8-10] Understanding the pathology and etiology of periodontitis is crucial to developing effective approaches to periodontitis treatment.

Oxidative Stress in Periodontitis Genesis

Currently, more than 200 diseases associated with the involvement of free radicals are known. They are characterized by changes in the internal environment and vascular disorders, which indicate a single mechanism of development – an

imbalance in the "lipid peroxidation (LPO) – antioxidant defense (AOD) "LPO – AOD system. The term oxidative stress (OS) is widely used to describe this imbalance.[11] LPO-AOD plays an important role in adaptive reactions, reducing the activity of inflammatory processes, pathology, and maintaining homeostasis.[12] The predominant role of this type of reaction in modifying cell membrane structure, xenobiotic metabolism, regulating the immune response, cell proliferation, vascular permeability, and receptor sensitivity is well established.[13] The activation of LPO reactions in the membranes of the endoplasmic reticulum, mitochondria, and lysosomes undoubtedly plays a crucial role in the functioning of normal cellular systems, presumably determining overall reactivity and resistance to pathogenic factors.[14]

Modern studies confirm that the insufficiency of AOD factors contributes to the uncontrolled intensification of LPO processes, which play a crucial role in the development of various pathologies, including those associated with periodontal disorders.[15] Moreover, the development of OS occurs not only due to a decrease in the buffer capacity of the AOD system, but also due to a violation of its mobilization in response to an increase in the activity of prooxidant factors. Protection of cells from LPO at different stages is implemented by various systems of both enzymatic and non-enzymatic nature.[16] At the same time, LPO reactions in the membranes of various cellular compartments play a crucial role in determining the overall reactivity of the body and its resistance to pathogenic influences.[17]

It was proven that OS plays a key role in the pathogenesis of periodontitis. Studies revealed changes in the expression of genes associated with oxidative stress (OS genes) in patients with periodontitis.[18,19] In total, 74 genes were isolated in periodontitis, the expression of which changes during OS, including 65 genes with increased expression and 9 genes with reduced expression. Six key genes (CXCR4, SELL, FCGR3B, FCGR2B, PECAM1, and ITGAL) are involved in leukocyte intercellular adhesion, phagocytosis, and cellular extravasation, which highlights their role in the pathogenesis of the disease.[20] CXCR4 is one of the most expressed OS genes in periodontal tissues. It plays a key role in podocyte damage, proteinuria, and glomerular sclerosis under oxidative stress. The neutralization of CXCR4 suppresses the resorption of the alveolar bone in periodontal inflammation. CXCR4 also suppresses the release of nitric oxide from macrophages and is involved in modulating mechanical sensitivity in periodontitis. The interaction of PECAM1 and CXCR4 genes enhances the transendothelial migration of leukocytes, promoting tissue infiltration by neutrophils and monocytes. The SELL and ITGAL genes ensure the adhesion of immune cells to the endothelium, which exacerbates periodontal damage.[20] Another study also identified the OS genes ITGAM, FCGR3A, and PECAM1, which perform a crucial function in the development of periodontitis.[21] Under the influence of pathogenic microflora, increased involvement and activation of neutrophils in periodontal tissues is noted, which, in turn, synthesize reactive oxygen species (ROS).[22] There is an aberrant activation of neutrophils, the increased release of pro-inflammatory mediators, which ultimately leads to tissue damage and disease progression.[23] It is interesting to discover the special structure of neutrophils – neutrophil extracellular traps (netosis), which they use for their function. Numerous studies indicate violations of local and/or systemic OS indicators.[24] Thus, clinical studies demonstrate an increase in the levels of LPO products, such as diene conjugates and malondialdehyde, in saliva and gingival fluid in patients with periodontitis.[25,26] These changes correlate with the severity of the disease and can serve as markers of its progression.[25,27] In periodontitis, there was also an increase in other markers of OS – 8-OHdG, carbonylated proteins, nitric oxide (NO), and 8-isoprostanes.[28,29] Several studies have investigated the level of nitrosative stress in the saliva of patients with periodontitis.[30] Basically, an increased level of these biomarkers was found, correlating with the risk of developing comorbidity of periodontal pathology and cardiovascular diseases.[24] Patients with periodontitis also exhibited an increase in less common markers, such as those indicating nuclear abnormalities and shortening of leukocyte telomeres.[31,32] Periodontitis-induced OS can trigger pro-inflammatory mechanisms and, significantly, osteoclastogenesis, which then leads to bone loss observed in patients with periodontitis.[20] Studies of the AOD system in periodontitis primarily focus on the activity of GR, SOD, CAT, GPx, myeloperoxidase, vitamin C, uric acid, GSH, melatonin, and the integral indicator of overall antioxidant status.[23] Negative changes in periodontitis often occur in the saliva. In patients with periodontitis, there were disturbances in glutathione homeostasis in peripheral blood neutrophils, which significantly impaired the chemotactic ability of these cells to combat infectious agents.[33] In patients with stage IV periodontitis, vitamin C levels were significantly lower than those in patients with early-stage periodontitis.[34] It was also noted that vitamin D deficiency led to a decrease in bone density, osteoporosis, and, as a result, the progression of periodontal diseases.[35] It is believed that the traditional treatment of periodontitis, which aims to combat bacterial pathogens, is insufficient. The use of additional antioxidants, such as resveratrol, quercetin, biochanin A, pyonol, and curcumin, which react stoichiometrically with ROS, has become a promising method for treating periodontitis.[36]

Oral Microbiota and Periodontitis

The human oral cavity is home to a diverse array of microorganisms that form a complex ecosystem, which, in terms of the number of species and complexity of organization, is second only to the microbiota of the gastrointestinal tract.[37] The complexity of the microbiota is due to the diverse environmental conditions in various parts of the oral cavity, which form microenvironments for colonization and growth of specific microorganisms forming highly organized surface-associated communities (biofilms) immersed in an extracellular polymer matrix, which consists of a complex of extracellular polymeric substances (water, polysaccharides, proteins, lipids, and DNA).[38] The oral microbiota plays a key role in the development and progression of periodontitis.[39] Plaque bacteria are the main culprits of periodontal diseases.[40] Plaque is present in both the supra-gingival and sub-gingival regions, forming microbial biofilms that multiply on the tooth surface. The slit-like epithelium and gingival fissure serve as the main

habitats of microbes, supported by gingival slotted fluid and a favorable anaerobic environment.[41] It has been identified that the subgingival plaque, comprising more than 500 species, changes composition as the disease progresses.[42] In healthy conditions, gram-positive cocci and rods predominate as early colonizers, while *Fusobacterium nucleatum* promotes bacterial coagulation.[43] Pathogenic microorganisms, such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, are capable of triggering a systemic inflammatory response and exacerbating the course of the disease.[44] It was found that OS can suppress the tolerance of macrophages to endotoxins induced by lipopolysaccharides produced by *Porphyromonas gingivalis* bacteria, thereby contributing to the progression of periodontitis through the suppression of tolerance to endotoxins.[45] It is known that *Aggregatibacter actinomycetemcomitans* can migrate from stress factors to a more protected subgingival region due to the activation of hexosaminidase, which attacks matrix polysaccharides containing hexosamine.[46] When faced with an innate subgingival reaction, *Aggregatibacter actinomycetemcomitans* can activate complement resistance genes and leukotoxin production to modulate the host's local immune response and ensure the proliferation of a consortium of pathobionts. Working together, the consortium can suppress the natural resistance of the host organism and produce inflammatory cytokines, which can lead to loss of connective tissue and bone tissue, as well as impaired attachment.[47]

Microbial imbalance (dysbiosis) contributes to the activation of OS and chronic inflammation. The formation of ROS, which has primarily antimicrobial effects, can be considered a double-edged sword, as ROS can help destroy invading pathogens during treatment; however, when overactivated, they can become cytotoxic to host cells. ROS play an essential role in cell signaling, gene regulation, and antimicrobial defense. Still, an overabundance of reactive oxygen species leads to increased oxidative stress, along with unchanged or reduced antioxidant capacity, which in turn leads to OS in the affected tissues. This subsequently results in pathological changes and, consequently, cell destruction of the host tissues.[48]

Periodontitis and Systemic Diseases

Periodontitis is often associated with systemic pathologies such as oral cancer, Alzheimer's disease, Parkinson's disease, hypertension, diabetes mellitus, and chronic kidney disease.[49] The connection arises from chronic low-grade inflammation, bacterial dissemination, and shared pathogenic mechanisms between periodontal and systemic diseases. Every year, the dentists' interest in disorders of systemic and local hemodynamics is expanding, and the links between periodontal pathology and cardiovascular diseases were established. The presence of systemic diseases, taking medications, and hormonal changes can certainly have a significant effect on periodontal tissue. Thus, it was established that comorbid associations of periodontitis, particularly with arterial hypertension (AH) in adolescence, are accompanied by disorders of systemic hemodynamics and contribute to a more active course of inflammatory processes in periodontal tissues.[50] Circulatory disorders in periodontal diseases correlate with the severity and degree of hypertension, as manifested by changes in vascular tone and permeability, endothelial dysfunction in the arterial network, and impaired autonomic regulation of vascular tone in tissues.[50] The risk factors for periodontal disease on the background of hypertension include common factors: socio-economic, smoking, stress, and age; hence, hypertension and periodontitis have a common mechanism of development.[51] In particular, the dynamic balance in the LPO-AOD underlies the functioning of systems that regulate the contraction of vascular smooth muscle cells and, consequently, systemic blood pressure.[52] It was established that the disorganization of the homeostatic mechanisms of the microvascular periodontal bed in arterial hypertension causes chronic hypoxia of the periodontal complex tissues, in which the processes of LPO of biomolecules are activated, leading to a violation of the structure and function of periodontal biomembranes correlations between the parameters of blood flow of the microcirculatory bed of the periodontium and the content of the final products of LPO thiobarbituric acid reactants (TBARs). The reinforcing effect of damaging factors may be due to the accumulation of prooxidants in periodontal tissues, their subsequent decomposition, leading to the formation of free radicals that have a destructive effect on the vascular wall, resulting in fibrosis, thickening of capillaries, and partial or complete obliteration.[53]

Oxidative stress plays a key mediating role, as stress-related overproduction of ROS overwhelms antioxidant defenses, accelerating periodontal tissue breakdown and worsening systemic disease progression. Stress factors play a significant role in the development of periodontitis. It is known that adaptation to stress is associated with the activation of stress-limiting systems, including prostaglandin and antioxidant systems, as well as an increase in the number of adenosinergic receptors. This suggests that the protective effects under stress are based on the coordinated activation of central and local stress-limiting systems. At the same time, adaptation to stress factors is impossible in cases where the regulatory stress systems responsible for implementing stress reactions have congenital or acquired defects. It can be assumed that an innate predisposition to hypertension reduces the body's functional reserves, which may serve as a risk factor for further disease progression.[54]

In conclusion, periodontitis is a multifactorial disease, the pathogenesis of which is influenced by oxidative stress, dysbiosis of the oral microbiota, and systemic inflammation. The relationship of periodontitis with cardiovascular and other chronic diseases was established, which underlines the need for an integrated approach to its prevention and treatment. Further studies of the pathogenetic mechanisms of periodontitis will help develop personalized therapies aimed at correcting oxidative stress and restoring microbial balance.

Conflicts of Interest

The authors declare that they have no competing interests.

References

1. Ayati A, Khodabandelu S, Khaleghi S, Nourmohammadi A, Jafari F, Ahmadianghalehsorkh M, et al. A systematic review and network meta-analysis of the association between periodontitis and inflammatory bowel diseases. BMC Oral Health. 2025;25(1):463. doi: 10.1186/s12903-025-05830-9.
2. World Health Organization. Global oral health status report: towards universal health coverage for oral health by 2030; 2022.
3. de Pablo P, Chapple IL, Buckley CD, Dietrich T. Periodontitis in systemic rheumatic diseases. Nature reviews. Rheumatology. 2009; 5(4):218–224. doi: 10.1038/nrrheum.2009.28
4. Wang Z, Saxena A, Yan W, Uriarte SM, Siqueira R, Li X. The impact of aging on neutrophil functions and the contribution to periodontitis. International journal of oral science. 2025;17(1):10. doi: 10.1038/s41368-024-00332-w
5. Ray RR. Periodontitis: an oral disease with severe consequences. Applied biochemistry and biotechnology. 2023;195(1):17-32. doi: 10.1007/s12010-022-04127-9
6. Hung M, Kelly R, Mohajeri A, Reese L, Badawi S, Frost C, et al. Factors associated with periodontitis in younger individuals: A scoping review. Journal of Clinical Medicine. 2023;12(20):6442. doi: 10.3390/jcm12206442
7. Orlandi M, Munoz Aguilera E, Marletta D, Petrie A, Suvan J, D'Aiuto F. Impact of the treatment of periodontitis on systemic health and quality of life: A systematic review. Journal of Clinical Periodontology. 2022;49:314-327. doi: 10.1111/jcpe.13554.
8. Schenkein HA, Papapanou PN, Genco R, Sanz M. Mechanisms underlying the association between periodontitis and atherosclerotic disease. Periodontology 2000. 2020;83(1):90–106. doi: 10.1111/prd.12304.
9. Genco RJ, Sanz M. Clinical and public health implications of periodontal and systemic diseases: An overview. Periodontology. 2000. 2020;83(1):7–13. doi: 10.1111/prd.12344.
10. Ishai A, Osborne MT, El Kholy K, Takx RAP, Ali A, Yuan N, et al. Periodontal Disease Associates With Arterial Inflammation Via Potentiation of a Hematopoietic-Arterial Axis. JACC Cardiovasc. Imaging. 2019;12:2271–2273. doi: 10.1016/j.jcmg.2019.05.015.
11. Kolesnikova LI, Darenskaya MA, Kolesnikov SI. [Free radical oxidation: a pathophysiologist's view]. Bulletin of Siberian Medicine. 2017;16(4):16-29. doi: 10.20538/1682-0363-2017-4-16-29. [Article in Russian].
12. Darenskaya MA, Grebenkina LA, Sholokhov LF, Rashidova MA., Semenova NV, Kolesnikov SI, et al. Lipid peroxidation activity in women with chronic viral hepatitis. Free Radical Biology & Medicine. 2016;100(S):192. doi: 10.1016/j.freeradbiomed.2016.10.525.
13. Darenskaya MA, Kolesnikova LR, Rychkova LV, Grebenkina LA, Semenova NV, Druzhinina EB, et al. Comparative Analysis of Lipid Peroxidation System in Humans and Rats with Arterial Hypertension. International Journal of Biomedicine. 2019;9(4):292-296. doi: 10.21103/Article9(4)_OA3
14. Darenskaya M, Kolesnikova L, Kolesnikov S. The association of respiratory viruses with oxidative stress and antioxidants. implications for the COVID-19 pandemic. Current Pharmaceutical Design. 2021;27(13):1618-1627. doi: 10.2174/1381612827666210222113351
15. Kolesnikova LR, Darenskaya MA, Pogodina AV, Grebenkina LA, Natyaganova LV, Kolesnikova LI, et al. [The relationship of hemodynamic parameters of periodontal microvascular bed and lipid peroxidation products in adolescents with arterial hypertension]. Stomatology. 2020;99(4):914. doi: 10.17116/stomat2020990419 [Article in Russian]
16. Kolesnikova LI, Darenskaya MA, Grebenkina LA, Osipova EV, Dolgikh MI, Semenova NV. [Analysis of antioxidant status and actual diet of students]. Voprosy pitaniia. 2015;84(4):66-73.[Article in Russian]
17. Kolesnikova LI, Rychkova LV, Kolesnikova LR, Darenskaya MA, Natyaganova LV, Grebenkina LA., et al. Coupling of lipoperoxidation reactions with changes in arterial blood pressure in hypertensive isiah rats under conditions of chronic stress. Bulletin of Experimental Biology and Medicine. 2018;164(6):712-715.doi: 10.1007/s10517-018-4064-3
18. Halliwell B. Understanding mechanisms of antioxidant action in health and disease. Nature Reviews Molecular Cell Biology. 2024;25(1):13-33. doi:10.1038/s41580-023-00645-4
19. Sies H, Mailloux RJ, Jakob U. Fundamentals of redox regulation in biology. Nature Reviews Molecular Cell Biology. 2024;25(9):701-719. doi:10.1038/s41580-024-00730-2
20. Zhang Z, ZhengY, Bian X, Wang M, Chou J, Haifeng L, et al. Identification of key genes and pathways associated with oxidative stress in periodontitis. Oxidative Medicine and Cellular Longevity, 2022;(1):1-27. doi: 10.1155/2022/9728172.
21. Zhou W, Zhang P, Li H. Identifying Oxidative Stress-Related Genes (OSRGs) as Potential Target for Treating Periodontitis Based on Bioinformatics Analysis. Comb Chem High Throughput Screen. 2024;27(8):1191-1204. doi:10.2174/1386207326666230821102623
22. Bassani B, Cucchiara M, Butera A, Kayali O, Chiesa A, Palano MT, et al. Neutrophils' contribution to periodontitis and periodontitis-associated cardiovascular diseases. International Journal of Molecular Sciences. 2023;24(20):15370. doi: 10.3390/ijms242015370
23. Palomino-Segura M, Sicilia J, Ballesteros I, Hidalgo A. Strategies of neutrophil diversification. Nature Immunology. 2023;24(4):575-584. doi: 10.1038/s41590-023-01452-x
24. Patil RT, Dhadse PV, Salian SS, Punse SD, Dhadse P, Salian SS. Role of Oxidative Stress in Periodontal Diseases. Cureus. 2024;16(5). doi: 10.7759/cureus.60779
25. Mohideen K, Chandrasekaran K, Veeraraghavan H, Faizee SH, Dhungel S, Ghosh S. Meta-Analysis of Assessment of Total Oxidative Stress and Total Antioxidant Capacity in Patients with Periodontitis. Disease Markers. 2023;2023(1):9949047. doi: 10.1155/2023/9949047
26. Skutnik-Radziszewska A, Zalewska A. Salivary redox biomarkers in the course of caries and periodontal disease. Applied Sciences. 2020;10(18):6240. doi: 10.3390/app10186240
27. Leong XF, Ng CY, Badiah B, Das S. Association between hypertension and periodontitis: possible mechanisms. The Scientific World Journal. 2014;(1):11-41. doi:10.1155/2014/768237
28. Goriuc A, Cojocaru KA, Luchian I, Ursu RG, Butnaru O, Foia L. Using 8-Hydroxy-2′-Deoxiguanosine (8-OHdG) as a Reliable Biomarker for Assessing Periodontal Disease Associated with Diabetes. International Journal of Molecular Sciences. 2024;25(3):1425. doi: 10.3390/ijms25031425
29. Maciejczyk M, Zalewska A, Ładny JR. Salivary antioxidant barrier, redox status, and oxidative damage to proteins and

lipids in healthy children, adults, and the elderly. Oxidative Medicine and Cellular Longevity. 2019;2019(1):4393460. doi: 10.1155/2019/4393460
30. Toczewska J, Konopka T, Zalewska A, Maciejczyk M. Nitrosative Stress Biomarkers in the Non-Stimulated and Stimulated Saliva, as well as Gingival Crevicular Fluid of Patients with Periodontitis: Review and Clinical Study. Antioxidants. 2020;9(3):259. doi: 10.3390/antiox9030259
31. de Mello Lobro WJ, Zajdenverg L, Lopes GC, de Barros MCM, Sansone C, Silva-Boghossian CM. Redox biomarkers in saliva and nuclear abnormalities in jugal epithelial cells of individuals with type 2 diabetes mellitus and periodontitis. Archives of Oral Biology. 2024;161:105915. doi: 10.1016/j.archoralbio.2024.105915
32. Sonoki K, Muraoka K, Morishita M, Awano S, Nakashima K. Periodontal Disease Shortens the Telomere Length in Human Gingival Crevicular Epithelium Cells and Human Umbilical Endothelial Cells. Journal of Biomedical Research & Environmental Sciences. 2024;5(9):1168-1175. doi: 10.37871/jbres2005
33. Binti Badlishah Sham NI, Grant MM. Role of Glutathione in Neutrophil Chemotaxis in Periodontitis. Oral. 2023;3(4):526-538. doi: 10.3390/oral3040043
34. Munday MR, Rodricks R, Fitzpatrick M, Flood VM, Gunton JE. A Pilot Study Examining Vitamin C Levels in Periodontal Patients. Nutrients. 2020;12(8):2255. doi: 10.3390/nu12082255
35. Nascimento GG, Leite FR, Gonzalez-Chica DA, Peres KG, Peres MA. Dietary vitamin D and calcium and periodontitis: A population-based study. Frontiers in Nutrition. 2022;9:1016763. doi: 10.3389/fnut.2022.1016763
36. Wu Y, Zhang X, Chen Y, Chen W, Qian W. Identification the Low Oxidative Stress Subtype of Periodontitis. International Dental Journal. 2024;74(1):119-128. doi:10.1016/j.identj.2023.07.011
37. Huttenhower C, Gevers D, Knight R, Abubucker S, Badger JH, Chinwalla AT, et al. Structure, function and diversity of the healthy human microbiome. Nature. 2012;486:207–214. doi: 10.1038/nature11234.
38. Di Stefano M, Polizzi A, Santonocito S, Romano A, Lombardi T, Isola G. Impact of Oral Microbiome in Periodontal Health and Periodontitis: A Critical Review on Prevention and Treatment. International Journal of Molecular Sciences. 2022;23(9):5142. doi: 10.3390/ijms23095142
39. Gao L, Xu T, Huang G, Jiang S, Gu Y, Chen F. Oral microbiomes: More and more importance in oral cavity and whole body. Protein Cell. 2018;9:488–500. doi: 10.1007/s13238-018-0548-1.
40. Lu M, Xuan S, Wang Z. Oral microbiota: A new view of body health. Food Sci. Hum. Wellness. 2019;8:8–15. doi: 10.1016/j.fshw.2018.12.001
41. Malla MA, Dubey A, Kumar A, Yadav S, Hashem A, Abd Allah EF. Exploring the Human Microbiome: The Potential Future Role of Next-Generation Sequencing in Disease Diagnosis and Treatment. Front. Immunol. 2019;9:2868. doi: 10.3389/fimmu.2018.02868.
42. Moore WE, Moore LV. The bacteria of periodontal diseases. Periodontology 2000. 1994;5:66–77. doi: 10.1111/j.1600-0757.1994.tb00019.x.
43. Rajasekaran JJ, Krishnamurthy HK, Bosco J, Jayaraman V, Krishna K, Wang T, et al. Oral Microbiome: A Review of Its Impact on Oral and Systemic Health. Microorganisms. 2024;12(9):1797. doi: 10.3390/microorganisms12091797
44. Mukherjee S, Chopra A, Karmakar S, Bhat, SG. Periodontitis increases the risk of gastrointestinal dysfunction: an update on the plausible pathogenic molecular mechanisms. Critical Reviews in Microbiology. 2024;51(1):187–217.doi: 10.1080/1040841X.2024.2339260
45. Yamaguchi T, Yamamoto Y, Egashira K, Sato A, Kondo Y, Saiki S, et al. Oxidative Stress Inhibits Endotoxin Tolerance and May Affect Periodontitis. Journal of Dental Research. 2022;102(3):331-339. doi:10.1177/00220345221138523
46. Ramasubbu N, Thomas LM, Ragunath C, Kaplan JB. Structural analysis of dispersin B, a biofilm-releasing glycoside hydrolase from the periodontopathogen Actinobacillus actinomycetemcomitans. Journal of Molecular Biology. 2005;349(3):475-486. doi:10.1016/j.jmb.2005.03.082
47. Fine DH, Patil AG and Velusamy SK. Aggregatibacter actinomycetemcomitans (Aa) Under the Radar: Myths and Misunderstandings of Aa and Its Role in Aggressive Periodontitis. Front. Immunol. 2019;10:728. doi: 10.3389/fimmu.2019.00728
48. Sczepanik FSC, Grossi ML, Casati M, Goldberg M, Glogauer M, Fine N, et al. Periodontitis is an inflammatory disease of oxidativestress: We should treat it that way. Periodontol 2000. 2020;84:45-68. doi: 10.1111/prd.12342
49. Albahri J, Allison H, Whitehead KA, Muhamadali H. The role of salivary metabolomics in chronic periodontitis: bridging oral and systemic diseases. Metabolomics. 2025;21(1):24. doi:10.1007/s11306-024-02220-0
50. Kolesnikova LR, Darenskaya MA, Kolesnikova LI, Grebenkina LA, Kolesnikov SI, Korytov LI, et al. Morphofunctional state of the periodontal tissues in humans and rats with arterial hypertension. Bulletin of Experimental Biology and Medicine. 2020;169(6):831-835. doi: 10.1007/s10517-020-04990-8
51. Stepanov EA, Kurashvili LV, Mikulyak NI, Moiseev YaP, Kinzirskiy AS. [The features of parodentium's microcirculation in various systemic diseases (a literature review)]. Izvestiya Vysshikh Uchebnykh Zavedeniy. Povolzhskiy region. Meditsinskie Nauki. 2021;2:137–150. doi:10.21685/2072-3032-2021-2-13. [Article in Russian]
52. Bairova TA, Kolesnikov SI, Kolesnikova LI, Pervushina OA, Darenskaya MA, Grebenkina LA. Lipid peroxidation and mitochondrial superoxide dismutase-2 gene in adolescents with essential hypertension. Bulletin of Experimental Biology and Medicine. 2015;158(2):181-184. doi: 10.1007/s10517-014-2717-4
53. Kolesnikova LR, Darenskaya MA, Pogodina AV, Grebenkina LA, Natyaganova LV, Kolesnikova LI, et al. [The relationship of hemodynamic parameters of periodontal microvascular bed and lipid peroxidation products in adolescents with arterial hypertension]. Stomatology. 2020;99(4):914. doi: 10.17116/stomat2020990419 [Article in Russian]
54. Kolesnikova LI, Kolesnikova LR, Darenskaya MA, Natyaganova LV, Grebenkina LA, Korytov LI, et al. Comparison of Reactivity of the Lipid Peroxidation–Antioxidant Defense System in Normal and Hypertensive Rats at Different Stages of Stress-Reaction. Bulletin of Experimental Biology and Medicine. 2019;166(5):613-616. doi: 10.1007/s10517-019-04403-5

***Corresponding author**: Prof. Marina Darenskaya, PhD, ScD. E-mail: marina_darenskaya@inbox.ru,*