ORIGINAL ARTICLE

CONTENTS

Condition of periodontal tissues in experimental animals under the model of periodontitis combined with intestinal dysbiosis

Valentina N. Kulygina[1], Olha V. Polishchuk[2], Elvira M. Danko[1], Halyna M. Poberezhna[3], Yuliia O. Slynko[1], Roman S. Arshynnikov[4], Larysa F. Kurdysh[3]

[1]UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE
[2]POLISHCHUK DENTAL CENTER, KHMELNYTSKYI, UKRAINE
[3]NATIONAL PIROGOV MEMORIAL MEDICAL UNIVERSITY, VINNYTSYA, UKRAINE
[4]SHUPYK NATIONAL HEALTHCARE UNIVERSITY OF UKRAINE, KYIV, UKRAINE

ABSTRACT

Aim: To study the nature of clinical and morphological changes in periodontal tissues under combined modeling of periodontitis and intestinal dysbiosis in an animal experiment.

Materials and Methods: The study involved 30 rats (1 control and 2 experimental groups of 10 animals each). Histological changes in the gingiva were examined during periodontitis modeling in 10 animals over 30 days and its combination with intestinal dysbiosis in the remaining 10 animals over 30–35 days. The degree of alveolar bone ridge atrophy was assessed, and the composition of the intestinal microflora was analyzed to confirm intestinal dysbiosis.

Results: It was established that the reproduction of experimental periodontitis in animals and its subsequent combination with intestinal dysbiosis contributed to the development of a pathological process in the periodontal tissues in 100% of rats, resembling an exacerbated course of human periodontitis, with increased severity and progression. In rats with simultaneous modeling of periodontitis and intestinal dysbiosis, more pronounced pathological changes were observed—compared to those without dysbiotic lesions—in the gingival epithelium, the connective tissue of the mucous membrane, and especially in the blood vessels of the microcirculatory bed and perivascular areas.

Conclusions: Morphological studies confirmed that disturbances in the intestinal microecological system, accompanied by suppression of its saprophytic flora, aggravate the course of periodontitis, promote its generalization, and contribute to the development of abscess-forming inflammation.

KEY WORDS: periodontal disease, intestinal dysbiosis, experimental research

Wiad Lek. 2026;79(5):918-928. doi: 10.36740/WLek/220834 DOI

INTRODUCTION

Experimental studies hold considerable significance in modern medicine [1-3]. Conducting experiments on animals allows for an objective assessment of the nature of morphological changes in body tissues during disease development. This is particularly relevant for the study of comorbid conditions, including the combination of periodontal diseases with disorders of the digestive tract.

Scientific research has demonstrated a pathophysiological interconnection between the functional elements of the digestive system and the oral cavity, due to the unity of their functions and morphological structure, as the oral cavity represents the initial segment of the digestive tract [4-6]. The relationship and mutual influence between periodontal diseases and digestive system pathologies have been noted by numerous authors [7-10].

In a limited number of studies [11-13], attention has been given to the peculiarities of periodontal disease progression when combined with intestinal dysbiosis. According to the literature [14], symptoms of dysbiosis are found in up to 80% of the healthy global population. Such a latent (compensated) stage of dysbiosis contributes to disturbances in absorption mechanisms, leading to changes in the mineral metabolism of macro- and microelements and their regulators in the blood and oral fluid, to the development of immunological imbalance, alterations in the oral microbiocenosis, and other homeostatic constants of this biotope [15].

In this context, modelling a pathological process in animals that closely resembles that in humans, and

studying the nature of periodontal tissue changes during the reproduction of a comorbid condition—specifically, the combination of periodontitis and intestinal dysbiosis—presents considerable scientific interest.

AIM

To study the nature of clinical and morphological changes in periodontal tissues during combined modelling of periodontitis and intestinal dysbiosis in an animal experiment.

MATERIALS AND METHODS

To achieve the aim, an experimental study was conducted on 30 laboratory animals — white outbred rats aged three months, with an average weight of 273±20 g (1 control and 2 experimental groups, each consisting of 10 animals).

The control group consisted of intact rats (10 animals) kept on a standard vivarium diet. Group II included 10 rats in which experimental periodontitis was induced over 30 days using the reduced masticatory function method by maintaining the animals on a special paste-like diet [16]. In Group III, after induction of periodontitis, 10 experimental animals received oral ciprofloxacin (50 mg/kg) from day 31 to day 35 to create experimental intestinal dysbiosis using the selective decolonization method [17].

Once a week, the degree of alveolar bone atrophy was visually assessed based on the periodontal tissue condition in each rat, according to the following scoring system: 0 – healthy periodontium; 1 – gingivitis (hyperemia in the frontal teeth area, slight gum swelling); 2 – periodontitis of mild to moderate severity (hyperemia, edema, bleeding of the gums in the frontal and lateral tooth regions); 3 – severe periodontitis (pronounced gingival hyperplasia, swelling, bleeding along the gingival margin, and spontaneous tooth loss). The total score for each animal was divided by the number of rats in the group.

At the end of the experiment (animals in Groups I and II – after 30 days, Group III – after 35 days), the rats were sacrificed by exsanguination. After euthanasia, the large intestine was isolated from each rat, ligated at both ends, and its contents were cultured on nutrient media to determine the qualitative and quantitative composition of the microbiota.

For isolation of pure microbial cultures, differentiation, and identification, the following media were used: meat–peptone agar, blood and serum agar, Endo, Chestovych, and Sabouraud media.

Microscopic, cultural, and biochemical methods were applied to differentiate and identify microorganisms, and their absolute values were calculated as logarithmic colony-forming units per 1 ml (lg CFU/ml).

After extraction of the jaw bone tissue, the nature of the dystrophic process in periodontal tissues was evaluated using biometric methods by determining the linear dimensions of molar root exposure with a binocular loupe equipped with an eyepiece scale (graduation value 0.05 mm).

The degree of relative exposure of the molar roots (K) was calculated using the formula and expressed as a percentage: $\hat{E} = \frac{l \times 100}{l}$,

where M – distance from the edge of the dental alveolus to the cusp tip of the tooth, and l – distance from the edge of the dental alveolus to the anatomical neck of the tooth. Intact rats served as the control.

For histological examination of the gingival structures, sections 5 μm thick were prepared and stained with hematoxylin and eosin, Van Gieson's stain, and toluidine blue. Microscopic analysis was performed using a light microscope with objectives ×4, ×10, ×40 and an eyepiece ×10. Photographs were taken with a digital camera.

The reliability of the results was evaluated using Student's t-test. Statistical processing of the obtained data was performed according to the recommendations [18].

ETHICS

This work complies with the principles of the Declaration of Helsinki.

FRAMEWORK

The study was carried out within the framework of the scientific topic "*Individualization of approaches to dental treatment within the structure of a comprehensive model for predicting therapeutic outcomes*" state registration number 0123U104050 of the state university "Uzhhorod National University".

RESULTS

At the beginning of the study, clinical observation of the animals' general condition, appearance, behavior, and reactions revealed no changes that would prevent the creation of the experimental model of periodontitis and its combination with intestinal dysbiosis.

The anatomical and histological structure of the soft periodontal tissues (gingiva and periodontium) of intact rats did not differ from those described in the literature [19] (Fig. 1).

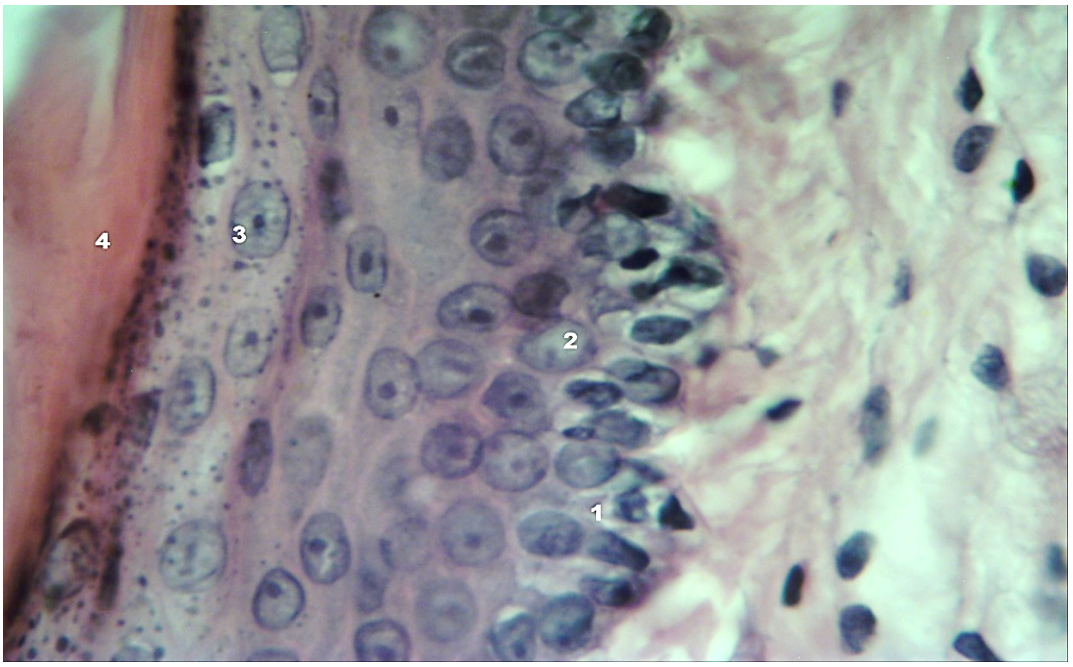

Fig. 1. Gingiva of intact rat No. 5, Group I. Hematoxylin and eosin staining. Magnification: ×400. 1 – basal layer epithelial cells; 2 – prickle layer epithelial cells; 3 – granular layer epithelial cells; 4 – keratinized layer
Picture taken by the authors

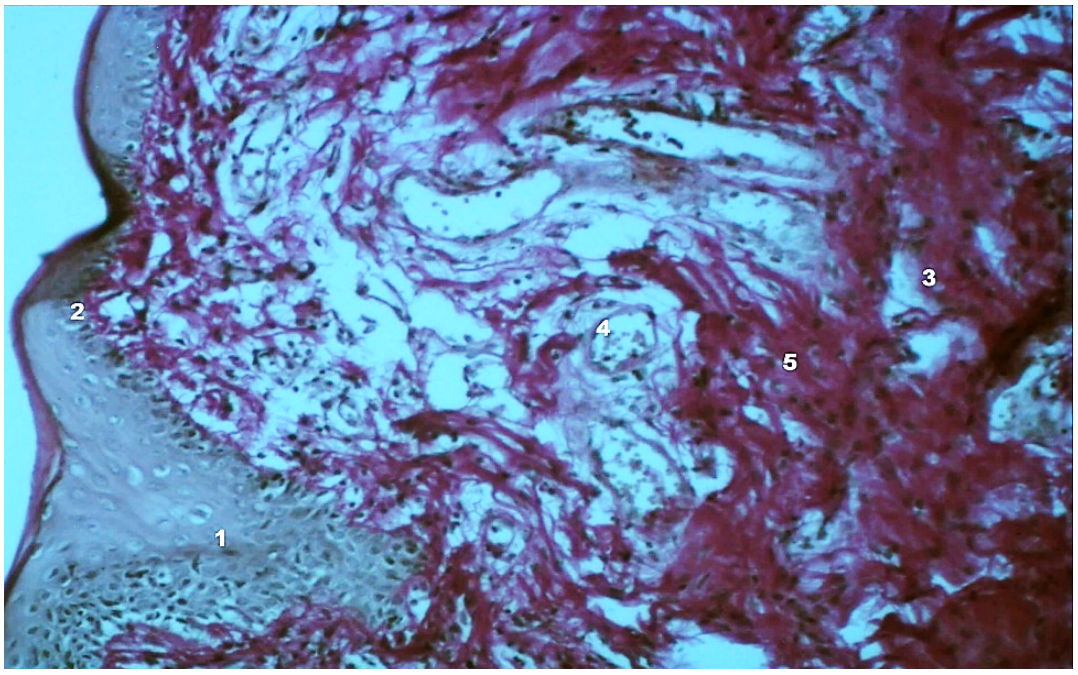

Fig. 2. Gingiva of rat No. 1, Group II, day 30 of the experiment. Diagnosis: experimental periodontitis. Destruction of collagen fibers and leukocytic infiltration observed in the basal membrane of the epithelial lining of the oral mucosa. Hematoxylin and eosin staining. Magnification: ×400. 1 – basal layer epithelial cells; 2 – prickle layer epithelial cells; 3 – basal membrane; 4 – leukocytic infiltration
Picture taken by the authors

When modeling periodontitis, after one week of the experiment, 2 out of 10 animals (20%) showed hyperemia and swelling of the marginal gingiva. The gingival mucosa of the remaining rats in Group II was pale pink, firm on palpation, non-bleeding, with no pathological pockets, and the teeth remained immobile. The periodontal tissue condition score was 0.2 points.

After two weeks, 7 animals (70%) in Group II developed gingival hyperemia, edema, and bleeding; however, the tooth–gingival attachment remained intact and the teeth were not mobile. The clinical evaluation score of the periodontal condition was 0.8 points.

After three weeks of the experimental study, 3 animals (30%) in this group exhibited gingival hyperemia, swelling, bleeding, loss of tooth–gingival attachment, and tooth mobility. In 5 animals (50%), the clinical condition of the gums corresponded to gingivitis. The total periodontal tissue condition score was 1.1 points.

After 30 days, the periodontal tissue condition in experimental rats of Group II was as follows: in 4 animals (40%) – severe periodontitis (marked gingival hyperemia, swelling, bleeding, presence of periodontal pockets, and tooth mobility); in 4 animals (40%) – moderate to mild periodontitis (gingival hyperemia, swelling,

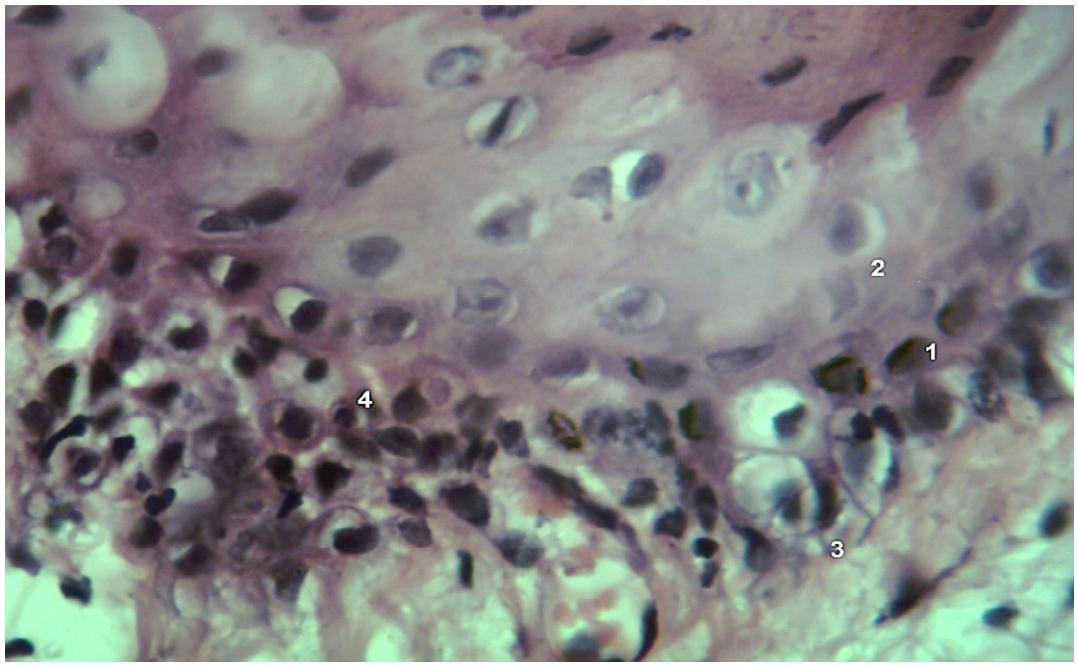

Fig. 3. Gingiva of rat No. 3, Group II, day 30 of the experiment. Diagnosis: experimental periodontitis. Destruction of collagen fibers observed in the papillary layer of the oral mucosa. Van Gieson staining. Magnification: ×100. 1 – stratified keratinized squamous epithelium; 2 – papillary layer of the oral mucosa; 3 – reticular layer of the oral mucosa; 4 – blood vessels; 5 – collagen fibers
Picture taken by the authors

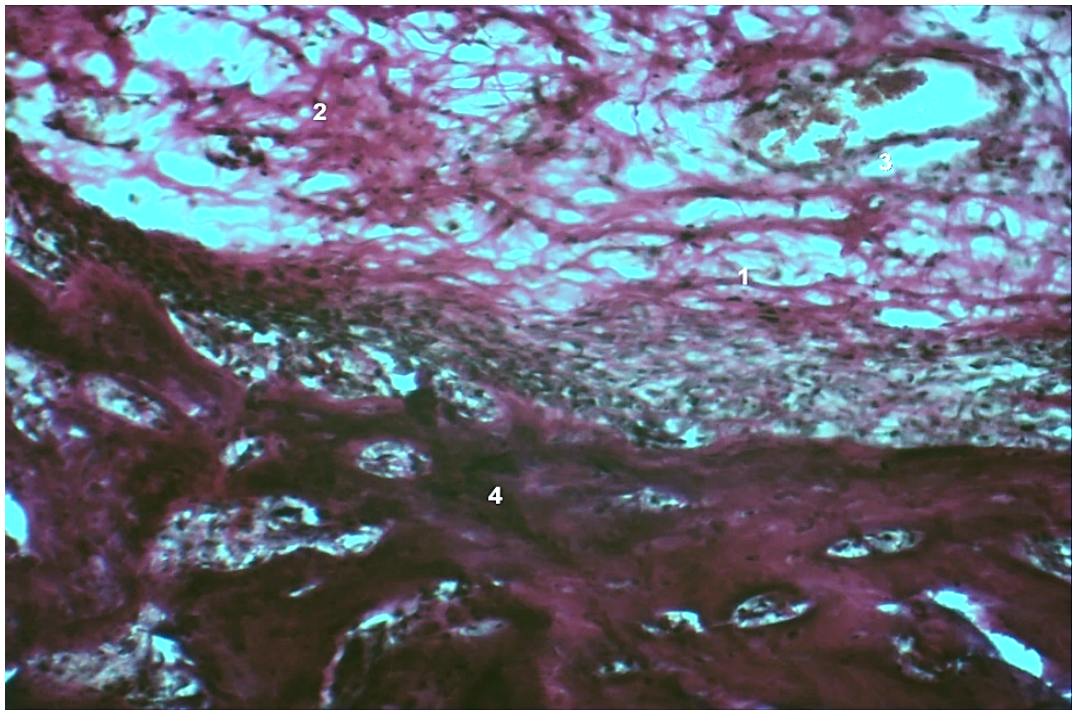

Fig. 4. Gingiva of rat No. 6, Group II, day 30 of the experiment. Diagnosis: experimental periodontitis. Vascular resorption of bone tissue observed. Van Gieson staining. Magnification: ×100. 1 – reticular layer of the oral mucosa; 2 – collagen fibers; 3 – perivascular interstitial edema; 4 – bone tissue
Picture taken by the authors

bleeding, destruction of the tooth–gingival attachment, and shallow periodontal pockets detected by probing); in 2 animals (20%) – gingivitis (slightly pronounced hyperemia and swelling of the marginal gingiva).

The average periodontal tissue condition score was 2.2 points. The degree of dystrophy of the alveolar process of the jaws was 36.8±0.33% (compared with 28.3±0.21% in the control group), $p < 0.001$.

On the 30th day of the experiment, morphological examination revealed changes in the epithelial layer and connective tissue of the gingiva. The epithelial layer was uneven in thickness — thinned in some areas and thickened in others. Compared with rats of the intact group, the keratinized layer was thicker and showed detachment over large portions of the epithelial surface. Nucleoli were often absent in the nuclei of prickle-cell layer cells, indicating a decrease in their functional activity. In the basal layer, intercellular spaces were widened, and the cells appeared vacuolated.

In some areas, the boundary between the epithelium and connective tissue was flattened. Collagen fibers of the basal membrane were loosened, and among them

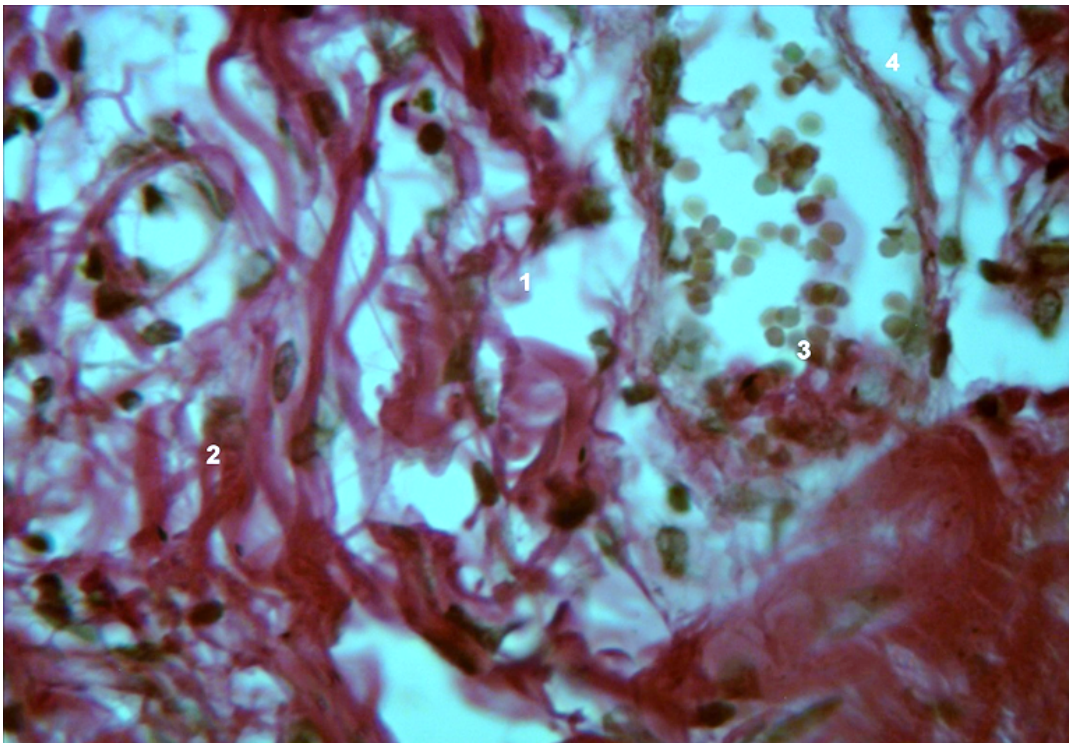

Fig. 5. Gingiva of rat No. 4, Group II, day 30 of the experiment. Diagnosis: Experimental periodontitis. Dilated vascular lumens, leukocyte stasis, and marginal accumulation in venules. Staining: Van Gieson method. Magnification: ×400. 1 – reticular layer; 2 – collagen fibers; 3- leukocyte stasis and marginal accumulation in venules; 4 – perivascular interstitial edema
Picture taken by the authors

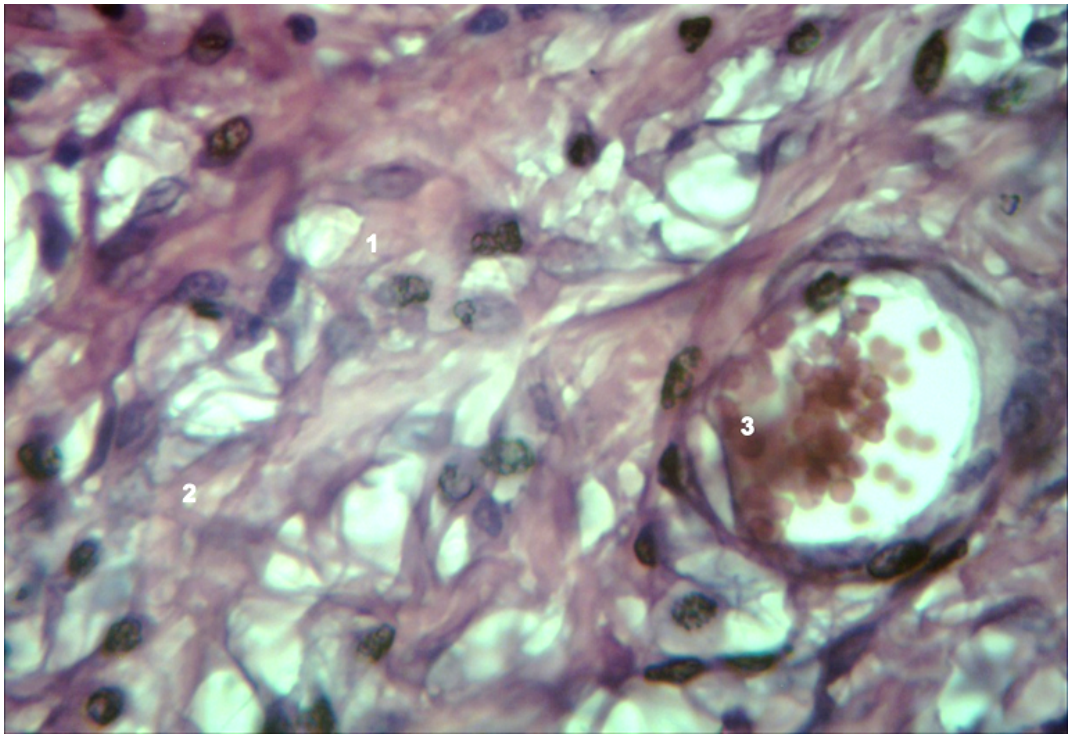

Fig. 6. Gingiva of rat No. 7, Group II, day 30 of the experiment. Diagnosis: Experimental periodontitis. Presence of mural thrombi in arterioles. Staining: Hematoxylin and eosin. Magnification: ×400. 1 – reticular layer; 2 – collagen fibers; 3 – mural thrombi in arterioles
Picture taken by the authors

were lymphocytes, histiocytes, and neutrophilic leukocytes. In certain regions, the collagen fibers appeared disorganized (Fig. 2).

In the papillary layer of the gingival connective tissue, areas of edema, destruction, and disorganization of collagen fibers were detected; the fiber bundles were separated and loosened. The cytoplasm of fibroblasts and fibrocytes appeared pale and swollen, and their nuclei were pyknotic and often showed destructive changes. Blood vessels were engorged, with dilated lumina (Fig. 3).

In the deep regions of the reticular layer, leukocytic infiltrates were observed. Changes were also found in the bone tissue of the alveolar processes of the jaws: lacunar resorption, dilation of the central vascular channels of osteons filled with leukocytes, and proliferation

Table 1. Results of the study of intestinal microbiocenosis in experimental animals, lg CFU/ml

Microorganisms	Groups of examined animals		
	Group I (control) n=10	Group II (with simulated periodontitis) n=10	Group III (with simulated periodontitis and intestinal dysbiosis) n=10
Total bacteria count	9.5±0.11	9.6±0.08 p>0.05	9.8±0.36 p>0.05
E.coli	6.2±0.08	6.3±0.10 p>0.05	6.0±0.09 p>0.05
Pseudomonas aeruginosa	1.0±0.05	1.2±0.08 p>0.05	1.9±0.06 p<0.001
Enterococus faecalis	1.0±0.11	1.2±0.09 p>0.05	1.9±0.07 p<0.001
Staphylococcus aureus	2.5±0.23	2.6±0.10 p>0.05	3.7±0.12 p<0.001
Fungi Candida	1.9±0.04	2.0±0.06 p>0.05	3.0±0.14 p<0.001
Bifidobacterium	3.1±0.18	2.8±0.18 p>0.05	1.0±0.04 p<0.001
Lactobacillus	4.0±0.15	3.7±0.10 p>0.05	1.4±0.04 p<0.001
Unidentified microorganisms	+	+	+

Note: p – is the significance of the difference in indicators between the experimental groups of animals (II and III) and the control group
Source: compiled by the authors of this study

of loose connective tissue around them. Osteoclasts were located along the edge of the bone lamella, while osteocytes showed signs of edema and cytoplasmic clearing (Fig. 4).

Significant alterations of blood capillaries, arterioles, and venules were noted. The walls of some capillaries were discontinuous. In certain regions, desquamation and swelling of endothelial cells were detected. The basal membrane in the capillary walls appeared loosened, and diapedetic hemorrhages were found around some blood capillaries.

The venules were dilated and engorged. Their lumina contained numerous leukocytes (both granular and agranular), exhibiting stasis, margination, and diapedesis through the vessel walls. Occasionally, mural thrombi were observed. The integrity of most venular walls was disrupted, with pronounced interstitial edema and perivascular hemorrhages. The perivascular spaces contained increased numbers of tissue basophils and leukocytes (Fig. 5).

The walls of the arterioles were thickened, with proliferation of collagen fibers in the adventitial layer and hyperplasia and hypertrophy of smooth muscle cells in the middle layer. The lumina of these vessels were narrowed. In some arterioles, mural thrombi almost completely occluded the vessel lumina (Fig. 6). The lumina of lymphatic vessels were dilated and filled with lymph.

On the 35th day of the experiment, when reproducing the model of experimental periodontitis in combination with intestinal dysbiosis, 100% of the rats exhibited gingival hyperemia with a bluish tint, swelling of the gingival papillae, the presence of periodontal pockets containing serous-purulent exudate, and tooth mobility, which were clinically assessed as periodontitis. In one rat, a periodontal abscess was diagnosed, indicating an aggressive nature of the pathological process in the periodontal tissues of this animal.

To confirm intestinal dysbiosis in Group III rats, the state of the colonic microbiota was compared with that of Groups I and II after completion of the experiment (Table 1). The obtained data demonstrated a generally stable species structure of the colonic microbiota, which did not change significantly during the modeling of periodontitis and intestinal dysbiosis. It was represented by monocultures and associations of conditionally pathogenic gram-negative bacteria of the family *Enterobacteriaceae* (*Escherichia coli*, *Enterococcus*), pathogenic microorganisms of the genus *Pseudomonas* (*Pseudomonas. aeruginosa*), as well as individual species of coccal (*Staphylococcus aureus*) and fungal (*Candida*) flora, and anaerobic antagonistically active bifidobacteria and lactobacilli, which suppress the growth and reproduction of pathogenic and conditionally pathogenic enteroba cteria.

The total microbial load in both experimental groups did not differ significantly from that of the control group

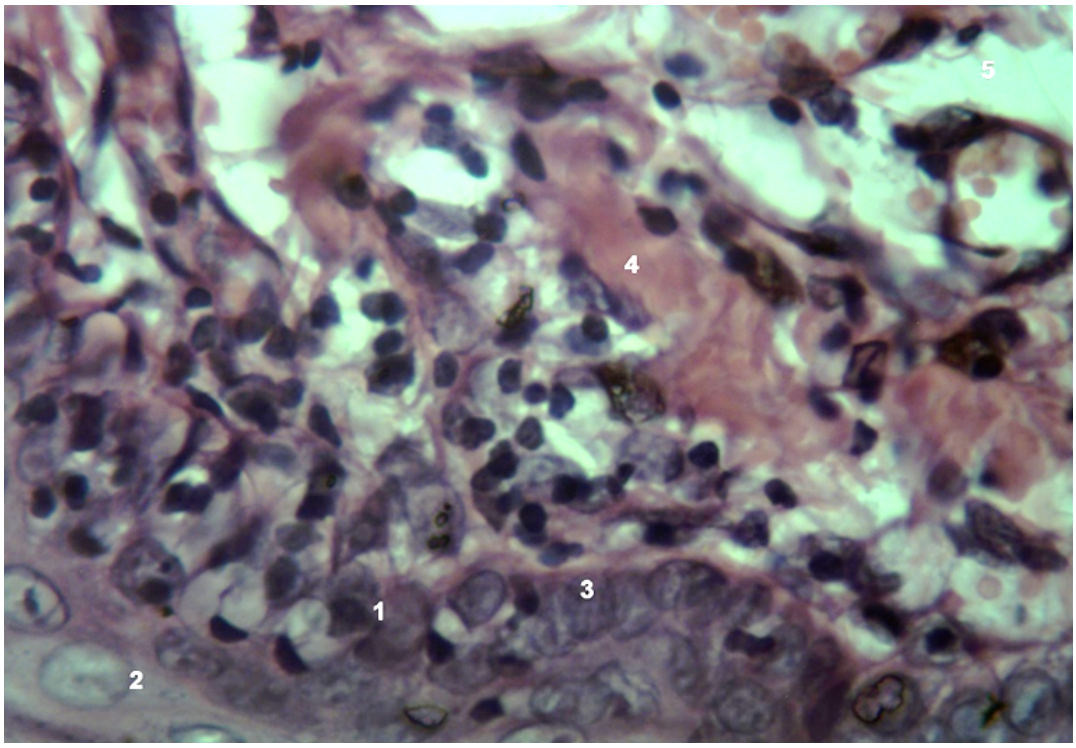

Fig. 7. Gingiva of rat No. 5, Group III, day 35 of the experiment. Diagnosis: Experimental periodontitis combined with intestinal dysbiosis. Destruction of collagen fibers and leukocyte infiltration within the basal membrane of the epithelial lining of the mucosa. Staining: Hematoxylin and eosin. Magnification: ×400. 1 – basal layer epithelial cells; 2 – prickle layer epithelial cells; 3 – basal membrane; 4 – collagen fibers; 5 – perivascular interstitial edema
Picture taken by the authors

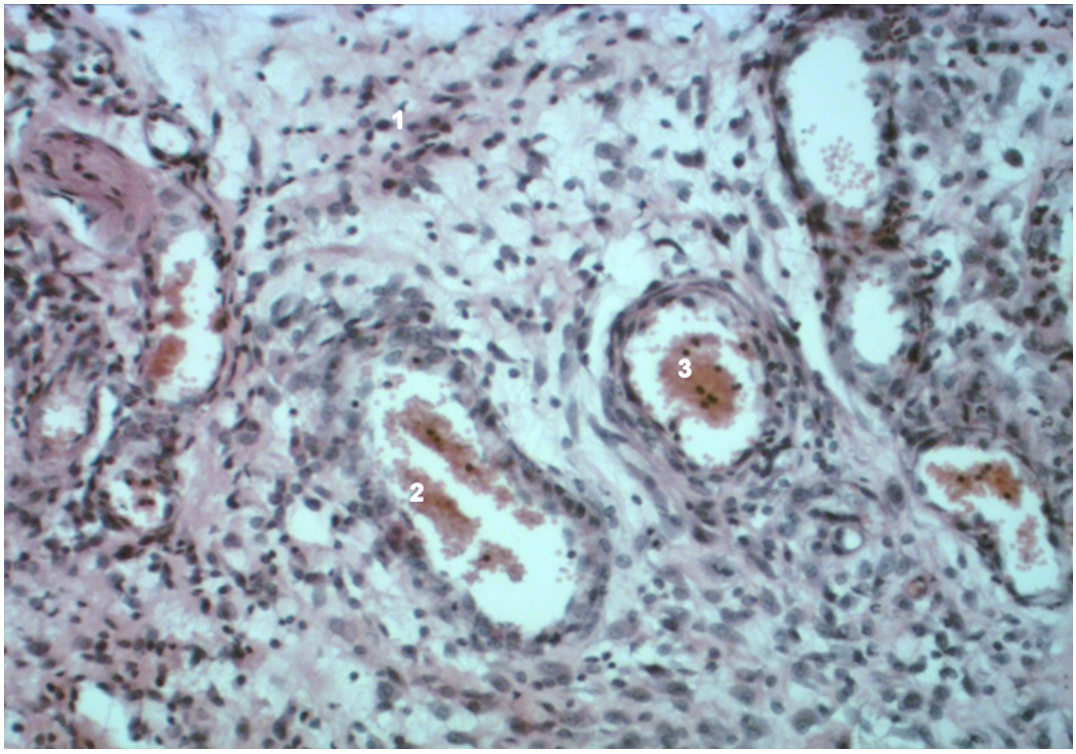

Fig. 8. Gingiva of rat No. 7, Group III, day 35 of the experiment. Diagnosis: Experimental periodontitis combined with intestinal dysbiosis. Diffuse infiltration by polymorphonuclear leukocytes. Mural thrombi in venules and arterioles. Staining: Hematoxylin and eosin. Magnification: ×100. 1 – reticular layer of the mucosa; 2 – mural thrombi in venules; 3 – mural thrombi in arterioles; 4 – infiltration by polymorphonuclear leukocytes
Picture taken by the authors

($p > 0.05$). However, keeping the experimental animals on a paste-like diet led to a slight decrease in the colonization of the large intestine by indigenous probiotic microflora (*Bifidobacterium* and *Lactobacillus*). Administration of ciprofloxacin to Group III rats, against the background of the induced experimental model of periodontitis, resulted in a significant decrease in the autochthonous intestinal microflora responsible for the colonization resistance of the gastrointestinal tract (bifidobacteria and lactobacilli), accompanied by a corresponding increase in the number of pathogenic and conditionally pathogenic microorganisms, confirming the development of dysbiosis in this biotope.

Using the biometric method, a higher intensity of the dystrophic process in the bone tissue of the periodontium was established during the combined modeling of periodontitis and intestinal dysbiosis, amounting to 41.1±0.61%, with a highly significant difference compared to Groups I and II ($p < 0.001$).

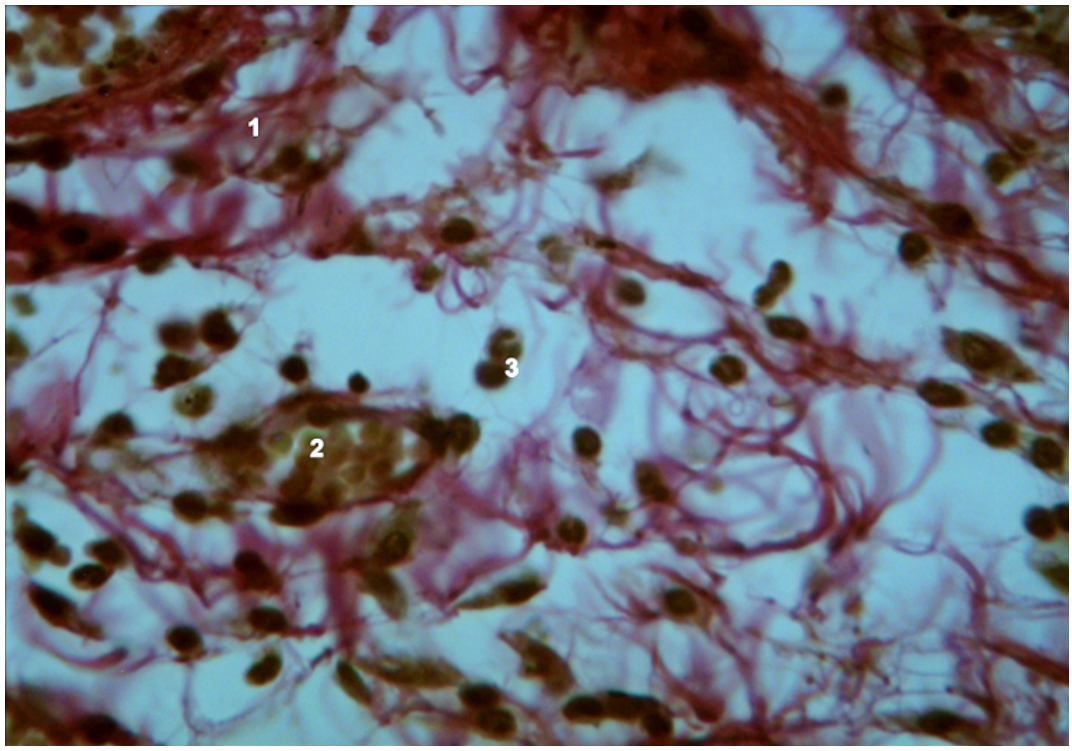

Fig.9. Gingiva of rat No. 9, Group III, day 35 of the experiment. Diagnosis: Experimental periodontitis combined with intestinal dysbiosis. Mural thrombi in venules. Pronounced interstitial edema in the reticular layer of the mucosa. Staining: Van Gieson method. Magnification: ×400. 1 – collagen fibers; 2 – thrombi in venules; 3 – infiltration by polymorphonuclear leukocytes
Picture taken by the authors

Morphological examination in Group III animals revealed more pronounced structural changes in the gingiva compared to Group II. In certain areas of the epithelial covering, disorganization and cellular damage in the form of necrosis were observed. In some regions, the keratinized, granular, and prickle-cell layers of the epithelium were absent. Individual basal layer cells appeared deformed and vacuolated, with widened intercellular spaces filled with lymphocytes and neutrophilic granulocytes. The basement membrane was discontinuous; its collagen fibers were loosened and disorganized, and lymphocytes, histiocytes, and neutrophilic leukocytes were present among them (Fig. 7).

In the connective tissue of the papillary layer of the gingival mucosa, fibroblast proliferation was observed in the region of the gingival papillae. Signs of edema in this layer and hypertrophy of collagen fibers were more pronounced than in rats of Group II. In the microcirculatory bed of the papillary layer, blood vessel lumina were dilated and engorged. The integrity of the capillary walls was disrupted, the endothelial lining was discontinuous, and the basement membrane appeared loosened. Numerous hemorrhages were found around the capillaries. In addition, polymorphonuclear leukocyte infiltrates were present in the papillary layer. The lymphatic vessels were dilated and filled with lymph.

In the reticular layer, edema of the connective tissue was more pronounced than in the papillary layer. The lumina of the microcirculatory vessels were markedly dilated and hyperemic (Fig. 8). Some blood vessels in this layer exhibited irregular blood filling.

The walls of the arterioles were thickened, and their lumina were narrowed. The endothelial lining was discontinuous, with areas showing both desquamation and regeneration. In the middle layer of the arterioles, hypertrophy of smooth muscle cells was observed.

The capillary lumina were also dilated and engorged; the endothelial lining was discontinuous, and the basement membrane was loosened. In some areas, desquamation of endothelial cells was detected. The perivascular connective tissue was loosened, with histiolymphocytic infiltration visible in many microscopic fields, and isolated hemorrhages found around capillaries.

The venules were dilated and markedly engorged. In some cases, mural thrombi were detected (Fig. 9). The endothelial lining of the venules was discontinuous, with frequent foci of endothelial desquamation. Numerous areas of leukocyte stasis, margination, and diapedesis through the venular walls were observed. Compared with the previous group, there was a more pronounced interstitial edema of the gingival reticular layer and diffuse inflammatory infiltration with neutrophilic leukocytes. In some regions, lymphocytes and histiocytes were also found. The lumina of lymphatic vessels in this layer were dilated and filled with lymph.

DISCUSSION

Thus, the results of this study demonstrated the expediency of conducting experimental research on animals to gain a more detailed understanding of the course of periodontal tissue diseases when combined

with other lesions of the digestive tract, particularly intestinal dysbiosis.

The widespread prevalence of dysbiotic conditions observed in all open cavities of the human body (oral, nasal, intestinal, etc.) makes it necessary to study this issue comprehensively from the standpoint of comorbidity. Meanwhile, both domestic and international scientific studies have focused on many aspects of dysbiosis as an independent process in dental diseases (such as dental caries, periodontal and oral mucosal diseases) and in the intestine [20-22]. However, the question of the negative impact of intestinal microflora imbalance and the replacement of its ecological niches on the course of periodontal diseases—frequently encountered in clinical practice—remains insufficiently addressed in the literature, and morphological studies in this context are virtually absent.

In this study, our results confirmed previous experimental findings regarding changes in periodontal tissues during periodontitis [23, 24] and alterations in intestinal microbiota during dysbiosis [25]. At the same time, we performed a comparative assessment of these parameters under conditions of consecutive modeling of periodontitis followed by intestinal dysbiosis.

It was established that disturbances in the microecological system of the intestine—even subclinical ones—accompanied by suppression of its saprophytic flora, complicate the course of periodontitis, promote its generalization, and contribute to the development of aggressive inflammatory manifestations in the gingiva, including abscess formation. This was supported by morphological findings: simultaneous modeling of periodontitis and intestinal dysbiosis in rats revealed more pronounced pathological changes than in those without dysbiotic disorders. These included alterations in the gingival epithelium, connective tissue of the papillary and reticular layers of the mucosa, and especially in the vessels of the microcirculatory bed and perivascular areas. In our opinion, the observed increase in the number and dilation of blood and lymphatic capillaries may represent a compensatory mechanism, while a slight increase in lymphocytes should be regarded as an adaptive response.

CONCLUSIONS

It was established that the induction of experimental periodontitis in animals using the reduced masticatory function model, followed by its combination with intestinal dysbiosis via selective decolonization, led to the development of a pathological process in the periodontal tissues in 100% of rats. This process resembled the exacerbated course of human periodontitis, with increased severity and progression. These findings indicate the high adequacy of this model for studying aggravating factors in the course of inflammatory-dystrophic lesions of human periodontal tissues.

It was found that modeling intestinal dysbiosis against the background of experimental periodontitis results in disruption of the colonic microbiome: a statistically significant decrease in bifidobacteria and lactobacilli, along with pronounced contamination by pathogenic and opportunistic enterobacteria and Candida fungi. This leads to a marked deficiency of autochthonous bacteria, impairing the colonization resistance of the intestinal mucosa and weakening the nonspecific anti-infective defense of the gastrointestinal tract, thereby intensifying the negative impact on periodontal tissues.

Assessment of the degree of dystrophic changes in the periodontium of experimental animals using biometric analysis revealed a higher intensity of alveolar process degeneration under sequential modeling of periodontitis and intestinal dysbiosis. This indicates early generalization of the pathological process in periodontal tissues and its progression under the influence of dysbiotic disturbances in the gastrointestinal tract.

In experimental animals with combined modeling of periodontitis and intestinal dysbiosis, compared to those without dysbiotic disorders, more pronounced pathological changes were observed in the gingival epithelium (intercellular space widening, vacuolar degeneration and necrosis of epithelial cells, focal absence of the keratinized, granular, and prickle layers, loosening and disorganization of collagen fibers in the basal membrane) and in the connective tissue (edema of the papillary and reticular layers, leukocytic infiltration, fibroblast hypertrophy and hyperplasia, signs of edema, disorganization and destruction of collagen fibers, their delamination and loosening). Vascular changes in the microcirculatory bed included: in arterioles – thickened walls, narrowed lumens, discontinuous endothelial lining with areas of desquamation and regeneration, hypertrophy of smooth muscle cells in the tunica media; in capillaries – dilated and congested lumens, discontinuous endothelial lining, desquamation of endothelial cells, histio-lymphocytic infiltration in perivascular connective tissue, and occasional hemorrhages around capillaries; in venules – markedly dilated and congested lumens, mural thrombi, multiple zones of leukocyte stasis, marginal positioning, and diapedesis. Lymphatic vessel lumens were dilated and filled with lymph. These findings confirm the development of severe complications in the clinical course of experimental periodontitis when combined with intestinal dysbiosis, up to its most aggressive manifestation: periodontal abscess formation.

REFERENCES

1. Dias IE, Dias IR, Franchi-Mendes T et al A Comprehensive Exploration of Therapeutic Strategies in Inflammatory Bowel Diseases: Insights from Human and Animal Studies. Biomedicines. 2024;12(4): 735. doi:10.3390/biomedicines12040735. DOI
2. Nasibullina BA, Gushchi SG, Oleshko OYa. Robota z laboratornymy tvarynamy: dohlyad ta vidtvorennya modeley patolohichnykh staniv (posibnyk). [Working with laboratory animals: care and reproduction of models of pathological conditions (manual)]. Odesa: "Poligraph". 2023, p.96. (Ukrainian)
3. Khimich OS, Rautskis VP, Kryvonos MI. Sanitarno-hihiyenichni, deontolohichni ta medyko-pravovi zasady uspishnoyi orhanizatsiyi provedennya eksperymental'noyi roboty na tvarynakh]. [Sanitary, hygiene, ethical and medico-legal principles of successful organization of experimental work on animals]. Zhurnal hromads'koho zdorov'ya. 2023;4:77–81. doi:10.32782/pub.health.2023.4.11. (Ukrainian) DOI
4. Capodiferro S, Limongelli L, Favia G. Oral and Maxillo-Facial Manifestations of Systemic Diseases: An Overview. Medicina. 2021;57(3):271. doi:10.3390/medicina57030271. DOI
5. Elzayat H, Mesto G, Al-Marzooq F. Unraveling the Impact of Gut and Oral Microbiome on Gut Health in Inflammatory Bowel Diseases. Nutrients. 2023;15(15):3377. doi:10.3390/nu15153377. DOI
6. Gevkaliuk N, Drevnitska R. Synbativity of the angioarchitectonics of the tongue and gastrointestinal tract mucosa in the disorders of homologous organs. Eastern Ukrainian Medical Journal. 2024;12(4):892-904. doi:10.21272/eumj.2024;12(4):892-904. DOI
7. Kitamoto S, Nagao-Kitamoto H, Hein R et al. The Bacterial Connection between the Oral Cavity and the Gut Diseases. J Dent Res. 2020; 99(9):1021–1029. doi:10.1177/0022034520924633. DOI
8. Mukherjee S, Chopra A, Karmakar S, Bhat SG. Periodontitis increases the risk of gastrointestinal dysfunction: an update on the plausible pathogenic molecular mechanisms. Crit Rev in Microb. 2024;51(1):187–217. doi:10.1080/1040841X.2024.2339260. DOI
9. Oh H, Lee DH, Giovannucci EL, Keum N. Gastric and duodenal ulcers, periodontal disease, and risk of bladder cancer in the Health Professionals Follow-up Study. Cancer causes & control: CCC. 2020;31(4):383–391. doi:10.1007/s10552-020-01274-4. DOI
10. Koveshnikov KI, Schneider SA. Vzayemozv yazok mizh zakhvoryuvannyamy parodontu ta shlunkovo-kyshkovoho traktu [The relationship between periodontal and gastrointestinal diseases]. XL international scientific and practical conference «Mechanisms of Development of the Scientific and Technical Potential of Modern Society». Salzburg, Austria. International Scientific Unity. 2024, pp.131-134. doi:10.70286/ISU-25.09.2024. (Ukrainian) DOI
11. Kamer AR, Pushalkar S, Hamidi B et al. Periodontal Inflammation and Dysbiosis Relate to Microbial Changes in the Gut. Microorganisms. 2024; 12(6):1225. doi:10.3390/microorganisms12061225. DOI
12. Rotaru M, Singeap A-M, Ciobica A et al. Oral Health and "Modern" Digestive Diseases: Pathophysiologic and Etiologic Factors. Biomedicines. 2024; 12(8):1854. doi:10.3390/biomedicines12081854. DOI
13. Yamazaki K. Oral-gut axis as a novel biological mechanism linking periodontal disease and systemic diseases: A review. The Japanese dental science review. 2023;59:273–280. doi:10.1016/j.jdsr.2023.08.003. DOI
14. Xie L, Chen Q, Xu H et al. The research progress on periodontitis by the National Natural Science Foundation of China. Int J Oral Sci. 2025;17(1):44. doi:10.1038/s41368-025-00371-x. DOI
15. Hontsariuk DO, Hristych TM. Znachushchist' dysbiozu ta osoblyvosti yoho perebihu pry poyednanni z khronichnym pankreatytom [Chronic pancreatitis: the mechanisms of development and progression that are taken into account during treatment and rehabilitation]. Herald of Pancreatic Club. 2024;64(3):6-12. doi: 10.33149/vkp.2024.03.01. (Ukrainian) DOI
16. Schneider SA. Morfohenez eksperymental'noho khronichnoho periodontytu [Experimental chronic periodontitis morphogenesis]. Morphologia. 2011;5(1):38-41. doi:10.26641/1997-9665.2011.1.38-41. (Ukrainian) DOI
17. Van Der Waaij D. Colonization resistance of the digestive tract — Mechanism and clinical consequences. Nahrung. 1987;31:507-517. doi:10.1002/food.19870310551. DOI
18. Kravchun PG, Babazhan VD, Myasoyedova VV. Metodolohiya naukovykh doslidzhen' v medytsyni: navchal'nyy posibnyk. [Methodology of scientific research in medicine: study guide]. 2020. Kharkiv: KhNMU. (Ukrainian)
19. Hontsariuk DO, Hristych TM. Znachushchist' dysbiozu ta osoblyvosti yoho perebihu pry poyednanni z khronichnym pankreatytom. [Chronic pancreatitis: the mechanisms of development and progression that are taken into account during treatment and rehabilitation]. Herald of Pancreatic Club. 2024;64(3):6-12. doi:10.33149/vkp.2024.03.01. (Ukrainian) DOI
20. Abdulkareem AA, Al-Taweel FB, Al-Sharqi AJB et al. Current concepts in the pathogenesis of periodontitis: from symbiosis to dysbiosis. J Oral Microbiol. 2023;15(1):2197779. doi: 10.1080/20002297.2023.2197779. DOI
21. Hrncir T. Gut Microbiota Dysbiosis: Triggers, Consequences, Diagnostic and Therapeutic Options. Microorganisms. 2022;10(3):578. doi:10.3390/microorganisms10030578. DOI
22. Godovanets OI, Kotelban AV, Grinkevich LG, Romanyuk DG. Chynnyky ryzyku rozvytku zakhvoryuvan' tverdykh tkanyn zubiv u ditey. Suchasnyy stan pytannya. [Factors that cause caries among children. current state of question]. Medytsyna s'ohodni i zavtra. 2021;85(4):111–120. doi:10.35339/msz.2019.85.04.16. (Ukrainian) DOI

23. Elhaieg A, Farag A, Elfadadny A et al. Effect of experimental periodontitis on cardiac functions: a comprehensive study using echocardiography, hemodynamic analysis, and histopathological evaluation in a rat model. Front Vet Sci. 2023;10:1327484. doi: 10.3389/fvets.2023.1327484. DOI
24. Remeziuk I, Avdeev O. Otsinka zastosuvannya mistsevykh likuval'nykh zasobiv u tvaryn z eksperymental'nym parodontytom [Evaluation of local therapeutic agents in animals with experimental periodontitis]. Ukrayins'kyy stomatolohichnyy al'manakh. 2023;3:9-16. doi:10.31718/2409-0255.3.2023.02. (Ukrainian) DOI
25. Wang S, Martins R, Sullivan MC et al. Diet-induced remission in chronic enteropathy is associated with altered microbial community structure and synthesis of secondary bile acids. Microbiome. 2019;7(1): 126. doi:10.1186/s40168-019-0740-4. DOI

CONFLICT OF INTEREST
The Authors declare no conflict of interest

CORRESPONDING AUTHOR
Elvira M. Danko
Uzhhorod National University
1 Narodna Sqr, 88000 Uzhhorod, Ukraine
e-mail: elvira.danko@uzhnu.edu.ua

ORCID AND CONTRIBUTIONSHIP
Valentina N. Kulygina: 0000-0001-7846-441X A D
Olha V. Polishchuk: 0009-0008-8037-9183 B D
Elvira M. Danko: 0000-0002-3997-9311 E F
Halyna M. Poberezhna: 0000-0002-2938-1252 C
Yuliia O. Slynko: 0000-0002-9718-5202 E
Roman S. Arshynnikov: 0000-0002-0136-3474 E
Larysa F. Kurdysh: 000-0002-8259-9963 B

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 14.01.2026
ACCEPTED: 24.04.2026