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The Oral-Gut Microbiome Axis: Mechanisms Influencing Periodontal Therapeutic Response and Strategies for Microbiome Restoration

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Abstract

The oral-gut axis represents a bidirectional relationship between oral and intestinal microbial communities and plays an important role in the development and progression of periodontal diseases. Periodontitis, traditionally regarded as a localized inflammatory disorder, is increasingly recognized as a condition with systemic implications. This review summarizes current evidence on the biological mechanisms linking oral and gut microbiota, with particular emphasis on the translocation of periodontal pathogens, including *Porphyromonas gingivalis* and *Tannerella forsythia,* into the gastrointestinal tract. These pathogens may promote gut dysbiosis, impair intestinal barrier integrity, and contribute to systemic inflammation. Conversely, gut dysbiosis may aggravate periodontal inflammation through circulating pro-inflammatory mediators and bacterial endotoxins, creating a vicious cycle that can impair tissue healing and reduce treatment effectiveness.Individual differences in baseline microbiome composition and host immune responses may partly explain the variable outcomes observed following conventional periodontal therapies such as scaling and root planing. Therefore, microbiome assessment may support the development of personalized periodontal treatment strategies. Microbiome-modulating interventions, including probiotics, prebiotics, dietary modifications, engineered probiotics, and fecal microbiota transplantation, have emerged as potential adjunctive approaches to restore microbial homeostasis and improve clinical outcomes. Furthermore, multi-omics technologies may facilitate microbial profiling and prediction of treatment responses within a precision-medicine framework.Overall, targeting both oral and gut microbial health may represent a promising paradigm shift toward integrated and personalized periodontal care. However, large-scale randomized controlled trials are required to establish the clinical efficacy and standardized application of microbiome-focused therapies.

Keywords: Oral-Gut Axis, Periodontal Disease, Microbiome Dysbiosis, Probiotics; Antimicrobial Stewardship.

Introduction

Growing evidence indicates that communication between the oral and intestinal microbiota plays an important role in shaping the development of periodontal diseases and influencing their clinical response to treatment. Accumulating evidence indicates that disturbances in the oral microbial ecosystem can extend beyond localized inflammation.

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Such microbial imbalance may promote the dissemination of periodontal pathogens into the gastrointestinal tract, where they can modify the composition of the gut microbiota and compromise intestinal barrier function. This oral-gut axis influences systemic immune homeostasis, potentially modulating the severity of periodontitis and its response to conventional therapies such as scaling and root planing. Understanding this bidirectional communication is crucial for elucidating why patients exhibit heterogeneous responses to standard periodontal interventions, highlighting the need to consider the broader microbial ecosystem beyond the periodontal pocket (1, 2, 25, 28).

Furthermore, the restoration of microbial balance through targeted interventions offers promising avenues for improving therapeutic efficacy in periodontal diseases. Strategies aimed at correcting dysbiosis, including probiotics, prebiotics, and microbiome-transplant therapies, are being investigated for their ability to synergize with traditional treatments and enhance clinical outcomes. By modulating the oral and gut microbiota, these adjunctive therapies may reduce systemic inflammation and promote tissue regeneration, addressing the limitations of mechanical debridement alone. Integrating microbiome-based approaches into clinical practice represents a paradigm shift towards personalized periodontal care, potentially leading to more sustainable and effective management of periodontal diseases (3, 4, 24, 29, 30).

The Oral-Gut Microbiome Axis: Conceptual Framework and Historical Context

Periodontal disease is now understood from a broader systemic perspective rather than solely as an infection restricted to the periodontal pocket. This evolving view highlights the two-way interactions that occur between the oral and intestinal microbiota and their potential contribution to disease development.This “oral-gut axis” suggests that dysbiosis in one site can precipitate microbial shifts in the other, influencing systemic health and disease progression. Current models of the oral-gut connection suggest that certain oral pathogens, including *Porphyromonas gingivalis*, may withstand gastric conditions and subsequently establish themselves within the intestinal environment. Their presence in the gut may interfere with the integrity of the intestinal barrier and modulate host immune responses.This paradigm shift necessitates a reevaluation of periodontal therapy, moving beyond local mechanical debridement to consider the broader microbial ecosystem (12, 22).

Furthermore, the historical context of this relationship highlights a growing recognition of the interconnectedness of mucosal surfaces in the body. Evidence from experimental and clinical studies indicates that microorganisms originating in the oral cavity may contribute to the intestinal microbial pool. Conversely, inflammatory processes within the gut can intensify periodontal tissue damage by promoting the systemic release of pro-inflammatory cytokines (25, 26).

Understanding the evolutionary and ecological principles governing these microbial communities is essential for developing effective therapeutic strategies. By acknowledging the oral-gut axis, clinicians can better predict patient responses to treatment and identify individuals at higher risk for systemic complications associated with chronic periodontitis (7, 25).

Mechanisms of Oral Pathogen Translocation to the Gut

The translocation of oral bacteria to the gastrointestinal tract occurs through several mechanisms, including swallowing, hematogenous spread, and lymphatic dissemination. Periodontal pathogens, particularly anaerobic gram-negative bacteria, are highly adapted to survive in hypoxic environments and can evade host immune responses in the gut. Following their arrival in the intestinal tract, these microorganisms may impair the protective mucosal barrier and consequently increase intestinal permeability, a phenomenon often described as “leaky gut.” As a result, microbial products such as lipopolysaccharides (LPS) may gain access to the bloodstream and promote persistent, low-grade systemic inflammation. This inflammatory response may, in turn, contribute to the aggravation of periodontal disease as well as other systemic disorders (25, 26, 28).

Beyond this,the metabolic activity of translocated oral bacteria can alter the gut microbial metabolome, influencing the synthesis of short-chain fatty acids (SCFAs) and other signaling molecules. (SCFAs), particularly butyrate, are essential for preserving intestinal homeostasis and modulating host immune activity.A reduction in SCFA-producing bacteria due to oral pathogen invasion can compromise gut barrier function and promote inflammation. Understanding these underlying mechanisms helps explain the relationship between the severity of periodontal disease and alterations in the gut microbiota. These findings also suggest that therapeutic strategies aimed at modulating the microbiome may offer a promising approach for restoring microbial equilibrium (28).

Impact of Gut Dysbiosis on Periodontal Inflammation and Healing

An imbalance in the gut microbiota, marked by a reduction in beneficial microorganisms and an expansion of potentially pathogenic species, may

intensify periodontal inflammation by activating systemic immune pathways. The intestinal microbiota is an important regulator of immune system development and function. Disruption of this microbial environment may alter the balance between Th17 and Treg cells, potentially enhancing pro-inflammatory immune activity in distant tissues, including the periodontal tissues.Systemic circulation of gut-derived inflammatory mediators, including LPS and pro-inflammatory cytokines, can sensitize periodontal tissues to bacterial challenges, accelerating tissue destruction and impairing healing after periodontal therapy (28).

Moreover, The composition and activity of the gut microbiota may affect periodontal treatment outcomes by shaping the host immune response following mechanical debridement.Patients with significant gut dysbiosis may exhibit a blunted healing response to scaling and root planing due to persistent systemic inflammation. Conversely, restoration of gut microbial balance can enhance the anti-inflammatory environment, facilitating tissue regeneration and stability. These observations highlight the need to consider intestinal health as part of periodontal disease management. Integrating strategies aimed at maintaining or improving gut health may therefore contribute to better overall therapeutic outcomes (23, 28).

Heterogeneity in Therapeutic Response: The Role of Microbial Variability

One of the greatest challenges in periodontal therapy is the heterogeneity in patient responses to standard treatments such as scaling and root planing (SRP). This variability is increasingly attributed to differences in the baseline composition of the oral and gut microbiomes. Individuals with a more stable and diverse gut microbiota, marked by a greater representation of beneficial microbial taxa, may exhibit a more favorable response to scaling and root planing (SRP) compared with patients experiencing pronounced microbial dysbiosis. Microbial profiling can therefore serve as a predictive tool for identifying patients who are likely to be non-responders and may require adjunctive therapies (22, 23).

Furthermore, the presence of specific pathogenic consortia in the oral cavity, often supported by gut-derived inflammatory signals, can render periodontal pockets resistant to conventional cleaning. These resilient biofilms are protected by an extracellular matrix that shields bacteria from antimicrobial agents and host immune cells. Understanding the microbial ecology of these resistant communities is crucial for developing targeted strategies to disrupt biofilm integrity and restore health. Personalized treatment plans based on microbiome analysis offer a promising avenue for improving therapeutic success rates (7, 21).

Probiotics and Prebiotics as Adjunctive Therapies

Probiotics and prebiotics are increasingly being considered as valuable adjuncts to conventional periodontal treatment, with the potential to improve therapeutic effectiveness (24, 29, 30).

Probiotics are beneficial live microorganisms that may limit the establishment of pathogenic bacteria by competing with them for available nutrients and attachment sites. Through this competitive interaction, they may help reduce the colonization of harmful microorganisms in both the oral cavity and the gastrointestinal tract.Specific strains, including *Lactobacillus* and *Bifidobacterium*, may provide additional benefits when combined with scaling and root planing (SRP). Studies have reported their potential to alleviate periodontal inflammation and promote improvements in clinical attachment levels. Beyond their potential periodontal benefits, probiotics may contribute to the reestablishment of a balanced gut microbial community. By supporting microbial homeostasis, they may help attenuate systemic inflammation and promote overall physiological health (24, 29).

Prebiotics are non-digestible dietary components that selectively promote the proliferation of beneficial microorganisms. By supporting the growth of these bacteria, they may contribute to the regulation and maintenance of a balanced microbiome. By providing substrates for SCFA-producing bacteria, prebiotics can enhance gut barrier function and reduce systemic inflammation. Synbiotics, which combine probiotics with prebiotics, may exert complementary effects by supplying beneficial microorganisms while simultaneously providing substrates that support their growth. However, further clinical investigation is still required to determine the long-term safety and therapeutic effectiveness of these approaches in the management of periodontal disease (30).

Microbiome-Based Approaches: FMT and Microbial Engineering

Fecal microbiota transplantation (FMT) is a microbiome-based intervention in which stool obtained from a healthy donor is administered to a recipient with the aim of reestablishing microbial diversity and restoring normal microbial functions. While primarily used for gastrointestinal disorders, FMT has shown potential in treating systemic conditions influenced by gut dysbiosis, including periodontal disease. Restoration of a balanced intestinal microbiota through FMT may help attenuate systemic inflammation and enhance the host immune response against periodontal pathogens.Although direct application of FMT to periodontal disease is still in its early stages, the concept of microbiome

engineering offers exciting possibilities for targeted therapeutic interventions (30).

Microbiome engineering techniques, such as the use of engineered probiotics or bacteriophages, allow for precise manipulation of microbial communities. These approaches can target specific pathogenic species while sparing beneficial bacteria, minimizing the risk of unintended ecological disruptions. For example, bacteriophages can be designed to lyse Porphyromonas gingivalis in the oral cavity, while engineered Lactobacillus strains can produce anti-inflammatory molecules in the gut. These innovative strategies represent the future of personalized periodontal therapy, offering highly targeted and effective treatments (26, 30).

Dietary Interventions and Microbiome Modulation

Dietary patterns are important determinants of the composition and functional activity of both oral and intestinal microbial communities. Frequent consumption of refined carbohydrates and foods rich in saturated fats may favor the proliferation of potentially pathogenic microorganisms while diminishing microbial diversity. These alterations can contribute to the progression of periodontal inflammation and further disrupt the balance of the gut microbiota. In contrast, a diet abundant in dietary fiber, fruits, and vegetables may promote the proliferation of beneficial microorganisms and increase SCFA production. These metabolites can contribute to maintaining microbial homeostasis and exerting anti-inflammatory effects within the host.Nutritional interventions, therefore, offer a non-invasive and accessible means of modulating the microbiome to improve periodontal health (25, 26).

Certain dietary constituents, including polyphenolic compounds and omega-3 fatty acids, may positively influence the composition and activity of the microbiome while contributing to the reduction of inflammatory processes. Polyphenol-rich foods, including tea, coffee, and berries, may influence the microbiome by limiting the proliferation of periodontal pathogens while supporting beneficial intestinal bacteria. In addition, omega-3 fatty acids obtained from sources such as fish and flaxseeds possess anti-inflammatory properties that may contribute to the resolution of periodontal inflammatory processes.Incorporating these dietary elements into daily habits can support microbial balance and enhance the outcomes of periodontal therapy (25).

Precision Medicine Approaches in Periodontal Therapy

Precision medicine in periodontal therapy involves tailoring treatment strategies to the individual patient's microbial profile, genetic background, and lifestyle factors. The integration of metagenomic, metabolomic, and transcriptomic information can provide clinicians with a more comprehensive view of an individual's microbial environment and immune profile, potentially supporting a more precise assessment of host–microbiome interactions. This information can be used to predict disease progression, identify risk factors, and select the most effective therapeutic interventions. Precision medicine aims to move away from a one-size-fits-all approach towards personalized care that maximizes efficacy and minimizes side effects (22, 27).

The implementation of precision medicine in periodontics requires the development of robust diagnostic tools and decision-support systems. Rapid microbial testing platforms can provide real-time information on pathogen load and resistance patterns, guiding antibiotic selection and treatment planning. Artificial intelligence algorithms can analyze complex microbial data to generate personalized treatment recommendations. With the increasing availability and accessibility of these advanced technologies, precision medicine has the potential to transform periodontal disease management. Such an approach could enable more effective patient care, improve clinical outcomes, and potentially reduce the overall burden of healthcare costs (27).

Clinical Trials and Evidence-Based Guidelines

The evidence base for microbiome-targeted interventions in periodontal disease is growing, with numerous clinical trials investigating the efficacy of probiotics, prebiotics, and dietary modifications. These studies have demonstrated varying degrees of success, highlighting the need for standardized protocols and larger sample sizes to draw definitive conclusions. Systematic reviews and meta-analyses are essential for synthesizing current evidence and identifying gaps in knowledge. Based on this evidence, professional organizations are developing evidence-based guidelines to recommend microbiome-targeted therapies as adjuncts to conventional periodontal treatment. Despite the promising results, challenges remain in translating research findings into clinical practice. Issues such as strain specificity, dosage, and duration of treatment need to be addressed to ensure optimal outcomes. Additionally, patient adherence to probiotic and dietary regimens can be a barrier to success. Further studies should incorporate extended follow-up periods to determine whether microbiome alterations can be maintained over time and to clarify their long-term effects on periodontal health. Collaboration between researchers, clinicians, and industry partners is crucial for advancing the field

and implementing evidence-based guidelines (24, 29, 30).

Future Perspectives and Limitations of Microbiome-Based Therapies

The future of microbiome-based therapies in periodontal disease holds great promise, but also faces significant challenges. Advances in sequencing technologies and computational bioinformatics are expected to facilitate a more comprehensive analysis of microbial communities, allowing researchers to better elucidate their composition, diversity, and functional activities.However, standardization of methods and data interpretation remains a critical issue. Additionally, the complexity of host-microbe interactions requires a multidisciplinary approach involving microbiologists, immunologists, and clinicians. Regulatory frameworks for probiotics and microbiome therapies need to be established to ensure safety and efficacy (25, 26, 27).

Furthermore, public education and awareness are essential for the successful implementation of microbiome-targeted interventions. Patients need to understand the role of the microbiome in health and disease and the importance of lifestyle modifications. Ethical considerations, such as privacy and consent in microbiome data collection, must also be addressed. As the field matures, it is expected that microbiome-based therapies will become an integral part of routine periodontal care, offering new hope for patients with chronic periodontitis (26, 27).

Conclusion

The integration of the oral-gut microbiome axis

Table 1. Overview of Key Studies Investigating the Oral–Gut Microbiome Axis and Its Implications for Periodontal Disease and Therapeutic Outcomes.

Ref	Author and Publication Year	Study Characteristics & Participants	Primary Intervention / Research Focus	Major Findings
(25)	Wang et al. (2019)	Cross-Sectional Study (Chronic Periodontitis Patients)	Oral-Gut Microbiome Comparison	Identified significant dysbiosis in both oral and gut microbiomes in periodontitis patients. Porphyromonas gingivalis was detected in the gut, correlating with increased intestinal permeability markers.
(28)	Zhang et al. (2019)	Longitudinal Cohort Study	Impact of SRP on Gut Microbiota	Scaling and root planing (SRP) significantly altered gut microbial composition, increasing diversity and reducing pathogenic taxa. This shift was associated with reduced systemic inflammation (CRP levels).
(29, 18)	Zhao et al. (2018)	Randomized Controlled Trial (Periodontitis)	Adjunctive Probiotics (L. reuteri)	Adjunctive administration of *Lactobacillus reuteri* alongside SRP resulted in a significant reduction in probing depth and bleeding on probing compared with SRP alone.Gut microbiome analysis showed improved microbial balance.
(26)	Zaura et al. (2019)	Review & Mechanistic Study	Oral-Gut Axis Mechanisms	Detailed mechanisms of oral pathogen translocation to the gut. Highlighted that oral anaerobes can survive gastric acid and colonize the intestine, triggering local and systemic immune responses.
(6)	Chen et al. (2019)	Case-Control Study	Microbial Biomarkers in Saliva and Stool	Identified specific microbial signatures in saliva and stool that could distinguish periodontitis patients from healthy controls. Proposed a combined oral-gut diagnostic model for early detection.
(24)	Wagener et al. (2018)	Systematic Review	Probiotics in Periodontal Therapy	Meta-analysis confirmed that probiotics reduce periodontal inflammation and improve clinical attachment levels. Suggested that strain-specific effects are crucial for therapeutic success.
(30)	Zhu et al. (2019)	Experimental Animal Study	FMT-Based Microbiome Therapy	Administration of FMT derived from healthy donors to mice with experimentally induced periodontitis resulted in reduced alveolar bone loss and attenuation of gingival inflammation. Demonstrated that gut microbiota modulation can directly impact periodontal health.
(20)	Ramseier et al. (2018)	Systematic Review	Periodontitis and Systemic Health	Reviewed the bidirectional relationship between periodontitis and diabetes. Highlighted that improving periodontal health can improve glycemic control, partly mediated by gut microbiome changes.
(7)	Darveau (2018)	Hypothesis Paper	Dysbiosis and Homeostasis	Proposed that periodontitis is a state of dysbiosis where the host fails to maintain homeostasis with the microbiome. Suggested that restoring microbial balance is key to treatment success.
(22)	Tonetti et al. (2018)	Consensus Statement	Periodontitis as a Multifactorial Disease	Emphasized the role of environmental and microbial factors in periodontitis. Advocated for personalized treatment approaches based on individual microbial profiles and host response.

into periodontal science represents a transformative shift in our understanding of periodontal disease pathogenesis and management. The evidence reviewed underscores that periodontitis is not an isolated oral condition but a systemic inflammatory disorder influenced by the complex interplay between oral and gut microbial ecosystems. Dysbiosis in either compartment can precipitate or exacerbate disease in the other, creating a feedback loop that drives chronic inflammation and tissue destruction. This bidirectional relationship explains the heterogeneity in patient responses to conventional mechanical therapies and highlights the limitations of treating the mouth in isolation from the gut (25, 28).

A comprehensive microbiome-targeted approach may provide substantial benefits for improving clinical outcomes and enhancing patients' quality of life. The incorporation of probiotics, prebiotics, and dietary interventions as adjuncts to conventional periodontal therapy may support microbial homeostasis, alleviate systemic inflammation, and increase the therapeutic effectiveness of established treatments such as scaling and root planing.Emerging technologies, including precision medicine approaches and microbiome engineering, hold promise for delivering highly personalized and effective interventions. Nevertheless, further evidence from large-scale, long-term randomized controlled trials is necessary before these microbiome-based approaches can be reliably incorporated into routine clinical practice (24, 29, 30).

Despite the promising prospects, challenges remain in standardizing diagnostic tools, defining optimal therapeutic protocols, and ensuring cost-effectiveness. Future research must focus on elucidating the specific mechanisms of host-microbe interactions and developing robust biomarkers for predicting treatment response. Additionally, public health initiatives are needed to educate both healthcare providers and patients about the importance of microbiome health in periodontal and overall systemic well-being. By adopting a multidisciplinary approach that bridges periodontology, gastroenterology, and microbiology, the medical community can develop comprehensive strategies to combat periodontal disease, ultimately improving global health outcomes and reducing the burden of chronic inflammatory conditions (24,27,30).

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Data Availability

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Competing Interests

The author declares no competing interests.

Ethics Approval and Consent to Participate

Ethics approval and consent to participate were not applicable because this study is a literature review and involved no human or animal participants.

Consent to Publish

Not applicable.

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