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From Plaque to Dysbiosis: Evolving Concepts in Periodontal Pathogenesis: A Narrative Review

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Abstract

Periodontal diseases are chronic inflammatory conditions and a leading cause of tooth loss globally. Traditionally viewed through a plaque-centric lens, the understanding of periodontal pathogenesis has evolved significantly from the non-specific and specific plaque hypotheses to the contemporary dysbiosis model. This narrative review explores the transition from simple bacterial infection theories to a complex framework where periodontitis is recognized as a host-mediated dysbiotic inflammatory disease. The review details the roles of "keystone pathogens" like *Porphyromonas gingivalis*, the "inflammophilia" of microbial communities, and the critical "IMPEDE" model which links inflammation to disease progression. Furthermore, it examines the mechanisms of host-mediated tissue destruction, including the RANK–RANKL–OPG pathway and the impact of systemic modifiers like diabetes and smoking. Integrating these modern concepts is essential for moving beyond mechanical debridement toward precision-based periodontal therapy and host modulation.

Keywords: Periodontitis; Dysbiosis; Dental Plaque; Inflammation; Keystone Pathogens

1. Introduction

Periodontal diseases are chronic inflammatory conditions affecting the supporting structures of the teeth including the gingiva, periodontal ligament, cementum, and alveolar bone—and remain a primary driver of tooth loss on a global scale[1,2]. Historically, dental plaque was identified as the sole etiological factor responsible for the destruction of these tissues. Early clinical models established a direct correlation between the accumulation of plaque and the onset of gingival inflammation, which reinforced a simplistic, plaque-centric view of the disease[3].

However, this traditional perspective failed to account for clinical heterogeneity, specifically why individuals with comparable levels of plaque often exhibit vastly different severities of disease. Such observations necessitated an evolution in thinking, leading to models that integrate microbial ecology, the host immune response, and various environmental modifiers. The contemporary scientific consensus now defines periodontitis not as a conventional bacterial infection, but as a host-mediated dysbiotic inflammatory disease[2,3]. This paradigm shift emphasizes that while bacteria are necessary, the host's own immune-inflammatory response—often triggered or subverted by a dysbiotic microbial community—is the actual driver of tissue destruction. Understanding this transition from "plaque to dysbiosis" is critical for developing modern therapeutic strategies that target inflammation and host susceptibility alongside traditional biofilm management[2,4].

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2. Dental Plaque: Classical Concepts

Dental plaque is a structured microbial biofilm adherent to the tooth surface, embedded within an extracellular matrix of bacterial and host-derived products. Plaque formation begins with the development of an acquired pellicle, followed by colonization by Gram-positive facultative bacteria such as Streptococcus and Actinomyces species. As plaque matures, ecological changes favor Gram-negative anaerobic organisms associated with periodontal disease[3,5].

The non-specific plaque hypothesis proposed that periodontal disease results from the overall mass of plaque irrespective of its microbial composition. This theory was supported by the experimental gingivitis model, which demonstrated that plaque accumulation leads to gingival inflammation that resolves upon plaque removal[1,3]. While this hypothesis established plaque control as the cornerstone of periodontal therapy, it failed to explain differences in disease susceptibility and progression among individuals[5,6].

2.1. Specific Plaque Hypothesis and Pathogen-Centered Models

With advances in microbiology, the specific plaque hypothesis emerged, suggesting that only certain microorganisms are responsible for periodontal destruction. Socransky and colleagues identified microbial complexes associated with disease severity, particularly the red complex consisting of Porphyromonasgingivalis, Tannerella forsythia, and Treponema denticola. These pathogens possess virulence factors such as lipopolysaccharides, proteases, and fimbriae that contribute to immune evasion and tissue damage [2,3,4].

Despite strong associations, these organisms were also detected in periodontal health, and their presence alone did not consistently predict disease progression. This highlighted the limitations of pathogen-centric models and emphasized the importance of microbial interactions and host response [2,4].

2.2. Ecological Plaque Hypothesis and Microbial Homeostasis

The ecological plaque hypothesis integrated microbial composition with environmental influences, proposing that disease results from shifts in the local environment that favor pathogenic bacteria[4]. In health, the oral microbiome exists in a symbiotic state, contributing to immune tolerance and microbial stability. Inflammation-induced changes such as increased gingival crevicular fluid flow, altered pH, and reduced oxygen tension selectively promote the growth of anaerobic, proteolytic bacteria [2,6]. Thus, periodontal disease is viewed as a consequence of disrupted microbial homeostasis rather than exogenous infection.

2.3. Dysbiosis: A Contemporary Model

Dysbiosis refers to an imbalance in the microbial community that disrupts host–microbe equilibrium. In periodontitis, dysbiosis is characterized by a shift toward inflammophilic microbial communities that perpetuate chronic inflammation [5,7]. Rather than single pathogens, disease arises from synergistic interactions within a pathogenic microbial consortium.

The keystone pathogen hypothesis proposes that low-abundance species such as Porphyromonasgingivalis can disproportionately modulate the host immune response and remodel the microbial community, leading to dysbiosis [6,8]. By interfering with complement and Toll-like receptor signaling, keystone pathogens impair immune clearance and promote microbial survival.

Dental plaque biofilm development is influenced by microbial succession, which involves selective adaptation over time. This process is a bidirectional relationship with the host defense system and follows principles of natural selection. The time scale for succession in dental plaque can be shorter, starting with a small number of pioneer species and continuing to become stable and self-perpetuating. The "engines" of succession include the impact of established organisms upon their environments and environmental or host defense-mediated perturbations [5,7].

Various mechanisms have been proposed to explain microbial succession in dental plaque, including nutritional networks between bacteria controlling plaque development and the attachment of bacteria to teeth being essential for bacterial colonization and plaque development. Periodontitis is believed to be the result of true polymicrobial activity, with a variety of bacteria associated with disease. Molecular microbiome studies show both cultivable and never-cultivated bacteria among the diverse group of microbes associated with disease. Metatranscriptomic analysis reveals that certain metabolic signatures are consistent with disease progression, suggesting the whole community drives disease progression[8,9].

Hajishengallis and Lamont proposed a model where periodontitis is initiated by a dysbiotic and synergistic microbiota, rather than a conventional infectious disease caused by a single or a few select species. They argued that diverse bacteria fulfill distinct roles that converge to form a stable, disease-provoking microbiota. The microbes within the biofilm work together to resist host responses and drive inflammation, with increased proteolytic activity and cytokine induction that results in tissue destruction [1,4].

2.4. Host Immune Response and Immune Dysregulation

The host immune response plays a pivotal role in periodontal pathogenesis. Neutrophils serve as the primary defense against subgingival biofilms, and their dysfunction can result in excessive tissue damage or ineffective microbial clearance[7]. Pattern recognition receptors such as Toll-like receptors initiate inflammatory signaling cascades upon microbial recognition [8,9].

Adaptive immune responses further amplify inflammation, with Th1 and Th17 cells producing pro-inflammatory cytokines including interleukin-1β, tumor necrosis factor-α, and interleukin-17. These mediators contribute to connective tissue degradation and alveolar bone resorption [10,12].

2.5. Inflammation-Induced Dysbiosis and Inflammophilia

Modern concepts emphasize that inflammation actively drives dysbiosis rather than merely resulting from it. The term inflammophilia describes the tendency of dysbiotic microbial communities to thrive in inflammatory environments[8,12]. Tissue breakdown products such as peptides and heme serve as nutrient sources for periodontal pathogens, creating a self-perpetuating cycle of inflammation and microbial imbalance.

2.6. Inflammatory response of the host to the dental biofilm in periodontal disease

The inflammatory response to dental biofilm in periodontal disease is characterized by a dynamic interplay between a healthy biofilm and the host's immune response. A stable, symbiotic biofilm exists until environmental changes disrupt the microbial balance, leading to a dysbiotic microbiota. The host’s immune defense, primarily involving inflammatory cells, plays a crucial role in maintaining periodontal health[3,6].

Key defense mechanisms include mucosal barriers, salivary factors, and various immune cells like PMN leukocytes, which exert antimicrobial effects. Bioactive lipids and antimicrobial peptides also contribute to this protective environment. The interaction between microbial components and pattern recognition receptors (PRR) on gingival epithelium triggers the release of inflammatory cytokines (e.g., IL-6, IL-8, IL-1α), promoting epithelial cell activation and expression of additional antimicrobial substances.

PMNs are central to combating bacterial invasion through mechanisms such as phagocytosis and the release of cytotoxic substances. Their role transitions during different stages of gingivitis and periodontitis, especially evident in acute exacerbations of periodontitis. Ongoing inflammation often leads to a switch from protective to destructive responses, where neutrophils may cause tissue damage and facilitate microbial invasion, ultimately resulting in bone loss[8,9].

The protective versus pathological role of neutrophils is influenced by their recruitment and function, and genetic factors also play a crucial role in maintaining homeostasis. Inefficient neutrophil function can lead to dysbiosis and increased tissue breakdown. Neutrophils further impact bone metabolism by upregulating RANKL, promoting osteoclast activity, and interact with Th17 cells linked to bone loss. Transitioning to advanced periodontal lesions involves a shift from neutrophil-mediated responses to those mediated by Langerhans dendritic cells and γδ-T cells, which release pro-inflammatory cytokines and signify a shift from innate to adaptive immune responses[4,8].

2.7. Microbial dysbiosis in peri-implantitis

Peri-implantitis is a condition characterized by microbial dysbiosis, where specific pathogens, such as P. gingivalis and Fusobacterium nucleatum, are found in peri-implant biofilms. However, there is no consistent microbial profile for peri-implantitis, as these pathogens can also be found in periodontitis and healthy sites. Staphylococcus epidermidis, a less commonly associated species with natural teeth, is often detected in peri-implantitis cases, suggesting a potential role in planktonic bacteria infections. The microbial composition varies between individuals and across studies, highlighting the complexity of peri-implant biofilms and the influence of host and environmental factors on microbial communities[2,5]. **(Table 1)**

The host immune system reacts to peri-implant biofilms by recognizing microbial components through receptors like Toll-like receptors, initiating a cascade of inflammatory responses. This response, which controls the microbial threat,

often leads to persistent inflammation, tissue damage, and bone loss around implants. Peri-implantitis generally presents a more exaggerated inflammatory response, with increased levels of cytokines and greater recruitment of neutrophils. It is also marked by an imbalance between Th17 cells and regulatory T cells, exacerbated inflammation [7,8].

2.8. Mechanisms of Tissue Destruction and Bone Loss

Periodontal tissue destruction is predominantly host-mediated. Matrix metalloproteinases degrade collagen, while cytokines and prostaglandins stimulate osteoclastogenesis. The RANK–RANKL–OPG pathway is central to alveolar bone resorption, with increased RANKL expression tipping the balance toward bone loss[9]. These mechanisms highlight the indirect role of bacteria in periodontal destruction.

RANKL is expressed in various cells within periodontal tissue, including osteoblasts, T cells, chondrocytes, osteocytes, and synovial fibroblasts. Notably, periodontal ligament cells can produce proinflammatory cytokines and modulate osteoclast formation when exposed to periodontal bacterial lipopolysaccharide (LPS), although osteoclasts formed from these cells lack bone resorption ability. In contrast, gingival epithelial cells can form functional osteoclasts capable of bone resorption, while osteoclasts formed from gingival fibroblasts do not exhibit this capability. Cementoblasts are also involved in RANKL expression, contributing to osteoclastogenesis, which can be enhanced by interleukin-1 (IL-1) and parathyroid hormone-related peptide (PTHrP)[6,9]. **(Table 2)**

Table 1 Evolution of Concepts in Periodontal Pathogenesis

Concept	Central Concept	Major Limitation	Impact on Current Understanding
Non-specific plaque hypothesis	Plaque quantity drives disease	Does not explain host variability	Established plaque–gingivitis relationship
Specific plaque hypothesis	Specific pathogens cause disease	Pathogens also present in health	Introduced microbial specificity
Ecological plaque hypothesis	Environmental changes select pathogens	Limited immune focus	Laid groundwork for dysbiosis
Dysbiosis model	Host-mediated microbial imbalance	Complex to quantify clinically	Current accepted paradigm

Table 2 Integrated Microbial–Host–Clinical Framework of Periodontal Dysbiosis

Domain	Key Components	Pathogenic Mechanism	Clinical Implication
Microbial	P. gingivalis (keystone pathogen)	Immune subversion and community remodeling	Persistent dysbiosis
Microbial	Red complex bacteria	Proteolysis and inflammophilia	Progressive tissue destruction
Host immune	Neutrophils, TLRs	Hyper/hyporesponsive inflammation	Collateral tissue damage
Inflammatory pathways	RANKL, cytokines, MMPs	Bone resorption and collagen breakdown	Attachment and bone loss
Clinical translation	Host modulation, maintenance therapy	Control of inflammation and risk factors	Long-term disease stability

Various inflammatory cytokines such as IL-1, IL-6, IL-11, IL-17, and TNF-α promote osteoclastogenesis, while others like IL-4 and IL-12 inhibit it. The involvement of immune cells, particularly CD4+ T cells, is emphasized, as they can enhance RANKL expression and subsequently osteoclast activity, leading to alveolar bone destruction[9,10]. Th17 cells, known for producing IL-17, accumulate in periodontal tissues during periodontitis and are implicated in tissue

destruction[11,12].

Porphyromonas gingivalis, Tannerella forsythensis, and Treponema denticola, referred to as the "red complex," which are associated with the condition's progression. Bacterial infections can cause significant alveolar bone resorption, with studies showing that multiple bacterial infections are more damaging than single ones. Research indicates that periodontal bacteria like P. gingivalis increase RANKL expression in osteoblasts while decreasing osteoprotegerin (OPG), which antagonizes RANKL, thereby influencing osteoclastogenesis and bone resorption dynamics in periodontitis[13,14].

2.9. Risk and Modifying Factors

Systemic and environmental factors significantly influence periodontal disease progression. Smoking alters immune function and microbial composition, increasing disease severity[10]. Diabetes mellitus exacerbates inflammation through hyperglycemia-induced immune dysfunction and impaired wound healing, reinforcing dysbiosis. Genetic susceptibility, aging, and systemic inflammatory burden further modulate host–microbe interactions[2,5.10].

2.10. Clinical Implications of the Dysbiosis Model

Viewing periodontitis as a dysbiotic inflammatory disease underscores the limitations of plaque control alone. While mechanical debridement remains fundamental, adjunctive strategies targeting inflammation, host response, and risk factor modification are essential. Supportive periodontal therapy and individualized treatment planning are critical for long-term disease stability[14,15].

2.11. Unifying Concept

In response to the assessment of the role of inflammation in dysbiosis and its exacerbation of periodontal damage, the authors propose the “Inflammation-Mediated Polymicrobial-Emergence and Dysbiotic-Exacerbation” (IMPEDE) Model. This model aims to complement the current Classification of Periodontal Diseases, which views periodontitis on a continuum from health to disease across four stages of severity, complexity, extent, and distribution. The IMPEDE Model illustrates how inflammation acts as a principal driver across each classification stage, acknowledging five distinct stages (0–4) related to the development, containment, or progression of health, gingivitis, and periodontitis.[13] The stages progress from health (Stage 0) through gingivitis (Stage 1), early periodontitis (Stage 2), inflammation-mediated exacerbation of dysbiosis (Stage 3), to late-stage periodontitis (Stage 4). The model articulates that bacterial transitions from health to late-stage periodontitis are characterized by inflammation, pocket formation, and changes in bacterial composition, identifying a self-sustaining feedforward loop contributing to disease progression[16]. (Table2)

2.12. Future Direction

Advances in metagenomics and proteomics have shifted focus from microbial identification to functional activity. Salivary and gingival crevicular fluid biomarkers show promise for early diagnosis and monitoring. Future periodontal therapy may emphasize microbiome modulation and precision-based approaches.

3. Conclusion

The transition from plaque-based theories to dysbiosis-driven models represents a paradigm shift in periodontal pathogenesis. Periodontitis is now understood as a host-mediated inflammatory disease driven by disrupted microbial homeostasis. Integrating these concepts into clinical practice enhances prevention, diagnosis, and therapeutic outcomes.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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