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**Review Article**

# Investigating IL-17A's Contribution to Periodontitis and Oral Dysbiosis in Relation to Systemic Inflammatory Pathways

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## ABSTRACT

The oral microbiome is fundamental to maintaining equilibrium within the mouth, protecting tissues, and preventing disease onset. Disruptions in microbial balance—known as oral dysbiosis—can provoke inflammation and immune dysfunction, adversely influencing systemic health. This imbalance is recognized as a principal causative factor in periodontitis. Both the emergence and persistence of dysbiosis have been shown to initiate inflammatory responses locally and in distant organs. The intensified inflammatory state characteristic of oral dysbiosis is largely driven by interleukin-17A (IL-17A), secreted by diverse immune cell populations. IL-17A plays a key defensive role by inducing antimicrobial peptides, attracting neutrophils, and amplifying localized inflammation through cytokine and chemokine activation. This review consolidates current evidence on oral dysbiosis and preventive approaches, emphasizing IL-17A's contribution to dysbiosis-related periodontitis and its broader systemic inflammatory implications.

**Keywords:** Oral dysbiosis, Periodontitis, Systemic inflammation, Interleukin-17A, Immune modulation

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## Introduction

The mouth functions as a primary interface between the body and the environment, where resident microorganisms critically sustain both local and systemic health [1, 2]. It harbors the second largest microbial population in humans, encompassing bacteria, fungi, archaea, viruses, and protozoa [3]. These communities colonize distinct habitats—such as saliva, tongue, teeth, gingiva, mucosa, palate, and tonsils—forming structured biofilms with niche-specific bacterial compositions [4, 5]. A healthy oral cavity typically accommodates around 100–200 species from a pool exceeding 700 identified microorganisms [6]. Inter-individual differences are shaped by factors including genetics, age, diet, hygiene, and environmental conditions [7].

Bacterial diversity ensures ecosystem stability and functional resilience [8]. High microbial diversity and community balance are hallmarks of oral health, as reductions in these traits often correspond to chronic or metabolic diseases [9]. Within biofilms [10], commensal bacteria sustain homeostasis, defend mucosal surfaces, and suppress disease development [11]. Pathogenic species, however, can disturb this equilibrium, converting commensal assemblages into dysbiotic ones [1, 12]. The inflammatory cascade typically arises from collective microbial shifts rather than a single pathogen [1, 13]. Porphyromonas gingivalis (P. gingivalis), a Gram-negative bacterium,

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is a central etiological agent of periodontitis. Despite its low abundance, it can disrupt commensal balance and foster dysbiosis. Such microbial imbalances can evoke inflammatory and immune disturbances contributing to oral pathologies, including caries, endodontic lesions, and oral malignancies [14, 15]. Oral dysbiosis is therefore recognized as a major etiologic determinant of periodontitis [16, 17], altering nutrient competition and microbial gene expression in ways that heighten pathogenic potential and activate inflammatory networks [1, 18]. Consequently, oral dysbiosis provokes immune dysregulation and chronic inflammation that underpin periodontal destruction. Nevertheless, the cytokine-mediated molecular mechanisms remain incompletely understood.

Periodontitis represents a chronic inflammatory condition initiated by oral microbes, leading to progressive degradation of tooth-supporting structures such as the gingiva, periodontal ligament, and alveolar bone [19]. Host responses manifest as gingival edema, bleeding on probing, increased pocket depth, and alveolar resorption. Moreover, periodontitis has been epidemiologically linked to multiple systemic disorders, including diabetes mellitus [20, 21], cardiovascular disease [9, 22], respiratory ailments [23, 24], rheumatoid arthritis [25, 26], adverse pregnancy outcomes [22, 27], malignancies [28, 29], and osteoporosis [30, 31]. Thus, a comprehensive understanding of dysbiosis-induced periodontitis mechanisms and strategies for sustaining a balanced oral microbiome is crucial.

The interleukin-17 (IL-17) signaling axis contributes to ecological conditions favorable to microbial imbalance. Emerging studies highlight IL-17A's capacity to remodel the oral environment toward a pro-inflammatory, pathogen-enriched state that accelerates periodontal breakdown. IL-17A has gained recognition as a pivotal cytokine in immune regulation and inflammation. Its downstream targets include chemokines, cytokines—such as TNF-α, IL-1β, IL-6, GM-CSF—and RANKL. Synergistic interactions between IL-17A and other mediators, including TNF-α, IL-1β, and IFN-γ, further amplify inflammatory cascades. Consequently, IL-17A is integral to the pathogenesis of periodontitis [1, 32]. This cytokine, produced by multiple innate and adaptive immune subsets, orchestrates inflammatory cascades involved in both periodontal and systemic inflammatory diseases [33, 34]. In addition, IL-17A stimulates the generation of antimicrobial peptides essential for controlling pathogenic and commensal microbes at mucosal barriers. IL-17A–producing γδ T cells, NK cells, and ILC3s—strategically positioned at barrier interfaces—serve as early responders modulating neutrophil activity [35]. Clinical samples from patients with periodontitis reveal elevated IL-17A expression, along with increased γδ T cell and neutrophil infiltration, compared to healthy tissues [36]. Understanding the pathways linking oral dysbiosis, IL-17A signaling, and systemic inflammation is therefore critical for developing effective interventions to restore microbial homeostasis. This review synthesizes recent advances concerning oral dysbiosis and its management, with a particular focus on IL-17A's mechanistic role as a pathophysiological mediator connecting periodontitis and systemic inflammatory disorders.

*Role of oral bacteria in preserving periodontal tissue balance*

Oral microorganisms provide considerable advantages to the host by preventing pathogen colonization and influencing both cellular architecture and immune system maturation [37]. Experiments using germ-free (GF) mice have revealed that although microbial colonization is not required for survival, it is indispensable for sustaining health and modulating immune and physiological responses associated with disease resistance [38, 39]. Within the mouth, the immune system sustains equilibrium through continuous interaction between resident bacteria and epithelial surfaces, while also addressing ongoing tissue turnover [4]. Prior findings demonstrated that oral microbes drive structural and functional adaptations in oral tissues [40, 41]. Moreover, microbial colonization limits nutrient availability and attachment sites for invading pathogens, a phenomenon known as colonization resistance [42].

Analogous to the intestinal microbiome, commensal microorganisms in the oral cavity promote tissue stability by stimulating immune activity. They facilitate immune cell recruitment within the mucosa, aid in the formation of organized lymphoid tissue [43], and enhance epithelial defense functions, such as mucus secretion and antimicrobial peptide synthesis [44]. Consequently, oral bacteria may act as an additional functional "tissue" of the host, maintaining physiological balance; impairment of this function can contribute to disease onset [45].

The epithelial barrier plays a pivotal role in oral protection. The soft-tissue epithelium—particularly the junctional epithelium adjacent to vascular gingiva—ensures a steady influx of immune cells that patrol and control bacterial populations within the gingival sulcus [37, 46]. Under normal conditions, this junctional epithelium remains poorly differentiated, with a

turnover time of approximately 4–6 days [47]. Comparative studies show that conventionally raised mice possess a substantially larger junctional epithelial region than GF mice [37]. Collectively, these findings indicate that oral bacteria are integral to periodontal tissue development and to the modulation of immune defenses against pathogens.

*Effects of oral bacteria on the innate defense system*

Comparative analyses between conventional and germ-free mice indicate that bacterial colonization strongly influences neutrophil dynamics and regulation [37, 41]. Furthermore, when P. gingivalis lipopolysaccharide (LPS) was applied to gingival tissues, GF mice exhibited reduced CD4+ T-cell infiltration and diminished TNF-α and Foxp3 expression compared to specific pathogen-free counterparts [48]. The presence of oral microbes triggers well-coordinated immune activation via neutrophil recruitment into gingival tissues, which surveils and restricts microbial proliferation.

Responses to bacterial endotoxins from periodontal pathogens engage both innate and adaptive arms of immunity. These include macrophages, dendritic cells, NK cells, monocytes, and neutrophils, as well as B and T lymphocytes, all contributing to the secretion of pro-inflammatory mediators such as IL-17A, IFN-γ, IL-1β, and IL-6 [49]. Innate and adaptive systems function in close synergy, with innate mechanisms initiating and directing adaptive responses. For instance, helper T cells produce IFN-γ, a potent cytokine that enhances macrophage and NK cell activity, strengthening both phagocytosis and cytotoxic function [35]. In summary, the oral microbiota orchestrates a tightly regulated innate defense network—particularly involving neutrophils—which migrate from blood vessels through gingival tissues to the sulcus, forming a protective shield between the epithelium and microbial biofilms.

*Overview of human oral dysbiosis*

Dysbiosis describes alterations in the microbial equilibrium within a specific ecological niche [50]. It can occur through three overlapping phenomena: (1) an overall decline in microbial diversity, (2) depletion of beneficial commensals, and (3) an overgrowth of pathogenic taxa [51]. Dysbiotic changes within the periodontal microbiome are strongly correlated with periodontitis. Under healthy conditions, pathogenic bacteria form a minor fraction of the subgingival flora; however, their prevalence increases markedly as periodontal pockets develop. Notably, dysbiotic microbial communities display reduced diversity yet greater compositional similarity compared to those from healthy sites [52]. Understanding the molecular basis of oral dysbiosis could provide insight into preventing the transition from microbial symbiosis to imbalance.

Oral dysbiosis most frequently stems from poor oral hygiene and inadequate care routines [53]. In periodontal tissues, excessive biofilm accumulation elicits inflammatory responses that enhance gingival crevicular fluid (GCF) exudation—often accompanied by bleeding. Elevated sulcular fluid not only participates in host defense but also nourishes proteolytic and anaerobic species dominant in gingival biofilms [54]. Additional contributors include compromised systemic health, unbalanced diets, smoking, immune deficiencies, genetic predispositions, and salivary gland dysfunction **(Figure 1)** [11, 55–57]. A dysbiotic shift ultimately promotes the establishment of complex microbial biofilms [14]. Hence, oral pathologies in humans largely originate from endogenous microbial alterations rather than from external infections [58].



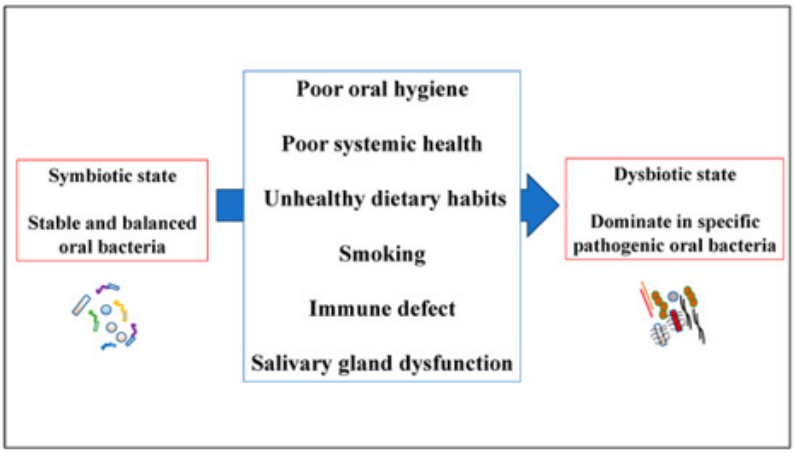


**Figure 1.** Multiple determinants influencing alterations within the oral microbiome.

*Human oral dysbiosis within periodontal tissues*

Periodontitis represents a multifactorial condition associated with microbial shifts from a balanced, symbiotic state to a pathogenic, dysbiotic state [2]. The transition from periodontal health to disease involves a substantial reorganization—from commensal-dominant species (mainly Actinomyces and Streptococcus) to an anaerobe-rich consortium consisting primarily of Bacteroides, Porphyromonas, Treponema, and Prevotella [1]. This sequence constitutes the biological process underlying oral dysbiosis, which evolves progressively within the gingival sulcus. Early microbial settlers of the gingiva are mostly Gram-positive and exhibit minimal pathogenicity [59]. The initial step involves salivary protein coating on tooth surfaces, after which bacterial adhesion and nutrient availability drive biofilm establishment [60]. As biofilms mature, they become structurally complex and contribute to gingival inflammation (gingivitis). Several genera, including Streptococcus, Fusobacterium, Actinomyces, Veillonella, Treponema, Bacteroides, and Capnocytophaga, are strongly linked to this condition [61].

The dysbiotic transformation of the periodontal microbiome is a gradual process that shifts the microbial partnership with the host from a symbiotic to a pathogenic state. Among these bacterial communities, the earliest disease-related assemblage is the orange complex, composed of anaerobic Gram-negative organisms such as Prevotella intermedia (P. intermedia), Prevotella nigrescens (P. nigrescens), Prevotella micros (P. micros), and Fusobacterium nucleatum (F. nucleatum). With disease advancement, this community gives way to the red complex, containing Treponema denticola (T. denticola), Tannerella forsythia (T. forsythia), and P. gingivalis [14]. The red complex displays a strong association with increased probing depth and bleeding upon examination.

Both complexes comprise the key microorganisms responsible for periodontitis. Members of the orange complex demonstrate the ability to adhere to other oral species, serving as bridging organisms that facilitate the colonization of later pathogens [62]. The presence of these intermediate species is critical since the virulence of the red complex depends on them for persistence in the oral niche. The red complex bacteria are predominantly Gram-negative and produce endotoxins, contributing to high pathogenic potential [16]. These microbes can intensify the growth of resident flora, leading to increased microbial burden, chronic inflammation, and tissue degradation.

During early colonization, P. gingivalis notably interferes with innate immunity, altering both the abundance and distribution of commensal bacteria. This imbalance disrupts host–microbe harmony and promotes inflammatory bone resorption. Hence, P. gingivalis is regarded as a keystone pathogen capable of reprogramming the commensal community toward dysbiosis, even when present in low numbers [16, 62]. Furthermore, P. gingivalis can influence adaptive immunity by selectively inducing Th17 cell differentiation and migration—cells that, while maintaining homeostasis under normal conditions, are implicated in tissue destruction during disease progression [63].

Recent research has also highlighted emerging Gram-positive anaerobic pathogens, such as Filifactor alocis (F. alocis) and Peptoanaerobacter stomatis (P. stomatis), as significant contributors to periodontitis. Growing evidence suggests that these species alter microbial community dynamics and play essential roles in dysbiosis development [64]. In contrast to other Gram-positive organisms, F. alocis exhibits strong synergistic effects within the host proteome, provoking extensive systemic immune responses [64]. It can invade gingival epithelial cells, produce trypsin-like proteases, tolerate oxidative environments, and modulate neutrophil functions [65]. Meanwhile, P. stomatis enhances the recruitment of neutrophils and monocytes, intensifying inflammation and promoting granule exocytosis [66]. Collectively, such dysbiotic microbial states act as direct pathogenic drivers rather than mere by-products of an altered inflammatory environment.



*Interaction between oral dysbiosis and the junctional epithelium*

Oral dysbiosis alters junctional epithelial cell behavior during infection and impacts signaling pathways, metabolic processes, and intercellular communication within host tissues [67]. Elevated concentrations of lipopolysaccharides (LPS)—originating from Gram-negative bacteria such as P. gingivalis, F. nucleatum, and Aggregatibacter actinomycetemcomitans—stimulate epithelial cells to produce inflammatory mediators and cytokines, promoting chronic inflammation [68]. Specifically, LPS activates the secretion of TNF-α, IL-1β, and IL-6 by junctional epithelial cells [69].

As a result, oral dysbiosis induces neutrophil infiltration, activates immune cells including macrophages and dendritic cells, and triggers inflammatory signaling that regulates Th-cell responses [70]. This heightened activation leads to excessive production of pro-inflammatory factors such as IL-1β, TNF-α, and prostaglandin $E_2$, intensifying microbial-induced inflammation and potentially resulting in systemic spread [71]. When infection persists, continuous secretion of these inflammatory mediators sustains adaptive immune activation through B- and T-cell pathways [36].

*Oral dysbiosis in periodontitis and systemic disease*

Imbalance within the oral microbiota can promote systemic inflammatory responses, either by amplifying existing inflammation through toxin dissemination or by enabling microbial by-products to enter the bloodstream [72]. Typically, this microbial disruption activates immune mechanisms encompassing both innate (neutrophils, dendritic cells, macrophages) and adaptive (B and T lymphocytes) components, resulting in elevated secretion of pro-inflammatory factors such as interferon [IFN]-γ, IL-17A, TNF-α, IL-1β, IL-6, and matrix-degrading enzymes, including metalloproteinases and collagenases [1, 62]. Consequently, oral dysbiosis observed in periodontitis is mechanistically tied to the initiation and worsening of systemic inflammatory illnesses—among them diabetes mellitus, cardiovascular disorders, and rheumatoid arthritis—since cytokines generated during chronic low-grade inflammation are distributed through the circulatory system [1, 9, 12, 22, 26, 30, 53, 72, 73].

Several of these cytokines influence naïve $CD4^+$ T cells, prompting their differentiation into Th1, Th2, Th17, follicular helper T, and regulatory T (Treg) subsets in response to inflammatory cues [74]. Th1 cells (producing IL-12 and IFN-γ) and Treg cells (expressing IL-2, TGF-β, and IL-10 family members) exhibit both suppressive and pleiotropic roles in periodontal inflammation. Th17 (IL-17A and IL-23) and Th2 (IL-4, IL-5, IL-13) subsets contribute to diverse immunomodulatory processes as well [75]. Maintenance of oral mucosal equilibrium strongly depends on the Th17/Treg balance [33]. Disturbance of this ratio has been linked to periodontitis progression [76], emphasizing the importance of synchronized activity between Th17 effectors and Tregs for immune stability and host protection [77].

Tregs act as inhibitory cells, dampening immune activation either through cytokine secretion or direct cellular interaction and are crucial for self-tolerance. Interestingly, under certain inflammatory contexts, Tregs can convert into IFN-γ-producing Th1-like cells or IL-17A-secreting Th17-type cells, processes implicated in the development of autoimmune disorders [78]. A subset known as exFoxp3Th17 cells—originating from $Foxp3^+$ Tregs—display potent pro-inflammatory and pro-osteoclastogenic features that aggravate autoimmune arthritis [79]. Their osteoclastogenic potential surpasses that of conventional Th17 cells, underscoring their involvement in bone resorption. Th17 cells are also central to inflammatory conditions such as rheumatoid arthritis, psoriasis, multiple sclerosis, asthma, and inflammatory bowel disease [34].

Understanding systemic inflammation requires considering IL-17A signaling, as a wide range of cells—including osteoblasts, fibroblasts, epithelial and endothelial cells, keratinocytes, macrophages, and chondrocytes—express IL-17A receptors [75]. IL-17A mobilizes neutrophils from bone marrow into the circulation, directing them toward periodontal infection sites [80]. Although IL-17A contributes to bone protection during P. gingivalis infection, excessive IL-17A activity has been associated with bone loss in rheumatoid arthritis [81]. Therefore, dysregulation among IL-17A and other pro-inflammatory mediators may alter oral microbial equilibrium, linking periodontitis-associated dysbiosis to systemic chronic inflammation. This section explores how IL-17A-driven mechanisms mediate systemic disease in the presence of oral dysbiosis.



*Role of IL-17A production induced by oral dysbiosis in systemic inflammatory disease*

IL-17A functions as a key mediator in both protective and pathological immune responses. It is rapidly synthesized following microbial invasion by bacteria, viruses, or fungi. In chronic inflammatory settings, IL-17A amplifies pathological inflammation, sustaining disease onset and chronicity [75]. It influences a broad spectrum of tissue-specific genes and enhances epithelial barrier defense against neutrophil-sensitive microorganisms and other pathogens linked to periodontal infections. At the same time, IL-17 contributes to tissue restoration by regulating reparative gene expression [82].

Multiple immune cell types—including NK cells, ILC3s, γδT cells, Tc17 cells, and regulatory T cells—serve as IL-17A sources [34]. These populations play pivotal roles in inflammatory disorders such as diabetes mellitus, psoriasis, and rheumatoid arthritis [1, 83] **(Figure 2)**. Increasing evidence supports a close connection between periodontitis and chronic systemic

inflammation, and cytokine-targeted therapies have demonstrated simultaneous benefits for both oral and overall health [84]. Recent research further shows that pharmacologic or genetic suppression of Th17 cells or IL-17A signaling can prevent periodontal bone resorption, suggesting that these immune pathways represent promising therapeutic targets [85, 86].

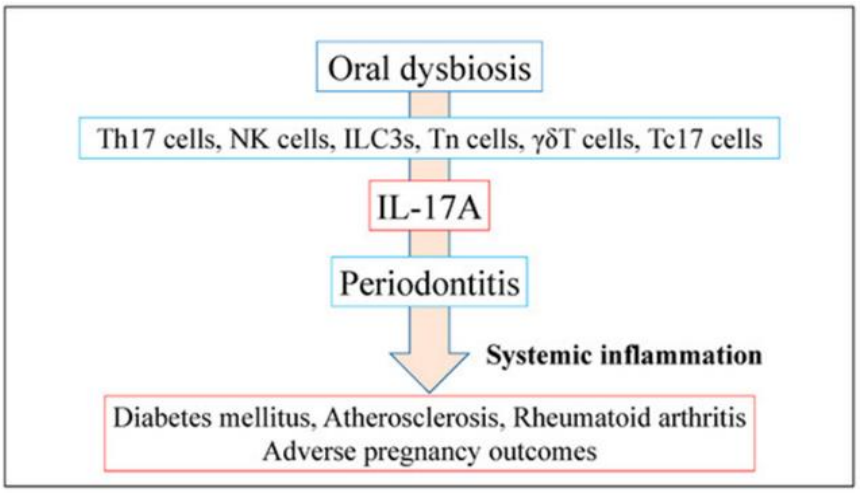



**Figure 2**. A schematic representation illustrating a potential pathway linking oral dysbiosis to systemic inflammation. Various innate and adaptive immune cells secrete IL-17A, which is elevated during dysbiosis. This heightened IL-17A response alters host immunity, worsens microbial imbalance, and drives the progression of systemic inflammatory diseases.

*Periodontitis, IL-17A, and their association with diabetes mellitus*

Diabetes mellitus (DM) is a metabolic condition defined by persistent hyperglycemia, arising from insufficient insulin output, impaired insulin action, or both mechanisms combined [87]. Type 2 diabetes mellitus (T2DM)—the non-insulin-dependent form—is the dominant subtype and typically results from concurrent insulin resistance and defective insulin release [87]. A reciprocal relationship exists between DM and periodontitis, with each capable of intensifying the other's pathology [88]. Elevated blood glucose levels are strongly associated with both the onset and progression of periodontal disease [89]. The inflammatory immune reaction driven by periodontitis can induce insulin resistance, thereby worsening diabetic control [90].

Furthermore, DM is known to diminish gut microbial diversity, aligning with observations that bacterial heterogeneity is also reduced in other tissues of diabetic subjects [91]. Within the oral cavity, diabetic individuals—regardless of periodontal status—display distinct microbial features, including altered community structure, greater biological diversity, and an increased abundance of certain bacterial taxa when compared with non-diabetic controls [92]. In diabetics with clinically healthy gums, the subgingival flora shows lower species richness than in healthy non-diabetic subjects, together with a relative predominance of opportunistic species belonging to the orange and red complexes and a reduction in health-associated taxa [93]. This microbial shift toward pathogenic organisms likely heightens susceptibility to periodontitis in diabetic patients.

Experimental findings show that oral administration of P. gingivalis in murine models provokes systemic inflammation and insulin resistance simultaneously [94]. Moreover, patients with both diabetes and chronic periodontitis exhibit markedly elevated salivary IL-17A levels compared with healthy individuals, suggesting IL-17A overexpression is a key risk factor for chronic periodontal inflammation in this population [95]. Altogether, these data indicate that oral dysbiosis can influence the bidirectional connection between DM and periodontitis, where IL-17A-driven immune activation and microbial imbalance contribute to systemic inflammation, increased insulin resistance, and aggravated hyperglycemia.

*Periodontitis, IL-17A, and their association with atherosclerosis*

Atherosclerosis represents a chronic vascular inflammatory disorder characterized by plaque accumulation in the intimal layer of medium- and large-caliber arteries and is the principal cause of cardiovascular disease [96]. Periodontitis has been identified as a major contributing factor in its initiation [97]. Periodontal pathogens—such as P. gingivalis, T.

forsythia, and P. intermedia—can translocate into vascular lesions, actively participating in plaque formation [98]. Additionally, P. gingivalis promotes oxidation of low-density lipoprotein, thereby accelerating atherosclerotic changes [99].

This organism can also induce endothelial dysfunction, foam-cell generation, vascular smooth-muscle proliferation and calcification, and disturbances in the Th cell/Treg equilibrium [100]. Its lipopolysaccharides (LPS) and virulence factors activate monocytes, enhance Th17/IL-17A signaling, and raise circulating TNF-α, IL-1β, IL-6, and IL-17A concentrations through TLR2/TLR4-mediated pathways, ultimately fostering plaque development [33]. Elevated IL-17A expression is observed in atherosclerotic lesions, contributing to lesion expansion and vascular inflammation [101]. Collectively, oral dysbiosis often induces transient bacteremia, which damages vascular endothelium, while continual LPS release sustains systemic immune activation, promoting atherogenesis.

*Periodontitis, IL-17A, and their association with pheumatoid arthritis*

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder primarily targeting synovial membranes, resulting in systemic inflammatory cascades [102]. Periodontitis is now regarded as a potential risk factor for RA onset [103, 104]. Both diseases share immunopathogenic similarities—such as excessive inflammatory cell infiltration, elevated pro-inflammatory cytokine production, suppression of anti-inflammatory mediators, and activation of NF-κB/RANKL pathways [105]. RANKL expression is driven either by IL-23-stimulated Th17 cells or by IL-17A-activated fibroblasts [106].

Synovitis comprises a complex interplay of cytokines and immune cells, including macrophages, fibroblasts, plasma cells, T and B lymphocytes, mast cells, dendritic cells, and neutrophils, all contributing to tissue vascularization and hyperplasia [107]. When dendritic cells or macrophages are stimulated by LPS, they release IL-23, which binds IL-23R on Th17 cells, encouraging their proliferation and secretion of IL-17A and RANKL [108]. Patients suffering from RA and concurrent periodontitis display significantly higher serum IL-17A concentrations compared with those who have periodontitis alone [109].

Interestingly, P. gingivalis uniquely expresses the enzyme peptidylarginine deiminase, implicated in citrullination processes associated with RA pathogenesis [110]. Hence, periodontitis involves a dysregulated subgingival ecosystem coupled with abnormal host immune activity, leading to chronic autoimmune inflammation that damages synovial tissue and joint cartilage. Consequently, IL-17A upregulation linked to periodontal inflammation may exacerbate joint destruction and contribute to RA progression.

*Periodontitis, IL-17A, and their association with adverse pregnancy outcomes*

Periodontal disease is common among pregnant individuals, as hormonal and immunological fluctuations significantly alter the oral microbiome. Maternal periodontitis has been associated with negative pregnancy outcomes, including premature birth, miscarriage, low-birth-weight infants, and stillbirth [111, 112]. Gingival crevicular fluid from women experiencing adverse pregnancy outcomes often shows elevated inflammatory mediator levels, implying a role for cytokine-driven induction of labor [113, 114].

Compared with non-pregnant controls, pregnant women exhibit an overrepresentation of Neisseria, Porphyromonas, and Treponema species, alongside decreased levels of Streptococcus and Veillonella [3]. Physiological and immune adjustments during pregnancy heighten susceptibility to infection by pathogenic oral species, resulting in dysbiosis that may trigger systemic complications. Analogous to mechanisms underlying atherosclerosis and rheumatoid arthritis, cytokines such as TNF-α, IL-1β, IL-6, and IL-17A produced in periodontal inflammation can enter systemic circulation and provoke acute-phase responses that detrimentally affect placental function and fetal development [115].

*Prevention of human oral dysbiosis*

Preventing oral dysbiosis requires an understanding of the harmful role played by bacterial accumulation in periodontal pockets. During periodontitis, the microbial diversity of the oral cavity increases markedly, with the subgingival plaque showing the highest species richness within the mouth [116]. The main preventive measure against oral dysbiosis, aimed at disrupting bacterial colonization in supra- and subgingival zones, is mechanical removal of biofilm from tooth surfaces [117]. Strong evidence supports that consistent personal plaque control methods—such as regular tooth brushing combined with chemical plaque inhibitors—can substantially reduce gingival inflammation and plaque buildup, provided cleaning is done effectively and at proper intervals [118]. Nevertheless, total bacterial eradication is not ideal; rather, methods to maintain ecological balance and restore a healthier oral environment are preferred.

Recently, systemic antibiotics [119], probiotics [120], and photodynamic therapy [121] have been explored for reducing pathogenic bacterial load, though robust evidence is still lacking. A critical mechanism influencing oral microbial balance appears to be the upregulation of IL-17A. This cytokine interacts synergistically with other inflammatory mediators, and the combined imbalance may drive host changes that foster dysbiosis. Experimental studies have shown that continuous delivery of IL-17A-neutralizing antibodies to periodontal tissues can prevent inflammatory bone loss in mice with induced periodontitis [122]. Further comprehensive clinical studies on IL-17A inhibitors are warranted. At present, no standardized preventive protocol for oral dysbiosis exists. Assessing the diversity and composition of oral flora could guide the creation of new preventive strategies and help evaluate their effectiveness.

## Conclusion

Oral dysbiosis plays a central role in the etiology of periodontitis. Hence, identifying the physiological and metabolic traits underlying this imbalance is vital for developing novel treatments that restore a healthy microbial community. Dysbiosis of the oral microbiota promotes IL-17A expression in periodontal tissues. Moreover, IL-17A works synergistically with other pro-inflammatory cytokines, and disruption in these mediators contributes to host alterations leading to dysbiosis, influencing the onset of diseases such as diabetes mellitus, atherosclerosis, rheumatoid arthritis, and adverse pregnancy outcomes.

Although IL-17A inhibitors are proven effective in managing psoriasis [123] and rheumatoid arthritis [124], their application in periodontitis therapy remains limited, likely due to the unclear role of IL-17A in periodontal disease progression. Because IL-17A has both protective and damaging functions, and its inhibition can cause notable side effects, the causal relationship between periodontitis and associated systemic conditions remains uncertain. Advancing the understanding of oral dysbiosis in disease mechanisms, prevention, and treatment may contribute to improved management of systemic inflammatory disorders. Furthermore, studying the oral microbiome's diversity and composition could enable the development of innovative preventive measures and methods to evaluate their success.

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