

MICROBIAL ECOLOGY AND DYSBIOSIS IN PERI-IMPLANT DISEASES: A NARRATIVE REVIEW

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Abstract

Dental implants represent the contemporary gold standard for prosthetic rehabilitation; however, their long-term success is increasingly jeopardized by peri-implant diseases, primarily peri-implant mucositis and peri-implantitis. These bacterially induced inflammatory conditions are driven by oral microdysbiosis, wherein a previously symbiotic microbiome transitions into a structurally complex, highly pathogenic biofilm. This narrative review examines the distinct microbiological profiles characterizing peri-implant health and disease, delineates the functional roles and virulence mechanisms of key pathogens, and evaluates the emerging significance of cross-kingdom interactions. The immunological cascades underpinning progressive tissue and bone destruction are reviewed alongside advances in metagenomic detection technologies. Current intervention strategies, including adjunctive chemical, antibiotic, and probiotic therapies as well as implant surface modifications, are critically assessed. The evidence underscores that peri-implantitis represents a polymicrobial, infection requiring targeted, ecology-driven therapeutic approaches to secure implant longevity.

Keywords: dental implants, peri-implantitis, biofilm, antibiotic resistance

Introduction

The advent of osseointegrated dental implants has fundamentally transformed prosthetic dentistry, providing a highly effective solution for restoring mastication, occlusion, and aesthetics following tooth loss. Despite reported survival rates approaching 95% over ten years,¹ the global burden of peri-implant diseases has escalated considerably, posing a major threat to implant longevity and generating substantial healthcare costs.² A recent AO/AAP systematic review and meta-analysis reported that peri-implant mucositis affects up to 43% of implants and 46% of patients, while peri-implantitis prevalence ranges from 19% to 22% at implant and patient levels, with estimates varying substantially according to diagnostic criteria and population studied.³

Peri-implant diseases encompass two principal conditions. Peri-implant mucositis is a reversible inflammatory lesion confined to the peri-implant soft tissues, clinically identified by bleeding on probing, erythema, and swelling without accompanying bone loss.⁴ When left unmanaged, mucositis can progress to peri-implantitis, a chronic pathological state characterized by mucosal inflammation and progressive,

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irreversible loss of crestal supporting bone.⁵ While aetiology is multifactorial, encompassing systemic conditions such as diabetes mellitus, tobacco smoking, genetic predisposition, and iatrogenic factors including excess residual cement, one of the primary precipitating factor is the accumulation of a dysbiotic microbial biofilm on implant surfaces.^{6,7} This review synthesizes current evidence on the microbiology, pathogenesis, detection, and management of peri-implant diseases, incorporating microbial interactions and advances in functional metagenomic profiling.

Microbial Ecology, Peri-Implant Health, and the Transition to Disease

Oral Microbiome and Peri-Implant Health

The oral cavity constitutes one of the most microbially diverse ecosystems in the human body, harbouring more than 700 distinct bacterial species alongside fungi, viruses, and archaea in a dynamic equilibrium with the host immune system.⁸ Colonization follows highly organized sequential succession: pioneer Gram-positive streptococci attach to salivary pellicle-coated surfaces and scaffold subsequent adhesion of secondary and late colonizers.^{9,10} This successional model applies directly to implant surfaces; immediately following placement, a titanium implant is coated by salivary proteins, after which commensal bacteria colonize in a pattern mirroring natural tooth surfaces but with notable compositional differences.¹¹

Under healthy conditions, the peri-implant microbiome is characterized by a stable, symbiotic relationship with the host, a relatively low microbial load, and reduced species diversity compared to diseased sites. Healthy peri-implant sulci are predominantly colonized by bacteria from the phyla Firmicutes and Proteobacteria, including *Streptococcus*, *Actinomyces*, *Rothia*, *Neisseria*, and *Corynebacterium* species.¹² These commensals fulfil critical protective roles through

competitive exclusion, bacteriocin secretion, and immunomodulation. Notably, *Fusobacterium nucleatum* in its symbiotic state stimulates gingival epithelial cells to constitutively express human beta-defensin-2 (hBD-2), defending against invading microorganisms.¹³ The absence of a periodontal ligament, the distinct surface chemistry of titanium, and the unique junctional anatomy around implants render peri-implant tissues inherently more susceptible to microbial perturbation than natural dentition.¹⁴

Peri-Implant Mucositis: Early Biofilm and Inflammatory Transition

Within minutes of implant exposure to the oral environment, a conditioning film of salivary glycoproteins forms on the titanium surface, providing adhesion receptors for initial bacterial colonization.¹⁵ Early colonizers, predominantly *Streptococcus* and *Actinomyces* species attach via specific adhesin-receptor interactions, establishing the primary biofilm scaffold.⁹ Over days to weeks, this nascent biofilm matures through incorporation of secondary colonizers, with increased prevalence of *Fusobacterium nucleatum*, *Treponema* species, *Prevotella intermedia*, and *Campylobacter* species. Metagenomic analyses of mucositis sites reveal enrichment in bacterial chemotaxis and flagellar assembly pathways, suggesting active tissue invasion capacity is established early in disease progression.¹⁶

The transition from microbial homeostasis to mucositis involves disruption of the epithelial barrier and onset of a host inflammatory response.¹⁷ Pattern recognition receptors, including Toll-like receptors detect microbial-associated molecular patterns (MAMPs), triggering release of pro-inflammatory mediators including IL-1 β , IL-6, and TNF- α .¹⁸ Critically, mucositis is reversible with effective mechanical plaque removal, reinforcing the bidirectional relationship between biofilm accumulation and early peri-implant inflammation.¹⁹ Without

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intervention, the deepening inflammatory pocket creates an anaerobic microenvironment that selectively favours the emergence of late-colonizing pathogens, driving progression to peri-implantitis.

Peri-Implantitis: Microbial Dysbiosis, Key Pathogens, and Biofilm

Pathogenic Consortium and Anaerobic Colonization:

Peri-implantitis is driven by a dysbiotic microbiome sharing considerable overlap with subgingival periodontitis but exhibiting distinct compositional and functional features.^{20,21} The pathogenic consortium is frequently characterized using the Socransky complex framework. The Red Complex, comprising *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* represents the most strongly implicated keystone pathogens.²² *Porphyromonas gingivalis*, an anaerobic Gram-negative rod abundantly detected in diseased sites, possesses cysteine proteases (gingipains), lipopolysaccharides, and fimbriae that mediate binding to host β 1-integrin, facilitating intracellular invasion and immune evasion.²³ *Tannerella forsythia* utilizes its surface glycoprotein BspA, facilitates epithelial invasion and bacterial adhesion, while *Treponema denticola*'s motility and proteolytic capacity enable deep tissue penetration and sustained inflammation. *Treponema denticola* acts synergistically with *Porphyromonas gingivalis* in sustaining dysbiosis and enhancing inflammatory tissue destruction.²³

As peri-implant pockets deepen and become increasingly hypoxic, anaerobic taxa are strongly favoured in a self-amplifying ecological shift.²⁰ Orange Complex bacteria, including *Prevotella intermedia*, *Parvimonas micra*, and *Campylobacter rectus* act as critical sentinel pathogens, facilitating biofilm maturation toward a fully pathogenic state.²² Recent metagenomic investigations have also highlighted the enrichment of *Filifactor alocis* and *Fretibacterium*

fastidiosum in peri-implantitis microbiomes. These organisms are less frequently detected in periodontitis, suggesting peri-implant-specific ecological niches.¹⁷ *Staphylococcus aureus* and *S. epidermidis* have been isolated from peri-implantitis lesions at levels rarely encountered in periodontitis, owing to their high affinity for titanium surfaces and drug-resistant biofilm-forming capacity.²⁴ Opportunistic enteric bacteria also appear at elevated frequencies, particularly in cases of late implant failure.²⁵ *Aggregatibacter actinomycetemcomitans* has also been implicated in peri-implant dysbiosis, particularly through leukotoxin-mediated immune modulation and inflammatory tissue destruction.²⁶

Polymicrobial Biofilm Formation and Microbial Succession:

Biofilm formation on dental implant surfaces is a temporally organized, multistep process beginning immediately upon implant exposure to the oral cavity. Early colonizers (*Streptococcus gordonii*, *S. oralis*, *Actinomyces naeslundii*) attach via specific lectin-carbohydrate and protein-protein adhesin interactions within hours, begin producing extracellular polysaccharide matrix, and locally deplete oxygen through metabolic activity.¹⁵

In the second phase, *F. nucleatum* acts as the pivotal bridging organism, coaggregating with early colonizers through specific molecular interactions (RadD with *Streptococcus*, FomA with multiple species), physically linking the established commensal community to late pathogens, including *P. gingivalis*, *T. denticola*, and *T. forsythia* that could not otherwise colonize the surface independently.²² The final maturation phase establishes a structurally complex, multi-layered biofilm with distinct microcolonies, fluid-filled channels, and a protective extracellular matrix functioning as a diffusion barrier against antimicrobials.¹⁰ The presence of *Candida albicans* further amplifies this phase by upregulating glucosyltransferase genes in streptococci, dramatically increasing

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extracellular glucan polymer synthesis and thickening the matrix scaffold.²⁷ The implant macro-geometry, particularly screw threads and surface microroughness provides protected niches that resist mechanical disruption and promote biofilm accumulation.¹¹

Antimicrobial Resistance in Peri-Implant Pathogens:

The clinical management of peri-implantitis is significantly hampered by inherent and acquired antimicrobial resistance operating at multiple levels. At the organism level, *S. aureus* strains isolated from peri-implantitis lesions frequently carry the *mecA* gene encoding penicillin-binding protein 2a (PBP2a), conferring methicillin resistance (MRSA) and rendering β -lactam antibiotics ineffective.²⁴ Gram-negative anaerobes, including *P. gingivalis* and *Prevotella* species, demonstrate resistance through outer membrane impermeability, efflux pump overexpression, and β -lactamase production.¹⁷ *C. albicans* strains carry ERG11 mutations and CDR1/CDR2 efflux transporter overexpression conferring azole resistance.²⁷

At the biofilm level, the polymicrobial matrix provides collective resistance mechanisms exceeding the sum of individual resistances. The dense extracellular polysaccharide matrix reduces antibiotic penetration, while metabolic gradients create zones of phenotypically tolerant persister cells that survive antibiotic courses and act as reservoirs for re-colonization.⁹ Horizontal gene transfer within the biofilm further facilitates the spread of resistance determinants between taxa.²¹ These multilevel resistance mechanisms underscore the inadequacy of antibiotic monotherapy and the need for strategies that physically disrupt the biofilm matrix prior to antimicrobial administration.

Host–Microbe Interactions and Immunopathology

The progression of peri-implant disease is fundamentally a consequence of a

hyperactivated, self-sustaining host immune response directed against a dysbiotic biofilm, ultimately resulting in collateral tissue and bone destruction.⁴ The host innate immune system detects dysbiotic microbiota through pattern recognition receptors including TLR-4, TLR-5, and NOD-like receptors (NLRs). Pathogenic stimuli, particularly *P. gingivalis* lipopolysaccharides and flagellin activate multiprotein inflammasome complexes (NLRP3 and AIM2) within peri-implant tissues, leading to caspase-1 activation and the massive release of IL-1 β , IL-6, IL-8, and TNF- α , initiating a destructive inflammatory cascade.^{18,28}

As inflammation transitions to a chronic state, the immune cellular infiltrate shifts from predominantly neutrophilic to a dense infiltrate of T cells (CD4+, CD8+), B cells, and macrophages.²⁹ The dysbiotic biofilm forces macrophage polarization predominantly toward the pro-inflammatory M1 phenotype rather than the pro-healing M2 phenotype. The sustained elaboration of TNF- α , IL-1 β , and IL-6 by M1 macrophages aggressively stimulates osteoclastogenesis via the RANK/RANKL/OPG axis, resulting in progressive resorption of alveolar crestal bone.¹⁷ Matrix metalloproteinases, particularly MMP-1, are simultaneously upregulated, causing severe degradation of the extracellular connective tissue matrix.²⁹ Host genetic factors further modulate response severity: composite IL-1 genotype polymorphisms nearly double the risk of developing peri-implant diseases, explaining interindividual variation in disease susceptibility.⁴

Implant Surface Characteristics and Periodontal–Peri-Implant Microbiota Comparison

Role of Implant Surface in Microbial Colonization:

The physicochemical properties of the titanium implant surface profoundly influence early microbial adhesion, subsequent biofilm

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maturation, and host-implant-microbe interactions.¹⁰ Surface roughness is among the most extensively studied parameters: rough surfaces provide increased adhesion area, protected micro-niches, and reduced shear forces, collectively favouring greater bacterial accumulation. Surface energy and hydrophilicity also modulate colonization dynamics, though the clinical significance of hydrophilicity diminishes rapidly as the pellicle neutralizes surface energy differences.¹¹ Surface chemistry modifications including nitrogen ion implantation, titanium nitride coatings, and incorporation of antimicrobial peptides have demonstrated variable efficacy in reducing early biofilm formation in vitro.³⁰

Titanium corrosion, particularly microbiologically influenced corrosion driven by acid-producing and sulfate-reducing bacteria, can degrade the titanium oxide passive layer, releasing ions that affect both biofilm composition and host tissue responses, potentially contributing to implant rejection.³¹ Surface nanotopography presents a promising frontier. Nano-textured surfaces can selectively promote osseointegration while reducing biofilm accumulation.³⁰

Periodontal vs. Peri-Implant Microbiota

While both periodontal and peri-implant diseases are polymicrobial conditions driven by Red and Orange Complex bacteria, with Gram-negative anaerobes predominating in advanced disease, significant compositional, anatomical, and functional differences exist.^{20–22} *P. gingivalis* detection rates in peri-implantitis are comparable to or exceed those in chronic periodontitis, and the general inflammatory pathways (TLR activation, cytokine release, RANKL-mediated osteoclastogenesis) are shared.¹⁸

However, peri-implant biofilms harbour notably higher burdens of staphylococci and enteric bacteria that are rarely implicated as primary periodontal pathogens.²⁴ Metagenomic studies consistently detect species strongly

enriched in peri-implantitis, including *Filifactor alocis*, *Fretibacterium fastidiosum*, and specific Mollicutes, suggesting the implant microenvironment selects for distinct ecological communities.¹⁷ Functionally, peri-implant microbiomes display greater enrichment of motility-related pathways (bacterial chemotaxis, flagellar assembly), reflecting enhanced tissue invasion capacity.¹⁶ The anatomical absence of a periodontal ligament removes a key mechanical barrier to biofilm apical migration, and the straight-walled implant pocket geometry combined with titanium surface microroughness provides distinct retention sites not replicated in natural teeth.^{11,14} Furthermore, *Candida albicans* is an emerging cross-kingdom pathogen in peri-implantitis, while rarely implicated in classical periodontitis.²⁷

Advances in Molecular Microbial Detection

The characterization of peri-implant microbiota has been revolutionized by the transition from culture-based methods to culture-independent molecular technologies.²² 16S ribosomal RNA gene sequencing, chiefly targeting hypervariable V3–V4 regions enables comprehensive culture-independent profiling of bacterial community composition and has been pivotal in identifying non-cultivable organisms such as *Filifactor alocis* and *Fretibacterium fastidiosum* in peri-implantitis.²⁰ Whole-genome shotgun (WGS) metagenomics represents an advancement beyond taxonomic profiling, enabling simultaneous characterization of all microbial genomes and the functional gene content of the community.³²

Checkerboard DNA-DNA hybridization and quantitative PCR (qPCR) provide targeted, quantitative detection of specific pathogens with high sensitivity, making them practical clinical monitoring tools for *P. gingivalis*, *T. forsythia*, and *T. denticola*.²¹ Comparative metagenomic studies tracking microbial communities across

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disease states, from health through mucositis to peri-implantitis and remission have revealed distinctive transitional compositional and functional signatures, providing potential diagnostic and prognostic biomarkers. These functional metagenomic traits increasingly serve not merely to identify which organisms are present, but to determine what pathogenic functions they are actively executing, of paramount importance for precision treatment planning.^{32,33}

Clinical Management: Prevention, Treatment, and Emerging Strategies

Clinical management of peri-implant diseases targets the microbial biofilm as the primary etiological agent, with interventions spanning from preventive maintenance to surgical reconstruction. Mechanical debridement remains the cornerstone of treatment at all disease stages, aimed at physically disrupting and removing the biofilm from implant surfaces and surrounding tissues.¹⁹ However, the complex macro-geometry of implant surfaces, particularly threaded designs and rough micro-surfaces significantly limits the efficacy of conventional instrumentation, necessitating adjunctive strategies.³⁴ Antiseptic adjuncts, including chlorhexidine (0.12–0.5%) delivered as mouth rinses, gels, or local delivery systems, produce modest but statistically significant reductions in bleeding on probing in mucositis.¹⁹ Despite its widespread use, chlorhexidine is associated with well-documented adverse effects including tooth staining, taste alteration, and mucosal irritation. More critically, chlorhexidine has been shown to alter implant surface properties, and in vivo evidence demonstrates that post-surgical chlorhexidine use suppresses fibroblast proliferation, upregulates proapoptotic BAX expression, promotes myofibroblast differentiation, and drives a fibrotic “scar wound healing” response mediated through COL1A1, α SMA, SERPINE1, and TIMP1 dysregulation, fundamentally compromising peri-implant

soft tissue regeneration rather than facilitating it.^{35–37} Systemic antibiotics like amoxicillin with metronidazole or azithromycin are utilized for tissue-invasive pathogens in peri-implantitis, but their efficacy is compromised by the high prevalence of antibiotic-resistant strains and biofilm-mediated tolerance.¹⁷

Probiotic therapy, particularly preparations containing *Lactobacillus reuteri*, has demonstrated promise in competitive exclusion of pathogens, reduction of probing depths, and normalization of bleeding on probing in randomized controlled trials.⁷ By restoring rather than eradicating the microbial community, probiotics align with the contemporary understanding of peri-implant disease as an ecological dysbiosis requiring community-level rebalancing rather than simple antimicrobial suppression.³⁸ Surgical interventions, including resective and regenerative approaches, are employed for advanced peri-implantitis with significant bone defects, providing access for thorough decontamination. Emerging surface decontamination technologies like photodynamic therapy, air abrasion, and laser-assisted protocols are under active investigation for their capacity to address biofilm within complex implant geometries.⁷

Limitations of Existing Evidence

Despite significant advances, several critical limitations constrain the clinical applicability of current evidence. First, a substantial proportion of published studies employ cross-sectional designs that establish association rather than causation; longitudinal cohort studies tracking microbial community dynamics from health through disease development remain limited, hindering identification of truly predictive microbial signatures.⁸ Second, significant methodological heterogeneity in sampling sites and methods, DNA extraction protocols, sequencing platforms, and bioinformatic pipelines renders direct comparison and meta-

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analysis challenging.²⁷ Third, the vast majority of studies have focused on the bacterial component; fungal (mycobiome), viral (virome), and archaeal communities remain largely uncharacterized, and the clinical significance of cross-kingdom interactions identified *in vitro* has not been fully validated *in vivo*.³⁹ Fourth, the influence of host factors including specific genetic polymorphisms, systemic disease status, medications, and implant geometry is insufficiently controlled for in most studies.⁴ Finally, evidence on microbiota of specific disease stages (mucositis versus early versus advanced peri-implantitis) remains fragmented, and inconsistent case definitions complicate direct comparisons.¹⁶

Discussion

The shift from a single-pathogen paradigm to an integrated dysbiosis model represents a critical evolution in our understanding of peri-implant disease dynamics. In this review, cross-sectional and clinical sequencing datasets underscore that while classical periodontal pathogens like *Porphyromonas gingivalis* and *Fusobacterium nucleatum* remain heavily enriched in both early and late implant failure, late-stage failure is uniquely characterized by an expanded ecological complexity and heightened microbial diversity, including taxa such as *Treponema* and *Fretibacterium*. Interestingly, global diversity metrics do not always exhibit statistically significant deviations between healthy and diseased states, suggesting that overall community structure can remain superficially stable even as profound taxonomic shifts and an increased Gram-negative anaerobic burden take place locally. Furthermore, within-subject longitudinal tracking during active and remission phases reveals that these communities are highly dynamic; active destructive lesions select heavily for aggressive proteolytic anaerobes, whereas remission states revert to a predominance of commensal, health-associated Gram-positive

organisms. This confirms that disease activity is driven by an ongoing ecological imbalance and network-level interactions between the biofilm and the host immune system, rather than the mere presence of isolated marker species.

Beyond the microbiological profile, a critical finding highlighted in contemporary literature is the bidirectional feedback loop established between the microbial biofilm and the prosthetic biomaterial interface itself. Translational and pilot models demonstrate that titanium surfaces experience significantly accelerated biofilm accumulation compared to control substrates, which subsequently triggers microbiologically influenced corrosion and surface degradation. This electrochemical and structural breakdown compromises the physical integrity of the implant-bone interface. Crucially, it also alters surface topography and roughness, which in turn facilitates renewed, persistent pathogenic colonization. When superimposed onto a highly activated host innate immune response, this material-microbe loop explains the accelerated tissue destruction frequently observed in peri-implantitis compared to conventional periodontitis. Consequently, relying solely on late-stage clinical diagnostic markers, such as increased probing depths or radiographic bone loss, creates a substantial diagnostic gap where therapeutic intervention occurs only after irreversible destruction has manifested. Moving forward, clinical monitoring must transition toward multi-domain triage models that integrate early microbial signatures, host inflammatory biomarkers from peri-implant crevicular fluid, and material-wear tracking to enable risk-stratified, proactive interceptive care.

Future Directions

Longitudinal metagenomic studies tracking the full oral microbiome including bacteria, fungi, viruses, and archaea, from implant placement through health, disease development, and treatment response are urgently needed to

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establish causal microbial-disease relationships and identify early biomarkers of dysbiosis. The integration of metatranscriptomics and metaproteomics with metagenomics will enable real-time characterization of active virulence gene expression, metabolic states, and host response modifications. Artificial intelligence and machine learning models trained on large-scale microbiome datasets hold significant promise for predicting implant failure risk at early disease stages.

Conclusion

Peri-implant diseases represent a complex, dynamically evolving interplay between a shifting dysbiotic microbiome and an exaggerated, self-sustaining host immune response. The transition from health to disease is orchestrated by the progressive enrichment of Red and Orange Complex bacteria, alongside unique opportunistic pathogens that distinguish peri-implantitis from classical periodontitis. The physicochemical properties of titanium surfaces, particularly surface roughness, chemistry, and nano-topography represent modifiable determinants of biofilm accumulation.

Advances in whole-genome shotgun metagenomics and functional pathway analysis have shifted the field beyond community cataloguing toward understanding the active virulence functions of the peri-implant microbiome. These insights, combined with recognition of the multilevel antimicrobial resistance characterizing peri-implant biofilms, underscore the inadequacy of conventional antibiotic-centered approaches and the imperative for ecology-guided, precision therapeutic strategies. Securing the long-term success of dental implants demands an integrated understanding of the microbiome not as a contaminant to be eradicated, but as a dynamic ecosystem to be guided toward health.

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