

The Oralome Spectrum: Microbial Balance Between Health and Disease

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Abstract: The human body harbours a diverse array of symbiotic and commensal microorganisms across various sites, including the skin, oral cavity, digestive, and reproductive tracts, where they contribute to health and homeostasis. Among them, one of the most diverse microbial communities is found in the oral cavity. This complex ecosystem includes bacteria, archaea, fungi, and viruses, which interact dynamically with the host. The oralome, the diverse microbial community within the oral cavity, plays a crucial role in maintaining periodontal health or driving disease progression. A balanced oralome supports homeostasis, while dysbiosis can lead to chronic inflammation and periodontal destruction. This review explores microbial shifts, oralome dysbiosis, and its role in diagnostics and therapy, paving the way for precision-based periodontal management.

Keywords: Oralome, Oral Microbiome, Periodontal Health, Microbial Dysbiosis, Precision Periodontology

1. Introduction

Symbiotic and commensal microbes inhabit the human body's skin, oral cavity, digestive, and reproductive systems, accounting for more than 90% of total cellular composition. These bacteria constitute dynamic ecological communities whose composition shifts within and across individuals due to factors such as age, genetics, and lifestyle choices.¹ The term "microbiome" refers to the community of microorganisms that inhabit our bodies. According to contemporary estimates, the human body is home to 3.8×10^{13} microbes, which make up around half of all cells. In aggregate, these organisms are known as the human microbiome.²

Joshua Lederberg won Nobel Prize for coining the phrase "microbiome" to refer to the biological community that consists of commensal, symbiotic and pathogenic microorganisms. The National Institute of Health Human Microbiome Project (HMP) began in 2007 and included 18 investigations to map and characterize the human microbiome and its impact on health and disease. The human microbiome can be found in almost every part of the body and HMP has identified 48 distinct microbial habitats.²

The Human Microbiome Project found that 34% of primary microbial habitats relate to human skin, 25% with the gastrointestinal tract, and 20% with head and neck cavities. The oral cavity is a challenging environment for microbial survival due to daily fluctuations in nutrient supply, temperature, pH, mechanical forces from mastication and routine oral hygiene.²

Nonetheless, it preserves a rich and varied ecosystem, hosting various micro-colonizers that flourish in this changing environment. The oral cavity hosts a diverse variety of microorganisms, including bacteria, fungi, viruses, archaea, and protozoa, totalling up to 1000 species. These include a

number of important pathogens that are implicated in the genesis of dental caries and periodontal disease, such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Streptococcus mutans*.³

Oral Microbiome

The oral cavity hosts 392 taxa, making it one of the most researched microbiomes. The reference genome and overall genome count are approaching up to 1500 species. The oral microbiome/oralome refers to the community of microorganisms found in the oral cavity, which can include up to 1000 different species. These species include bacteria, fungi, viruses, archaea, and protozoa.¹ (Figure 1)

The oral cavity is a difficult habitat for microbial life because it experiences frequent daily variations in nutrition supply, temperature, pH, shear and mechanical pressures from mastication and hygiene activities, and chemical exposure from hygiene, pharmaceutical, or toxic/smoking goods. However, it preserves a rich and varied ecosystem, supporting various micro-colonizers that flourish in this changing environment.

The microbial composition is also significantly affected by interspecies and host-microbial interactions, which in turn, can impact the health and disease status of the host. The promotion of health or progression toward disease is critically influenced by the microbiota, wherein in a balanced oralome brings homeostasis and dysbiosis causes chronic inflammation and destruction.

The community of microorganisms essential for maintaining oral health. Predominant genera include *Streptococcus*, *Neisseria*, *Actinomyces*, *Veillonella*, and *Corynebacterium*. The composition of this complex microbiome evolves throughout life, influenced by maternal transmission, host genetics, and environmental factors such as diet, oral hygiene, medications, stress, and systemic health.

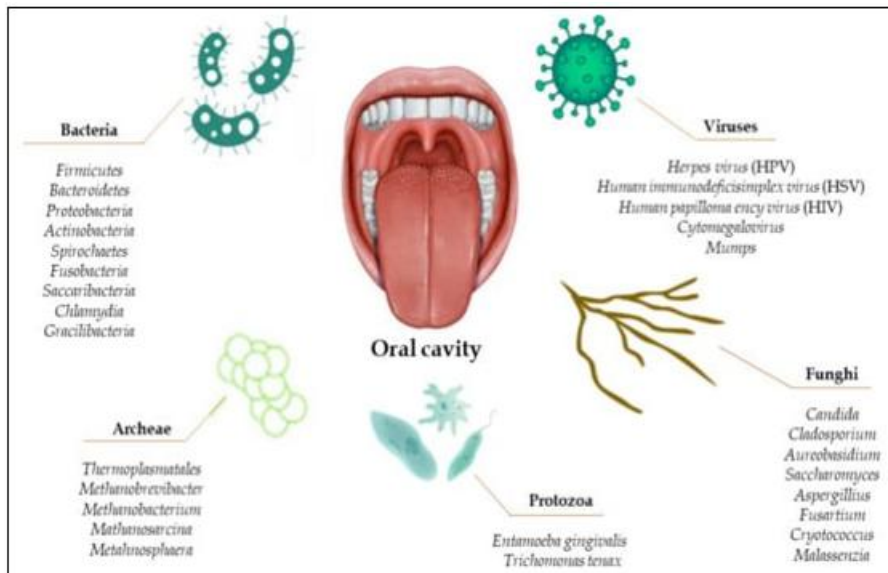


Figure 1: Various oral microbiomes present in the oral cavity⁵

From Birth to Biofilm: The Origins and Evolution of the Oral Microbiome

Microbial colonization of newborns begins at birth, primarily through maternal microbiota transfer. Factors such as mode of delivery, vaginal exams, and antibiotic use influence this process. (Figure 2) Pregnancy alters the maternal gut and vaginal microbiomes and acts as a key source for initial microbial seeding. Early colonizers, like *Streptococcus*

salivarius, establish the oral microbiome, which by the first year includes aerobes such as *Streptococcus*, *Lactobacillus*, *Actinomyces*, *Neisseria*, and *Veillonella*. Tooth eruption introduces non-shedding surfaces, promoting further colonization. Microbial community development is shaped by selective adherence, cell-to-cell interactions, and environmental changes—laying the foundation for oral disease.

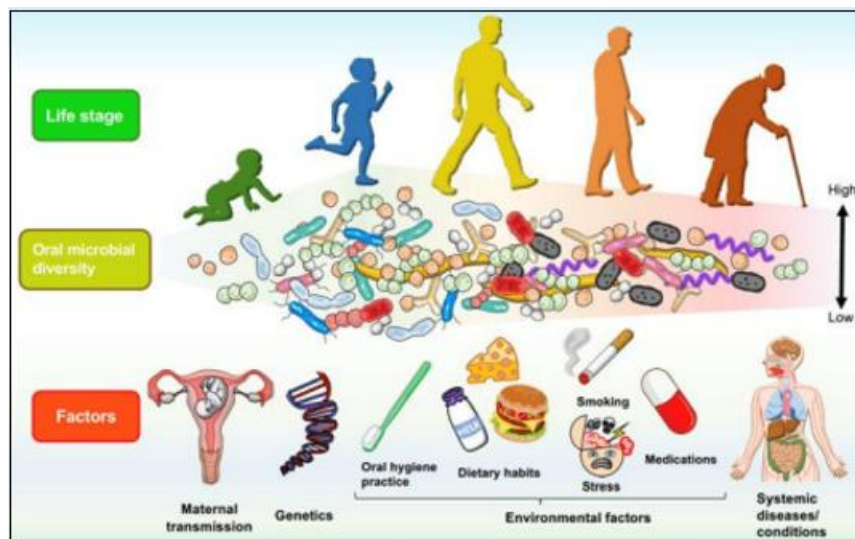


Figure 2: The evolution of oral microbiome³

The human microbiome is made up of a core microbiome and a changeable microbiome. The core microbiome is made up of dominant species that live in many parts of the body under normal circumstances. The varied/changeable microbiome has evolved in response to distinct lifestyle and genotypic variables and is exclusive to one individual.

Oral Microbiome and Periodontal Disease

The oral microbiome is a complex bacterial ecosystem vital for dental health. Disruption of its balance leads to dysbiosis, a key factor in periodontal disease, an inflammatory condition beginning with gingivitis and potentially progressing to periodontitis, marked by bone and connective tissue loss.

Periodontal damage arises from host immune responses to microbial plaque and its enzymes (lipases, proteases, nucleases), compounded by genetic susceptibility, lifestyle factors, tobacco use, and systemic diseases like diabetes and osteoporosis. Dysbiosis of subgingival microbes triggers uncontrolled inflammation, impairing immune regulation and tissue repair.¹

Key pathogens such as *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola* which reshape the microbiota and drive inflammation. The disease reflects a shift from symbiotic bacteria (*Actinomyces*, *Streptococcus*) to dysbiotic communities (*Firmicutes*, *Proteobacteria*, *Spirochaetes*, *Bacteroidetes*, *Synergistetes*).^{2,3}

Mature biofilms, composed of extracellular polymers (water, polysaccharides, proteins, lipids, DNA), anchor bacteria to host tissues, facilitate microbial interactions, and shield against immune defences and treatments.⁶

Host-Microbial Interactions

The current state of the art about bacterial host cell interactions that take place during periodontal disease pathogenesis are⁷:

- 1) Microbiological aspects of the microbial host interactions
- 2) Immunological elements of host- microbial interactions.

Periodontal disease is influenced by dental plaque, which is an important microbiological factor. Many bacteria and their virulence factors play a role in the development of many inflammatory conditions by controlling targeted inflammasomes. *Porphyromonas gingivalis*, lipopolysaccharide and pili activate the NLRP3 inflammasome and regulate IL-1 β processing, contributing to periodontal inflammation⁸.

- 1) The processes that have been extensively described in the microbiological aspects of host microbial interaction are⁸:
 - a) Bacterial colonization and survival in the periodontal tissues
 - Bacterial evasion of host defensive mechanisms.
 - Entry mechanism of various periodontal bacteria
 - b) Microbial processes causing host

- 2) Immunological Elements of Host Microbial Interactions. Periodontal pathogenesis includes the immune system responding to bacterial infections through
 - a) The Innate Defence System
 - b) The Adaptive Defence System

2. Systemic Implications of Oral Dysbiosis

Oral dysbiosis has been linked to a spectrum of systemic diseases, including⁹:

1) Cardiovascular Disease

Mechanism:

- Periodontal pathogens such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans* can enter the bloodstream during routine oral activities (e.g., chewing, brushing).
- These bacteria promote endothelial dysfunction, foam cell formation, and atheromatous plaque development via inflammatory mediators like IL-6, TNF- α , and CRP

2) Diabetes Mellitus

Mechanism:

- Chronic periodontal inflammation exacerbates insulin resistance through systemic elevation of pro-inflammatory cytokines.
- Hyperglycemia alters the subgingival microbiome, favoring pathogenic species and impairing neutrophil function

3) Adverse Pregnancy Outcomes

Mechanism:

- Oral pathogens such as *Fusobacterium nucleatum* can translocate to the placenta, triggering inflammatory

responses that lead to preterm low birth weight and preeclampsia.

4) Cancer

Mechanism:

- Dysbiotic oral biofilms produce carcinogenic metabolites (e.g., acetaldehyde, nitrosamines) and promote chronic inflammation, which can lead to DNA damage and tumorigenesis.
- Specific pathogens like *F. nucleatum* are implicated in colorectal and oral squamous cell carcinomas

5) Rheumatoid Arthritis

Mechanism:

- *P. gingivalis* expresses Peptidyl Arginine Deiminase (PAD), which catalyses citrullination a process implicated in the generation of Anti-Citrullinated Protein Antibodies (ACPAs), a hallmark of Rheumatoid arthritis.

6) Respiratory Diseases

Mechanism:

Aspiration of oral pathogens into the lower respiratory tract can contribute to pneumonia, Chronic Obstructive Pulmonary Disease (COPD), and exacerbations of asthma

3. Therapeutic Strategies for Modulating Oral Dysbiosis

Contemporary approaches aim to restore microbial balance rather than eliminate the oralome. Key strategies include²:

- 1) **Oral Hygiene:** Routine mechanical plaque control using fluoridated toothpaste and interdental cleaning remains foundational.
- 2) **Probiotics and Prebiotics:** Administration of beneficial strains (e.g., *Lactobacillus reuteri*, *S. salivarius*) and substrates that promote their growth can enhance microbial resilience and modulate host immunity¹⁰.
- 3) **Antimicrobial Peptides (AMPs):** AMPs offer targeted antimicrobial activity with reduced resistance potential, though challenges remain in stability and delivery².
- 4) **Nano-Drug Delivery Systems:** Nanoparticles enable precise delivery of therapeutics, improving bioavailability and minimizing systemic toxicity².
- 5) **Extracellular Matrix Disruption:** Targeting biofilm architecture through cyclic-di-GMP inhibitors can prevent maturation and enhance antimicrobial penetration.²
- 6) **Host Response Modulators:** Agents such as doxycycline (Periostat®) inhibit matrix metalloproteinases, reducing tissue degradation without directly altering microbial composition.²

4. Future Directions

Advances in metagenomics, proteomics, and artificial intelligence are transforming our understanding of the oralome. Longitudinal studies and high-resolution imaging may elucidate microbial biogeography and identify predictive biomarkers for personalized therapy. Integration of multi-omics data will facilitate targeted interventions and improve outcomes in periodontal and systemic diseases.

5. Conclusion

The oralome is integral to periodontal and systemic health. Maintaining microbial homeostasis through evidence-based hygiene practices and innovative therapeutics is essential. As research continues to unravel the complexities of host-microbe interactions, a paradigm shift toward precision oral healthcare is on the horizon.

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