

# Role of the Oral Microflora in Health and Disease

Mahesh Kumar, DN Umashankar, Deepak Viswanath, G Girish

## ABSTRACT

Oral microbial flora refers to the population of microorganisms that inhabit skin and mucous membrane of the oral cavity of the normal healthy persons. The microbial cells in a human body outnumber the total number of cells in the human body 10 folds. The mouth harbors a diverse, abundant and complex microbial community on varied surfaces of the oral cavity including both hard and soft oral tissues as biofilms. Oral bacteria have evolved mechanisms to sense their environment and evade or modify the host. Bacteria occupy the ecological niche provided by both the tooth surface and gingival epithelium. The equilibrium is maintained by the innate host defense system constantly which monitors the bacterial colonization and prevents bacterial invasion of local tissues. The analysis of the microbiome and its genomes will pave the way for more effective therapeutic and diagnostic techniques and, ultimately, contribute to the development of personalized medicine and personalized dental medicine. An understanding of the oral environment and microbial interactions leads to understanding the main causes for the onset of oral diseases.

**Keywords:** Oral and gingival microbial flora, Microbiome, Pathogens, Disease.

**How to cite this article:** Kumar M, Umashankar DN, Viswanath D, Girish G. Role of the Oral Microflora in Health and Disease. J Indian Aca Oral Med Radiol 2013;25(3):184-187.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Oral microbiome is a complex ecosystem where several species of microorganisms have been identified.<sup>1</sup> The predominant groups present in the mouth include *Streptococcus*, *Neisseria*, *Veillonella*, *Actinomyces* and other obligate anaerobes.<sup>2</sup>

The oral microbiome is particularly crucial to health because it can cause both oral and systemic disease. The oral microbiome lodges within biofilms throughout the oral cavity, forming an ecosystem that maintains health when in equilibrium. Every human body contains a characteristic microbiome that is necessary to maintaining homeostasis. These bacteria have an inherent capability of synthesizing vitamins like B and K, helping in digestion, and preventing colonization by pathogens, but can possibly evoke disease in case of imbalance with a shift in the equilibrium state allowing pathogens to manifest and cause disease.

Oral microflorae can cause dental plaques and are also a common cause of two major dental diseases: dental caries and periodontal disease.<sup>3-5</sup> A dynamic equilibrium exists between dental plaque bacteria and the innate host defense

system.<sup>5</sup> The human microbiome can be classified into a core microbiome and a variable microbiome.<sup>6</sup> The core microbiome is shared among all individuals and is comprised of the predominant species that exist under healthy conditions at different sites of the body.<sup>6-8</sup>

## ORAL ENVIRONMENT

The teeth, gingival sulcus, tongue, cheeks, hard and soft palates, and tonsils each provide the favorable environment for microbial survival.<sup>9</sup> The oral cavity lodges several species of bacteria that contribute to the health and physiological status of the oral cavity namely the resident flora, supplemental flora and transient flora. The residential flora consists of organisms which are regularly present in a given area at a given age. Supplemental flora comprises of species that are nearly always present but in low numbers (< 1%). Transient flora consists of both nonpathogens and pathogens that inhabit skin or mucous membrane for a limited period of time.

Within the oral cavity, there are two types of surfaces for which bacteria can colonize; the hard surfaces of teeth and the soft tissue of the oral mucosa.<sup>7</sup> Different types of microorganisms prefer distinct niches according to varying surface structures and functions.<sup>10</sup> Each niche provides the optimal environment for populating certain microbes.<sup>2</sup> In fact, research has shown the maxilla, hard palate, soft palate, and even the tongue's lateral sides and dorsal side each to have a different bacterial profile.<sup>10</sup>

Oral microflora are most commonly found in gingival crevices, coronal plaques, tongue dorsum, buccal mucosa and saliva.<sup>11</sup> The gingival crevices have the highest concentration of anaerobes (mainly spirochetes, vibrios and *S. melaninogenicus*) because it has an ideal redox potential and anoxygenic environment which helps select for the growth of these microorganisms.<sup>11</sup> *Streptococcus salivarius* is found mostly in the dorsal tongue and the saliva, *Streptococcus mitis* is commonly found in buccal mucosa and *Streptococcus sanguinis* present on the teeth. Saliva plays a major role in maintaining the microbial ecology as it is an important source of nutrients for microorganisms and contains proteins and glycoproteins. Saliva controls microbial communities with immunoglobulins and lactoferrins which prevent growth of pathogenic microorganisms.

The emerging field of research that targets the microbiome for therapeutic purposes is known as microbiomics. Bacteria, as a determining factor of disease was a

concept that emerged in 1882 when physicist Robert Koch wrote an article discussing bacteria as the etiological agents of tuberculosis.<sup>12</sup> Koch's article triggered years of microbiology and disease etiology research that eventually led to microbiomics. Microbiome research must develop a deeper understanding of the fundamentals and specifics of microbial activity within the body during health and disease before it can contribute to personalized care. First, there should be a clear picture of which microorganisms exist in the body and how they affect the host's physiology and health condition. Then, microbial characteristics of specific diseases should be studied to recognize microbiome patterns that distinguish one disease from another.

## ORAL DISEASES

The two main etiologies of oral diseases have been attributed to *Porphyomonas gingivalis* which causes periodontal diseases and *Streptococcus mutans* which causes dental caries.<sup>13</sup> Both these bacteria are not ubiquitously found in the mouth because the normal flora in the oral cavity is commensal and work together to prevent pathogenic bacteria from affecting the host. Thus caries and periodontal diseases is a result of a combined poor oral hygiene and high sugar based diet which causes constant recolonization by the pathogenic bacteria.<sup>13</sup> Empirical studies by Kigure et al have found that there is higher concentration *P. gingivalis* and *Treponema denticola* are found in the periodontal pockets of adults suffering from periodontitis.<sup>3</sup> A third oral disease that deserves substantial attention is oral cancer.

### Mechanism

Development of the adherent populations of microorganisms in the oral cavity begins with the association and irreversible adhesion of certain bacteria to the tooth surface. Components of the host oral cavity, such as proteins and glycoproteins from the saliva, also adhere. This early coating is referred to as the conditioning film. The conditioning film alters the chemistry of the tooth surface, encouraging the adhesion of other microbial species. Over time, as the biofilm thickens, gradients develop within the biofilm. For example, oxygen may be relatively plentiful at the outer extremity of the biofilm, with the core of the biofilm being essentially oxygen-free. Such environmental alterations promote the development of different types of bacteria in different regions of the biofilm.

This changing pattern represents what is termed bacterial succession. Examples of some bacteria that are typically present as primary colonizers include *Streptococcus*, *Actinomyces*, *Neisseria* and *Veillonella*. Examples of secondary colonizers include *Fusobacterium nucleatum*, *Prevotella intermedia* and *Capnocytophaga* species. With

further time, another group of bacteria can become associated with the adherent community. Examples of these bacteria include *Campylobacter rectus*, *Eikenella corrodens*, *Actinobacillus actinomycetemcomitans* and the oral spirochetes of the genus *Treponema*.

The proposed mechanism for periodontitis is that the causative organisms have shown hemolytic activity (by possible virulence factor) and this affects the attachment of the gums with the teeth.<sup>3</sup> In case of dental caries, Sucrose has been shown to help *S. mutans* colonize by helping it adhere better.<sup>11</sup> *S. mutans* break sucrose down to produce glucans (extracellular polymer) which can then be used for building a biofilm which is different from biofilms produced by normal flora. This biofilm has increased porosity and allows acids to freely diffuse to the enamel and cause a pH drop, which can lead ultimately lead to dental caries.<sup>13</sup> The onset for both periodontitis and dental caries is a result of a shift in the normal composition of the oral flora.

A third oral disease that deserves substantial attention is oral cancer. Oral cancer is the sixth most prevalent cancer, affecting over 300,000 people each year around the world.<sup>14</sup> Studies suggest that there is a correlation between the structure and function of the oral microbiome and oral cancer.<sup>14,15</sup> Most patients infected with oral cancer practice poor oral hygiene.<sup>15</sup> In general, various studies conducted around the world have shown poor oral health and tooth loss to increase the risk of gastric, pancreatic and other cancers. The mouth is in general an inhospitable place for pathogenic bacteria and thus it is interesting to know that is possible to prevent these diseases by ensuring good oral hygiene and avoiding high sugar diets.

## EQUILIBRIUM OF MICROBIAL FLORA AND ORAL CAVITY

Once a pathogen possesses virulence factors, exists in abnormal proportions and demonstrates parasitism, all of the following conditions which are required for disease have been satisfied: the local environment is one in which the species can express its virulence properties, the pathogen is in numbers that exceed the threshold for that host; other bacterial species can foster, or at least not inhibit, the diseases manifestation; and the host is susceptible to this pathogen, i.e. currently compromised immune system or specific genetic composition.<sup>12</sup> Overall, it is crucial that there be an ecological balance among microorganisms to prevent pathological changes and disease from occurring. A healthy microbiome can only be maintained with good oral hygiene and a well functioning immune system.<sup>16</sup>

### Dental Infection and the Oral Commensal Flora

The commensal oral flora plays a significant role in dental infections where it is in a constant and dynamic flux. This

is partly in response to the intake of food and also influenced by oral hygiene measures including brushing of teeth and flossing. The hard surfaces of the teeth and the gingival crevices are the sites of accumulation of dental plaque. This is a complex structure comprising microbes, microbial products, food particles, host secretions and host cells. Plaque is continually altering in composition in response to microenvironmental changes. It differs in response to its location in the mouth and in response to the length of time that it has been established.

On the surface of a tooth, *S. mutans* is the first important colonizer; particularly in people with a high sucrose diet. This bacterium can metabolize sucrose to produce extracellular polysaccharide (glucans) that enable the bacterial cells to stick onto the surface of the tooth. Metabolism of the sucrose by *S. mutans* also leads to the formation of large quantities of lactic acid. In turn this provides the low pH environment that favors colonization by lactobacilli. Next in the microbial succession are the actinomycetes. These are filamentous bacteria that provide a web of cells that can provide a niche for the colonization of anaerobic bacteria, including those belonging to genera such as *Bacteroides*, *Capnocytophaga*, *Veillonella* as well as spirochaetes and fusobacteria. An array of poorly-characterized bacteria can also be found in plaque, which may contain up to 100,000,000,000 bacteria per gram wet weight.

## SYSTEMIC DISEASE AND ORAL FOCI OF INFECTION

The oral cavity is the primary gateway to the human body; therefore, microorganisms that inhabit that area are very capable of spreading to different body sites.<sup>9</sup> Pathogens that originate in the oral cavity can be frequently detected in blood cultures as they destroy and pass through oral mucous membranes and periodontal pockets.<sup>17</sup> Pathogens may enter the blood stream, alter proper immune responses, or produce excessive and deregulated amounts of inflammatory mediators, and in turn, cause disease at different body sites.<sup>18</sup> Persistent inflammation and frequent bacterial attacks not only lead to bacterium, but also organ abscesses and severe systemic diseases, such as diabetes and cardiovascular disease.<sup>17,18</sup> This correlation further supports the importance of the oral microbiome to overall health.

## TREATMENT

### Antibiotics

Systemic drugs target pathogens at sites around the body in addition to the oral cavity but are limited to the species

they target. They are also known to reduce any bleeding in the periodontium. However, systemic drugs are conventionally used as a last resort in the treatment of periodontal diseases for cost effective purpose. Effective use of antibiotics in the future requires genomic analysis of the patient's oral microbiome to recognize the microbes that are present and to determine whether they will respond to specific treatments.

### Probiotics and Prebiotics

Both probiotics and prebiotics would strengthen the beneficial microflora so the body can naturally fight off disease-causing agents. The production process would have to consider factors, such as the technology used, temperature and fermentations conditions, oxygen content, organic ingredients used, etc. Therapeutic antibiotics and probiotics face limitations because of a lack of knowledge of the oral microbiome and its numerous, complex constituents.

### Vaccination Against Oral Infections

Dental caries and periodontitis have an infectious etiology and immunization has been proposed as a means of controlling them. However, the approaches vary according to the nature of the bacteria involved and the mechanisms of pathogenesis for these two very different diseases. In the case of dental caries, proteins involved in colonization of teeth by *Streptococcus mutans* can produce antibodies that inhibit the cariogenic process. Periodontal vaccines are less well-developed, but some antigenic targets have been identified.<sup>19</sup>

## CONCLUSION

The oral microbial ecosystem is particularly vital to maintaining both oral and systemic homeostasis in the body. Salivary flow and biofilms on the teeth and soft tissue maintain microbial equilibrium within the oral cavity and protect pathogenic microbes from manifesting. Disturbing the homeostasis of the oral cavity can stir pathogen activity and lead to oral disease. Since oral cavity is the primary gateway to the body, severe cases of oral disease may result in the spread of infection to other body sites, producing systemic diseases such as cardiovascular disease or exacerbating an already compromised immune system, as in diabetes. Practicing good oral hygiene and maintaining stable oral biofilms is essential to keeping a body healthy and also preventing rapid spread of disease to other individuals. In addition, the analysis of the human microbiome will significantly contribute to the development of personalized medicine and personalized dental medicine.

## REFERENCES

1. Palmer RJ Jr, Chalmers NI, Rickard AH, Kolenbrander PE. Community development in bacterial biofilms of the oral cavity. *Microscopy and Microanalysis* 2008;14:1554-1555.
2. Avila M, Ojcius DM, Yilmaz O. The oral microbiota: living with a permanent guest. *DNA and Cell Biology* 2009;28(8):405-411.
3. Kigure T, Saito A, Seida K, Yamada S, Ishihara K, Okuda K. Distribution of porphyromonas gingivalis and treponema denticola in human subgingival plaque at different periodontal pocket depths examined by immunohistochemical methods. *J Periodontal Research* 1995 Sep;30(5):332-341.
4. Sbordone L, Bortolaia C. Oral microbial biofilms and plaque-related diseases: microbial communities and their role in the shift from oral health to disease. *Clinical Oral Investigations* 2003 Dec;7(4):181-188.
5. Rogers AH. *Molecular oral microbiology*. Caister Academic Press 2008. Chapter 22 P. 482.
6. Turn Baugh PJ, Ley RE, Hamady M, Fraser-Liggett CM, Knight R, Gordon JI. The human microbiome project: a strategy to understand the microbial components of the human genetic and metabolic landscape and how they contribute to normal physiology and predisposition to disease. *Nature* 2007;449:804-810.
7. Zaura E, Keijsers BJ, Huse SM, Crielaard W. Defining the healthy core microbiome of oral microbial communities. *BMC Microbiol* 2009;259:12.
8. Sonnenburg JL, Fischbach MA. Community healthcare: therapeutic opportunities in the human microbiome. *Sci Transl Med* 2011;3:1-5.
9. Dewhirst FE, Chen T, Izard J, et al. The human oral microbiome. *J Bacteriol* 2010;192:5002-5017.
10. Aas JA, Paster BJ, Stokes LN, Olsen I, Dewhirst FE. Defining the normal bacterial flora of the oral cavity. *J Clin Microbiol* 2005;43:12.
11. Gibbons RJ, Houte JV. Bacterial adherence in oral microbial ecology. *Annual Review of Microbiology* 1975;29:19-44.
12. Socransky SS, Haffajee AD. The bacterial etiology of destructive periodontal disease: current concepts. *J Periodontol* 1992;63:322-331.
13. Liljemark WF, Bloomquist C. Human oral microbial ecology and dental caries and periodontal diseases. *Critical Reviews in Oral Biology and Medicine* 1996;7(2):180-198.
14. MF Zarco, TJ Vess, GS Ginsburg. The oral microbiome in health and disease and the potential impact on personalized dental medicine. *Oral Diseases* 2012;18:109-120.
15. Meurman JH. Oral microbiota and cancer. *J Oral Microbiol* 2010;2:51-95.
16. Nieuw Amerongen AV, Veeman ECI. Saliva—the defender of the oral cavity. *Oral Dis* 2002;8:12-22.
17. Horz HP, Conrads G. Diagnosis and anti-infective therapy of periodontitis. *Expert Rev Anti infect Ther* 2007;5:11.
18. Williams RC, Barnett AH, Claffey N, et al. The potential impact of periodontal disease on general health: a consensus view. *Curr Med Res Opin, Infoma UK Ltd* 2008;24:1635-1643.
19. Pei-Fung Liu, Wen-Hung Zhu, Chun Ming Huang. Vaccines and photodynamic therapies for oral microbial-related diseases. *Current Drug Metabolism* 2009 Jan;10(1):90-94.

## ABOUT THE AUTHORS

**Mahesh Kumar (Corresponding Author)**

Reader, Department of Oral and Maxillofacial Surgery, Krishnadevaraya College of Dental Sciences, Bengaluru, Karnataka, India, Phone: 9845417365, e-mail: mahu017@gmail.com

**DN Umashankar**

Reader, Department of Oral and Maxillofacial Surgery, Krishnadevaraya College of Dental Sciences, Bengaluru, Karnataka, India

**Deepak Viswanath**

Professor and Head, Department of Pedodontics and Preventive Dentistry, Krishnadevaraya College of Dental Sciences, Bengaluru Karnataka, India

**G Girish**

Senior Lecturer, Department of Oral and Maxillofacial Surgery Krishnadevaraya College of Dental Sciences, Bengaluru Karnataka, India