

# THE ORAL MICROBIOME IN HEALTH AND DISEASE

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**Abstract:** Every human body has many microbial communities, there are certain group of microbial communities called as the oral microbial community, these microbiomes are healthy unless and until they are triggered by certain environmental factors that enable them to produce disease. The microbes are being identified and sequenced by certain methods such as DNA hybridization and the PCR techniques and these microbes are found to be specific at specific sites which are given by site specialist hypothesis and it is also found that specific microbes are for specific persons hence it can help with the concept of the personalised medicine. It is found in recent years that tolerance to these microbes can also be developed to the foetus prenatally itself with the help of the mother's microbiome.

**Keywords:** Oral microbiome, DNA hybridization, prenatal tolerance, personalised medicine.

## 1. INTRODUCTION:

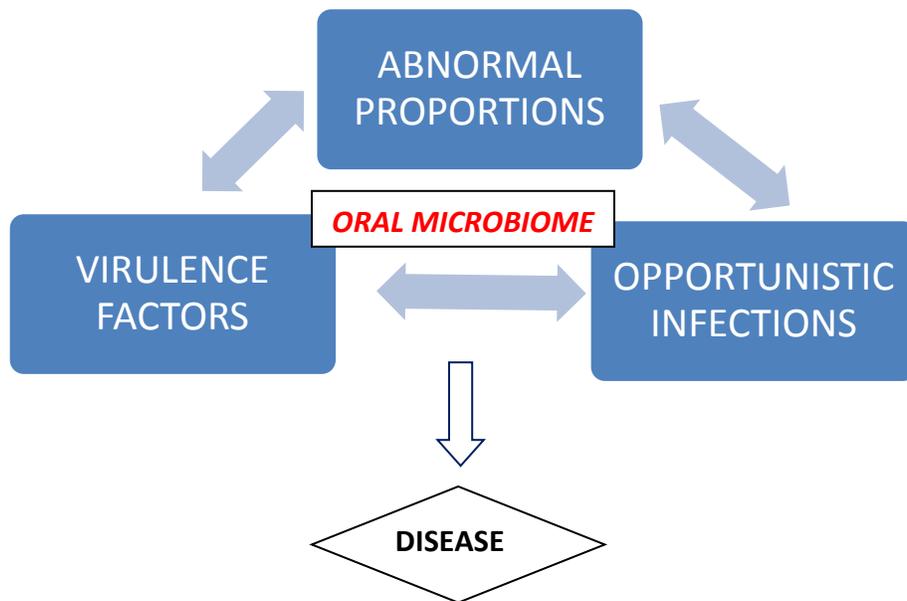
Every human body consists of a specialised microbiome for their own self which maintains the health of an individual which is also capable of producing disease. These microbial communities are being distributed widely such as the gut microbiome, oral microbiome etc. The oral microbiome is a large community which plays several important part in the health as well as disease of an individual.

## THE ORAL MICROBIOME:

The human microbiome can be classified into a **CORE** microbiome and a **VARIABLE** microbiome. The core microbiome is comprised of the predominant species that exist under healthy conditions at different sites of the body. Every individual have certain microbiome evolved due to their lifestyle and genes known as the variable microbiome.

**THE HEALTHY MICROBIOME:** The healthy oral microbiome is 10 times higher in number than the normal cells of the body(1). There are about 25000 phylotypes of the healthy core microbiome. Firmicutes (Granulicatella and streptococcus genus and family veillonellaceae) Bacteroides (genus capnocytophaga, prevotella, porphyromonas) Fusobacteria (genus fusobacterium) actinobacteria (genus corynebacterium, Rothia, Actinomyces) Proteobacteria (genus Neisseria , haemophilus) are found to be the predominant taxa of the healthy microbiome.(2)

**TRANSFORMATION OF HEALTHY MICROBIOME TO DISEASE:** In health, microbes prevent disease progression by: They occupy the niche preferred by a pathogen, and thereby prevent the pathogen's adherence to specific surfaces, They prevent a pathogen from occupying a site, they suppress a pathogen's abilities to multiply, and can degrade virulence factors of them(1). However, certain pathological changes can make a beneficial microorganism to produce disease. Ecological shifts that cause pathological changes are: a change in the relationships between the microbes and host, an increase in relative abundance; and acquiring virulence factors.(3)



### TECHNIQUES FOR SEQUENCING MICROBES:

The discovery of the double helical structure of the DNA molecule, helped to study the process by which the genetic information can be stored and copied known as the base pairing, which provided the way to detect, and understand the microbes and to develop certain nucleic acid – based technologies and techniques. The identification DNA sequences such as the 16S rRNA gene made information about relativeness among various groups of organisms. The recent advances in sequencing technologies and computational approaches are propelling scientists even closer towards complete understanding of human-microbial interactions. The powerful sequencing platforms are rapidly producing huge amounts of nucleotide sequence data which are compiled into huge databases. This sequence data can be retrieved, assembled, and analyzed for identification of microbial pathogens and diagnosis of diseases (4). In turn, this has provided a universal system for categorization of bacteria.

### DNA HYBRIDIZATION:

For the study of microorganisms a technique called DNA-DNA hybridisation has been developed which is the process of pairing of complementary strands of double –helix nucleic acid. DNA probes which bind to complementary base of a specific DNA which forms a duplex and which can be identified by appropriate instrument or chemical agents are utilised, these DNA PROBES are labelled with radioactive isotopes or fluorescent tag. Hybridization techniques used in oral microbiological research include 1. whole-genome checkerboard DNA– DNA

hybridization, 2. reverse-capture oligonucleotide hybridization, 3. fluorescence in situ hybridization (FISH) and 4. DNA microarray technology. (5)

### **POLYMERASE CHAIN REACTION:**

From any DNA molecule specific fragment can be amplified which was invented by Kary Mullis in 1985. The basic PCR technique is that the target DNA sequence known as the template is being framed by 2 specific oligonucleotide primers, this in turn is being amplified by a thermostable DNA polymerase enzyme. The dsDNA template is first heat denatured (>94 °C) followed by cooling to 50–55 °C to allow the primers to bind to the template. For the synthesis of new DNA strands the temperature is raised to 68–72 °C after annealing. After annealing these are called as extensions. Each newly-synthesized DNA strand then acts as a new template in the next cycle. On the extension period, DNA fragments of more than 20 kbp in length can be generated. Because amplification of the target DNA fragments is exponential, minute amounts of DNA can be multiplied billions of times in a matter of hours. PCR is extremely sensitive and highly specific. However, there are limitations, particularly within heterogeneous bacterial samples such as oral biofilms. These include: (i) errors from the need for different methods for lysis of gram-negative and gram-positive bacteria; (ii) oral samples containing amplification inhibitors such as blood; (iii) DNA sequence differences leading to unequal DNA denaturation and annealing causing amplification bias; and (iv) erroneous findings from the amplification of contaminating DNA. (5)

### **DNA SEQUENCING:**

In 1977, Sanger and Gilbert developed a DNA sequencing method that has been the gold standard for four decades. The prototype method was expensive, labour-intensive and potentially dangerous. It involved the use of a heat-labile DNA polymerase enzyme, radioactively-labelled chain terminators and X-ray films. (5)

### **SITE SPECIALIST HYPOTHESIS OF ORAL MICROBIOME:**

A salient feature of the oral microbiome that emerged from the oligotyping work of Erenetalis that there are subtypes for the microbial genera specially for three habitat zones such as the keratinized gingival, dorsum of tongue and the dental plaque. For example, that the genus *Actinomyces* has species strongly specialized to either tongue or teeth, dental plaque has *A. naeslundii*, *A. graevenitzii* and *A. odontolyticus* (and its close relatives) on the tongue. *A. graevenitzii* is extremely special, since it has a mean relative abundance of 3,900-fold higher on the tongue than on teeth. The genus *Fusobacterium* has subtypes in all three of the habitats: *F. nucleatum* on teeth, *F. periodonticum* on tongue, and an unnamed species, *Fusobacterium* sp. HMT (Human Microbial Taxon) 248, on the keratinized gingiva (6). Within the genus *Streptococcus*, *S. salivarius* and *S. parasanguinis* are for tongue and *S. sanguinis* and *S. gordonii* are specialised for dental plaque (6). *S. mitis* and its close relatives are abundant in all habitats, although in keratinized gingiva they reach an exceptionally high mean relative abundance of approximately 50%. Other apparent generalists are *Haemophilus parainfluenzae*, *Porphyromonas pasteri* which are equally abundant in all habitats. Thus, most microbes in the mouth are site specialists, found majorly in a single habitat. The hypothesis predicts these microbes will be present in their preferred habitats and outside which their abundance is relatively low and they may show altered metabolism gene expression and spatial organisation. (7)

**PERSON SPECIFIC MICROBES:**

Numerous studies have shown that individuals usually have distinctive oral microbiomes. However, it has been found that certain species are abundantly distributed in all individuals and that they are differentiated by set of strains within these species as well as by proportions of the major taxa. Thus, the distinctiveness of individual oral microbiomes appears to arise from strain-level divergence and the long-term stability of strain profiles within individuals. This presence of specific microbes for each individual can help with the success of “THE PERSONALISED MEDICINE” (3).

**ACQUIRING NORMAL MICROBIOME: DEVELOPMENT OF PRENATAL TOLERANCE TO MOTHER’S ORAL MICROBIOME**

Although the encounter of microbiota in a new born is postnatal, there is clinical evidence for presence of microbes in placenta, umbilical cord blood, amniotic fluid, and meconium in full-term pregnancies without infection. These studies suggest that there is a biological function for these placental microbes. It was proposed that during pregnancy for the foetal immune system to be “trained” in antigen tolerance, the placenta becomes an antigen collecting site. Hence a hematogenous route for indigenous microbes to placenta during pregnancy has been proposed. Increased gingival bleeding in pregnant women is known as pregnancy gingivitis (Niederman, 2013). Proposed a new role for the increased gingival bleeding: by opening the vascular bed, oral bacteria from the mother become available in blood and thus gain access to the placenta. Jeurink and colleagues have introduced a similar mechanism for the formation of the breast milk microbiome. This involves immune cell education by the pregnancy hormone progesterone resulting in transportation of bacteria from the mother to her mammary glands (Jeurink et al., 2013). A similar process is found to be responsible for transporting bacteria to the placenta. Placental tissue traps the microbial cells to be presented to the immune system of foetus. Foetal antigen presenting cells (APCs) interact with the mother’s microbial antigens and return to foetal peripheral lymphoid organs during the prenatal period. The human foetus has large numbers of peripheral regulatory T cells (Tregs) with immune suppressive activity (Takahata et al., 2004). Foetal Tregs can be retrieved also from umbilical cord blood, which offers a perspective for medicine transplantation, while new-borns have higher proportions of thymically derived Tregs than adults (Rabe et al., 2014). These foetal Tregs are preventing undesirable alloreactivity to maternal derivatives during the pregnancy (Takahata et al., 2004). As a result, the foetus is found to develop tolerance prenatally to the microbiome of the mother and regards it “safe” during postnatal encounters with these bacteria. (8)

**2. REFERENCES:**

1. Cornejo Ulloa P, van der Veen MH, Krom BP. Review: modulation of the oral microbiome by the host to promote ecological balance. *Odontology*. 2019 Oct;107(4):437–48.
2. Zaura E, Keijsers BJ, Huse SM, Crielaard W. Defining the healthy “core microbiome” of oral microbial communities. *BMC Microbiol*. 2009;9(1):259.
3. Zarco M, Vess T, Ginsburg G. The oral microbiome in health and disease and the potential impact on personalized dental medicine: The oral microbiome. *Oral Diseases*. 2012 Mar;18(2):109–20.
4. Yadav BS, Ronda V, Vashista DP, Sharma B. Sequencing and computational approaches to identification and characterization of microbial organisms. *Biomed Eng Comput Biol*. 2013;5:43–9.

5. Benn A, Heng N, Broadbent J, Thomson W. Studying the human oral microbiome: challenges and the evolution of solutions. *Aust Dent J*. 2018 Mar;63(1):14–24.
6. Frédéric L, Michel B, Selena T. Oral Microbes, Biofilms and Their Role in Periodontal and Peri-Implant Diseases. *Materials*. 2018 Sep 22;11(10):1802.
7. Welch JLM, Dewhirst FE, Borisy GG. Biogeography of the Oral Microbiome: The Site-Specialist Hypothesis. *Annu Rev Microbiol*. 2019 Sep 9;73(1):annurev-micro-090817-062503.
8. Zaura E, Nicu EA, Krom BP, Keijser BJJ. Acquiring and maintaining a normal oral microbiome: current perspective. *Front Cell Infect Microbiol* [Internet]. 2014 Jun 26 [cited 2019 Aug 26];4. Available from: <http://journal.frontiersin.org/article/10.3389/fcimb.2014.00085/abstract>