Asian Journal of Applied Science and Technology (AJAST)
Volume 6, Issue 3, Pages 47-55, July-September 2022

The Oral Cavity and its Ecosystem – A Narrative Review

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DOI: http://doi.org/10.38177/ajast.2022.6307

Article Received: 28 May 2022 *Article Accepted: 26 August 2022* *Article Published: 29 September 2022*

ABSTRACT

The oral cavity is the hub of several species of microorganisms that protect the oral environment as well as cause the destruction of the hard and soft tissues namely the teeth and the periodontium. The acquisition and maturation of these microbes depend on factors that come into play even before a child takes birth. This article looks into the various aspects that could affect the oral microbiome and its dynamics in the human body.

Keywords: *Biofilm, Dental plaque, Oral cavity, Microflora, Microbiome, Window of infectivity.*

1. Introduction

Ecology is the study of the relationship between living organisms and their environment. Pathogens or microbes are the living agents that produce disease in humans. The science of microbiology encompasses the study of these organisms, the host response to infection, and ways in which such infection can be prevented. Biofilm is a complex, functional community of one or more species of microbes encased in an exopolysaccharide matrix and attached to one another or to a solid surface.

1.1. Oral microflora

The oral cavity is unique with regard to microbial colonization. Several organisms commonly isolated from neighbouring ecosystems such as gut and skin are not found in the mouth. The oral cavity has a diverse array of microorganisms like *Eubacteria, Archaea, Fungi, Mycoplasmas, Protozoa*, and possible viral flora. Bacteria are predominant with 350 different cultivable species and a further proportion of unculturable flora (the archaebacterial). This, together with the fact that the oral cavity has a wide range of habitats with different environmental conditions makes oral microbiology very difficult and complex.

1.2. The oral ecosystem

The oral microflora along with their habitat and the surrounding structures encompass the oral ecosystem (Table 1 shows the characteristic features of habitats of the oral cavity). The major oral habitats are the buccal mucosa, the dorsal surface of the tongue, supra- and sub-gingival tooth surfaces, the crevicular epithelium, and any prosthetic or orthodontic appliances placed in the mouth. The two types of oral microbes within the oral ecosystem are the resident flora (indigenous or commensal) and the transient flora.

The human mouth is lined by stratified squamous epithelium interrupted by teeth (primary and permanent dentition) and ducts (of the three major and several salivary glands) with modifications based on function. The gingival tissues form a cuff around the tooth with a 2 to 3-mm gingival sulcus and a continuous flow of gingival crevicular fluid into the sulcus.

Table 1. Characteristic features of habitats of the oral cavity	
Habitats	**Characteristic Features**
Buccal mucosa Dorsum tongue	Cheek mucosa – sparsely colonized. Papillary surface tongue – highly colonized, has low redox potential (E_h). Keratinized and non-keratinized.
Teeth	Only non-shedding areas in the body to harbor microbes. Large bacterial masses and their products accumulate to produce plaque. The nature of the bacterial community varies on the tooth surface and degree of exposure. Eg: Pits and fissures (lesser number of species), and sub-gingival surfaces (more anaerobic species).
Gingival crevice	Bacterial colonization in the crevice plays a critical role in the initiation and development of gingival and periodontal disease.
Appliances	Can act as reservoirs and may cause denture stomatitis.

2. Factors modulating microbial growth

Table 2 enlists the general and miscellaneous factors that modulate microbial growth in the oral cavity.

Table 2. Factors modulating microbial growth in the oral cavity	
Factors	**Features modulating microbial growth**
General Factors	
Anatomic	Bacterial stagnation due to tooth shape, topography, malalignment, poor restorations, and non-keratinized sulcular epithelium.
Saliva	Organic constituents like proteins and glycoproteins modulate bacterial growth. The concentrations of inorganic constituents like Na^+, K^+, Ca^+, Cl^-, PO_4 vary diurnally in stimulated vs resting saliva.
GCF	Slow continuous flow in health with an altered flow in inflammation.
Microbial	Microbial interaction leads to 'colonization resistance' and competition for receptors. Toxins produced have metabolic end products which are either noxious or nutritious. Eg. *Veillonella* use acids from *S.mutans* for co-aggregation (homotypic, heterotypic).
Miscellaneous Factors	
Local environmental pH	Most microbes require neutral pH to grow. Acidophilic bacteria grow at lower pH while others are eliminated by competitive inhibition.
Redox potential	Fluctuates from +200mV to -141mV, favors the growth of different groups
Antimicrobial therapy	Systemic, topical antibiotics affect oral flora. Tetracycline can wipe out endogenous flora and favor the emergence of yeast species
Diet	Fermentable carbohydrates – a major source of proteins, promote the growth of acidogenic flora. Extracellular polysaccharides facilitate adherence, intracellular polysaccharides serve as food resources.
Iatrogenic factors	Treatment procedures alter the composition of the periodontal pocket
Resources of bacterial nutrition	Host – diet remnants, saliva components, GCF, and O_2. Microbial – extracellular microbial products, intracellular food storage granules.

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3. Dental plaque biofilm

Dental plaque is a tenacious microbial community that develops on soft and hard tissue surfaces of the mouth and contains bacteria (living, dead, dying, and their extracellular products) and host components that are chiefly derived from saliva. The microorganisms are embedded in an inorganic matrix which comprises 30% of the total plaque volume. The composition of this plaque biofilm varies at different sites of the same tooth, at the same site in different teeth, and at different times on the same tooth site. This biofilm is found on all dental surfaces and intra-oral appliances, especially in the absence of oral hygiene. Surfaces like the inter-proximal areas, occlusal fissures, and areas around the gingival crevice are regions that are anatomically protected from the host defenses.

3.1. Biofilm formation

The formation of biofilm is a complex, competitive, sequential, and dynamic colonization process. It occurs in 5 stages which are pellicle formation, transport, long-range interactions, short-range interactions, and co-aggregation/co-adhesion which finally lead to the formation of the biofilm. A prerequisite for the formation of a biofilm is adherence. The pioneer group of organisms is gram-positive cocci and rods which are followed by gram-negative cocci, rods, filaments, fusobacteria, and spirochetes.

3.1.1. Pellicle formation

Salivary glycoproteins are deposited on the tooth surface within moments of exposure to the oral environment. Adsorption of bacterial molecules to tooth surfaces via acquired salivary pellicle where the oral bacteria initially attach to the pellicle and not directly to the enamel.

3.1.2. Transport

Before attachment, bacteria approach the tooth surface by salivary flow, chemotaxis, and Brownian motion (random motion of particles suspended in a medium).

3.1.3. Long-range and short-range interactions

The long-range interactions are the physiochemical interactions between the microbial cell surfaces and the pellicle-coated tooth surface. The interplay of van der Waals forces and electrostatic repulsion produces a reversible phase of net adhesion. The short-range interactions are an irreversible phase and involve stereochemical reactions between adhesions on microbial cell surfaces and the receptors present on the acquired pellicle. This polymer bridging between organisms and surfaces helps the organisms to anchor and multiply on virgin surfaces. Quorum-sensing bacteria produce and release chemical signal molecules called autoinducers (Eg: Acyl homoserine lactones or acyl-HSLs) which increase in concentration as a function of cell density.

3.1.4. Co-aggregation or co-adhesion and biofilm formation

Fresh bacteria, either from the same genus or a different genre, now attach to the already present first generation of cells. Co-adhesion continues resulting in confluent growth. The biofilm matures in complexity over time and attaches to any solid surface like a tooth or any intra-oral appliance. Metabolic products of early colonizers radically alter the immediate environment while the new colonizers inhabit the plaque resulting in increased thickness, biomass, and microbial complexity. This biofilm mass reaches a critical size at which a balance between the deposition and the loss of plaque bacteria is established leading to the formation of the 'climax community'. As the number of organisms increases, quorum-sensing signals increase and activate the genes responsible for additional extracellular polysaccharide production, reduction of metabolism, and production of virulent factors (drug-destroying genes).

3.1.5. Detachment

The bacteria that colonize the climax community detach and enter a planktonic phase and are transported to new colonization sites. Table 3 shows the three distinct sites and the viable count range of predominant bacteria in dental plaque. Table 4 shows mechanisms involved in the process of bacteria evading the oral defenses.

Table 3. Predominant bacteria in dental plaque at 3 distinct sites (% viable count range)

Bacterium	Fissures	Approximal surfaces	Gingival crevice
Streptococcus	8 – 86	<1 – 70	2 – 73
Actinomyces	0 – 46	4 – 81	10 – 63
An G+R	0 – 21	0 – 6	0 – 37
Neisseria	-	0 – 44	0 – 2
Veillonella	0 – 44	0 – 59	0 – 5
An G-R	-	0 – 66	8 – 20
Treponema	-	-	+
Environment			
Nutrient source	**Saliva & diet**	**Saliva & GCF**	**GCF**
pH	Neutral-low	Neutral-low	Neutral-high
Eh	Positive	Slight -ve	Negative

Table 4. Mechanisms by which bacteria evade host defenses

Mechanisms	Features
Antigen masking	Oral bacteria bind host molecules to their surface ('stealth technology')
Molecular mimicry	Bacterial epitopes resemble those of the host
Enzyme degradation	Pioneer Strep produces IgA 1 protease. Other bacteria produce general proteases that cleave other host defense factors
Immune suppression /immune indifference	Some species are immuno-modulatory or produce factors that instruct the host defenses to recognize them as 'self'
Antigenic variation	Constant subtle antigenic changes
Unfavorable environment	Local conditions may be unsuitable for optimal functioning of host defenses

4. Role of oral microflora in health

The resident microflora play an important role in the maintenance of a healthy state in the oral cavity by contributing to the host defenses and by preventing the colonization of exogenous microorganisms. Approximately 0.7 to 1.5 l of saliva is secreted per day from the three major (parotid, submandibular, and sublingual salivary glands) and several other minor salivary glands present in and around the oral cavity. The major organic constituents of saliva are proteins and glycoproteins namely, amylase, mucin, salivary IgA (sIgA), lysozyme, lactoferrin, and sialoperoxidase. Salivary components act as primary nutrients and exert their influence on the oral microflora via tissue tropism (adsorption), bind to bacterial surfaces and mask their antigens, facilitate microbial clearance by aggregation, and inhibit attachment and growth of exogenous organisms.

Distinct habitats exist in the oral cavity for bacterial colonization (Table 5) because of the unique biological features of the teeth and the mucosal surfaces. These habitats undergo major changes during the lifetime of a human. During the first few months after birth, only the mucosal surfaces are available for colonization. The event of teeth eruption creates a novel habitat along with a major nutrient source. With the eruption of the deciduous dentition, teeth provide hard non-shedding surfaces for colonization. These teeth allow the accumulation of large masses of microorganisms and their extra-cellular products, especially at retentive and stagnant sites. A gram of oral biomass contains about one hundred million microbes. The process of tooth eruption-shedding along with any intra-oral appliances, prostheses, and dental treatment procedures affects the ecological conditions. Table 6 shows the different environmental factors that modulate the growth of microbes in a healthy mouth.

Table 5. Distinct microbial habitats in a healthy mouth

Habitat	Predominant group	Features
Lips, cheek, palate	*Streptococci, Neisseria, Veillonella*	Desquamation restricts biomass. Surfaces have distinct cell types. *Candida* – opportunistic pathogen. *Staph* may be seen.
Tongue	*Streptococci, Veillonella, Obligate anaerobes*	*Candida* – opportunistic pathogen. *Staphylococcus* may be present. Highly papillated surfaces – reservoirs for anaerobes.
Teeth	*Streptococci, Veillonella, Actinomyces, Hemophilia Spirochetes, Obligate anaerobes, Eubacterium*	Non-shedding surfaces promote biofilm. Distinct surfaces for colonization support characteristic flora due to intrinsic properties like – fissures, approximal and gingival crevices. Teeth harbor the most diverse oral microbial communities.

Table 6. Environmental factors modulating microbial growth in a healthy mouth

Factor	Range	Features
Temperature	35^0C to 36^0C	
Oxygen	0 % to 21%	Oxygen is abundant on mucosal surfaces. Gradients exist in dental plaque enabling obligate anaerobes to grow.
Redox potential	+200 to -200 mV	Gradients exist in biofilms. Value is lowest in gingival crevice.

pH	6.75 to 7.25	Plaque pH falls during dietary sugar metabolism. Sub-gingival plaque pH increases during inflammation.
Nutrients	Endogenous	Peptides, proteins, and glycoproteins in saliva and GCF.
	Exogenous	Dietary sugars facilitate selection of acidogenic, acid-tolerating species in plaque which decreases pH, and demineralizes enamel.

4.1. Key defense factors in a healthy mouth

The integrity of the enamel, mucosa, and both the oral secretions (saliva and GCF – gingival crevicular fluid) are the key defense factors in a healthy oral cavity. Saliva has anti-microbial peptides like statins and cystatins. It also contains active proteins and glycoproteins like lysozyme, lactoferrin, and sialoperoxidase. Immunoglobulins (predominantly IgG, along with IgM and IgA) reach the mouth via the GCF. This GCF can influence the ecology of the gingival crevice by removing the weakly adherent microbial cells, adding serum components (immunoglobulins) to host defenses, and also providing a source of nutrients.

4.2. Acquisition and maturation of oral microflora

The process of acquiring newer microflora and their maturation is a continuous process throughout childhood. As the newborn ages, the microbial load increases but the diversity of the microorganisms decreases. The nature of the initial colonizers depends on the method of delivery (vaginal birth or cesarean section), living conditions, and proximity-personal relations with the caretakers. Such early microbial communities play a major role in the development of the adult microbiota as they represent a source of pathogenic as well as protective microbes at a very early stage in life. Approximately 19,000 phylotypes of oral microorganisms are present, most of which are uncultivable. Such organisms can be detected by molecular technique from samples taken from the oral cavity.

4.2.1. Intrauterine life and microbial colonization

Fusobacterium nucleatum has been reported in 70% of pregnant women in the intrauterine environment, especially in the amniotic fluid. Transient bacteremia may carry bacteria from the maternal oral cavity to amniotic fluid. So oral screening and oral hygiene maintenance should be a concern throughout pregnancy.

4.2.2. Immediately after birth (within five minutes after birth)

The predominant species in the mouth of a child born via vaginal birth are *Lactobacilli, Prevotella,* and *Sneathia*. Birth via C-section shows a microbial picture of *Staphylococcus, Corynebacterium,* and *Propionibacterium.*

4.2.3. Within the first twenty-four hours

Activities like breathing, breastfeeding, and contact with parents, caretakers, and medical staff lead to the pioneer colonization of *Staphylococcus* and *Streptococcus*. Thereafter, microbial succession leads to diverse colonization.

4.2.4. At the age of five months

Changes occur due to increased contact with caretakers and family members, ingestion of food, hygiene routine, and habits. The most prevalent phyla are *Bacteriodites, Fusobacteria, Actinobacteria, Spirochetes,* and

Proteobacteria with the most abundant genera being *Streptococcus, Neisseria, Veillonella, and Haemophilus. S.mitis* and *S.oralis* produce IgA proteases which help in surviving the IgA-rich environment from the breast milk.

4.2.5. As the first tooth erupts (around the age of six months)

The 'Window of infectivity' is defined as the time of initial colonization of the infant's oral environment with cariogenic *S.mutans*. With the eruption of the first primary tooth around the age of six months, new adhesion surfaces are available to the *S.mutans* and this stage was referred to as the 'Window of infectivity' by Caufield et al. The second window of infectivity is speculated at about 6 years of age at the time of eruption of the first permanent molar. Straetemans (1998) found that 75% of children uninfected at the age of five years became infected by the time they were eleven years old.

4.2.6. At the age of three years

The predominant microbes belong to *Pseudomonas, Moraxellaceae, Enterobacteriaceae,* and *Pasturellaceae*. By the time complete permanent dentition eruption occurs the microbial picture changes to *Veillonella, Selenomas, Prevotella,* and *Carnobacteriaceae*.

At around puberty, there is an increase in perio-pathogenic bacteria. The major hormonal changes and the nutritional enrichment for the microbes see an increase in Gram-negative anaerobes and spirochetes as a result of which there is an increased incidence of gingivitis seen during puberty.

Additionally, any prosthetic or orthodontic appliance act as plaque retentive areas leading to impaired plaque removal. The physicochemical properties of appliances like surface roughness, hydrophobicity, and elemental composition can influence factors like bacterial attachment, plaque retaining capacity, microbial diversity, the interaction of microorganisms, and the biofilm matrix itself. Host health status can influence the composition of the oral microbiome and the host's oral health. Archaea are detected in healthy individuals with an increased prevalence of periodontitis.

4.2.7. Oral fungal colonization

Infants have fungal colonization, especially *Candia* species. During the first year of life, this incidence is in the range of 40% to 82%, whereas in older children it is in the range of 3% to 36%. The reasons for this variation are immune maturation, diet alteration, and environmental changes.

4.2.8. Oral parasitic colonization

Very few parasites like *Entamoeba gingivalis* and *Trichomonas tenax* colonize the oral cavity. This incidence is between 4% to 53% and the rate of colonization increases with age.

4.2.9. Oral viral colonization

Studies by Pride et al., demonstrated a persistent community of double-stranded DNA viruses in the saliva of healthy subjects, mostly bacteriophages. These regulate microbial diversity and act as reservoir pathogens.

5. Routes of transmission of oral microorganisms

The chief sources are the mother and/or the primary caregiver. *C.albicans* transmission is predominant in vaginal births (vertical transmission). Breast milk can be a source of transmission of *Veillonella, Prevotella,* and *Leptotrichia*. Horizontal transmission occurs via siblings and play companions.

5.1. Microbes associated with dental caries

The bacteria involved are *S.mutans*, *S.sobrinus*, and Lactobacilli with a possible association with *S.mitis* and Actinomyces. *S.mutans* is chiefly implicated due to its properties of adherence to the tooth surface, ability to produce greater amounts of acids from carbohydrates, being acid tolerant, and ability to produce extracellular polysaccharides from sucrose.

5.2. Microbes associated with Early Childhood Caries (ECC)

Bacteria associated with ECC are *Streptococcus*, *Propionibacterium*, *Veillionella*, *leptotrichia*, *Actinomyces*, *thiomonas*, and *Bifidobacterium*. As the child grows, the proportion of perio-pathogenic bacteria increases and the bacterial picture changes from aerobic or facultative gram-positive cocci to anaerobic fastidious gram-negative bacteria. Table 7 shows the microbes associated with periodontal conditions.

5.3. Microbes associated with periodontal conditions (Table 7)

Table 7. Microbes associated with periodontal conditions in the oral cavity

Condition	Microbe
Localized juvenile periodontitis	*Aa (Aggregatibacter actinomycetescomitans)*
Juvenile diabetes, Neutropenia, Immunocompromised condition	*Capnocytophaga* species
Rapidly progressive adult periodontitis Acute necrotizing ulcerative periodontitis	*Eikenella corrodens intermediate* *Spirochetes, Fusobacteria*
Acute necrotizing ulcerative periodontitis	*Prevotella intermedia*
Adult gingivitis	*Actinomyces viscosus, Some streptococci*
Adult periodontitis	*P gingivalis, Haemophilus sp, Campylobacter rectus, Fusobacteria spacing, Selenomonas sputigena*

6. Conclusion

The oral cavity is in a dynamic equilibrium and components of this equilibrium are both factors that improve oral health and that degrade it. The seemingly inconsequential acts that aid in maintaining oral health and oral hygiene such as brushing and flossing, even once a day, make sure that the equilibrium doesn't lead to an unfavorable shift and maintains the dynamic stability of the oral cavity.

Declarations

Source of Funding

This research did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Competing Interests Statement

The authors declare no competing financial, professional, or personal interests.

Ethical Approval

Based on institutional guidelines.

Consent for publication

The authors declare that they consented to the publication of this research work.

Availability of data and material

The authors are willing to share the data and material according to relevant needs.

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