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Dysbiosis of oral and Periodontal Ecologic System, Review of the Literature

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ABSTRACT

The gingival sulcus is colonized by several complexes of microorganisms, or microbiotas, which are adapted to the oral cavity. These microorganisms are characteristic of the normal healthy gingiva and periodontal structures. An unfavorable change of this normal flora of the mouth or periodontal tissues is called “*dysbiosis*” that may have an intense effect on periodontal normal ecologic system and lead to the development of gingivitis and periodontitis [1]. The aim of this article is to review periodontal bacterial transition, from utile flora to perilous periodontopathogens which is metaphorically called “Slime City”.

Key words: Periodontal infection, Dysbiosis, Dental plaque, Gingivitis.

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INTRODUCTION

Discovery of dental plaque dates back to the seventeenth century, when Anton Von Leeuwenhoek, who invented the Microscope, saw microbial aggregates on the scraping materials of teeth surface, but the term 'Biofilm' was first used by Bill Costerton in 1978 [2]. The process of plaque development starts by the formation of an organic material layer on the tooth surface known as the dental pellicle. This layer provides a protective layer for the enamel and consists of several salivary peptides, proteins, glycoproteins, phosphoproteins, proline-rich proteins and histidine-rich proteins. The pellicle can be formed on dental surfaces within 1 minute after tooth cleaning and provides adhesion molecules for oral bacteria. The specific interactions between microbial cell surface and salivary pellicle adhesion molecules are responsible for the initial adhesion and attachment of bacteria that are mainly *Streptococcus* species and can be found 2 hours after tooth cleaning. These bacteria are well known as the primary tooth surface colonizers. They have the ability to produce new binding sites for attachment of secondary colonizers through their specific receptors and stereochemical interactions as part of a process called co-adhesion or co-aggregation that leads to the development of mature biofilm which is called specifically dental plaque. At this stage the plaque can be seen as a white or yellow slime layer that is usually formed between the teeth and along the cervical margins. Oral hygiene should be prevented for at least 24 to 48 hours for a mature dental plaque development and within a few days, periodontal pathogens become visible and a mild gingivitis occurs [3-8].

TEN UNIQUE PROPERTIES OF DENTAL PLAQUE AS A BIOFILM

1. Dental plaque as a biofilm is described as the non-random accumulation of bacteria in the intermicrobial matrix or glycocalyx that accounts about 25% of the plaque volume (but up to 50-95% of the dry weight of the biofilm) that originates from plaque microorganisms, saliva and the gingival crevicular exudates and composed of exopolysaccharides, proteins, salts, and cell material. The remaining part of the biofilm that accounts about 75% is almost composed of bacteria and a few other cells including Mycoplasma species, Protozoa, Yeast and Viruses [9, 10].
2. Biofilms can form on almost all non-shedding surfaces in the natural aqueous environments. The biofilm provides specific properties for the growth and development of bacteria that are not seen outside the plaque. For this reason bacteria accumulation inside the plaque are not random in comparison to their planktonic state. In a mature biofilm, bacteria can communicate with each other through their adhesion molecules or by stereochemical interaction. Bacterial life inside biofilm is similar to the individual's life in cities. Cities and biofilms first extend laterally and then develop in a vertical direction [11, 12].
3. Dental plaque has a circulatory system. Inside the biofilms there are several small channels between the microcolonies. These channels provide the passage of water, nutrients and other agents throughout the biofilm and permit the disposal of waste products [5].
4. Another important issue is the protection that biofilm provides for the bacteria from other microorganisms and local factors such as host defense mechanisms and noxious materials like antibiotics or other chemical agents. It has been suggested that bacteria inside the plaque are 1000 to 1500 times more resistant to antibiotics in comparison with their planktonic state. The increased resistance may be explained by the presence of a glycocalyx matrix as a protective barrier, slower rate of bacterial growth inside the biofilm, different temperature and pH of the plaque that may deactivate the antibiotic and sub-dose concentrations of chemical agents when penetrates through the biofilm [13-17].
5. Dental plaque provides an anaerobic environment with reduced oxidation reduction potential that cannot find anywhere in the oral cavity. This special location permits the presence of key anaerobic gram negative periodontal pathogens in the deep portions of the biofilm. The interactions between these pathogens and host inflammatory cells lead to the production of destructive enzymes that are responsible for damaging the epithelial and connective tissue cells. The resulting inflammatory processes are responsible for the clinical signs of gingivitis and periodontitis [18-20].
6. The bacteria inside the biofilm can communicate with each other. This communication is achieved through the signals that regulate specific genes expressions and is called "Quorum sensing". This is an

important characteristic of the bacteria inside the plaque and provides the biofilm’s distinct properties such as modifying the growth of distinct species or genes expression for antibiotic resistance [12].

7. Bacteria inside the biofilm have different physiologic and ecologic functions. Even microbial cells of the same species can display completely different physiologic states in the dental plaque. One important function is the production of enzymes such as betalactamase for destroying of some antibiotics and the production of catalases and superoxide dismutases for deactivating of oxidizing ions released by phagocytes. These enzymes are secreted into the inter-microbial matrix of biofilm which is an important line of microbial defense shield. Bacteria of the plaque can also produce enzymes such as elastases and cellulases which is responsible for tissue damage and periodontitis [21].
8. In a mature dental plaque attachment of genetically distinct bacteria can occurs in a pattern which is called “co-aggregation” through their surface proteins and carbohydrates recognition [4]. Examples of this phenomenon include:
 - A. *Fusobacteria* spp. co-aggregate with all other bacteria such as *S. sanguinis*.
 - B. *Veillonella* spp., *Capnocytophaga* spp. and *Prevotella* spp. co-aggregate with streptococci or actinomyces.
 - C. *Prevotella loescheii* co-aggregates with *Actinomyces Oris*.
 - D. *Capnocytophaga ochracea* co-aggregates with *Actinomyces Oris*.
 - E. *F. nucleatum* Co-aggregates with *P. gingivalis* or *Treponema denticola*
9. Studies using whole genomic DNA probes and hybridization have revealed that bacterial species exist in complexes in the biofilm. In 1968 Sigmund Socransky by analyzing 13.261 subgingival plaque samples from 185 subjects divided bacterial species in groups, labeled by colors. The classification was based on the pathogenicity of the bacteria in the plaque [table1]. *Actinomyces* species and yellow complex comprise species that are related to the healthy conditions, green complex increases at the early stage of periodontitis and the species of the orange complex are more principal colonies in the advanced stages of the disease. The orange complex also has the bridging effect for connecting the previously mentioned complexes to the red complex which are thought to be the most critical periodontal pathogens [22].

Table 1. Microbial complexes in subgingival biofilm. (Sigmund Socransky, 1968)

Colonizing category	Complex color	Complex members
These groups of species are early colonizers of the tooth surface. <i>Actinomyces</i> , yellow and purple complex are considered the normal and healthy flora.	No color coded	<i>Actinomyces</i> species
	Yellow complex	<i>Streptococcus</i> species
	Purple complex	<i>Veillonella parvula</i> and <i>Actinomyces odontolyticus</i> .
	Green complex	<i>Capnocytophaga</i> species, <i>Aggregatibacter actinomycetemcomitans</i> serotype a, <i>Eikenella corrodens</i> and <i>Campylobacter concisus</i> .
These two complexes are considered to be the major etiologic bacteria of periodontal diseases. Red complex is related to deep periodontal pockets and bleeding on probing.	Orange complex	<i>Campylobacter gracilis</i> , <i>Campylobacter. rectus</i> , <i>Campylobacter showae</i> , <i>Eikenella. nodaium</i> , <i>Fusobacterium. nucleatum</i> subspecies, <i>Fusobacterium. periodonticum</i> , <i>Peptostreptococcus micros</i> , <i>Prevotella. iniermedia</i> , <i>Prevotella. nigrescens</i> , and <i>Streptococcus. constellatus</i> .
	Red complex	<i>Porphyromonas gingivalis</i> , <i>Tannerella forsythia</i> and <i>Treponema denticola</i> .

10. “Invasion” and “virulence” are the last but the most important features of pathogens inside biofilm. The ability of tissue invasion is an important factor especially for motile periodontal pathogens in progression of disease. The invasion of periodontal pathogens has been demonstrated by the adherence of *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Tannerella forsythia* and *Treponema denticola* to the basement membrane and collagen fibers that is necessary for invasion into periodontal tissues. Virulence factors may include bacterial substances that directly damage tissue cells (e.g. hydrogen sulphide) or bacterial substances that cause host cells to produce biologically active substances (e.g. lipopolysaccharide) or may be either microbial or host-cell released substances that damage the

intercellular matrix (e.g. collagenase). Table 2 shows special virulence factors of some periodontal pathogens [5].

Table 2. Special virulence factors of key periodontal pathogens. (Lindhe, 2008)

Bacterial species	virulence factors
<i>Aggregatibacter actinomijceiemcomitans</i>	Leukotoxin; collagenase; endotoxin; epitheliotoxin; fibroblast inhibitory factor; bone resorption inducing factor; induction of cytokine production from macrophages; modification of neutrophil function; degradation of immunoglobulins; cytolethal distending toxin (Cdt); induces apoptotic cell death. Invades epithelial and vascular endothelial cells <i>in vitro</i> and buccal epithelial cells <i>in vivo</i> .
<i>Porphyromonas gingivalis</i>	Collagenase; endotoxin; proteolytic trypsin-like activity; fibrinolysin; hemolysin; other proteases including gingipain; phospholipase A; degrades immunoglobulin; fibroblast inhibitory factor; H ₂ S; NH ₃ ; fatty acids; factors that adversely affect PMNs; capsular polysaccharide; bone resorption inducing factor; induction of cytokine production from various host cells; generates chemotactic activities; inhibits migration of PMNs across epithelial barriers; Invades epithelial cells <i>in vitro</i> .
<i>Tannerella forsythia</i>	Endotoxin; fatty acid and methylglyoxal production; induces apoptotic cell death; cytokine production from various host cells; invades epithelial cells <i>in vitro</i> and <i>in vivo</i> .

CONCLUSION

In summary, periodontal infection is caused by a relatively group of pathogens in a susceptible host. Several factors that affect periodontal disease development and progression through several pathways include environmental conditions, genetic susceptibility, nutritional status and the role of psychological stresses. Since the etiology of the disease is multi-factorial, no single treatment can control the infection, the choice of treatment should be selected by the nature of the infection and the aid of several physical or chemical anti-plaque strategies [23-26].

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Declarations of Interests

The authors confirm that this article content has no conflict of interest.

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