

BACKGROUND

Bacteria in natural as well as industrial and medical ecosystems grow in biofilms. These communities include bacteria that are beneficial for oral and general health but also can include bacteria that produce adverse outcomes, such as caries and periodontal disease. Dental plaque is a classic biofilm that creates problems known to pose public health challenges worldwide. The properties of dental biofilms and possible controlling mechanisms were explored.

DENTAL BIOFILMS

Formation

Immediately after the teeth are cleaned, dental biofilm re-forms through the adsorption of the pellicle, which is an organic film that provides a place where receptors for bacteria can be found. Pioneer bacteria have direct contact with the pellicle, then later bacteria adhere to the bacteria that are already attached (Figure 1). Streptococcal species are the most common early colonizers of dental biofilms. If left undisturbed, the dental biofilm would change from being dominated by gram-positive cocci to being composed of cocci, filamentous organisms, spirils, and spirochetes, with high numbers of gram-negative bacteria. When this mature biofilm is present, gingivitis develops.

Properties

Newer molecular techniques have identified coaggregation, or the adhesion of genetically distinct bacteria to each other, as another property of biofilm bacteria. Late colonizers may not directly coaggregate with early colonizing species but can join with strains of *Fusobacterium nucleatum*, which can coaggregate with both early and late colonizers.

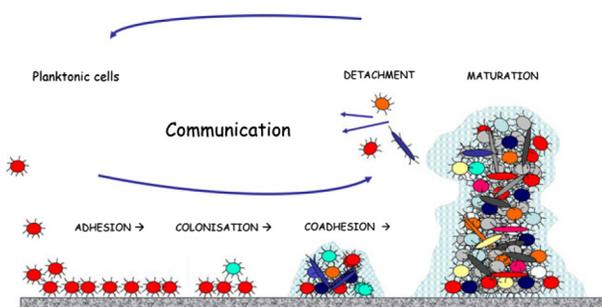


Figure 1. Formation of dental biofilm. Pioneer bacteria colonizing the dental hard tissue are dominated by streptococcal spp. The adhered bacteria start to produce an extracellular matrix and become ‘irreversibly’ attached. The biofilm matures and increases in bacterial diversity and complexity. Bacteria may detach from the oral biofilm, enabling colonization of other surfaces in the oral cavity. Bacterial communication may mediate several of the steps in biofilm formation. (Courtesy of Valen H, Scheie AA: Biofilms and their properties. *Eur J Oral Sci* 126:13-18, 2018.)

Sometimes bacteria detach from the biofilm, which can occur through a passive process or an active one mediated by the bacteria themselves. These detached bacteria can disperse and colonize new areas in the oral cavity.

Both synergistic and antagonistic interactions occur between the bacteria in the biofilm. When cooperating, nutritional food chains and webs are formed. Salivary molecules can be metabolized by cooperating bacteria. Bacteria begin to produce an extracellular matrix composed of polysaccharides, lipids, proteins, and extracellular DNA soon after they adhere to a surface. This matrix is an essential component in biofilm architecture and integrity. Several characteristic properties of biofilms, such as the higher tolerance to antimicrobial compounds, are also related to extracellular matrix development.

Communication

Bacterial communication is essential for several aspects of biofilm formation and maturation. Both quorum sensing communication and signaling molecule communication have been proposed as ways that biofilm bacteria share information. Interstrain and interspecies communication may also exist between bacteria in biofilms. Cross-talk between streptococcal species has been reported for various peptide pheromones.

Quorum sensing communication coordinates activities such as adhesion, biofilm formation, aggregation, virulence, motility, antibiotic resistance, and horizontal gene transfer. This method is dependent on bacterial density. Because communication in this way affects so many aspects of biofilm life, it has been suggested that interference with this mode of bacterial communication may be a way to formulate treatment strategies against bacterial infections.

Signaling molecules can be autoinducer peptide (AIP), autoinducer-1 (AI-1), or autoinducer-2 (AI-2) types. These molecules are produced, released, and accumulated in the biofilm, then, at a critical level of concentration, the molecules activate the receptor that switches the transcription of effector genes on or off. Quorum-sensing ability ensures that sufficient bacteria are present for signaling molecules to activate the effector genes.

Having different types of signaling molecules indicates that receptor specificity for their detection also differs. AI-1 molecules are used by gram-negative bacteria for intraspecies communication. AIPs are used by gram-positive bacteria. The AI-2 signaling molecule is produced by both gram-positive and gram-negative bacteria and allows communication across gram classification and species borders. The production of the AI-2 molecule is related to the *luxS* gene, which is widespread in bacteria. However, the known receptor proteins for AI-2 must be present

along with the AI-2 molecule for quorum sensing to be activated.

AI-2 signaling operates in a diverse sample of bacteria. If the *luxS* gene is inactivated, bacteria cannot produce AI-2, which reduces biofilm production. Some interactions can overrule this situation. Biofilm formation between *Streptococcus gordonii* and *Porphyromonas gingivalis* requires intact *luxS*. *S. gordonii* is an early colonizer, but *P. gingivalis* is a putative periodontal pathogen. Both species produce AI-2. When *luxS* is inactivated in just one of these species, the biofilm is still formed, but if inactivation of *luxS* occurs in both species, no biofilm is formed. One study has indicated that inactivation of the *luxS* gene and subsequent failure to produce AI-2 leads to an increased sensitivity to chlorhexidine. Antibiotic sensitivity can also be related to AI-2 signaling in bacterial biofilms.

Autoinducer Peptides

The competence stimulating peptide (CSP) pheromone was first found in *S. pneumoniae*. It induces competence for the uptake and incorporation of DNA into the host genome. CSP affects the biofilm formation abilities of various oral streptococci. In addition, adaptation to an acidic environment increases with CSP signaling. CSP also induces fratricide, killing, and lysis of noncompetent cells in the oral environment.

CONTROLLING BIOFILMS

Several hundred different bacterial species and strains inhabit the dental biofilm, with the result being a vastly expanded genetic pool of enzymes that can inactivate antibacterial agents, explaining why bacteria in a biofilm are considerably more resistant to these drugs than free bacteria. The extracellular matrix protects the bacteria, but the exact mode of protection remains to be revealed. Possibilities include matrix binding of the antibacterial compounds, which inhibits their penetration and their ability to reach the bacteria. In addition, biofilm bacteria may excrete and concentrate protective enzymes. Biofilm bacteria may also adopt a dormant state that reduces their susceptibility to antibiotics and antibacterial agents. Finally, genetic exchange and transfer of antibacterial-resistant genes may occur more readily in a biofilm environment.

Despite these challenges, novel compounds, technologies, and methods are being researched in an effort to eradicate or prevent the formation of oral biofilms. Agents may ultimately be added to toothpastes and oral rinses or incorporated into dental restorative materials. Reduced bacterial adhesion may be addressed by engineering the material and tooth surfaces of restored structures. Already available are products that work through photodynamic therapy to kill bacteria in biofilms. Probiotic bacteria have also been used to maintain biofilm ecology in a healthy state or restore it to this state. Efforts to interfere with bacterial communication do not kill bacteria but should make them less virulent.

DISCUSSION

Diseases related to the oral biofilm, including caries and periodontitis, develop when dysbiosis of the oral microbiome occurs. Because biofilm bacteria are significantly less sensitive to the antibacterial agents commonly used, research into new products and new methods is essential.

Clinical Significance

In pursuing new approaches to addressing the problems with a disbiotic dental biofilm, it's essential to understand the complex properties and interplay among biofilm bacteria. In addition, until those new agents and methods are available and even beyond that time, patients should be educated to perform daily mechanical biofilm disruption (tooth brushing) and to make lifestyle changes that support a healthy oral environment.

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ORAL HYGIENE

Dry brushing

BACKGROUND

The removal of plaque through routine oral hygiene is a well-accepted method of protecting teeth from becoming infected by bacteria, carious, and eventually lost from the dentition. Because caries remains an important public health concern, it's

clear that our tooth brushing practices could be improved. One method that has been proposed is brushing with a dry toothbrush rather than a prewetted one. The claim has been made that dry brushing will remove more dental plaque and will increase the subject's perception of smoothness of tooth surfaces,

