Taking oral care a step further
Clinical aspects of oral biofilm control and prevention

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There is growing interest in investigating the relationship between oral and systemic health. The association of oral biofilms and periodontal disease with systemic conditions such as diabetes, coronary heart disease, nosocomial (hospital-associated) pneumonia and preterm delivery (PTD), albeit non-causal, highlights the importance of biofilm control and good oral health. Thus, the limitations of mechanical cleaning (ie, brushing and flossing) in providing effective biofilm control need to be properly addressed.

A preliminary expert panel meeting, initiated by Johnson & Johnson, gathered a multidisciplinary group of oral healthcare professionals to discuss the role of biofilms in oral disease pathogenesis and the role of antiseptic mouthrinses in oral healthcare, focusing on the clinical aspects of biofilm control and prevention. The expert contributions, summarized in this report, will provide the basis for the long-term goal of producing a consensus report on the use of antiseptic mouthrinses in oral care.

The increasing significance of biofilm control in oral and systemic health

Biofilms are structured microbial communities that adhere to surfaces and are reported to cause 65% of all human infections. Bacterial biofilm formation in the mouth is a complex process that starts with the adhesion of bacterial colonizers on surfaces in the oral cavity (Figure 1). Once a foothold has been established, other bacterial species (secondary colonizers) adhere irreversibly to the primary colonizers to form a larger, confluent and more diverse microbiological community. In the course of biofilm formation, bacterial colonies produce an extrapoly saccharide matrix, which imparts specific properties on the bacterial biofilm, including resistance to antibacterial agents.

A 'climax community' consisting of numerous coexisting bacterial species in matrix-bound microcolonies eventually forms. Water channels within the structure provide diffusion pathways for nutrients and also for bacterial communication via chemical messengers known as 'quorum

Figure 1. Bacterial biofilm formation

- Invaders
- Detachment of biofilm fragments
- Mature biofilm
- Secondary colonizers (adhesion = coaggregation)
- EPS production
- EPS, extrapoly saccharide matrix
- Adhesion
- Detachment
- Initial colonizers
- Surface
sensing molecules. These bacterial colonies are able to regulate their gene expression according to their population density. In due course, biofilm fragments may detach from the community; although the exact mechanism involved remains to be determined, biofilm dispersal is critical in the biofilm lifecycle because it enables bacterial spread and colonization of new surfaces.

It is important to emphasize that not all oral biofilms are pathogenic; some of them constitute the oral cavity’s normal flora. Pathogenic bacteria, which colonize and form microcolonies within pre-existing oral biofilms, are the ones that have a causative role in oral infectious diseases such as periodontitis and caries.5

The complexity of the oral microbiome6 and the high resistance of biofilms to antibiotics, antiseptics and antifungals are the major challenges in oral biofilm management. Bacterial resistance may be due to the antibacterial agent’s poor penetrating capacity, the emergence of a resistant phenotype, or the effects of an altered microenvironment. Major ecological pressures favouring pathogenic bacteria may disrupt the balance between ‘good’ and ‘bad’ bacteria, resulting in, for example, periodontal disease (POD).

POD develops as bacterial infections trigger inflammatory reactions in the gum. Inflammatory cells that enter the systemic circulation induce a systemic response and a chronic inflammatory state. Inflammatory cytokines that are produced in periodontal pockets and surrounding blood vessels then enter the bloodstream and reach distant target organs, where they may cause systemic disease. Inflammatory cytokines induce the liver to produce acute-phase proteins such as C-reactive protein – a key cardiovascular disease (CVD) marker.6

**Oral infections are linked to preterm delivery**

Emerging literature supports the association between POD and the risk of adverse pregnancy outcomes.8 Preliminary evidence suggests a link between periodontal infections and preterm labour: periodontal bacteria and their products have been shown to induce PTD in animals. In relation to inflammatory mediators, maternal cytokine levels in oral and dental surface fluid (ie, gingival crevicular fluid) were highly correlated with those in amniotic fluid, suggesting that periodontal bacteria can invade the mother’s epithelial and endothelial cells and spread to amniotic fluid.

Further studies are necessary to establish whether POD prevention can prevent PTD and related complications. Professor Samaranayake stressed that while more compelling clinical evidence is necessary, oral healthcare providers are responsible for educating patients regarding the possible link between POD and adverse pregnancy outcomes, and that treating POD could benefit both the mother and newborn.

**Recommendating atherosclerotic-disease risk assessment in patients with periodontal disease**

Historical data demonstrate a non-causal relationship between myocardial infarction and POD.9 Moreover, a systematic review that included a meta-analysis concluded that POD is an independent risk factor for coronary heart disease.11 One study demonstrated that intensive periodontal treatment resulted in acute, short-term systemic inflammation and endothelial dysfunction. Furthermore, the benefits to oral health from treatment were associated with improved endothelial function 6 months after therapy.12

A consensus report from the editors of the American Journal of Cardiology and the Journal of Periodontology aims to provide ‘health professionals, particularly cardiologists and periodontists, a better understanding of the link between atherosclerotic CVD and periodontitis.’ On the basis of current information, it has been recommended that patients with moderate to severe periodontitis be informed of the possibility of having an increased risk of CVD, suggesting the need for atherosclerotic-disease risk assessment in patients with periodontitis.13

**Good oral hygiene reduces the risk of nosocomial pneumonia**

Oral health and systemic infections are directly connected, as the mouth is a reservoir of bacteria and inflammatory products of POD. Intensive-care patients were shown to have more dental plaque, which predominantly consisted of pathogenic bacteria such as *Staphylococcus aureus* and *Pseudomonas spp*. Additionally, common hospital bacteria which were resistant to antibiotics colonized the dental plaque and oral mucosa of these patients.14 When inhaled, these pathogens may cause pneumonia. A systematic review showed that oral disinfection with tooth brushing, antiseptics and topical antibiotics reduced the risk of nosocomial pneumonia by an average of 40%.15 Large-scale studies are needed to provide stronger evidence to demonstrate the efficacy of preventive oral hygiene procedures in high-risk patients.

**Clarifying the relationship between periodontal disease and diabetes**

Severe POD often coexists with diabetes mellitus and, conversely, diabetes has been identified as a risk factor for severe POD.16 Major inflammatory components common to both POD and diabetes could explain this two-way relationship. However, the evidence for this relationship is fraught with concerns over data interpretation owing to different POD classifications and complicated clinical parameters related to diabetes assessment. Results of interventional studies investigating the effects of POD on metabolic state have also been inconsistent. While some studies have shown that scaling, root planing and systemic doxycycline therapy improve glycaemic control, others have suggested otherwise.17,18

**Defining the role of antiseptic mouthrinses in better oral health**

Concern among healthcare professionals over the negative health consequences of inadequate plaque control with mechanical cleaning alone highlights the growing significance of antiseptic mouthrinses as an adjunct regimen for routine oral care. Brushing and flossing continue to be the standard routine for plaque removal; however, bacteria often remain in the oral cavity due to inadequate technique, limited dexterity and inaccessibility of certain oral regions.19,20 In addition, patient compliance and motivation to maintain proper oral care may decrease over time, as was observed in a study tracking flossing effectiveness.21 Antiseptic mouthrinses, when used in addition to mechanical cleaning with toothbrush and dental floss, may overcome this problem.22,23

"Inadequate plaque control with mechanical cleaning alone highlights the growing significance of antiseptic mouthrinses as an adjunct regimen for routine oral care."
Figure 2. Effect of mouthrinses on self-derived biofilms after (a) 30-second and (b) 60-second treatment

Addressing limitations of brushing and flossing
A systematic review confirmed that mechanical cleaning is insufficient in effectively reducing adult gingivitis, while another recent study also suggested the need for antibacterial approaches to improve oral care, especially caries control. A consensus statement published by the United States National Institutes of Health specified that additional cariostatic agents may enhance the effectiveness of fluoride in dental caries management. Effective antimicrobials counteract the decrease in oral pH by reducing bacterial load, while fluoride promotes remineralization, resulting in a healthy oral environment.

The majority of currently available chemical agents for biofilm control are broad-spectrum microbicides. Chlorhexidine (CHX), triclosan and essential oils (EO) (Listerine®, Johnson&Johnson) are the most common clinically tested antimicrobials. The panel agreed that, in clinical practice, antimicrobial mouthrinses with proven clinical activity based on generally accepted safety and efficacy criteria, may play a role in the control of supragingival plaque and gingivitis when used as an adjunct therapy. Patients who are unable to maintain adequate oral plaque control with mechanical cleaning alone are most likely to benefit from the use of antimicrobial mouthrinses. Large-scale studies are warranted to investigate the safety, efficacy and cost-effectiveness of including mouthrinses in an oral hygiene regimen.

The panel agreed that the adjunctive use of antiseptics in patients who do not manage proper oral hygiene practices is a behavioural matter. Although antiseptic mouthrinses offer some respite from oral health problems, regular practice in the optimal rinsing method is very important, as compliance gradually falls in the long term. It is therefore necessary to determine what is acceptable to patients and ensure mouthrinses are used according to protocols established by evidence.

In orthodontic patients, the level of oral hygiene is key in patient management – brushing, rinsing and frequent clinic attendance are recommended. Panel members concur that specific populations, such as the elderly, may benefit from the addition of antiseptic mouthrinses in their oral care, particularly for caries prevention. Over-the-counter mouthrinses may help improve oral hygiene practices in these specific groups.

It is important to emphasize that the use of mouthrinses does not replace standard oral hygiene practices. Mouthrinses can be used as an adjunct to regular brushing and flossing, together with visits to the dentist every 6 months. Some countries have started oral health campaigns to promote brushing, flossing and the proper use of mouthrinses, so as to ultimately encourage better oral health practices among the public. The panel concurred that dental professionals play a crucial role in educating patients on the most effective, complete oral care regimen.

Safety and effectiveness of antiseptic mouthrinses
Strong evidence of the anti-plaque and anti-gingivitis effects of different antimicrobial mouthrinses validate recommendations to make these agents part of oral care. The antimicrobial activity of commercially available antiseptic mouthrinses against plaque biofilms bathed in saliva has been tested in vitro, and marked differences in the antimicrobial capacity of these agents have been observed (Figures 2a and 2b). The EO-based mouthrinse was superior to other mouthrinses and had an antimicrobial activity comparable to that of CHX alone (p<0.001). Antibacterial mouthrinses may also contain biocides, surfactants, polymers and/or other ingredients that work against biofilms to effectively reduce plaque and gingivitis. Studies on the real-life use of oral care formulations with antiplaque biocides did not show the emergence of bacterial resistance.

Essential-oil mouthrinses offer the advantage of long-term safety and efficacy
When used as an adjunct to routine oral hygiene, a formula containing four EOs (i.e., eucalyptol, menthol, methyl salicylate and thymol) provided additional benefit against plaque and gingivitis compared with placebo and control. In vitro studies have demonstrated how EOs disrupt the bacterial cell wall and inhibit enzyme activity, thereby non-selectively killing bacteria within 30 seconds. In addition, EOs inhibit supragingival plaque and gingivitis by up to 56% and 36%, respectively, and eliminate bacteria in hard-to-reach areas of the oral cavity.

While the efficacy of CHX mouthrinses in improving oral health has been proven by numerous studies, their usage may be limited owing to coverage by certain prescription plans. Moreover, CHX mouthrinses stain the tongue and teeth, including aesthetic restorations, and promote supragingival calculus formation. Furthermore, CHX affects taste and is recommended for short-term use only. EO-containing mouthrinses, on the other hand, are indicated as a daily-use mouthrinse for gingivitis prevention. Apart from causing a transient tingling sensation, EO-based mouthrinses have a good safety profile and are suitable for long-term use without staining the teeth, altering taste, forming calculus or adversely affecting oral microflora.
Alcohol-containing mouthrinses do not cause oral cancer

Excessive consumption of alcoholic beverages is a commonly identified causative agent of oral cancer, especially when combined with smoking. This finding has led to speculation that there may be a link between using alcohol-containing rinses and an increased risk for oral cancer. It should be noted that the pharmaceutical-grade ethanol in EO-mouthrinses is not an active ingredient; it serves only as a solvent for the combination of EOs and acts as a delivery vehicle for the EO active ingredients to achieve superior plaque biofilm penetration. Unlike mouthrinses, alcoholic beverages contain numerous carcinogenic compounds. Because ethanol is non-carcinogenic, prolonged exposure to ethanol (> 1 hour) has been shown to increase the permeability of oral surfaces, allowing for increased mucosal penetration of carcinogens from alcoholic beverages and tobacco products. In contrast, typical-use exposure to EO-mouthrinses (2 minutes) does not affect mucosal permeability.49

Dr. Laiteerapong explained that although most oral antiseptics contain alcohol, commercial mouthrinses used non-antiseptic, carcinogen-free distilled alcohol.49 A review of nine epidemiological studies on oropharyngeal cancer and alcohol mouthrinses use revealed no causal link between the use of alcohol-containing rinses and oropharyngeal cancer.49 Similarly, the United States Food and Drug Administration, along with the National Cancer Institute and American Dental Association (ADA), have confirmed the lack of evidence of a causal relationship.49,50 The ADA recommends the use of antiseptic mouthrinses with appropriate professional advice.49

Conclusions

Oral biofilms, commonly known as dental plaque, are complex microbial communities encased within a cellular matrix. These structured bacterial colonies communicate, change genotypes, and mutate to stay together in the community. If left untreated, these biofilms may cause a series of oral problems, including caries, gingivitis, and periodontal disease. Importantly, P.gingivalis is associated with this disorder and has been shown to have a strong connection to the development of periodontitis.51,52,53

Listerine® has been in use for decades and is the most extensively tested mouthwash worldwide, with over 30 clinical studies having investigated its safety and efficacy. It has a good safety profile and is suitable for daily use.

References