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REVIEW ARTICLE

Dental biofilm infections – an update

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Teeth are colonized by oral bacteria from saliva containing more than 700 different bacterial species. If removed regularly, the dental biofilm mainly comprises oral streptococci and is regarded as resident microflora. But if left undisturbed, a complex biofilm containing up to 100 bacterial species at a site will build up and may eventually cause development of disease. Depending on local ecological factors, the composition of the dental biofilm may vary considerably. With access to excess carbohydrates, the dental biofilm will be dominated by mainly gram-positive carbohydrate-fermenting bacteria causing demineralization of teeth, dental caries, which may further lead to inflammation and necrosis in the pulp and periapical region, i.e., pulpitis and periapical periodontitis. In supra- and subgingival biofilms, predominantly gram-negative, anaerobic proteolytic bacteria will colonize and cause gingival inflammation and breakdown of supporting periodontal fibers and bone and ultimately tooth loss, i.e., gingivitis, chronic or aggressive periodontitis, and around dental implants, peri-implantitis. Furthermore, bacteria from the dental biofilm may spread to other parts of the body by bacteremia and cause systemic disease. Basically, prevention and treatment of dental biofilm infections are achieved by regular personal and professional removal of the dental biofilm.

Key words: Dental biofilm; oral biofilm; dental caries; gingivitis; periodontal disease; oral disease.

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More than 700 different bacterial species have been detected in the oral cavity of humans (1). Saliva contains 10^8 to 10^9 bacteria per milliliter, and some of these adhere to the teeth and initiate formation of a dental biofilm, previously called dental plaque. Generally, the dental biofilm is similar to biofilms elsewhere in the body, where bacteria colonize tissue surfaces or artificial implants and are embedded in a self-produced extracellular matrix of exopolymers (polysaccharides and proteins) and DNA
(2–4). There are, however, also differences from biofilms at other sites of the body (5).

Dental plaque and its relation to oral health and diseases have been studied for decades. A search in PubMed with the Mesh words "dental plaque" and "dental biofilm" yields 22.968 and 3.097 hits, respectively, and the earliest papers date back to 1946 and 1981. With the search words "lung biofilm", "urogenital biofilm", "hemodialysis biofilms", and "catheter biofilms", the number of hits are 639, 271, 203, and 1.386, respectively (searched on April 21, 2016), and early articles date from 1984 to 1989. So, dental biofilm research has been a pioneer in the field of human biofilm research.

The dental biofilm causes diseases in the teeth and their supporting tissues, i.e., dental caries and periodontal diseases. Dental caries is characterized by a demineralization of the teeth without concurrent inflammation in surrounding tissues, while its sequels if left untreated, pulpitis and apical periodontitis are infections. Similarly, the periodontal diseases, such as gingivitis, periodontitis, and peri-implantitis, induce an inflammatory response. Each of these biofilm-induced dental diseases will be described including the principles of biofilm control/elimination. Biofilm-induced infections on the oral mucosa are not included in this article, whereas bacteria in dental biofilms causing infections at other locations of the body are mentioned.

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DENTAL BIOFILM – DEVELOPMENT, STABILITY, AND VARIABILITY

A mature dental biofilm is of polymicrobial nature as it may consist of up to 100 different microbial species (3, 6). The biofilm is dominated by bacteria, but may also comprise yeasts, protozoa, *Archaea*, and virus (3). According to our present knowledge, biofilm bacteria are the primary cause of dental diseases.

The initial adherence of bacteria to dental surfaces is preceded by the formation of a conditioning film on the clean dental surfaces mainly consisting of salivary glycoproteins, the so-called acquired pellicle. The pioneer bacterial species adhere to the pellicle, initially with weak long-distance forces of physicochemical nature between charged molecules. Subsequently, stronger bacterial adherence to the pellicle is established via receptor-pairs between bacterial surface adhesins and glycoprotein receptors in the acquired pellicle (5). The predominant initial colonizers are oral streptococci, primarily from the *Streptococcus mitis* group followed by gram-positive rods, especially *Actinomyces* species. Gradually other gram-positive and gram-negative cocci and rods adhere to the early gram-positive biofilm. These bacteria are also present in saliva and may originate from the depth of the tongue papillae or crypts of the tonsils (7). *Fusobacterium* species play an important role in the formation of the mature dental biofilm as these bacteria co-aggregate with both the initial gram-positive bacteria and the following colonizers, including the majority of gram-negative and motile bacteria (8, 9) (Fig. 1). The composition of the developing biofilm is determined by local ecological factors at the site of colonization and varies considerably at different surfaces, even at the same tooth. Eventually, if left undisturbed, a very diverse biofilm is established (Fig. 2). During development of the biofilm, bacteria are metabolically active using mainly endogenous nutrients from saliva. This results in the formation of an extracellular matrix that contributes to the co-adherence of the bacteria on the tooth surface and offers protection of the biofilm bacteria (3). Like other types of human biofilms, the dental biofilm has a quorum sensing communication system; quorum signal molecules such as autoinducer-1 and -2 play a significant role in the structure and virulence of the biofilm (9).

The present knowledge on the dental biofilm microbiota is based upon studies carried out by culture methods and culture-independent molecular biological methods. The last-mentioned studies have revealed that only about 50% of the dental biofilm microbiota detected hitherto can be

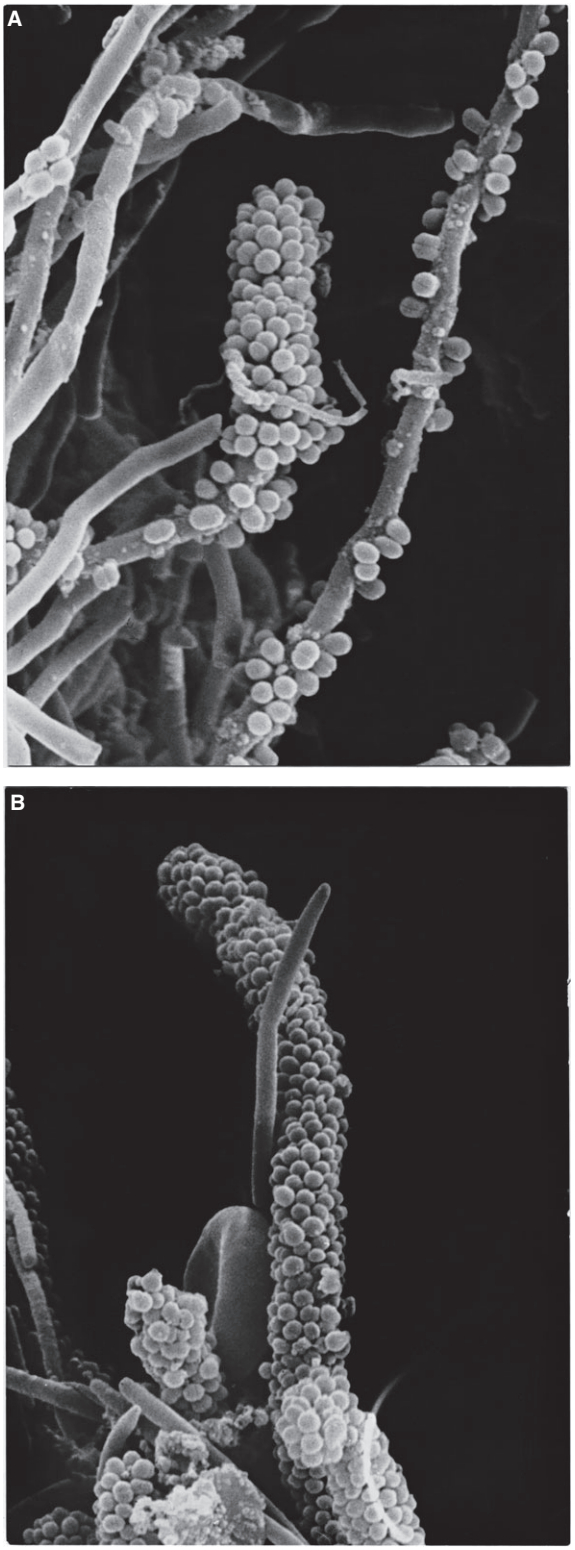

Fig. 1. (a) Coaggregation between streptococci and filaments in a developing dental biofilm; (b) A typical corncob formation.

Fig. 2. A typical mature diverse dental biofilm.

identified by use of traditional culture methods (3). The composition of the dental biofilm varies not only between different sites in the oral cavity but also between individuals. Despite this, a core microbiome has been proposed, and based on molecular approaches, it includes species of the following genera: *Streptococcus, Veillonella, Granulicatella, Neisseria, Haemophilus, Corynebacterium, Rothia, Actinomyces, Prevotella, Capnocytophaga, Porphyromonas*, *and Fusobacterium*. A supplemental microbiota is often observed in addition to the core microbiome adding to the variability of the oral microbiota (10). So, the bacterial profile of the dental biofilm may vary significantly between different individuals and between adjacent sites within the individual.

Dental biofilms are part of the resident oral microflora or oral microbiota which as a general rule is beneficial to the host, i.e., by providing colonization resistance against exogenous microorganisms/pathogens and by interacting with the immune system at a level compatible with health. This balance or stability is termed microbial homeostasis (10). If stressed, the balance may result in shifts in the microflora of the biofilm and diseases may develop (dysbiosis). The stress factors can be of different nature such as changes in diet or oral hygiene habits, medical treatment, e.g., antibiotics or medicine influencing salivary flow, or a change in host response due to medication or an immunosuppressive disease. These factors may cause a breakdown of the local ecological homeostasis in the oral cavity and result in a shift in the composition of the dental biofilm introducing or rather increasing the level of microbial species that may initiate disease. Thus, dental diseases are very seldomly caused by exogenous bacteria, but mainly by a reorganization of structure and composition of the biofilm allowing more virulent bacterial species to become dominant. This understanding of disease development based on shifts in local ecological factors concomitant with changes in proportions of mainly resident bacterial species is called the ecological biofilm/plaque hypothesis. The local ecological changes related to caries and periodontal diseases are different, but characteristic for each disease. The same applies to the bacterial virulence factors capable of causing demineralization of the teeth and destruction of the supporting periodontal tissues, respectively (11).

DENTAL DISEASES AND INFECTIONS

A dental biofilm is first established in stagnant areas of the teeth where the bacteria are protected, i.e., in fissures of the occlusal (biting) surfaces, approximally between adjacent teeth, and supragingivally along the gingival margin. If left undisturbed by insufficient dental hygiene procedures, the supragingival biofilm may gradually spread along the root of the tooth into the periodontal pocket, and a subgingival biofilm is formed. Biofilms on the tooth surfaces may cause dental caries, while supra- and subgingival biofilms along and under the gingival margin may cause periodontal diseases. If the tooth is replaced by a dental implant, peri-implantitis may develop.

Dental caries

Dental caries is characterized by local demineralization of the hard tissues of the tooth, initially the dental enamel and subsequently the dentine. The demineralization is caused by the production of low-molecular organic acids (of which lactate is most important) by carbohydrate-fermenting bacteria, which catabolize primarily mono- and disaccharides primarily from the food. When excess sugar is present, some of these carbohydrates, in particular sucrose, can also be polymerized by bacteria possessing glycosyl- or fructosyltransferases to extracellular glucans and fructans. These polysaccharides contribute to the extracellular matrix of the biofilm and consolidate the attachment of the bacteria to the tooth surface. Furthermore, the extracellular

polysaccharides make up a nutrient reserve for the biofilm bacteria, as they can be degraded during starving conditions allowing the acid production and degradation of dental hard tissues to continue. Demineralization of teeth takes place when pH in the biofilm at the tooth surface is below 5.5 which is called the critical pH value (11).

Until a few decades ago, development of caries was ascribed to only a few gram-positive bacterial species in the biofilm, i.e., the specific biofilm/plaque hypothesis, and *Streptococcus mutans*, *Streptococcus sobrinus* together with some *Lactobacillus* species were regarded as key pathogens. This understanding was based upon cultivation studies which often isolated these bacteria and found them to possess the cariogenic abilities described above. Furthermore, these bacteria are acid-tolerant/aciduric and thus able to catabolize carbohydrates and continue demineralization under acidic conditions which halt most bacteria. However, caries can be detected in the absence of these species, and they may, on the other hand, be present without development of caries, indicating that other bacteria can contribute to demineralization of the teeth. This led to the formulation of the ecological biofilm/plaque hypothesis proposing that whether caries develops or not is determined by the existing ecological balance in the biofilm on the tooth surface. Only if cariogenic bacteria possessing the above-mentioned characteristics are allowed to dominate the biofilm demineralization will occur. Bacteria with less carbohydrate-fermenting capabilities than *S. mutans* in conjunction may add to the process, or the presence of a majority of lactate-consuming or alkali-producing bacteria may neutralize the effect of carbohydrate-fermenting bacteria. Thus, development of caries is due to a shift in the local homeostasis of the resident microflora. The balance may be stressed by an increase in intake of fermentable carbohydrates, an insufficient oral hygiene or a decrease in salivary flow due to medication which allows an overgrowth of cariogenic, acid-tolerant bacteria resulting in lowering the pH in the biofilm and demineralization of the tooth (11).

Recent 16S rRNA-based molecular biological studies have revealed that the caries microflora is much more complex than assumed based on culture studies. While especially *S. mutans, Actinomyces*, and *Lactobacillus* species were previously regarded as responsible for caries, the list of caries-associated bacteria now includes species of the genera *Actinomyces, Lactobacillus, Dialister, Eubacterium, Olsenella, Bifidobacterium, Atopobium, Propionibacterium, Scardovir, Abiotrophia, Selenomonas, and Veillonella* in addition to carbohydrate-fermenting oral streptococci. Many of these bacteria are still uncultivable and their cariogenic potential, i.e., if they are acidogenic and aciduric and actually involved in the caries process remains to be determined (12).

Biofilm control

A prerequisite for preventing caries is good oral hygiene habits controlling the oral microbiota at levels compatible with health (10). Parents and public dental care for children and adolescents are the key persons for teaching and securing optimal oral hygiene until children and adolescents are able to take care of tooth brushing with dentifrice containing fluoride. This effort is also crucial in the dental care system for adults and for elderly in hospitals and nursing homes, and when necessary supplemented with inter-dental brushes, tooth picks, or dental floss. If demineralization of teeth is advanced, professional treatment including application of fluoride and ultimately filling therapy is warranted.

Pulpitis and apical periodontitis

Under healthy conditions, the dental pulp and the apical periodontium are sterile. The dental pulp can become infected as a consequence of profound dental caries, dental trauma, or via extra-radicular root canals from deep periodontal pockets. Most frequently, the dental pulp is infected via dentinal tubules in relation to caries and with access to the oral cavity (13). Bacteria from the caries lesion and saliva can penetrate to the vital pulp and initiate an inflammation in the pulp tissue, called pulpitis (14).

If early pulpitis is left untreated, the inflammation develops into an irreversible condition and the pulp gradually becomes necrotic. As the disease develops, the microflora in the root canal becomes more complex, and a biofilm will develop on the inner surfaces of the root canals (14). When the dental pulp is fully necrotic, the biofilm may extent through the apical foramen of the root to the outer wall of the apical part of the tooth resulting in an inflammation in the periapical tissue (14, 15).

In early pulpitis, the microflora is very simple and dominated by caries-related bacteria. As the biofilm advances through the dentinal tubules to the pulp the available nutrients change. Dentinal fluid and collagen and eventually necrotic tissue from the pulp and tissue surrounding the apex of the root will favor the growth of proteolytic bacteria like gram-negative anaerobic species such as *Prevotella, Porphyromonas, Eubacterium, Parvimonas*, and *Campylobacter* species (16, 17). Thus, as the disease develops, the complexity of the root canal microflora increases with dominance of gram-negative anaerobic rods and

proteolytic bacteria. When bacteria get access to the pulp via extra radicular root canals from periodontal lesions, the microbiota will be almost similar to the microbiome seen in chronic periodontitis (see below). As for dental caries, recent 16S rRNA-based molecular biological studies have shown that the microflora in the root canal is far more complex than previously assumed. Uncultivable bacteria such as species of the genera *Treponema*, *Dialister*, *Olsenella*, and unnamed clones of *Synergistes* have been found in addition to the cultivable microflora described above. At persistent infections in root canals, *Enterococus faecalis* has been observed as a bacterium difficult to eliminate (14).

Elimination of the biofilm

A matter of vital importance for a successful endodontic treatment is elimination of the biofilm on the root canal surfaces. This requires mechanical removal of the infected pulp tissue and cleaning of canal walls and dentinal tubules combined with irrigation with antiseptics such as sodium-hypochlorite followed by a total sealing of the root canal in order to prevent reinfection of the root canal.

The biofilm may be difficult to eradicate, in particular at the apex of the tooth where a labyrinth of accessory infected canals may be present. In such cases, surgical intervention may be necessary with resection of the apex of the root in order to remove the biofilm.

Periodontal diseases

Inflammation in the gingival tissues develops if insufficient oral hygiene allows a supragingival biofilm to accumulate along the gingival margin. If the biofilm is left undisturbed, periodontal pockets will develop and periodontitis will usually follow. Periodontitis is classified as chronic or aggressive periodontitis. Generally, chronic periodontitis appears from about the age of 40 years, whereas generalized or localized aggressive periodontitis appear earlier in young adults or even in adolescents or children. The different forms of periodontitis have different clinical pictures. Around dental implants, periimplantitis may occur, an inflammation with similarities to periodontitis.

Gingivitis

Under healthy conditions, the microflora at the gingival sulcus is sparse and gram-positive oral streptococci are dominating (11). When a biofilm develops, it causes gingival inflammation including marginal swelling, initiation of pocket formation, and increasing exudation of gingival crevicular fluid rich in proteinous nutrients. In 1–2 weeks, a mature biofilm develops consisting of a rather complex microflora comprising both gram-positive cocci and rods and gram-negative rods of different sizes of which many genera and species are anaerobic (11). The total amount of bacteria in the biofilm is about 10^8 to 10^9 per mg and members belong to the resident microbiota. The development of disease can be designated to the unspecific biofilm/plaque hypothesis where all bacteria present contribute to the inflammation, while the ecological biofilm/plaque hypothesis adds to the explanation by ascribing the shift in the microflora to local ecological changes (11).

Biofilm control. As for preventing caries, removal of the supragingival biofilm and reestablishing a microflora compatible with health by daily oral hygiene measures will eliminate the gingival inflammation. Professional mechanical cleaning of the teeth will reverse the inflammation of gingiva to a healthy condition, if it is followed by oral hygiene at home twice a day by use of toothbrush, toothpicks, and/or dental floss.

Chronic periodontitis

If a supragingival biofilm is left undisturbed, it will spread into the periodontal pocket establishing a subgingival biofilm. The biofilm and the ongoing inflammation will gradually result in deepening of the periodontal pockets, destruction of periodontal fibers providing attachment of the teeth in the alveolar bone, degradation of the bone, and ultimately loss of teeth. In contrast to gingivitis, the tissue destruction in periodontitis is irreversible.

The composition of the subgingival microbiota differs from that of the supragingival biofilm as it is dominated by different kinds of gram-negative rods like *Prevotella* species, *Porphyromonas gingivalis*, and *Fusobacterium nucleatum* and including motile bacteria and spirochetes located at the surface of the biofilm in direct relation to the pocket epithelium (Fig. 3). The majority of the bacteria are anaerobic and have a proteolytic metabolism. These are favored by the local anaerobic conditions in the periodontal pocket rich in gingival crevicular fluid, which is a tissue exudate resembling serum and rich in proteins and blood products. Thus, the ecological biofilm/plaque hypothesis can explain the shifts in composition of the biofilm and development of periodontal disease (11).

Based upon comprehensive DNA–DNA hybridization, cross-sectional association studies on the development of subgingival biofilm (plaque) in 1998, the microbiota was grouped in different colored complexes based on their typical interspecies associations and sequential colonization. The yellow complex comprises the oral streptococci which

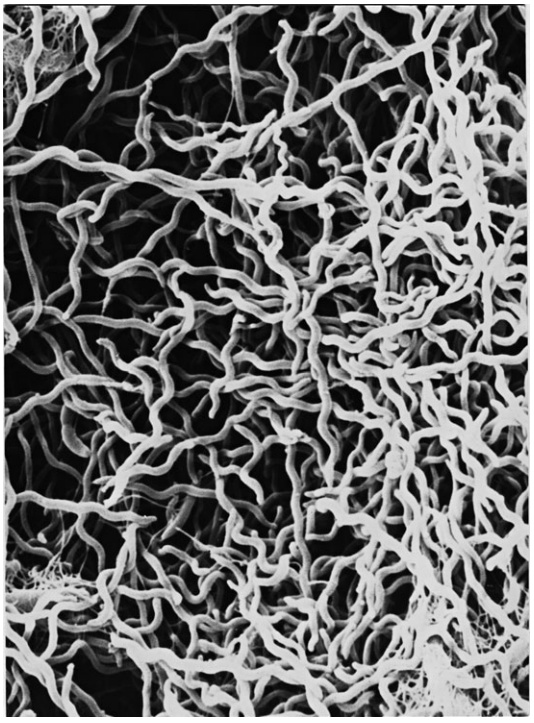

Fig. 3. A subgingival biofilm dominated by spirochetes.

together with *Actinomyces naeslundii* are primary colonizers and compatible with periodontal health; the violet and green complexes add *Veillonella parvula*, *Actinomyces odontolyticus*, *Eikenella corrodens*, *Aggregatibacter actinomycetemcomitans* serotype a, and different species of *Capnocytophaga* to the biofilm and initial disease emerges; the following orange complex contains anaerobic bacteria, e.g., *Prevotella* species, *F. nucleatum, Eubacterium,* anaerobic streptococci, and motile *Campylobacter* species, which are involved in development of periodontitis; finally, in the red complex, *P. gingivalis*, *Tannerella forsythia*, and *Treponema denticola* are observed (18). Especially bacteria of the orange and red complexes express tissue destructive virulence factors such as different proteolytic enzymes, cytotoxic substances, and toxins. They are, however, dependent on the adhesive properties of proceeding bacterial complexes to colonize the periodontal pocket. Thus, development of disease is a result of a concerted action of the total biofilm community. In addition to direct tissue destructive properties, some of the subgingival bacteria have different abilities to inhibit and interact with cells and components of the immune system interfering with host reactions. Thus, the biofilm bacteria both have a direct tissue destructive effect on the periodontium and an indirect inflammatory destructive effect via the immune system. It is generally agreed that direct bacterial destruction is responsible for initiation of disease, while the main tissue destruction is due to the host response (19).

The genera and species mentioned above belong to the resident oral microbiota recruited to the gingival area from different sites in the oral cavity. As for the supragingival microbiota, recent studies using more advanced molecular biological methods have added to the number of species identified, although not yet properly characterized. Further, a recent Dutch cultivation study showed that non-oral gram-negative facultative rods like *Bordetella bronchispetica, Pasteurella* species, and *Neisseria zoodegmatis* occurred in the subgingival biofilm in association with *P. gingivalis* and *T. forsythia* in patients recently treated with mechanical debridement therapy (20). So, it cannot be excluded that exogenous bacteria may be involved in chronic periodontitis.

Biofilm control. The main points in the treatment of chronic periodontitis are professional mechanical removal of the subgingival biofilm and instruction of the patient in thorough oral hygiene. The professional removal of biofilm including dental calculus is carried out with different types of scalers and ultrasonic devices, and the patient's own oral care is carried out with toothbrush, inter-dental brush, toothpicks, or dental floss at least twice a day. This treatment regime will result in a reduction of periodontal pockets and change the pocket biofilm microbiota to be dominated by bacteria from the yellow complex (and possibly the violet and green complexes) compatible with periodontal health. If the resulting pocket reduction is not sufficient, a supplemental surgical pocket reduction may be carried out leading to further improvement of the patients' own oral care.

Aggressive periodontitis

While about 50% of the adult population over 50 years of age develop chronic periodontitis, only a few percent develop aggressive periodontitis. The disease can be localized or generalized depending on the number of periodontal sites affected by tissue destruction. Tissue destruction can develop very rapidly and sometimes it is difficult to arrest disease progression. As in chronic periodontitis, the aggressive forms are initiated by bacteria located in the subgingival biofilm. However, very often the amount of bacteria is sparse and the supragingival biofilm barely visible. Aggressive periodontitis may be associated with functional abnormalities of the neutrophils or other parts of the immune system (21).

Cultivation studies of the subgingival biofilm have shown that bacteria in the orange and

particularly the red complex are associated with aggressive periodontitis. However, recent 16S rRNA-based molecular biological techniques have revealed that the microbiota is much more complex. Species of the genera *Parvimonas*, *Filifactor*, *Dialister*, *Granulicatella*, and *Synergistes* (many of which are uncultivable) are found together with cultivable species belonging to the orange and red complexes (22). So, it is still not fully elucidated which subgingival bacterial profiles are responsible for development of disease, and furthermore, the role of novel and uncultivable bacteria has not yet been clarified (23).

In localized aggressive periodontitis of juveniles, *A. actinomycetemcomitans* serotype b has for years been regarded as the key etiologic agent. In the studies that formed the basis for description of the complexes, this serotype was not associated with any other bacterial species (18). This has raised discussions on *A. actinomycetemcomitans* serotype b possibly being an (as intended) exogenous bacterium causing periodontitis. A particular clone (JP2) of this subspecies has been isolated from people of North West African origin and identified as a major risk factor for aggressive periodontitis. This clone is characterized by a 530-base pair deletion in the promotor region of the gene coding for production of leukotoxin, causing a significant increase in leukotoxin production, and consequently an increased risk of developing severe disease (24).

Following antibiotic therapy resulting in a decreased colonization resistance, some studies have observed that periodontal pockets can be colonized by non-oral bacteria such as staphylococci, pyogenic streptococci, enterobacteria, and *Candida* species (25). This may result in aggressive periodontitis.

Biofilm control. The main efforts in the control of the biofilm in aggressive periodontitis correspond to those described for chronic periodontitis. But as the tissue destruction takes place much faster in aggressive periodontitis, the patient must be controlled in the dental office more frequently. Furthermore, the basic control may be supplemented with biofilm reducing agents such as chlorhexidine rinsings. In the treatment of refractory cases, antibiotics may also be used as a supplement to mechanical or surgical debridement to change the subgingival microbiota to a profile compatible with periodontal health.

Peri-implantitis

Colonization of dental implants and the associated supra structures share similarities with biofilm formation around natural teeth, both in the development and in its role in initiation of disease. When the tissues supporting the osseointegrated implants are affected it is termed peri-implantitis (11). As for periodontitis, peri-implantitis can be aggressive with suppuration and bone loss and may lead to the loss of the "implant tooth". With the increasing use of dental implants, peri-implantitis is an emerging disease and it is too early to estimate the incidence of peri-implantitis. Again, a good oral hygiene is crucial for preventing development of disease.

The microbiological sampling around dental implants is complicated on account of the irregularities of implant surfaces making it difficult to reach the bottom of the "implant pocket". Based on both cultural studies and recent molecular biological studies, the microflora seems to be comparable with the subgingival biofilm at periodontitis teeth, despite variations are observed depending on the implant material used, the roughness of the surface, and the implant design. Roughness of the surface may in particular facilitate biofilm formation (26).

The peri-implant biofilm microbiota differs between implants placed in edentulous patients and partially edentulous patients. It seems that the last-mentioned group has a more pathogenic peri-implant microflora than do the edentulous patients (27). Very likely the source of the microbiota is the subgingival biofilm around natural teeth with periodontitis in the partially edentulous patients.

Biofilm control. The treatment principles for peri-implantitis do not differ from periodontitis, i.e., biofilm formation should ideally be prevented by proper oral hygiene measures and – when established – removed by mechanical procedures by the patient and professionally by the dentist. The rough surfaces of the implants can pose a challenge in achieving total biofilm removal making the prevention of biofilm formation even more important.

BACTERIA IN DENTAL BIOFILMS AND SYSTEMIC DISEASES

Bacteria from the dental biofilm may spread to other parts of the body via bacteremia. This may occur in connection with dental treatment causing bleeding, e.g., tooth extractions, oral surgery, and subgingival scaling in patients with periodontitis. Daily habits such as tooth brushing and chewing can also cause bacteremia, especially in periodontal patients. Generally, oral bacteria are eliminated from the vascular system within 30 min and do not cause health problems (28). But seldomly infections in other parts of the body may arise. Thus, several

casuistic papers have reported development of respiratory, gastrointestinal, and brain abscesses caused by oral bacteria following oral infection or treatment. However, the most well-established systemic infection caused by dental bacteria is infectious endocarditis, where oral streptococci are the second most commonly reported causative agents (29). Upon entering the circulation, the streptococci colonize the endocardium, especially in risk patients with previous endocardial lesions and establish a pathogenic biofilm initiating and maintaining disease. Thus, as bacteremia with oral bacteria is more prevalent in periodontal patients, establishing proper oral hygiene habits and professional periodontal treatment is an important prophylactic measure in preventing development of infectious endocarditis (30).

Aside from direct spreading, dental biofilm bacteria may influence other parts of the body and contribute to systemic diseases in a more indirect manner. A number of epidemiologic studies have shown a correlation between periodontitis and diabetes mellitus, atherosclerosis, and rheumatoid arthritis (31–33). This can be explained by the effect of inflammatory mediators induced by periodontal pathogens in subgingival biofilms and subsequently distributed systemically. This connection has been confirmed for diabetes mellitus, while it remains to be well established for the other diseases. As for diseases caused by direct spreading of oral bacteria, disease development can be prevented by controlling the dental biofilm by proper oral hygiene measurements.

CONCLUSION

All surfaces in the oral cavity are colonized by a resident microflora which is in balance with the oral tissues. This balance is referred to as homeostasis. The resident microflora is beneficial to the host and protects the tissues against colonization by exogenous microorganisms that may be pathogenic. If this homeostasis is stressed, the profile of the resident microflora changes and disease may develop. If homeostasis in the dental biofilm is broken, it may lead to development of caries and/or periodontal diseases. The treatment of these diseases must result in reestablishment of a dental biofilm which is compatible with health. This is referred to as biofilm control in this article. Only when a biofilm develops at a site which is sterile under healthy conditions, e.g., in infected root canals and at the apex of the root, the treatment must lead to an elimination of the biofilm. At all other sites, biofilm control implies reestablishment of a homeostatic biofilm comprising a resident microflora.

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