Caries and periodontal disease: Two diseases, one biofilm

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Introduction

Dental plaque, a natural oral biofilm is involved in the aetiology of dental caries and periodontal disease. Despite decades of research, the microbiology, aetiology and pathogenesis of these diseases remain controversial. A number of factors interplay in these diseases, the indigenous microbes that inhabit the oral cavity, diet, host susceptibility and time. The 'Non-Specific Plaque Hypothesis' (NSPH) was proposed where the overall mass of plaque interacted with the host and caused disease [1]. An alternative view was the 'Specific Plaque Hypothesis' (SPH) where, among the diverse microbial community, a limited subset of specific bacteria were associated with disease [2]. In recent years, the 'Ecological Plaque Hypothesis' (EPH) has been proposed that it be recognised that the oral ecology as a whole contributes to the aetiology of dental caries and periodontal diseases, with shifts in the composition of microbial communities being of particular importance [3].

Indigenous microbiota

The indigenous microbiota of human adults is a complex microbial community that grows and structures as a biofilm. Microbes in the biofilm are grouped into micro-colonies that communicate via water channels and these micro-colonies are protected by an extracellular matrix [3]. The structure of the biofilm enhances the survival, colonisation, retention and succession of different species. Species within the dental biofilm are more resistant to anti-microbials than planktonic bacteria [4] and this impacts significantly on the prevention and management of dental caries and periodontal diseases.

Dental caries

Dental caries is a 'chronic endogenic multifactorial bacterial infection' [5] with mutans streptococci and lactobacilli long being recognised as the primary cariogenic bacteria [2]. These Gram positive facultative bacteria are characterised by marked acidogenicity and aciduricity. In particular, *Streptococcus mutans* and *Streptococcus sobrinus* are important for the initiation of dental caries and lactobacilli are implicated with caries progression [2]. *S. mutans* has received much attention in scientific research since the 1960s when Keyes demonstrated its cariogenicity in experimental animals [6]. They were previously believed to colonise only non-desquamating surfaces and, thus, generally infect the oral cavity at the time of eruption of the primary incisors [7]. Studies by Wan *et al* [8,9] showed that mothers with high carriage rates of *S. mutans* and a history of frequent, sweetened fluids were a high risk factor for their infants (Figure 1). *S. mutans* was detected in the mouths of predentate infants as young as three months of age. This early colonisation amongst predentate infants was associated with the presence of oral developmental nodules (Figure 2) [9]. Earlier colonisation time has clinical significance and increases the risk of caries [10]. Therefore, preventive and interventive strategies may need to be implemented at a much earlier age than is currently recommended.

Recently, a group of low pH non-mutans streptococcus bacteria *Streptococcus oralis* and *Streptococcus mitis,* has also been implicated as important cariogenic bacteria [11]. These low pH bacteria species are believed to contribute to the development of dental caries as much as species labelled as cariogenic. Furthermore, it has been proposed that the overall amount of acids produced in the oral environment and the associated homeostatic imbalance matter more in dental caries development than specific bacteria, which are likely to play an associative rather than a causative role [12]. This concept shift has already begun to influence the preventive and interventive strategies employed against dental caries.

Figure 1. Early childhood caries – infant (A) and Mother (B) both with high *S. mutans* counts, history of sweetened fluids in bottle and frequent consumption.

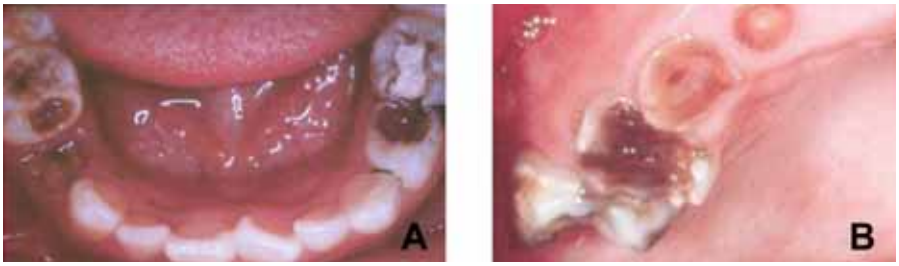
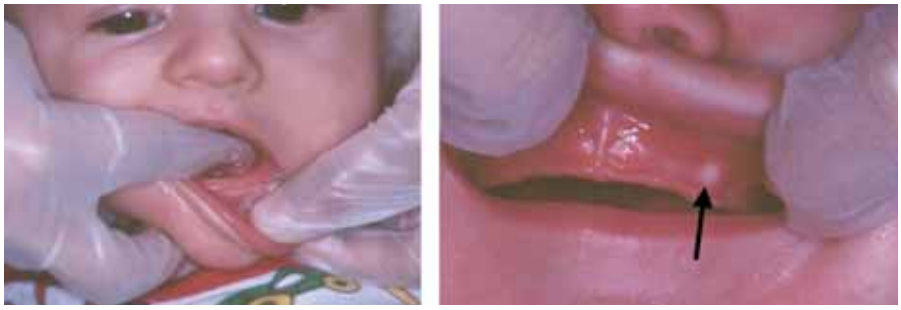


Figure 2. Oral developmental nodules (arrow) in predentate infants significantly increases the risk of early colonisation of *s. mutans.* Earlier intervention with chlorhexidine gel may reduce the risk of early colonisation.



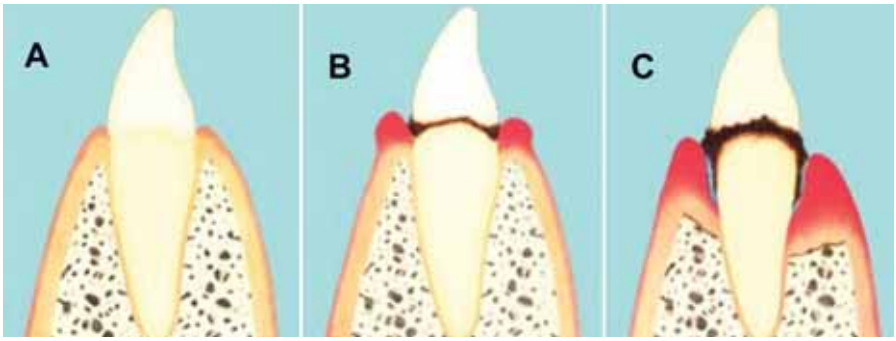
Periodontal Diseases

Periodontal diseases are those that affect the periodontium, the supporting structures of the tooth including the bone and periodontal ligament. Dental plaque is essential for the development of the common inflammatory periodontal diseases, gingivitis and periodontitis (Figure 3A). The pathogenesis of periodontal diseases depends again on whether presence of specific bacteria (SPH) are important or solely the magnitude (total mass) of plaque (NSPH).

Gingivitis (Figure 3B), a reversible condition leading to inflammation of the gingival margin, is almost ubiquitous in the population. This results from the interaction of supra-gingival plaque with the host with increased plaque deposits leading to more severe gingivitis. Furthermore, the observation that the removal of plaque leads to resolution of gingivitis suggests that the magnitude, rather than composition, of plaque is responsible for gingivitis. This has led to the acceptance that the NSPH applies to the pathogenesis of gingivitis.

Periodontitis differs from gingivitis in that it affects the deeper tissues of the periodontium and results in tissue loss around the tooth and ultimately tooth loss (Figure 3C). Approximately 40-50% of the population suffers from periodontitis. Periodontitis is caused by sub-gingival plaque which differs significantly from the supra-gingival plaque that causes gingivitis. The subgingival plaque is composed of at least 500 different bacterial species. In the early 90s, three bacteria, *Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans* and *Tannerella forsythenesis* were strongly associated with periodontitis and were labelled defined pathogens. Therefore, the specific plaque hypothesis applies to the pathogenesis and progression of periodontitis. However, it is now being recognised that complexes or groups of bacteria rather than single species are responsible for periodontitis and its progression [13]. This observation is supported by the findings that certain defined pathogens are transiently expressed in both periodontitis-affected and healthy subjects. Therefore, although it is recognised that the quality or composition of plaque does have an impact on periodontal attachment loss, it is the co-dependent groups of bacteria, rather than individual species, that are important in the pathogenesis and progression of periodontitis.

Figure 3. Diagrammatic representation of healthy periodontium (A), gingivitis presenting as marginal inflammation without associated attachment loss (B), and periodontitis presenting as inflammation associated with bone and soft tissue destruction (C).



Prevention and Intervention

Given that the aetiology of dental caries and periodontal diseases are multifactorial, effective prevention and intervention must target multiple factors by reducing risk / pathological factors, enhancing protective factors and promoting homeostasis in the oral environment. Currently, some of the most widely used strategies focus on the microbiological aspect of the two diseases.

Various chemotherapeutics, such as high concentration fluoride, xylitol and povidone-iodine have been used against cariogenic bacteria. In addition, anti-caries vaccines (including both passive and active immunisation methods), mutant microbial strains and microbial replacement therapy have also been proposed as preventive strategies against specific cariogenic bacteria. However the most potent anti-microbial agent used for the control and prevention of dental caries is chlorhexidine gluconate [14]. Various forms e.g. gels, mouth rinses, varnishes and concentrations (ranging from 0.1%-40%) of this bisbiguanide have been shown to reduce mutans streptococci in children and adults with active caries or high caries risks even with short term use [15]. Wan and co-workers [16] conducted the first placebo controlled randomised double-blind clinical trial using weekly applications of 0.2%

chlorhexidine gluconate gel in infants colonised with *S. mutans* and showed that the numbers of *S. mutans* were significantly reduced in the first three months especially for infants with relatively low initial *S. mutans* counts and suggested that the application of chlorhexdine gel pre-colonisation or immediately post-colonisation may prevent or delay *S. mutans* colonisation in infants. Chlorhexidine has also been used in mothers to prevent, reduce or delay transmission of mutans streptococci to their infants [17].

With regards to the treatment and intervention in periodontal disease, and more specifically periodontitis, it is important to recognise that the bacteria do not directly cause the tissue loss evident in these diseases. Indeed, the host response to the presence of the plaque is responsible for the tissue destruction associated with periodontitis. Furthermore, the nature of the response to the plaque is not only dependent on its composition but also on the inherent susceptibility of the host, which is determined by systemic (e.g. diabetes), environmental (e.g. smoking) and genetic factors [18]. Therefore, it is clear that the presence of plaque is essential, it is insufficient for the pathogenesis and progression of periodontitis in a non-susceptible patient.

These findings have important implications for the treatment and intervention of periodontitis. Mechanical debridement remains the primary mode of treatment as antibiotics and mouth rinses are unable to penetrate the subgingival biofilm. However, in patients suffering from periodontitis who already have attachment loss around the teeth, it is difficult to completely remove all plaque. If these patients are particularly susceptible to the presence of even small amounts of plaque, then periodontitis will progress. In these patients, a different therapeutic approach consisting of modulating the host response has been suggested as an adjunct to mechanical therapy.

Regenerative therapy aimed at reconstituting the tissues that have been lost due to periodontitis has been proposed in order to improve aesthetics, as well as remove the plaque retaining environment around the affected teeth, thus improving the prognosis. However, regeneration has proven difficult due to the challenging intraoral environment and the complex composition of the periodontium. The use of tissue engineering, stem cells and growth factors has shown promise in our efforts to regenerate the periodontium. The viability of this approach is supported by the finding that autologous periodontal ligament cells grown in-vitro can be re-implanted into the periodontal defect to induce regeneration [19]. Furthermore, cells derived from regenerating defects have been shown to have superior regenerative therapies and respond to growth factors [19].

Conclusion

Trends in oral disease will see a steady decline in caries in young people due to oral health strategies and reduction of cariogenic colonisation rates using chlorhexidine gel intervention to control the supra-gingival dental biofilms. However, in an aging populations, the retention of teeth will increase the risk of periodontitis. A concomitant improvement in oral care will be required in order to achieve a decline in the prevalence and severity of periodontal diseases. Furthermore, despite rapid advances in the areas of immunopathology and molecular genetics which are transforming and enhancing our understanding of oral pathogens, the nature of their interaction with the host environment during pathogenesis is still not fully understood. The most effective preventive and treatment strategies still aim to remove the microbial biofilm in order to prevent and control the pathological processes.

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