

## Microbes, Inflammation, Scaling and Root Planing, and the Periodontal Condition

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### Introduction

Typically, the term “periodontal disease” refers to gingivitis and periodontitis, both common inflammatory diseases that involve a variety of pathogenic bacterial species and an innate host response to those bacteria.<sup>1</sup> Gingivitis, the most familiar form of inflammatory periodontal disease, has a high prevalence rate, affecting 50%-90% of adults worldwide.<sup>2,3</sup> By definition, gingivitis is limited to an inflammation that involves only the gingival soft tissues, ie, gingival epithelium and subjacent fibrous connective tissues. In spite of its high prevalence rate and worldwide distribution, biofilm (plaque)-induced gingivitis is preventable and rather easily reversed by routine oral hygiene measures.

Inflammation that extends into the deeper tissues to involve bone, resulting in resorption of tooth supporting bone, is termed periodontitis. Concomitant with the loss of bone is the formation of a deepened space between the root of the tooth and the gingiva, a periodontal pocket. Periodontitis can present as a chronic and slowly progressing disease (most common form) or as an aggressive disease causing loss of bone over a relatively short period of time. Periodontitis of advanced severity can result in tooth mobility, occasional pain and discomfort (generally associated with abscess formation), impaired ability to masticate food, and eventual tooth loss.

Although more common to adults, epidemiologic data indicate that periodontitis can also be found in children and adolescents.<sup>4,5</sup> In the United States, chronic periodontitis is more prevalent in men than women, and in African Americans, Native Americans, and Mexican Americans than Caucasians.<sup>2,6,7</sup> Various epidemiology studies, when

### Abstract

Biofilms are a complex community of microorganisms characterized by the excretion of an adhesive and protective extracellular matrix, microbe-to-microbe attachment, structural heterogeneity, genetic diversity, and complex community interactions. Bacteria growing in dental biofilms display an increased tolerance to antibiotics and antimicrobial agents, including those used in dentifrices and mouthrinses.

The microbial challenge associated with the inflammatory periodontal diseases induces an immediate inflammatory and immune response in the host. The nature and magnitude of the response has an impact on the severity and rate of progression of the periodontal disease. It is this host inflammatory-immune response that ultimately leads to the clinical signs and symptoms of gingivitis and chronic periodontitis. The traditional treatment modality of scaling and root planing (SRP) remains the “gold standard” for the non-surgical management of chronic periodontitis. Even clinically successful treatment has a high probability of pocket re-infection. Re-infection of periodontal pockets results from residual biofilms, increased tolerance of microbes within a dense, mature biofilm to antibiotics, reservoirs of bacteria in calculus, and reservoirs of bacteria within the dentinal tubules of infected root surfaces. Thus, for maximum effect, a combination of scaling and root planing and locally delivered antimicrobials should be considered if non-surgical therapy is the treatment of choice.

**Keywords:** periodontal disease, periodontal infection, chronic periodontitis, scaling and root planing, dental biofilm

considered in aggregate, suggest a progressive decrease in the prevalence of periodontitis between the years 1988-2004.<sup>7-11</sup> The more recent of these studies indicate a prevalence rate for moderate to advanced periodontitis ranging from approximately 5% to 15% for individuals > 18 years of age.<sup>9-11</sup> Given the current US Department of Census projections, a 5% to 15% prevalence rate translates to 11 to 33 million US adults that may exhibit periodontitis of moderate to advanced severity.<sup>12</sup> If one includes slight severity, the prevalence rate for periodontitis increases to approximately 30% of the US adult pop-

ulation, or roughly 65 million individuals.<sup>9-12</sup> However, all epidemiology studies that have reported on the prevalence of chronic periodontitis have utilized partial-mouth examinations, which tend to underestimate prevalence, extent, and severity of disease.<sup>13-15</sup>

### Microbes and Biofilm

A biofilm is a complex community of microorganisms characterized by the excretion of an adhesive and protective extracellular matrix, microbe-to-microbe attachment, structural heterogeneity,

genetic diversity, and complex community interactions. Dental plaque is a microbial biofilm (Figure 1). As with any biofilm, the constituent microbes are tightly adherent to each other and to an oral substrate by means of an extracellular matrix, ie, slime layer or glycocalyx, into which they are embedded.<sup>16,17</sup> The microbial populations in biofilm have 2 strategies that enable them to successfully survive within their community. The first is a high rate of reproduction for continued survival, and the second is physiologic adaptation to the available environmental resources or life-supporting capacity of the environment.<sup>18</sup>

Biofilms inherently dictate profound changes in the behavior of individual microbes, their relationship to the host, and their response to environmental conditions.<sup>19</sup> Indeed, oral biofilms, as distinct entities, are the causative agents of biological processes such as dental caries, periodontal disease, and peri-implantitis, rather than any single microbe evading the host defense and causing disease.<sup>20</sup> Biofilms exhibit characteristics that impact the clinical management of inflammatory periodontal disease. For example, both altered patterns of microbial gene expression and the composition and density of the

extracellular matrix reduce the susceptibility of microbes to antimicrobial agents.<sup>21-23</sup> Bacteria growing in dental biofilms display an increased tolerance to antimicrobial agents, including those used in dentifrices and mouthrinses.<sup>24-27</sup> In addition, confocal microscopy of *in situ* established natural biofilms showed that chlorhexidine only affected the outer layers of cells in 24 and 48 hour plaque biofilms, suggesting either quenching of the agent at the biofilm surface or a lack of penetration.<sup>28</sup> Further, biofilms of oral bacteria are also more tolerant of antibiotics (eg, amoxicillin, doxycycline, minocycline, and metronidazole) than planktonic cells.<sup>29-31</sup> In this regard, biofilms of *Porphyromonas gingivalis* have been shown to tolerate 160 times the minimum inhibitory concentration (MIC) of metronidazole that was determined for planktonic cells.<sup>32</sup>

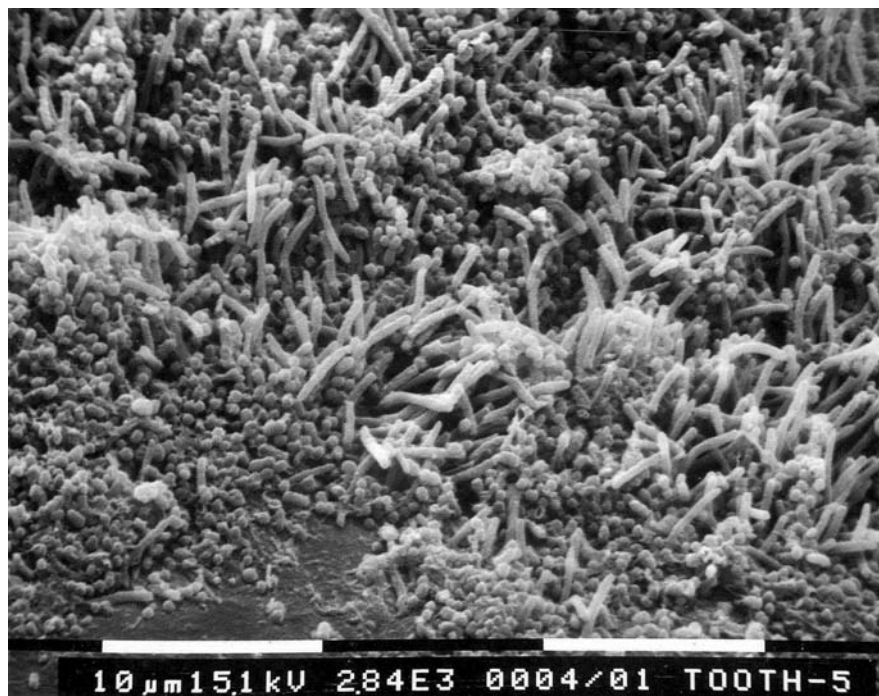
Over 700 species of aerobic and anaerobic bacteria have been identified in the human oral cavity.<sup>33,34</sup> The microbes grow as complex, mixed, interdependent colonies in biofilms, and may achieve considerable thickness, achieving a thickness of 1 mm within 96 hours, if left undisturbed.<sup>16,17</sup> Oral biofilms, like all microbial biofilms, exhibit a successional colonization with

gram-positive aerobic *Streptococci* species (spp.) being the initial colonizers, followed in sequence by *Actinomyces* spp., *Corynebacterium* spp., *Veillonella* spp., and then in more mature biofilm, a variety of gram-negative anaerobic microbes such as *Treponema* spp., *Fusobacterium* spp., *Porphyromonas* spp., *Prevotella* spp., and *Tannerella* spp.<sup>17,35,36</sup>

As the biofilm is allowed to mature with concomitant increases in thickness, the percentage of Gram-negative anaerobic microbes increases. Specific complexes of such microbes commonly cohabit subgingival sites and are consistently associated with inflammatory periodontal diseases.<sup>35</sup> These putative microbial pathogens include *Porphyromonas gingivalis*, *Tannerella forsythia*, and *Treponema denticola*.<sup>35</sup>

In the human host, the transition from gingivitis to periodontitis does not occur automatically, either in every patient or every site, but depends on 3 factors: 1) degree of host susceptibility, 2) presence and numbers of pathogenic bacteria, and 3) presence and numbers of protective bacteria.<sup>36</sup> Pathogenic bacteria exhibit virulence features that decrease the effectiveness of the host response by inducing tissue degradation and retarding attempts at healing.

Host defense mechanisms are impaired through a variety of mechanisms. As one example, consider that *Aggregatibacter* (formerly *Actinobacillus*) *actinomycetemcomitans* produces a leukotoxin that alters the cell membranes of neutrophils and monocytes and thereby alters chemotactic and phagocytic responses.<sup>36</sup> Infection with Gram-negative anaerobes is accompanied by the release of epitheliotoxins, endotoxins, leukotoxins, collagenase, gellanase, elastase, fibrinolysins, and other proteolytic enzymes.<sup>37</sup> These bacterial toxins and enzymes are tissue irritants and/or cytotoxic and viewed by the host immune system as foreign proteins (Figure 2). The aggregate cellular/tissue insult activates the host immune system locally and is generally visualized at a clinical level as inflammation with all the inherent gingival changes, eg, vasculitis, edema and swelling, change in tissue color from white-pink to red or red-purple, and spontaneous gingival bleeding or bleeding on provocation.<sup>38</sup>

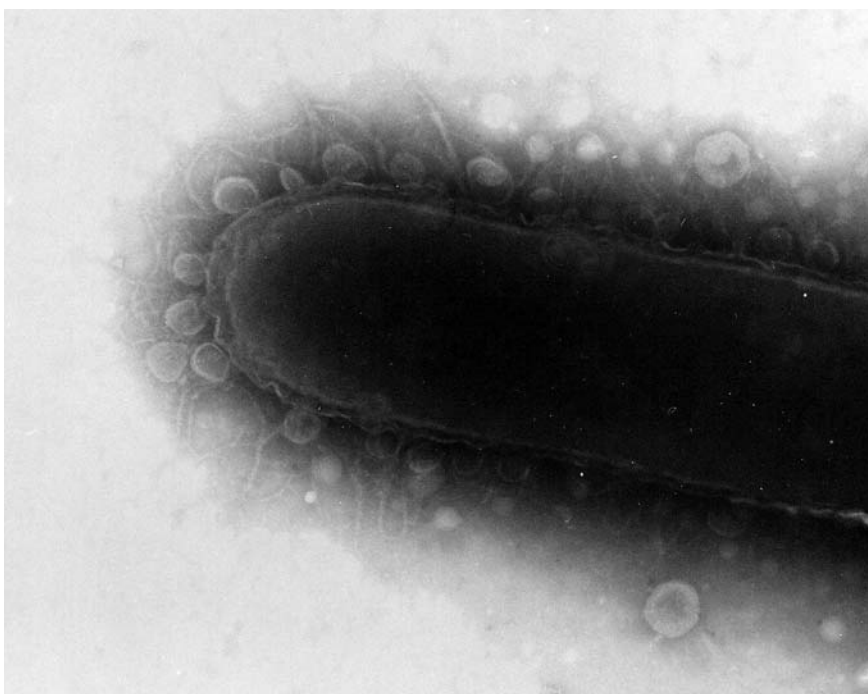


**Figure 1. Scanning electron microscopic photograph of root associated dental biofilm (plaque). Bar = 10 micron at an original magnification of 2840x.**

## Role of the Host Immune Response

Bacteria are necessary but not sufficient by themselves to produce a destructive periodontal disease. Disease initiation and progression requires a susceptible host.<sup>38</sup> The microbial challenge induces an immediate inflammatory and immune response in the host. The nature and magnitude of the response have an impact on the severity and rate of progression of the periodontal disease.<sup>39</sup> Locally, bacteria and their metabolic byproducts stimulate a cellular immune response within the affected gingiva represented by a dense infiltration of neutrophils, macrophages, and lymphoid cells. These cells and host connective tissue cells within the developing inflammatory lesion are stimulated to synthesize and release proinflammatory cytokines, prostanooids, and proteolytic enzymes, eg, interleukin-1 (IL-1), interleukin-6 (IL-6), interleukin-8 (IL-8), tumor necrosis factor-alpha (TNF- $\alpha$ ), prostaglandin E<sub>2</sub> (PGE<sub>2</sub>), matrix metalloproteinases.<sup>38</sup> It is this host inflammatory-immune response that ultimately leads to the clinical signs of gingivitis and chronic periodontitis and their characteristic features of fibrous connective tissue degradation, resorption of tooth supporting alveolar bone, and periodontal pocket formation.

In contrast to the epidermis of skin, the epithelial lining of the soft tissue wall of a periodontal pocket lacks a stratum corneum and stratum granulosum. Consequently, the pocket epithelium is easily ulcerated and breached by invasive subgingival pathogenic bacteria.<sup>40</sup> In addition, endotoxins and other microbial antigens may gain access to the underlying connective tissues and gingival vasculature, leading to bacteremia and endotoxemia. There is considerable evidence that the locally produced proinflammatory cytokines and prostanoids gain access to the circulatory system and may, in turn, induce the production of liver-derived markers of a systemic inflammatory reaction, such as C-reactive protein, fibrinogen, serum amyloid-A, and haptoglobin.<sup>41-45</sup> Elevations in both the locally generated inflammatory mediators and systemic markers of inflammation have been associated with various systemic diseases such as ath-



**Figure 2. Transmission electron microscopic photograph of a negatively stained *Phorphyromonas gingivalis* featuring fimbriae and numerous surface blebs that likely contain endotoxin. Both fimbriae and endotoxin are potent antigens that solicit a host immune response. Original magnification of 35 000x.**

erosclerosis,<sup>46</sup> cardiovascular disease,<sup>47</sup> ischemic stroke,<sup>48</sup> pre-eclampsia,<sup>49</sup> and poor glycemic control in diabetic patients.

## Risk Factors Associated With Development of Chronic Periodontitis

In addition to the accepted associations of pathogenic microbes to the pathogenesis of inflammatory periodontal diseases, several genetic and environmental risk factors have been identified that affect the host response. It is well established that the prevalence and severity of chronic periodontitis increases with advancing age, poor oral hygiene, marginally or poorly controlled type I and II diabetes, and use of tobacco.<sup>51,52</sup> In addition, data from twin studies indicate that about 50% of the population variance in periodontitis can be attributed to genetic factors.<sup>53,54</sup> Several studies indicate that genetic polymorphisms (variations) in a cluster of at least 3 genes on chromosome 2q13,

which control the production of proinflammatory cytokines, may affect the systemic inflammatory response in a significant percentage of people with chronic periodontitis.<sup>55,56</sup>

## Scaling and Root Planing in the Control of Chronic Periodontitis

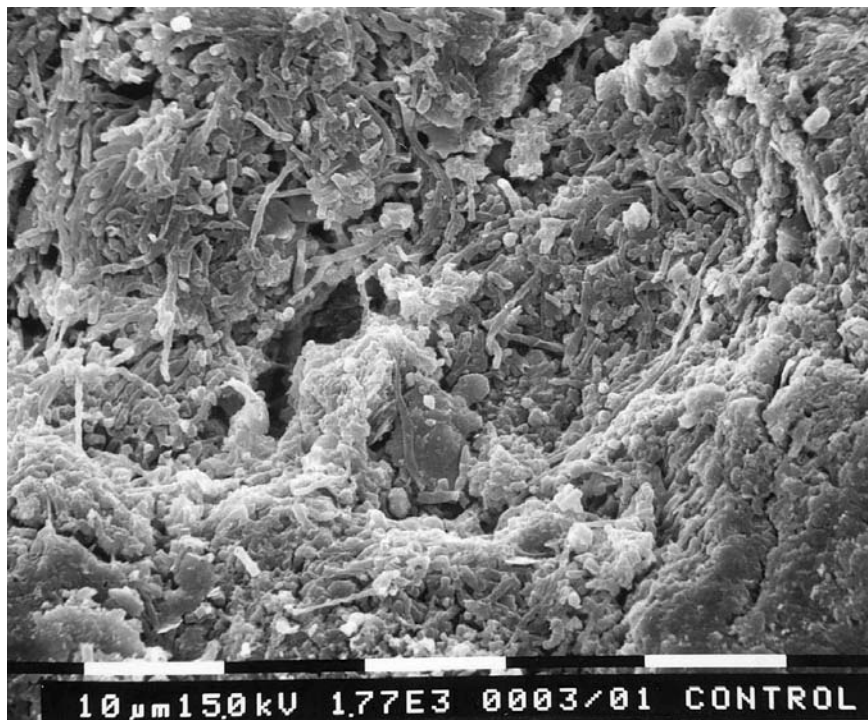
Periodontitis is a chronic and progressive inflammatory disease for which there is no known cure. It is now well-established that periodontitis is not associated with a single microorganism but rather the initiation and progression of periodontitis is the result of the host's immune response to a consortium of bacteria. For periodontopathic bacteria to initiate periodontitis, it is essential that they are able to colonize subgingival pockets and produce virulence factors that directly damage host tissue. Thus, a major goal of nonsurgical periodontal therapy is to suppress, to the extent possible, the subgingival pathogenic microbial flora and thereby signifi-

cantly reduce or eliminate the associated inflammatory lesion.

Dental calculus was the original etiologic agent associated with development of chronic periodontitis. In the 1960s and 1970s it was established that the rough, irregular surface of dental calculus was always covered with a non-mineralized microbial biofilm (Figure 3).<sup>57-59</sup> In addition to the surface biofilm, at least one recent study has identified the presence of several viable periodontal pathogens within the mass of dental calculus, ie, *Aggregatibacter actinomycetemcomitans*, *Treponema denticola* and *Porphyromonas gingivalis*.<sup>60</sup> Interestingly, the persistence of *Porphyromonas gingivalis* in the subgingival environment following periodontal therapy has been associated with progressive alveolar bone loss.<sup>61</sup> In support of this observation, Offenbacher et al<sup>62</sup> recently reported a significant association between serum immunoglobulin G (IgG) titers against *Porphyromonas gingivalis* in patients that exhibit deep PDs ( $\geq 4$  mm) and moderate ( $\geq 10\%$  to  $< 50\%$ ) and severe ( $\geq 50\%$ ) bleeding on probing.

In spite of the fact that calculus can serve as a reservoir for pathogenic microbes, the role of subgingival calculus, as an etiologic agent in chronic periodontitis, was relegated to secondary status once microbial biofilm was declared the primary, extrinsic etiologic factor. Thus, the need for complete removal of subgingival calculus became a subject for debate.<sup>63</sup> However, the traditional treatment modality of scaling and root planing (SRP) remains the “gold standard” for the nonsurgical management of periodontitis.<sup>64</sup>

The periodontal literature is replete with studies showing that treatment of periodontitis by SRP results in reductions in probing depth (eg, a mean reduction of 1.29 mm for 4-6 mm pockets and a mean of 2.16 mm for pockets of  $\geq 7$  mm) and subgingival bacterial loads and gains in clinical attachment.<sup>65-67</sup> Probing depth (PD) reduction is generally greater at sites with deeper initial probing depths. The decrease in PD is the result of 2 phenomena: shrinkage of the pocket soft tissue wall manifested as recession of the gingival margin which results from a decrease in soft tissue inflammation and the inherent edema; and gain in clinical attachment.



**Figure 3. Scanning electron microscopic photograph of dental calculus characterized by a superficial layer of microbial biofilm. Bar = 10 micron at an original magnification of 1,770x.**

The latter usually accounts for roughly one-half of the probing depth reduction.<sup>65-67</sup> In general, clinicians should evaluate post-SRP healing at 4 to 6 weeks following treatment. After 6 weeks, most of the healing has taken place but repair and collagen maturation may continue for an additional 9 months.<sup>67,68</sup>

Three relevant observations must be considered when deciding to use non-surgical therapy as the primary modality for treatment of early to moderate chronic periodontitis. First, regarding SRP, clinicians must be careful when interpreting data from published clinical trials as they may not accurately reflect the private practice setting in terms of time, skill level, severity of disease, and diversity of patient population.<sup>65</sup> For example, university-conducted clinical trials often use highly skilled clinicians, select patients for level of disease, and report spending 10 minutes per tooth when performing SRP.<sup>66,67</sup> Ten minutes per tooth equates to about 70 minutes per quadrant. It is the experience of this author that in private practice a quadrant of SRP may be completed in approximately 60 minutes, regardless of the level of disease, and

this allows approximately 10 minutes for setting of the patient and administration of anesthetic. Greenstein<sup>67</sup> has rightfully noted that decreased time devoted to SRP in more recent studies probably accounts for the diminished results reported when to the more classic clinical trials. Second, one must remember that microbes embedded in a mature, undisturbed subgingival biofilm may exhibit an increased tolerance to antimicrobial agents.<sup>28-32</sup> Third, even when chronic periodontitis is treated successfully, the reduction in subgingival pathogenic microbes is transitory. SRP of diseased root surfaces can open dentinal tubules, allowing invasion by periodontal pathogens into the exposed tubules, and possibly then serve as a reservoir for re-infection of the pocket.<sup>69,70</sup> Thus, the need for follow-up treatment, usually consisting of supra- and subgingival debridement at 3 to 4 month intervals, is necessary to maintain the initially gained beneficial effects.<sup>71,72</sup> Collectively considered, the distinct probability of less than ideal results from SRP and pocket re-infection by residual microbes is a forceful argument for the use of adjunctive treatment modalities in addition to SRP.

## Clinical Implications

1. The prevalence rate for chronic periodontitis (slight, moderate, and advanced severity) is approximately 30% of the US adult population or roughly 65 million individuals.
2. Bacteria growing in undisturbed dental biofilms exhibit a significant increased tolerance to antimicrobial agents and antibiotics.
3. The transition from gingivitis to periodontitis does not occur auto-

matically, either in every patient or every site, but depends on 3 factors: 1) degree of host susceptibility, 2) presence and numbers of pathogenic bacteria, and 3) presence and numbers of protective bacteria.

4. Even when chronic periodontitis is treated successfully, the reduction in subgingival pathogenic microbes is transitory. Thus, the need for follow-up treatment, usually consisting of supra- and subgingival debridement at 3 to 4 month intervals, is necessary to

maintain the initially gained beneficial effects.

5. Due to limitations of SRP and re-infection of the periodontal pocket, adjunctive treatment modalities may increase the likelihood of improvement in the periodontal condition.

## Disclosure

Dr. Cobb has served as a scientific advisor and consultant for OraPharma, Inc.

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