A REVIEW

Biofilm, the host response and treatment in periodontal disease

Fiona M. Collins, BDS, MBA, MA
A Review: Biofilm, the host response and treatment in periodontal disease

ABSTRACT

Periodontal disease, including gingivitis, is prevalent in the general population. Periodontal pathogens contained in dental biofilm play a central role in periodontitis; however, it is the interactions between the host and the biofilm that influence the onset and progression of the disease. Risk factors include environmental, acquired and genetic factors, some of which are modifiable risks. Initial periodontal therapy is typically nonsurgical scaling and root planing, followed by re-evaluation and periodontal maintenance. Antimicrobials may be used adjunctively, including systemic antibiotics, subantimicrobial doxycycline and locally applied antimicrobials. The use of adjuncts, where indicated, is guided by guidelines, and clinical judgment for the individual patient. The overall goal of therapy is to preserve the dentition and maintain or gain clinical attachment, and to prevent disease recurrence.

LEARNING OBJECTIVES

The overall goal of this article is to provide information on periodontal disease and the role of biofilm in its development and progression. After completing the article, the reader will be able to:

1. Review the role of biofilm in periodontal disease;
2. Describe the pathogenesis of periodontal disease, destructive and protective chemical mediators;
3. List and describe risk factors; and,
4. Review options for treating chronic periodontitis and their efficacy.

Introduction

The 1999 Classification of Periodontal Diseases and Conditions includes 2 main classifications: gingival conditions of plaque-induced and non-plaque-induced origins, and, periodontal diseases/conditions. Periodontitis involves clinical attachment loss (CAL) with loss of alveolar bone together with apical migration of the epithelial attachment. Increased probing depths (PD) and bleeding on probing (BOP) are present. Mild, moderate and severe periodontitis are, respectively, represented by CAL of 1 – 2 mm, 3 – 4 mm, and ≥5 mm. A comprehensive update of the current classification is planned for 2017, with the inclusion of risk assessment and prognosis for progression of periodontitis.

ABOUT THE AUTHOR

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Dr. Collins is a national and international speaker and author, and has presented on dental caries, xerostomia, biofilm, disease prevention, dentifrices, infection control, and tobacco cessation. She has given presentations in North America, Europe, the Pacific Rim and the Middle East. She has also participated as a faculty member at OSAP Boot Camps. Dr. Collins is a member of the American Dental Association and is the ADA representative to AAMI. She is also a member of the American Association for Dental Research, ADA Standards Committee working groups, the Organization for Safety, Asepsis and Prevention (OSAP), and is a Fellow of the Pierre Fauchard Academy. During her career, Fiona has lived and worked in five countries. Dr. Collins graduated as a general dentist from the University of Glasgow in Scotland, and holds an MBA and an MA from Boston University. Dr. Collins is the CE Editor for Dental Learning. She has no commercial interest or relationship with the commercial supporter of this course.
Prevalences

Based on the National Health and Nutrition Examination Survey (NHANES III) of 1988-1994, 50% of adults had gingivitis. One study found that 94% of adults had gingivitis (GI ≥0.50), and it is estimated that up to 75% of the global population experiences gingivitis. Plaque-induced gingivitis is an inflammatory host response to dental biofilm. Early gingivitis is reversible with thorough oral hygiene, while established gingivitis requires professional intervention to treat it. Persistent gingivitis is a risk factor for periodontitis and tooth loss, and in a 26-year longitudinal study (n=565; ages 16 to 59), 70% more CAL was observed in subjects approaching age 60 who had long-standing gingivitis vs. subjects with no gingivitis. However, the presence of gingivitis does not always lead to periodontitis, as shown by the higher prevalence of established gingivitis versus periodontitis in the general population.

Periodontitis in adults ≥30 years-of-age was estimated in the 2009-2010 NHANES. Based on the definitions, 47% of these adults were found to have periodontitis, of whom 8.7%, 30.0%, and 8.5% respectively had mild, moderate, and severe periodontitis. Among adults ≥65 years-of-age, an estimated 57% have mild or moderate periodontitis, and 11% have severe periodontitis. Occlusal trauma secondary to periodontitis may exacerbate periodontal destruction. Periodontal pathogens are a prerequisite for plaque-induced periodontitis.

Development and Structure of Dental Biofilm

Dental biofilm development begins with pellicle formation at the tooth surface. This is followed by early adhesion and colonization by Gram-positive cocci, then by Gram-positive rods and filaments. Next, a shift in the biofilm occurs with adhesion and colonization by Gram-negative bacteria. Bacterial production of extracellular lipopolysaccharides (EPS) results in a matrix that binds the biofilm together and protects microorganisms within it. Gingivitis can develop in a matter of days once periodontal pathogens are present. The subgingival biofilm matures over a period of several weeks, becoming structured and self-protective, and is most protected deep within the biofilm. The initial host response includes the production of antibodies to bacterial antigens, and the release of cytokines. Vasodilation and the release of polymorphonuclear leukocytes (PMNs), primarily neutrophils, then occur and the PMNs migrate to the inflamed area and enter the tissue along with Immunoglobulin G (IgG). In established gingivitis, plasma cells, IgG and IgA are present, with little IgM. PMNs are still present and T-cell lymphocytes are most abundant.

Plaque Hypotheses

Historically, oral bacterial disease was considered to be associated with dental plaque, not with specific bacteria. This was followed by the specific plaque hypothesis, which holds that specific pathogenic bacteria are responsible for disease. By the late 1990s, Socransky and Haffajee had identified six bacterial complexes in subgingival dental biofilms. These complexes were color-coded, based on their level of virulence. Bacteria in the yellow, green, purple and blue complexes colonize first during biofilm development, while red and orange complex bacteria are the most virulent. Red complex bacteria included Tannerella forsythia (Tf), Porphyromonas
gingivalis (Pg) and Treponema denticola (Td).21 (Figure 2)

The periodontal microbiota has been investigated in periodontally healthy patients, and in healthy and diseased sites. In young adults with a healthy periodontium,23 periodontal bacteria from interdental samples were assessed by polymerase chain reaction (PCR). For red complex bacteria, Pg was found in 19% of subjects, Tf in 93% and Td in 49% of subjects.23 Based on the analysis, the orange complex was the main one (70.17% on average) followed by the green complex (13.97%). (Figure 3) In addition, the red and orange complexes clustered together, while other complexes correlated with each other but did not cluster.

Dibart et al found that a majority of sites harbored Streptococcus oralis (So), while in diseased sites greater numbers of Tf, Prevotella intermedia (Pi), Capnocytophaga ochracea (Co) and Campylobacter rectus (Cr) were found.24 In a second study, A. actinomycetemcomitans (Aa), Fusobacterium nucleatum (Fn), Tf, Pg, Pi, and Peptostreptococcus micros (now Parvimonas micra; Pm) were abundantly present in patients with periodontitis.25 In a 2006 study assessing periodontal disease at baseline, after 7 years and a further 8 years later in subjects in Western Java, Aa was found to be a risk predictor for its onset and progression.26 In a study assessing gingival crevicular fluid (GCF) levels of inflammatory biomarkers, serum IgG and subgingival bacteria, higher levels of red complex bacteria were found at the biofilm-periodontal tissue interface for patients with deep periodontal lesions and at sites with moderate or high bleeding-on-probing. However, the differences between moderate and high bleeding-on-probing were determined by the overall increased level of bacteria.27 Dental biofilm is polymicrobial, with differing bacterial concentrations and virulence depending on the location.10,28,29 Additionally, significant differences exist in the prevalence and mix of periodontal pathogens found in periodontal pockets across ethnic groups.30,31,32

The Oral Microbiome

The oral microbiome has now been researched,33 with >1,000 intraoral species identified, many uncultured and unculturability using current methods.34 Up to 100 species are found in individual periodontal pockets,14 with variation in strains within species demonstrating the diversity that may be found within periodontal pockets. More bacteria have been found that are involved in periodontal disease, and it is believed that uncultured/uncultivable microorganisms may include as yet unidentified periodontal pathogens.7 Recent findings are discussed later in this article.

Host Influence on Biofilm

The ecological plaque theory holds that a state of health can be maintained provided an equilibrium exists, while changes in the ecology can favor transition to a disease
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state. Factors affecting the equilibrium include the local pH, temperature, 'lifestyle risk factors,' ethnicity, age, gender and genetics.37 In a state of health, the gingival crevice has a pH just under 7, while a pH of 7.2 to 7.4 and higher (up to around a mean of pH 7.8) occurs in the presence of inflammation.38 This may encourage preferential growth of periodontal bacteria, including Pg, Pi and Aa.39 Distinct temperature increases are part of periodontal inflammation and favor Pi, Aa and Pg.

Risk Factors

Numerous individual risk factors exist for periodontal disease and its progression. In addition, the presence of two/more of biofilm, tobacco use and alcohol consumption is a strong risk indicator.40 Modifiable environmental risk factors include poor oral hygiene, gingivitis, local factors such as calculus and restoration overhangs,14 and socioeconomic status. Acquired risk factors include tobacco use (modifiable), substance abuse, some systemic diseases and medications (some modifiable). Smoking tobacco is the primary modifiable risk factor for periodontitis.41 Based on NHANES III, smokers have a 4-fold risk and previous smokers a 1.6-fold risk, compared to never-smokers.42 Smoking tobacco has been shown to alter the host response, including collagenase activity.43-45 It is believed that smoking favors periodontal pathogens, including Tf, Pm, Fn and Cr.46 A poorer response to periodontal therapy is observed for smokers, with lower reductions in bacterial load, a greater risk of recurrence and tooth loss.47 A 4-fold risk for periodontitis up to 20 years after prior heavy consumption of alcohol has been observed,48 and higher levels of Fn, Pi, E. corrodens and IL-1B in alcohol-dependent individuals.49 Use of recreational drugs has also been implicated in risk for periodontitis.50

Diabetes mellitus (DM) is a strong risk factor for periodontitis,31,52 and inhibits periodontal repair. In one study, severe periodontitis was found in 58% of adults ages 40-69 years with long-duration diabetes vs. 7% without diabetes.53 An association between gestational DM (GDM) and periodontal disease has been found.54 In some studies, higher BOP, mean CAL and PD have been observed in patients with Sjögren’s syndrome.55,56 Possible mechanisms include changes in cytokine expression and in the levels of antimicrobial agents and other agents.57,58 Dry mouth itself reduces the availability of salivary antimicrobial agents.59 In patients with rheumatoid arthritis (RA), a two-fold risk for periodontitis and a risk for more severe periodontal disease have been found.60,61 Pg plays a role in both diseases, and is present in the synovial fluid of patients with RA.61 The conclusion in one study was that patients with RA would likely benefit from increased professional care, e.g., scaling and root planing (SRP).61

The role of genetics has been extensively investigated. One factor researched was genes associated with IL-1 production and the balance of pro- and anti-inflammatory chemical mediators.62 More recently, the role of epigenetics, whereby chemical alterations to the DNA and proteins (as opposed to encoded genetic changes) result in changes in gene expression, has been researched.63 Stress affects the immune system, can cause increased bacterial growth, is associated with periodontal disease and can affect treatment outcomes.64,65 Recent research suggests that obesity may be a risk factor and may alter periodontal inflammation.66,67

The Host Response

Periodontal destruction depends on the balance between destructive and protective inflammatory mediators.18,19

<table>
<thead>
<tr>
<th>TABLE 1. Risk Factors</th>
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<tr>
<td>Poor oral hygiene</td>
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<td>Tobacco use</td>
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<td>Alcohol consumption</td>
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<td>Calculus</td>
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<td>Socioeconomic status</td>
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<td>Diabetes mellitus</td>
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<td>Rheumatoid arthritis</td>
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<td>Genetics</td>
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Tumor necrosis factor alpha (TNFα), interleukin-1 (IL-1) and IL-6 are reported to be the first cytokines to appear. IL-1beta and IL-6 stimulate cell migration, and TNFα promotes neutrophil adhesion to blood vessels, aids vascular permeability, and upregulates IL-1beta and IL-6, further promoting cell migration. Neutrophil movement and vascular permeability are aided by complement factors, and GCF flow increases. IL-1beta, IL-6 and TNFα are involved in disease progression, and stimulate production of matrix metalloproteinases (MMPs) involved in bone destruction. The initiation of bone loss also involves toll-like receptor. Prostaglandins are involved in the disease process, T-lymphocytes secrete receptor activator of nuclear factor kappa-B ligand (RANKL) and RANKL is upregulated by TNFα. In addition, based on GCF samples from patients with CP vs. healthy patients, it has also been suggested that MMP-13 and MMP-9 together can overcome protection by tissue inhibitors of metalloproteinase-1 (TIMP-1).

Protective factors include transforming growth factor beta (TGF-beta), which downregulates IL-1beta, TNFα and MMPs, helping to prevent tissue destruction. TGF-beta1 levels are inversely related to levels of RANKL in active diseased sites. TIMPs inhibit MMPs, and osteoprotegerin inhibits RANKL. IL-4 increases production of TIMPs and osteoprotegerin, may downregulate IL-1 beta, and upregulates IL-10, which in turn downregulates MMPs and RANKL and upregulates TIMPs. IL-10 also inhibits production of interferon gamma, found at high concentrations in severe and progressive periodontitis. IL-10 is believed to limit the severity of periodontitis (Figure 4).

Recent Findings on Dental Biofilm and Periodontitis

The keystone pathogen hypothesis holds that specific bacteria present at a very low level may nonetheless direct the bacterial content of biofilm, initiating an inflammatory response.

Oral microbiome research, 16S rRNA sequencing and other techniques have made it possible to identify bacteria previously unknown, and dental biofilm is more diverse than previously thought. Periodontitis is now considered to be a polymicrobial inflammatory disease in which the microorganisms and specific strains within dental biofilm are dysbiotic. This means that their influence can result in a change in the biofilm into one favoring periodontal disease, with increased self-protection and pathogenicity. In addition, the whole biofilm community is believed to be associated with periodontal disease. Dental biofilm associated with periodontal disease is considered inflammospheric, i.e., likes inflammation, which also means that as inflammation occurs, the biofilm shifts further to bacteria that like inflammation, creating a vicious circle and progressing periodontal disease.

Bacteria previously considered nonpathogenic are now believed to be involved in periodontal disease, based on the research. Instead of mainly Gram-negative bacteria being associated with periodontal disease and Gram-positive with periodontal health, it has been discovered that Gram-positive bacteria are also involved in this disease. Eubacterium nodatum (En) is found in mature supragingival biofilm and in biofilm redeveloped after professional prophylaxis, together with Pg, Tf and Td. It is considered possible that Gram-positive bacteria, such as En, Pm and Filifactor alocis (Fa), as well as the bacteria Porphyromonas endodontalis and Prevotella tannerae, may be putative periodontal pathogens. In recent research, Fa, which is Gram-positive, was found to be associated with periodontal disease and to have a high incidence in periodontal pockets, while Veillonella (Gram-negative) was not.
Microorganisms within a mature biofilm interact and support each other, with various functions within the whole biofilm. Commonalities and differences have also been found in the response of periodontal tissues to recognized pathogens. The inter-relationship between the host and the microbial environment determines the onset and progression of periodontal disease. Interaction between different strains of species also occurs, and new bacterial-host interactions likely remain to be discovered.

**Microbial and host interactions**

In addition to binding to receptor sites, different species of bacteria co-aggregate (bind) with each other. *Pm* mediates co-aggregation with *Fn* and *Pg*, and co-aggregation of *Td* and *Pg* may increase the virulence of both species. Gingipains produced by *Pg* digest host proteins, provide nutrients to other microorganisms and alter the immune response by inhibiting the bactericidal activity of PMNs. In addition, gingipains play a role in the co-aggregation of *Pg* and *Pi* and may interact with other bacteria.

*In vitro*, *Fn*, *Fusobacterium necrophorum*, *Pe* and *Pd* have been shown to promote MMP release in gingival epithelial cells, and *Pg* may modify the adaptive immune response. Multi-species biofilms have been shown in vitro to elevate levels of interleukins. An example of a role for both Gram-positive and Gram-negative bacteria is the influence of *Sg* in recruiting *Pg* and other bacteria, and its crucial role in biofilm formation. Viruses may also play a synergistic role with bacteria, specifically human cytomegalovirus and Epstein-Barr virus.

In vivo, specific bacterial combinations influence the severity of periodontal disease: *Td* and *Pg* levels increase GCF levels of a bone destruction marker; and higher IL-8 levels are produced when *Aa* and *Fn* are both present. Inflammatory mediator levels were also shown to be lower with the commensal *S. gordonii* (*Sg*) and higher with periodontal bacteria. Specifically, IL-1b levels were higher with *Pg*, IL-8 with *Aa*, and *Fn* resulted in the highest levels of interleukins overall. Since many bacteria cannot currently be assessed, it is not known what their influence may be on the inter-relationships of bacterial species and the microbial-host relationship.

**Treatment for chronic periodontal disease**

The goal of periodontal therapy is to halt disease...
progression, to preserve the dentition and maintain or gain clinical attachment, and to prevent disease recurrence. Nonsurgical SRP is standard initial therapy for CP, followed by re-evaluation and long-term periodontal maintenance. Clinical judgment is required in determining appropriate treatment and considers the individual patient's medical and dental history, systemic health, risk factors, preferences, and severity and extent of periodontal disease. Levels of Tf, Fn, Pg and Td have been observed to initially decrease significantly after periodontal therapy, and to then slowly increase in the 3rd month onward in pockets with a PD of ≥6 mm.

In some patients, surgical therapy may be indicated for deep pockets or furcation areas, follow-up in specific areas following initial periodontal therapy, or for tissue regeneration. Patients with aggressive periodontitis or moderate to severe chronic periodontitis require more than only scaling and root planing. It has also been recommended that a periodontal referral be considered for co-management, evaluation and indicated therapy of these patients and for patients with DM. Tobacco cessation should be recommended to users, and has been shown to decrease the proportions of Pe, Dialister pneumosintes, Pm, Fa and Td. The outcome of periodontal therapy depends on an individual’s response to treatment, and compliance with appropriate periodontal maintenance and home care. Depending on the individual patient and clinical judgment, systemic or local adjunctive therapy may be indicated.

Systemic antimicrobials
Options include, but are not limited to, penicillins, tetracyclines and metronidazole, and combination therapy may be required. The adjunctive use of systemic antibiotics is supported by a systematic review finding their use benefitted periodontal patients. Considerations include the patient’s medical history, microorganisms present, and continuing disease activity. However, antimicrobial resistance is of increasing concern in part related to the use/misuse of systemic antibiotics and one of the potential disadvantages of selecting systemic antibiotics. Based on the current ADA EBD guidelines, adjunctive systemic antimicrobials may be considered in patients with moderate to severe chronic periodontitis.

Subantimicrobial dose doxycycline (SDD)
Orally administered SDD (20 mg bid) improves the host response and outcomes, while not promoting antimicrobial resistance. SDD use for 3 months after SRP resulted in mean PD reductions ≥3 mm in 80% of sites with an initial PD ≥7 mm vs. 51% of sites in patients receiving SRP + placebo in one study (p<0.05). SDD has been shown to increase levels of gingival crevicular fluid transforming growth factor-beta1, and to decrease levels of extracellular MMP inducer in GCF. In vitro, in the presence of Aa, SDD inhibits production of TNF-α, IL-1α, IL-1β, IL-6 and IL-8. Based on the current ADA EBD guidelines, the strength of the recommendation is 'in favor' of the adjunctive use of SDD for 3 to 9 months.

Locally applied antimicrobials (LAAs)
LAAs offer controlled, sustained release that keeps the level of antimicrobial above the minimum inhibitory concentration (MIC), while maintaining low levels systemically. Options in the United States include 2% minocycline hydrochloride microspheres (MM; Arestin) and 10% doxycycline hyclate gel (DG; Atridox). DG is applied pre-mixed in a syringe, sets and remains in the site for 7 days, while MM is applied in a syringe as a dry powder that sets in the presence of GCF and remains in the site for 14 to 21 days. In non-smokers, one study found mean PD reductions of 1.99 mm for SRP + MM vs. 0.98 mm for SRP alone at 9 months for pockets with an initial mean PD ≥7 mm following 3-monthly applications. In sites with an initial mean PD ≥6 mm, the difference in mean PD reductions was 0.41 mm, favoring SRP + MM (p≤0.01). A study with one application of MM found mean PD reductions of 1.3 mm for SRP + MM vs. 0.9 mm for SRP alone (NS). Two multi-center trials compared SRP vs. DG as a monotherapy in subjects with moderate to severe CP and ≥4 pockets with an initial PD of ≥5 mm and BOP, 2 of them ≥7 mm. Mean PD reductions in study 1 were 1.1 mm for DG vs. 0.9 mm for SRP (NS). In an evaluation of yearly application of DG during initial
SRP and periodontal maintenance (maintenance itself was 6-monthly), significantly greater reductions in BOP and PD were observed at 3 months only.106

In smokers, adjunctive use of MM for pockets with an initial PD ≥5 mm than SRP alone following treatment at baseline, 6 and 9 months. The mean difference in PD reductions was 0.29 mm (1.19 mm vs 0.90 mm).107 In a short-term study on the gene load of Aa, Fn, Pg and Pi 7 days post-treatment, only Pg responded to SRP alone, and only combination therapy significantly reduced the gene load of Pi (p=0.042).108 In patients with moderate to severe CP, at 25 weeks, use of MM resulted in more sites with PD reductions of ≥2 and ≥3 mm for smokers. For S only, these reductions were 74% and 32% respectively, and for the S + MM group were 85% (p=0.001) and 45% (p<0.0001), respectively.109 Machion et al assessed the outcome of SRP vs. SRP+DH in smokers with severe CP (n=43) and ≥4 pockets in anterior teeth with BOP and a PD ≥5 mm. Mean PD reductions at 6 months were 1.76 mm for SRP alone and 2.17 mm for SRP + DH (NS). For sites with an initial of PD ≥7 mm, the mean PD reductions were 2.6 mm for SRP alone and 3.78 mm for SRP + DH (p=0.01).110 Patients were retreated at 12 months. At the 2-year follow-up, 65% of sites with an initial PD ≥7 mm treated with DH had a PD reduction ≥2 mm versus 46% in the SRP-only group (p=0.01). Clinical attachment level gains were also superior and occurred at more sites.111

In two multi-center studies comparing smokers, previous smokers and nonsmokers with moderate to severe CP, similar improvements were observed with SRP+DH regardless of tobacco use history, while for the SRP group significant differences in treatment outcomes were observed.112

Based on the current ADA EBD guidelines, the strength of the recommendation is 'expert opinion for' the adjunctive use of minocycline microspheres (Arestin) and doxycycline hyclate (Atridox).98 The decision on whether to use an adjunctive LAA is based on current recommendations and clinical judgment.

Conclusions

Periodontitis is a multi-factorial disease associated with the presence of a polymicrobial bacterial biofilm, and research points to dysbiosis resulting from a change in the biofilm or a change in the host response. These changes favor a biofilm associated with disease and inflammation. The outcome depends on the host response, including bacterial-host interactions. Given the polymicrobial nature of the biofilm, one factor in choosing therapies is their effectiveness against a wide range of microorganisms and the severity of disease present. Another is addressing underlying risk factors and the inflammatory host response. It can be anticipated that new or additional therapies will be discovered in the future that address the inflammatory and dysbiotic nature of periodontitis. Standard initial therapy consists of nonsurgical SRP. Adjunctive systemic or local therapy may be indicated depending on the clinical circumstances and clinical judgment.98

Improvements in periodontal health rely on the host response and results of active therapy, removal and reduction of modifiable risk factors, thorough home care, and long-term regular periodontal maintenance.

References

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86. Kamaguchi A, Ohyama T, Sakai E, et al. Adhesins encoded by the gingipain genes of Porphyromonas gingivalis are responsible for co-aggregation with Prevotella intermedia. Microbiology. 2003;149:1257-64.


Webliography

1. Mild, moderate and severe periodontitis are, respectively, represented by a CAL of
   a. 0–1 mm, 2–3 mm, and ≥3 mm
   b. 1–2 mm, 3–5 mm, and >5 mm
   c. 1–2 mm, 3–4 mm, and ≥5 mm
   d. 1–2 mm, 3–5 mm, and ≥6 mm

2. The prevalence of gingivitis and moderate chronic periodontitis in adults in the US is
   a. 30%; 10%
   b. 40%; 20%
   c. 50%; 30%
   d. 60%; 40%

3. Persistent gingivitis always results in periodontitis and tooth loss.
   a. True
   b. False

4. The oral microbiome has since been investigated and around ___________ intraoral species have been identified, while up to ___________ species have been found in individual periodontal pockets.
   a. 250; 500
   b. 500; 750
   c. 1000; 100
   d. 1200; 50

5. The specific plaque hypothesis holds that ___________ are responsible for disease.
   a. all intra-oral bacteria
   b. specific pathogenic bacteria
   c. all microorganisms
   d. only Gram-positive bacteria

6. Dental biofilm ___________.
   a. is polymicrobial
   b. contains differing concentrations of bacteria
   c. varies across ethnic groups, with different prevalences and mix of periodontal pathogens in periodontal pockets
   d. all of the above

7. Tumor necrosis factor alpha (TNFa), interleukin-1 (IL-1) and IL-6 are reported to be ___________ in the inflammatory cascade.
   a. protective inflammatory mediators
   b. the first cytokines to appear
   c. required for osteogenesis
   d. all of the above

8. It has been suggested that MMP-13 and MMP-9 together can overcome protection by tissue inhibitors of metalloproteinase-1 to inhibit progression of CAL.
   a. True
   b. False

9. Osteoprotegerin inhibits ___________.
   a. TIMPs
   b. MMPs
   c. Interferon gamma
   d. RANKL

10. ___________ is considered the primary modifiable risk factor for periodontitis.
    a. Drinking alcohol
    b. Smoking tobacco
    c. The presence of calculus
    d. Poor oral hygiene

11. Bacteria previously considered nonpathogenic are now believed to be involved in periodontal disease, based on the research.
    a. True
    b. False

12. In one study, severe periodontitis was found in ___________ of adults 40-69 years-of-age with long-duration diabetes vs. ___________ without diabetes.
    a. 38%; 5%
    b. 48%; 6%
    c. 58%; 7%
    d. 68%; 8%

13. It was concluded in a recent study that patients with rheumatoid arthritis would likely benefit from ___________.
    a. increased professional dental care
    b. modification of the acquired pellicle
    c. higher cortisol levels
    d. a and b

14. Nonsurgical scaling and root planing (SRP) is standard initial therapy for CP, followed by ___________.
    a. re-evaluation and long-term periodontal maintenance
    b. re-evaluation and short-term periodontal maintenance
    c. re-evaluation and testing for rheumatoid arthritis
    d. irrigation and re-evaluation

15. The outcome of periodontal therapy depends on ___________.
    a. an individual’s response to treatment
    b. compliance with appropriate periodontal maintenance
    c. compliance with home care
    d. all of the above

16. Gingipains produced by Porphyromonas gingivalis ___________.
    a. promote the bactericidal activity of PMNs
    b. play a role in the co-aggregation of Porphyromonas gingivalis and Prevotella intermedia
    c. inhibit other microorganisms from accessing nutrients
    d. result in pain associated with periodontal disease

17. For some bacterial species, their influence on the inter-relationships of bacterial species and the microbial-host relationship is not known because ___________.
    a. they cannot currently be assessed
    b. the influence is likely minimal
    c. they are less important than others
    d. all of the above

18. Orally administered sub-antimicrobial dose doxycycline has been shown to ___________.
    a. improve the host response and outcomes
    b. promote antimicrobial resistance
    c. increase levels of MMP inducer in gingival crevicular fluid
    d. influence epigenetics

19. Available locally applied antimicrobials ___________.
    a. offer sustained release of the antimicrobial above the minimum inhibitory concentration
    b. maintain low levels of the antimicrobial systemically
    c. remain at the site for at least a week
    d. all of the above

20. Determining what would be appropriate treatment is based on ___________.
    a. current clinical recommendations and gut feel
    b. clinical judgment and patient education
    c. current clinical recommendations and clinical judgment
    d. the patient’s age
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EDUCATIONAL OBJECTIVES

- Review the role of biofilm in periodontal disease;
- Describe the pathogenesis of periodontal disease, destructive and protective chemical mediators;
- List and describe risk factors; and,
- Review options for treating chronic periodontitis and their efficacy.

COURSE EVALUATION

Please evaluate this course using a scale of 3 to 1, where 3 is excellent and 1 is poor.

1. Clarity of objectives ........................................... 3 2 1
2. Usefulness of content ........................................... 3 2 1
3. Benefit to your clinical practice .............................. 3 2 1
4. Usefulness of the references ................................. 3 2 1
5. Quality of written presentation ............................. 3 2 1
6. Quality of illustrations ........................................... 3 2 1
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11. Are there any other topics you would like to see presented in the future? __________________________________________________________________________

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Fill in the circle of the appropriate answer that corresponds to the question on previous pages.

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10. A B C D 25. A B C D
11. A B C D 26. A B C D
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