

Periodontal Inflammation: From Gingivitis to Systemic Disease?

Fotinos Panagakos and Frank Scannapieco
*Department of Oral Biology, School of Dental Medicine,
State University of New York at Buffalo, New York
USA*

1. Introduction

There has been a resurgence of interest in recent years in the systemic effects of oral infections such as periodontal diseases. The study of the various means by which periodontal infections and inflammation may influence a variety of systemic conditions is collectively referred to as periodontal medicine. The periodontium responds to tooth-borne biofilm (dental plaque) by the process of inflammation. Dental biofilms release a variety of biologically active products, such as bacterial lipopolysaccharides (endotoxins), chemotactic peptides, protein toxins, and organic acids. These molecules stimulate the host to produce a variety of responses, among them the production and release of potent agents known as cytokines. These include interleukin-1 beta, interleukin-8, prostaglandins, and tumor necrosis factor-alpha. There is a spectrum of periodontal response to these molecules, from mild gingivitis to severe destructive periodontitis. These and other host products and responses may influence a variety of important disease pathways, including atherosclerosis, mucosal inflammation, and premature parturition. The purpose of this chapter is to review the possible biological pathways by which periodontal diseases may influence these disease processes.

There has been increasing attention paid in recent years to the possibility that oral bacteria and oral inflammation, particularly periodontal diseases, may influence the initiation and/or progression of several systemic disease processes. This, of course, is not a novel concept. Indeed, the focal-infection hypothesis, which grew from the principles of infectious disease first established by Koch and Pasteur in the mid-19th century, put forth the notion that the invasion of the bloodstream by bacteria from a localized infection (such as periodontal diseases) could spread to distant organs and tissues to cause disease.¹⁻³ In fact, this hypothesis was so convincing to practitioners of the time that tonsillectomy and full-mouth extraction enjoyed widespread implementation to treat many diseases, regardless of whether or not infection could be proven to be the cause. However, because it became clear that it was impossible to correlate with confidence a particular systemic disease with a preceding oral infection or dental procedure, the focal-infection hypothesis fell from favor by the middle of the 20th century. Yet, interest in the systemic effects of periodontal infection was reignited in the early 1990s by a series of case-control and other epidemiologic studies that demonstrated statistical associations between poor oral health and several

systemic diseases. The goal of this chapter is to describe the biologically plausible circumstances that underlie these potential associations. The reader is further referred to recent definitive reviews on the pathogenesis of periodontal disease for specific details that are beyond the scope of this chapter.^{4,5}

The periodontium responds to the tooth-borne biofilm, long known as dental plaque, by the process of inflammation. Plaque is composed of numerous bacteria, comprising over 700 species, which tenaciously adhere to the tooth surface.⁶ Scientists are now beginning to understand the complex molecular interactions that occur, for example, between the bacteria and salivary pellicle that coats the tooth, and between gram-positive cocci of early plaque and gram-negative filamentous bacteria that populate the tooth as plaque matures.⁷ Recent work has elucidated complex signaling pathways (referred to as quorum sensing) between bacteria, mediated by soluble chemicals produced by the bacteria that control biofilm development.⁸ It is anticipated that this knowledge will eventually yield sophisticated strategies to limit the pathogenic potential of dental plaque.

Within a few hours of meticulous tooth cleaning, bacteria colonize the tooth surface primarily around the gingival margin and interdental spaces (Figure 1).⁹ The developing biofilm releases a variety of biologically active products, including lipopolysaccharides (endotoxins), chemotactic peptides, protein toxins, and organic acids.⁴ These molecules diffuse into the gingival epithelium to initiate the host response that eventually results in gingivitis and, in some circumstances, inflammatory periodontal diseases.⁴ Clinically, gingivitis is characterized by a change in color—from normal pink to red—with swelling and, often, sensitivity and tenderness.¹⁰ Gentle probing of the gingival margin typically elicits bleeding.¹⁰ Because gingivitis is often not painful, it may remain untreated for many years.

Epidemiologically, the prevalence of gingivitis in non-Hispanic whites is approximately 50% of the population, with up to 63% in Mexican Americans showing clinical signs of the disease.¹¹ It is quite possible that this rate is somewhat understated because it is possible that gingivitis, in its most nascent form, is clinically undetectable. Periodontitis affects approximately 35% of dentate US adults 30 to 90 years of age, with 21% having a mild form and 12% having a moderate or severe form of the disease.¹² Thus, gingivitis is much more widespread than periodontitis in the US population.

Histopathologically, gingival inflammation presents as a spectrum of severity in humans.⁷ In a relatively small subset of the population, the gingiva are virtually devoid of inflammatory infiltrate, the so-called “pristine gingiva” (Figure 2).⁷ These subjects practice impeccable oral hygiene and demonstrate no clinical signs of inflammation. More widespread would be the “normal healthy gingiva,” which demonstrates a mild-to-moderate inflammatory infiltrate. Clinically, these two conditions would appear indistinguishable in that the tissues would appear quite healthy.

Probably most prevalent in the population is established gingivitis that is associated with a more widespread biofilm and clear clinical symptomology (redness, swelling, and bleeding), and histopathologically showing significant inflammatory infiltration (Figure 3).⁷ The most severe form of periodontal diseases results in the destruction of the periodontal ligament and supporting osseous tissue and, ultimately, exfoliation of the teeth. Periodontitis is associated with extensive formation of biofilm dominated by anaerobic, gram-negative bacteria and spirochetes.¹³

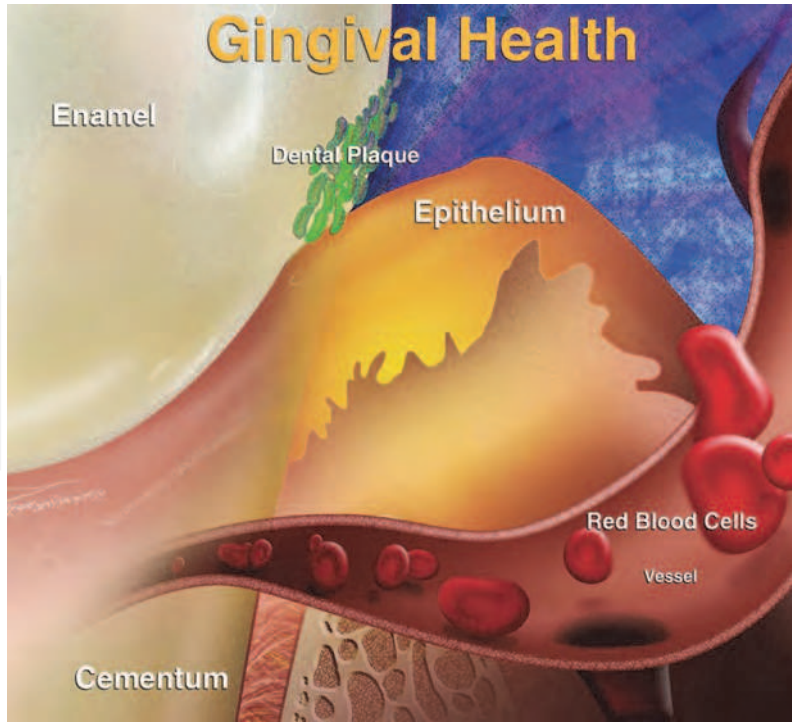


Fig. 1. Biochemical events in periodontal disease. Pristine gingiva are not exposed to significant numbers of plaque microorganisms to yield a host response. Few signs of acute inflammation or cellular infiltrate are noted.



Fig. 2. Left panel: Pristine gingiva is found in subjects with impeccable oral hygiene and minimal plaque. Gingival tissues are free of clinical signs of inflammation, and tissues are essentially free of inflammatory infiltrate. Right panel: Early gingivitis is found in subjects with some plaque formation. While the gingival tissues are free of clinical signs of inflammation, a mild inflammatory infiltrate is evident, consisting of vasculitis and the presence of neutrophils.

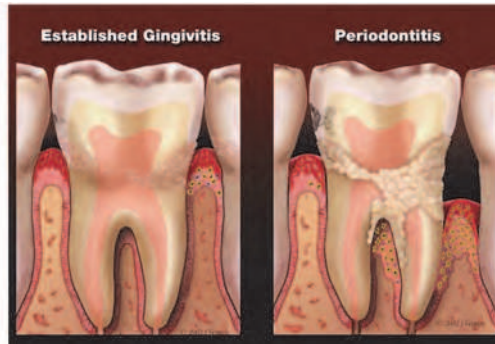


Fig. 3. Left panel: In the absence of effective plaque control, a robust inflammatory response results in clinical signs of inflammation (redness, edema, bleeding) and a significant inflammatory infiltrate, including neutrophils, lymphocytes, and evidence of collagen breakdown. Signs of periodontal attachment loss or alveolar bone loss are not evident. Right panel: The inflammatory response results in marked collagen breakdown, periodontal attachment and alveolar bone loss, and clinical signs of inflammation.

As mentioned previously, initial dental plaque bacteria (typically gram-positive cocci and filaments) release a variety of chemical compounds during their normal metabolism (organic acids, chemotactic peptides, etc). These products are soluble and penetrate the superficial layers of the sulcular epithelium. These substances signal the epithelium of the gingiva to produce a variety of biologically active mediators, most prominently cytokines such as interleukin-1 beta (IL-1 β), interleukin8 (IL-8), prostaglandins, tumor necrosis factor-alpha (TNF- α), and matrix metalloproteinases (Figure 4). These products influence a number of cellular processes, including the recruitment and chemotaxis of neutrophils to the site, with increased permeability of the gingival vessels that results in extravasation of plasma proteins from the blood vessels into the tissue. The epithelium also responds by induction of innate defense systems, which include the production of antimicrobial peptides, such as defensins, calprotectin, etc.¹⁴ In addition, the salivary defense system works to limit bacterial growth through the flushing action of simple fluid flow that clears bacteria from the oral surfaces, bacterial-aggregation factors, antimicrobial proteins, etc.¹⁵ Should the dental plaque biofilm continue to grow and expand to populate the subgingival space, these noxious compounds will stimulate the epithelium to produce bioactive mediators, resulting in further recruitment of a variety of cell types, including neutrophils, T-cells, monocytes, etc (Figure 5). The resulting established or chronic gingivitis is the most prevalent type of gingival inflammatory lesion in the population as a whole. Thus, continued exacerbation of the process results in signaling of underlying cell types, including fibroblasts, to increase production of proinflammatory cytokines in the tissues. Host systemic responses to this insult also can be documented. For example, evidence of specific antibodies to oral organisms can be demonstrated in peripheral blood. Also, the acute-phase response is associated with gingival inflammation, including the production of C-reactive protein (CRP), fibrinogen, complement, etc, by both local cells and the liver.^{16,17} These proteins not only possess biological activities that may further exacerbate the inflammatory response, they may also impact the initiation or progression of systemic disease processes, such as atherosclerosis.^{18,19}

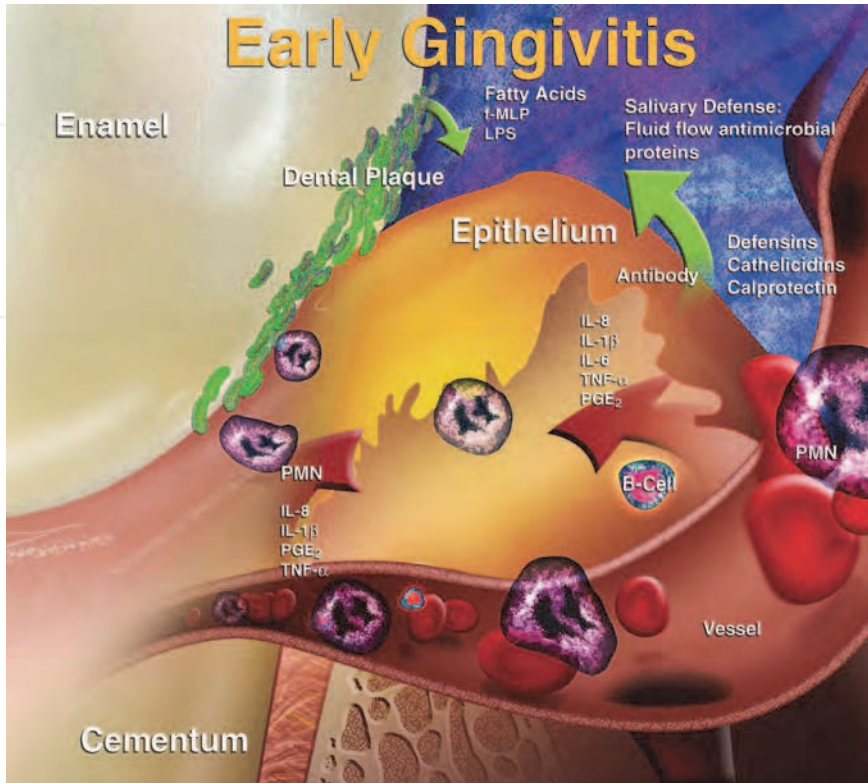


Fig. 4. Bacteria in dental plaque release biologically active components, including lipopolysaccharides, chemotactic peptides, and fatty acids. These components signal gingival epithelial cells to release proinflammatory cytokines that diffuse into the underlying connective tissues to stimulate acute vasculitis, which leads to dilation of blood vessels and extravasation of plasma components into the connective tissue compartment. Chemotactic peptides signal white cells to interact with and stick to vascular endothelium, after which the neutrophils enter the connective tissues. In addition to the inflammatory response, the host attempts to clear itself of microorganisms by responding to these signals with epithelial production of antimicrobial peptides. Saliva also affords numerous antimicrobial mechanisms to protect the host



Fig. 5. Increased numbers and increasing diversity of bacteria in dental plaque continue to release biologically active components that increase the intensity and spread of the inflammatory response. Increased numbers of neutrophils, monocytes, and macrophages infiltrate the tissues to release more diverse cytokines and prostaglandins that exacerbate the inflammatory response. Lymphocytes (T- and B-cells) and plasma cells also infiltrate, the latter releasing antibodies against the microorganisms that may also cross-react with the host tissues. The acute-phase response (including production of acute-phase proteins such as CRP, serum alpha amyloid A, and fibrinogen) also is evident.

To this point, rigorous tooth cleaning and oral hygiene procedures would reverse the course of gingivitis and return the periodontium to a healthy state.²⁰ Unfortunately, however, many people fail to maintain adequate hygiene and so the process of inflammation often continues unchecked for years. In some individuals, for reasons that are not entirely clear, the inflammatory process expands to involve the breakdown of collagen in periodontal ligament and bone resorption, resulting in periodontitis (Figure 6). The rate of breakdown varies between individuals. It has been suggested that there are underlying genetic mechanisms or other risk factors (e.g., smoking, diabetes, stress, etc) that provoke these processes in certain people and not in others. We've heard lately of polymorphisms and various genes that control, for example, interleukin or fibrinogen synthesis. There is an ongoing scientific effort to determine the role of host genetics in the susceptibility to periodontal infection.²¹

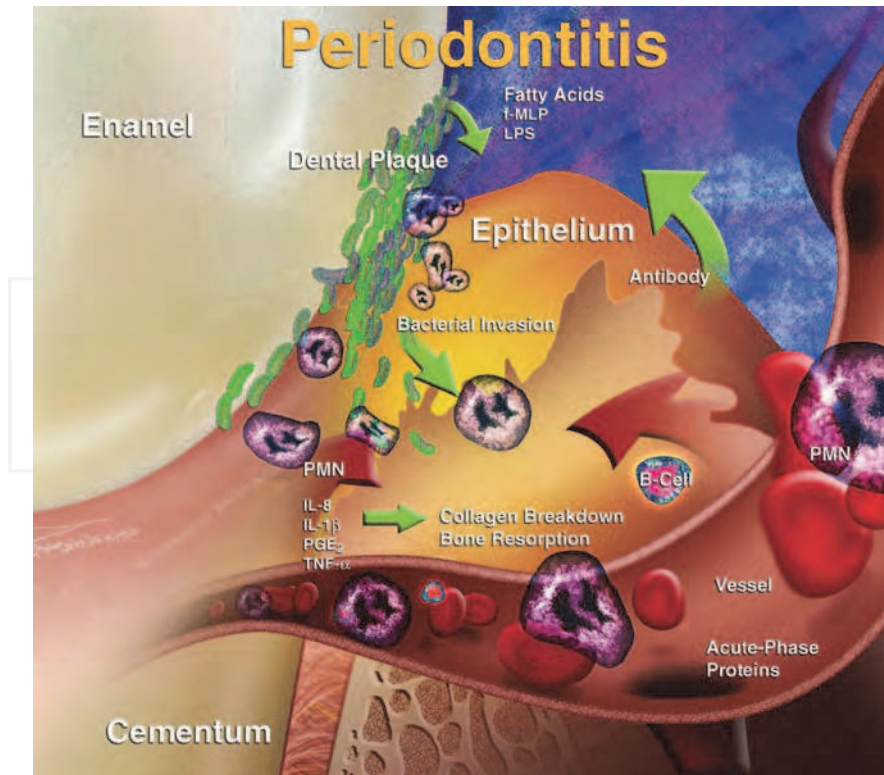


Fig. 6. In some subjects, for reasons that remain unknown, the chronic inflammation of established gingivitis spreads to provoke periodontal ligament and alveolar bone destruction.

2. Gingival health and bacteremia

A consequence of this inflammatory process is ulceration of the gingival sulcular epithelium, which allows bacterial translocation from the sulcus into the bloodstream. The surface area of the periodontal ligament has been calculated to cover about 75 square centimeters. Thus, a person having 50% horizontal bone loss and inflamed pocket epithelium would have a wound surface of approximately 30 to 40 square centimeters. Such a wound surface would likely increase the risk for bacterial translocation when compared to a healthy periodontium. In the most prevalent periodontal disease, established gingivitis, pockets of 4 to 5 millimeters may translate into a gingival wound surface area of 10 to 20 square centimeters. Considering that many people go a long time without having gingivitis treated, this chronic inflammatory condition may promote continuous, low-grade chronic bacteremia. Several studies have indeed shown that the incidence of bacteremia is elevated in subjects with increasing severity of gingival inflammation.^{22,23} When using rather insensitive bacterial culture techniques, bacteremia could be detected even in subjects with clinically healthy gingiva. The use of more sensitive molecular techniques, such as the polymerase chain reaction,^{24,25} would likely prove bacterial translocation from the periodontium to be even

more common than presently appreciated. While most studies of dentally related bacteremia have centered around purposeful activities such as tooth brushing, periodontal probing, and tooth extraction, it is possible that while participating in daily activities (chewing, speaking, habits, etc), minor disruptions to gingival integrity occur in a significant number of individuals with gingival inflammation.

3. Gingival inflammation: Pathways of systemic effects

Oral bacteria and gingival inflammation may theoretically influence systemic health through four potential pathways: bacteremia, systemic dissemination of locally produced inflammatory mediators, provocation of an autoimmune response, and aspiration or ingestion of oral contents into the gut or airway (Figure 7). Low-grade but persistent bacteremia may allow oral bacteria to aggregate platelets through receptor-ligand interactions. Studies have shown that infusing rabbits with aggregating bacteria caused significant hemodynamic changes, acute pulmonary hypertension, and cardiac abnormalities, including ischemia.²⁶ This very provocative work suggests that bacteremia of oral origin may have serious implications for systemic health.

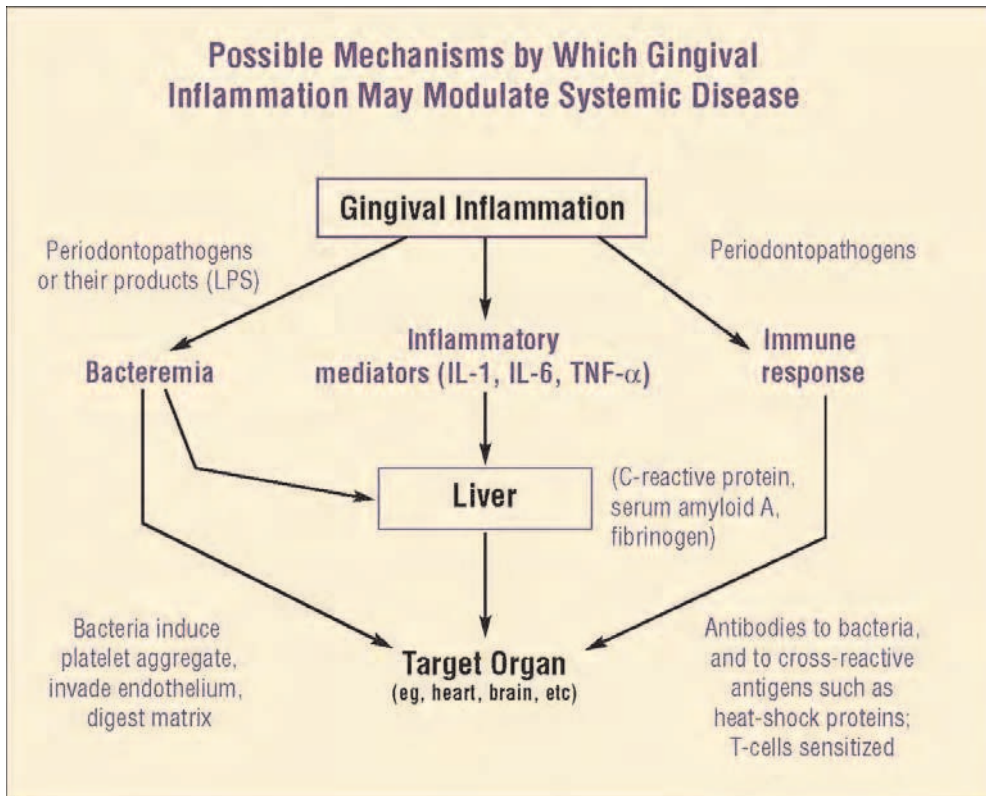


Fig. 7. Theoretical pathways by which the gingival inflammatory response may impact systemic inflammation and systemic processes such as atherosclerosis.

Several inflammatory mediators can be measured as being elevated in peripheral blood in subjects with periodontal disease,¹⁷ suggesting that periodontal inflammation either contributes directly to the elevation of the concentration of these substances in peripheral blood or signals distant organs (e.g., the liver) to produce them. The liver could respond, for example, through the acute-phase response by producing CRP, fibrinogen, etc. These proteins may have deleterious effects on other target organs (e.g., heart, brain) by modulating disease processes such as atherosclerosis. Recent studies have suggested a connection between chronic infections, such as *Chlamydia pneumoniae* infection or periodontal diseases, and atherosclerosis.²⁷ It has been suggested that immunity to bacterial pathogens plays a role in the atherosclerotic process and that this response may involve autoimmunity.²⁸ It has been observed that almost all humans have immune reactions against microbial heat-shock protein 60 (HSP60). The human version of this protein is highly homologous with bacterial HSP60. It is possible that the immune response generated against the microbial version of this protein could cross-react with human HSP60 on arterial endothelial cells to influence the course of atherosclerosis.²⁸ Bacteria thought to induce gingival inflammation may also stimulate an autoimmune response by presentation of cross-reactive epitopes that stimulate autoantibody or T-cell response reactive with host antigens, such as HSP60, to drive a proinflammatory response with cardiovascular effects.^{29,30}

Dental plaque and/or periodontal inflammation may influence pathogenic processes occurring in distally contiguous mucosal surfaces, for example, in the respiratory or digestive tracts.^{31,32} Salivary hydrolytic enzymes, observed to be elevated in patients with periodontitis, can promote the adhesion of pathogenic bacteria to the oral surfaces, thereby altering oropharyngeal colonization patterns. It is also possible that periodontopathic bacteria stimulate the periodontium to release proinflammatory cytokines that, when aspirated or swallowed, alter mucosal surfaces to promote adhesion of pathogenic bacteria that cause diseases such as pneumonia or gastric ulcers.^{31,32} Finally, cytokines released from inflamed periodontal tissues may enter the respiratory tract in aspirated saliva, triggering the sequence of neutrophil recruitment, epithelial damage, and infection.³¹

4. Gingival inflammation and systemic disease

Several case-control studies³³ published in the early 1990s found that patients with a history of myocardial infarction had worse oral health than control subjects (studies are summarized in the reference). This has led to a flurry of studies to verify these observations. While most of these studies support a modest association between periodontal diseases and the outcomes of atherosclerosis (of myocardial infarction, angina, or stroke), several studies have not supported this association. This is complicated by the absence of a standard definition or measures for periodontal diseases and that underlying mechanisms common to both periodontal diseases and atherosclerosis share common risk factors, such as lifestyle habits like cigarette smoking. It is possible that dental plaque stimulation of cytokine production in the periodontium may elevate levels of cytokines in the peripheral blood. This may in turn stimulate hepatic production of acute-phase proteins, such as CRP. These proteins could then induce vascular injury, atherogenesis, cardiovascular disease, and stroke. Several studies have shown that patients with periodontal diseases demonstrate elevated levels of CRP and fibrinogen, as well as peripheral white blood cells.^{17,34} Elevated

levels of these proteins have been suggested to be risk factors for cardiovascular disease.³⁵⁻³⁷ Additional evidence has been reported for the possible direct role of bacteria in atherosclerosis. It has been reported that chronic disease agents, such as *C pneumoniae*, play a role in atherosclerotic plaque development. Recently it has been reported that the DNA of oral bacteria could be amplified directly from atherosclerotic plaques. It is, therefore, possible that these pathogens may play a role in the development and progression of atherosclerosis leading to coronary vascular disease

Lung diseases such as hospital-acquired pneumonia and chronic obstructive pulmonary disease (COPD) also have been associated with poor oral health.^{31,38} It is possible that oral biofilms on the teeth may serve as a reservoir of infection for respiratory pathogenic bacteria. In subjects admitted to hospital intensive care units or nursing homes, bacteria such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and enteric bacteria have been shown to colonize the teeth. These bacteria may then be released into the oral secretions to be aspirated into the lower airway to cause infection. It is also possible that inflammatory mediators, such as cytokines produced by the periodontium, released into the secretions also can be aspirated to have pro-inflammatory effects in the lower airway.

Several epidemiologic studies have reported associations between poor oral health and COPD.^{39,40} One interesting observation found that lung function measured through spirometry is associated with measures of periodontal disease.⁴⁰ In subjects stratified by periodontal attachment loss, those with more severe attachment loss tended to demonstrate less lung function than those with less attachment loss. Further research is necessary to dissect the contribution of periodontal inflammation from those of established etiologies, such as smoking on lung function.

There also has been interest in the association between periodontal inflammation and adverse pregnancy outcomes.^{41,42} Unfortunately, adverse pregnancy outcomes, such as premature birth and low birth weight, are quite common events. This is a very significant public health problem in the United States, and has been associated with subclinical genitourinary or other infections. During parturition, the uterus is influenced by the hypothalamus through the production of oxytocin, which stimulates uterine contraction. Prostaglandins that are produced by the placenta also stimulate uterine contraction, which normally leads to birth in the third trimester (37 weeks). It is thought that chronic infections drive the inflammatory process, which leads to the release of inappropriate levels of prostaglandins and TNF- α , which prematurely stimulates uterine contraction to promote preterm birth.

It has been suggested that periodontal infection and the release of lipopolysaccharides and other biologically active molecules drive the process of inflammation, as described above. This results in the elevation of prostaglandins and TNF- α in the crevicular fluid. Lipopolysaccharides released from the oral cavity into the bloodstream may stimulate prostaglandins in the placenta, causing preterm birth. It is also possible, such as in atherosclerosis, that cytokines in the periodontium may lead to elevated peripheral blood cytokine levels and stimulate hepatic production of acute-phase proteins that may influence the birth process. Very recent work has also found that periodontal pathogens, such as *Fusobacterium nucleatum*, may travel from the gingival sulcus to the placenta to cause preterm birth.⁴³ Thus, it is possible that these bacteria may enter the bloodstream from the oral cavity to directly affect the birth process.

5. Summary

Dental plaque drives periodontal inflammation, with gingivitis being the initial manifestation of this process. With appropriate intervention, this process can be reversed and the periodontium returned to a state of health (Figure 8). However, an exuberant local host response, including the synthesis of cytokines and antibodies, in some cases results in the destruction of periodontal ligament and supporting bone (periodontitis). Periodontitis is typically treated by removing the etiology (dental plaque) and returning the gingival tissues to health. Unfortunately, in many cases, periodontal disease goes untreated for many years. It is possible, then, for the systemic host response to this insult to contribute to disease processes that result in cardiovascular disease and stroke, respiratory disease, and adverse pregnancy outcomes.

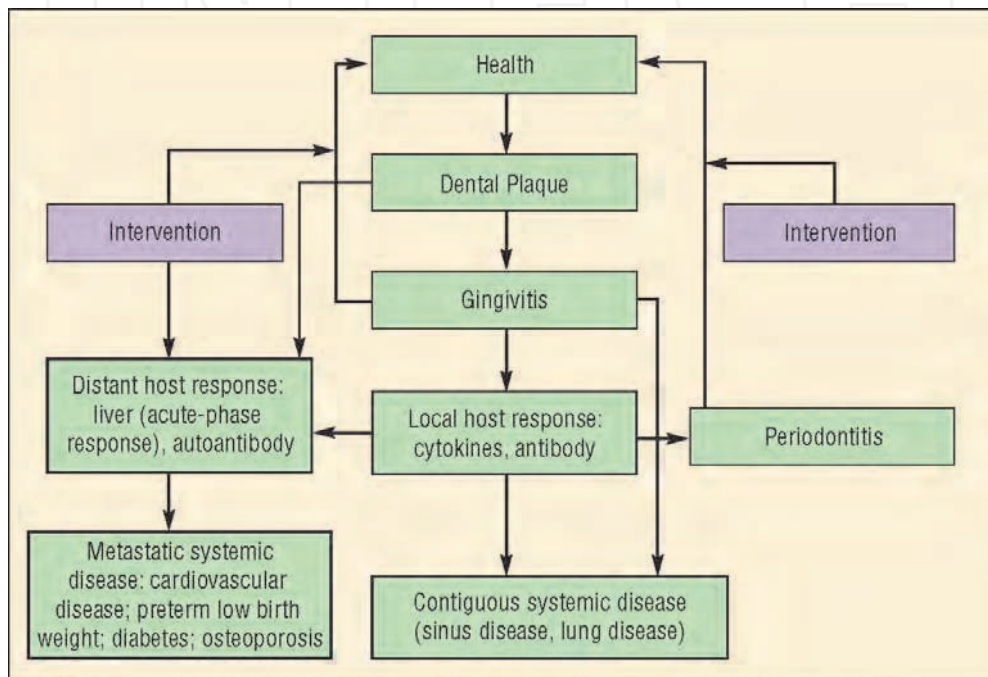


Fig. 8. Suspected interrelationships between gingival inflammation, systemic disease, and response to periodontal therapy.

What is the status of periodontal medicine today? While there are a number of preliminary studies that point to an association between periodontal inflammation and several systemic conditions, as mentioned above, the data are equivocal. In many cases, there has been an emphasis on linking periodontal attachment loss with systemic disease. It is possible that the use of this outcome measure, which represents “historical” evidence for the disease without indicating the temporal sequence or duration of disease activity, may cloud the role of periodontal inflammation in this process. Future investigations are needed that use better definitions for periodontal disease and measures of how gingival inflammation and tooth

loss may best determine the role this localized, chronic disease process plays in the progression and severity of important systemic diseases.

6. Acknowledgement

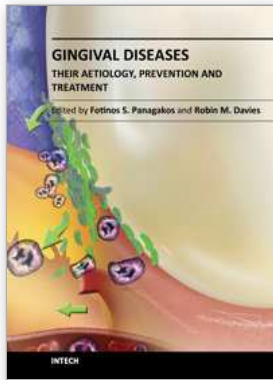
The editors would like to acknowledge that the preceding chapter was reprinted by permission of, and in cooperation with, the author and sponsor of the special issue in which it appeared. It was originally published in the *Compendium*, Vol. 25 Iss. 7 Special Issue.

7. References

- [1] Newman HN. Focal infection. *J Dent Res*. 1996;75:1912-1919.
- [2] Gibbons RV. Germs, Dr. Billings, and the theory of focal infection. *Clin Infect Dis*. 1998;27:627-633.
- [3] Pallasch TJ, Wahl MJ. The focal infection theory: appraisal and reappraisal. *J Calif Dent Assoc*. 2000;28:194-200.
- [4] Kornman KS, Page RC, Tonetti MS. The host response to the microbial challenge in periodontitis: assembling the players. *Periodontol 2000*. 1997;14:33-53.
- [5] Graves DT, Cochran D. The contribution of interleukin-1 and tumor necrosis factor to periodontal tissue destruction. *J Periodontol*. 2003;74:391-401.
- [6] Paster BJ, Boches SK, Galvin JL, et al. Bacterial diversity in human subgingival plaque. *J Bacteriol*. 2001;183:3770-3783.
- [7] Kinane DF, Lindhe J. Pathogenesis of periodontal disease. In: Lindhe J, ed. *Textbook of Periodontology*. Copenhagen, Denmark: Munksgaard; 1997.
- [8] Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. *Science*. 1999;284: 1318-1322.
- [9] Kolenbrander PE. Oral microbial communities: biofilms, interactions, and genetic systems. *Annu Rev Microbiol*. 2000; 54:413-437.
- [10] Armitage GC. Diagnosis of periodontal diseases. *J Periodontol*. 2003;74:1237-1247.
- [11] Albandar JM, Kingman A. Gingival recession, gingival bleeding, and dental calculus in adults 30 years of age and older in the United States, 1988-1994. *J Periodontol*. 1999;70:30-43.
- [12] Albandar JM, Brunelle JA, Kingman A. Destructive periodontal disease in adults 30 years of age and older in the United States, 1988-1994. *J Periodontol*. 1999;70:13-29.
- [13] Sbordone L, Bortolaia C. Oral microbial biofilms and plaque-related diseases: microbial communities and their role in the shift from oral health to disease. *Clin Oral Investig*. 2003;7:181-188.
- [14] Dale BA, Kimball JR, Krisanaprakornkit S, et al. Localized antimicrobial peptide expression in human gingiva. *J Periodontol Res*. 2001;36:285-294.
- [15] Scannapieco FA. Saliva-bacterium interactions in oral microbial ecology. *Crit Rev Oral Biol Med*. 1994;5:203-248.
- [16] Ebersole JL, Machen RL, Steffen MJ, et al. Systemic acute-phase reactants, C-reactive protein and haptoglobin, in adult periodontitis. *Clin Exp Immunol*. 1997;107:347-352.
- [17] Loos BG, Craandijk J, Hoek FJ, et al. Elevation of systemic markers related to cardiovascular diseases in the peripheral blood of periodontitis patients. *J Periodontol*. 2000;71:1528-1534.

- [18] Danesh J, Collins R, Appleby P, et al. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. *J Am Med Assoc.* 1998;279:1477-1482.
- [19] Ridker PM, Buring JE, Shih J, et al. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. *Circulation.* 1998;98:731733.
- [20] Löe H, Theilade E, Jensen SB. Experimental gingivitis in man. *J Periodontol.* 1965;136:177-187.
- [21] Schenkein HA. Finding genetic risk factors for periodontal diseases: is the climb worth the view? *Periodontol 2000.* 2002;30:79-90.
- [22] Silver JG, Martin AW, McBride BC. Experimental transient bacteraemias in human subjects with varying degrees of plaque accumulation and gingival inflammation. *J Clin Periodontol.* 1977;4:92-99.
- [23] Daly CG, Mitchell DH, Highfield JE, et al. Bacteremia due to periodontal probing: a clinical and microbiological investigation. *J Periodontol.* 2001;72:210-214.
- [24] Ley BE, Linton CJ, Bennett DM, et al. Detection of bacteraemia in patients with fever and neutropenia using 16S rRNA gene amplification by polymerase chain reaction. *Eur J Clin Microbiol Infect Dis.* 1998;17:247-253.
- [25] Kane TD, Alexander JW, Johannigman JA. The detection of microbial DNA in the blood: a sensitive method for diagnosing bacteremia and/or bacterial translocation in surgical patients. *Ann Surg.* 1998;227:1-9.
- [26] Meyer MW, Gong K, Herzberg MC. *Streptococcus sanguis*-level. *J Periodontol.* 2001;72:1221-1227. induced platelet clotting in rabbits and hemodynamic and cardiopulmonary consequences. *Infect Immun.* 1998;66: 5906-5914.
- [27] Mosorin M, Surcel HM, Laurila A, et al. Detection of *Chlamydia pneumoniae*-reactive T lymphocytes in human atherosclerotic plaques of carotid artery. *Arterioscler Thromb Vasc Biol.* 2000;20:1061-1067.
- [28] Wick G, Perschinka H, Millonig G. Atherosclerosis as an autoimmune disease: an update. *Trends Immunol.* 2001;22: 665-669.
- [29] Hinode D, Nakamura R, Grenier D, et al. Cross-reactivity of specific antibodies directed to heat shock proteins from periodontopathogenic bacteria and of human origin [published erratum appears in *Oral Microbiol Immunol.* 1998;13:193]. *Oral Microbiol Immunol.* 1998;13:55-58.
- [30] Sims TJ, Lernmark A, Mancl LA, et al. Serum IgG to heat shock proteins and *Porphyromonas gingivalis* antigens in diabetic patients with periodontitis. *J Clin Periodontol.* 2002;29:551-562.
- [31] Scannapieco FA. Role of oral bacteria in respiratory infection. *J Periodontol.* 1999;70:793-802.
- [32] Umeda M, Kobayashi H, Takeuchi Y, et al. High prevalence of *Helicobacter pylori* detected by PCR in the oral cavities of periodontitis patients. *J Periodontol.* 2003;74:129-134.
- [33] Scannapieco FA, Bush RM, Paju S. Associations between periodontal disease and risk for atherosclerosis, cardiovascular disease and stroke: a systematic review. *Ann Periodontol.* 2003;8:38-53.

- [34] Shah SH, Newby LK. C-reactive protein: a novel marker of cardiovascular risk. *Cardiol Rev.* 2003;11:169-179.
- [35] Blake GJ, Ridker PM. Inflammatory bio-markers and cardiovascular risk prediction. *J Intern Med.* 2002;252:283-294.
- [36] Hackam DG, Anand SS. Emerging risk factors for atherosclerotic vascular disease: a critical review of the evidence. *J Am Med Assoc.* 2003;290:932-940.
- [37] Scannapieco FA, Bush RM, Paju S. Associations between periodontal disease and risk for nosocomial bacterial pneumonia and chronic obstructive pulmonary disease: a systematic review. *Ann Periodontol.* 2003;8:54-69.
- [38] Hayes C, Sparrow D, Cohen M, et al. The association between alveolar bone loss and pulmonary function: the VA Dental Longitudinal Study. *Ann Periodontol.* 1998;3:257-261.
- [39] Scannapieco FA, Ho AW. Potential associations between chronic respiratory disease and periodontal disease: analysis of National Health and Nutrition Examination Survey III. *J Periodontol.* 2001;72:50-56.
- [40] Champagne CM, Madianos PN, Lief S, et al. Periodontal medicine: emerging concepts in pregnancy outcomes. *J Int Acad Periodontol.* 2000;2:9-13.
- [41] Scannapieco FA, Bush RM, Paju S. Periodontal disease as a risk factor for adverse pregnancy outcomes: a systematic review. *Ann Periodontol.* 2003;8:70-78.
- [42] Han YW, Redline RW, Li M, et al. *Fusobacterium nucleatum* induces premature and term stillbirth in pregnant mice: implication of oral bacteria in preterm birth. *Infect Immun.* 2004;72:2272-2279.



Gingival Diseases - Their Aetiology, Prevention and Treatment

Edited by Dr. Fotinos Panagakos

ISBN 978-953-307-376-7

Hard cover, 230 pages

Publisher InTech

Published online 22, September, 2011

Published in print edition September, 2011

Gingival diseases are a family of distinct pathological entities that involve the gingival tissues. These signs and symptoms of these diseases are so prevalent in populations around the world that they are often considered to be "normal" features. The diseases are now classified into two main groups namely: Plaque-Induced and Non-Plaque Induced Gingival Diseases. This book provides dentists, dental hygienists, dental therapists and students with a comprehensive review of gingival diseases, their aetiology and treatment.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Fotinos Panagakos and Frank Scannapieco (2011). Periodontal Inflammation: From Gingivitis to Systemic Disease?, *Gingival Diseases - Their Aetiology, Prevention and Treatment*, Dr. Fotinos Panagakos (Ed.), ISBN: 978-953-307-376-7, InTech, Available from: <http://www.intechopen.com/books/gingival-diseases-their-aetiology-prevention-and-treatment/periodontal-inflammation-from-gingivitis-to-systemic-disease->

INTECH

open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821