Overview of Oral Inflammation

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Over the last 25 years, the field of periodontology has witnessed remarkable changes in the understanding of disease processes and their relationship to the body as a whole. The focus on inflammation of the gingiva and periodontium, as important solely for disease of the oral cavity, has shifted to include significant associations with the health of other body systems.

Background

Gingival disease is an inflammatory process characterized by increased redness, swelling, and bleeding of the gingiva on probing. Gingivitis is an inflammation of the gums caused by plaque and bacteria accumulation. It can progress to a more severe state when the inflammatory process extends to the periodontal ligament and alveolar bone. Periodontitis is one of the causes of connective tissue loss, resorption of alveolar bone, and formation of periodontal pockets, eventually leading to loosening and the loss of teeth; periodontitis is one of the most common causes of tooth loss in adults. The process is believed to be episodic rather than continuous, with alternating periods of disease progression and remission.

According to a survey conducted in the United States in the mid 1980s, between 73% and 80% of adults displayed some loss of periodontal attachment (2 mm or more), while 15% of adults between the ages of 60 and 64 displayed advanced periodontitis (i.e., loss of attachment ≥ 6 mm). The risk of developing periodontal disease varies among patients based on factors including age, heredity, diabetes, poor oral hygiene, and smoking. While previously considered an inevitable consequence of aging, it is now recognized that the onset of periodontal disease can be delayed or the severity of the disease reduced once it develops.

Periodontal disease is bacterial in origin, and gingivitis and periodontitis are associated with extensive destruction of the collagen-proteoglycan-connective-tissue matrix. The development of disease occurs through two separately mediated mechanisms (see figure). In both the acute and chronic phases of infection, pathogenic manifestations may result directly from the bacterial invasion of the tissue and production of toxic substances that lead to inflammation, cell death, and tissue necrosis. Tissue damage results from the action of major inflammatory and immunopathologic components activated by the host response. These include alteration of fibroblast function, activation of macrophages that release collagenase and other lytic enzymes, activation of lymphocytes, modulation of fibroblast growth and collagen synthesis, and stimulation of bone resorption. Prostaglandins and cytokines appear to be critically involved in the tissue destruction caused by periodontitis.

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Oral Inflammation → Periodontal Disease

Acute and Chronic Phase
- Bacterial invasion of tissue
- Production of toxic substances
- Inflammation, cell death and tissue necrosis
- Immunopathologic components activated by host response
- Prostaglandins and cytokines involved
- Alteration of fibroblast function
- Activation of macrophages that release collagenase and other lytic enzymes
- Activation of lymphocytes
- Modulation of fibroblast growth and collagen synthesis
- Stimulation of bone resorption

Prevention, Control, and Treatment

Prevention and treatment of periodontal disease aims at slowing the progression of the disease process, increasing the regeneration of alveolar bone, periodontal ligament and root cementum.
and preventing recurrence after treatment. Elimination of gingival inflammation is a first step in reducing the risk for oral disease. Removal and control of bacterial plaque are key components towards this end, and involve mechanical interventions adjusted to the stage and severity of disease. Early control of bacterial plaque accumulation is essential to help slow the development of periodontal disease. Proper dental hygiene, with daily mechanical removal of bacterial plaque by tooth brushing supplemented with flossing, is recommended to control gingivitis.8

Antimicrobial agents can help to slow the progression of periodontal disease. Several antimicrobial agents have been incorporated into mouthrinses or dentifrice preparations to inhibit plaque accumulation. Triclosan, a well known antibacterial agent, has a wide spectrum of action against plaque-forming supragingival and subgingival bacteria, including many types of Gram-positive and Gram-negative non-sporulating bacteria, some fungi, Plasmodium falciparum, and Toxoplasma gondii. The combination of triclosan with a copolymer allows the agent to remain on the tooth surface for a prolonged period of time, providing effective inhibition of plaque formation and of gingivitis.4 A dentifrice containing triclosan/copolymer (Colgate® Total® Toothpaste) has been shown to effectively contribute to the control of bacterial infection, reduce gingival inflammation, and slow the progression of periodontitis.4

New avenues of treatment explore the use of histatins, histidine-rich proteins that are naturally found within parotid and submandibular secretions, and contain antimicrobial peptides that can effectively inhibit plaque accumulation. Animal studies have shown that topically applied synthetic histatins can significantly reduce bleeding and the presence of gingivitis. While still being tested clinically, histatins hold potential for the control of gingival inflammation because they are a natural component of human saliva with no apparent adverse effect on host tissue. Localized antibiotic treatments using novel delivery systems can also be used to control advanced periodontitis and halt acute infection.1

In parallel, the inflammatory nature of periodontitis suggests that blocking inflammatory pathways and modulating host responses via pharmacological treatment may also attenuate periodontal tissue destruction.14 In this research area, trials of topically applied cyclooxygenase inhibitors (e.g., ketoprofen) have been shown to significantly reduce the rate of alveolar bone loss compared to placebo in animal studies.4

The Relationship Between Oral and Systemic Health

It has long been recognized that systemic conditions can contribute to the expression of periodontal disease; metabolic disorders (e.g., diabetes), blood dyscrasias (e.g., leukemia), autoimmune disease (e.g., pemphigus), pregnancy, and puberty all increase the incidence of periodontal disease.1 In recent years, increasing evidence has supported the concept that the relationship between systemic and oral health is bi-directional.15 Much research has documented the association between periodontitis and its effects on preterm delivery and low birth weight newborns.10,12 Studies have also indicated that periodontal disease can increase the risk for cardiovascular disease, respiratory diseases, osteoporosis, and accelerate the progression of diabetes (see figure).

Conclusion

Over recent years, we have increasingly begun to focus on inflammation of the oral cavity, not only as important for disease of the periodontal tissues, but also as a risk factor for systemic diseases. It is evident that we can no longer view gingivitis simply as a precursor of periodontitis, but we should treat it as oral inflammation that needs to be controlled and eliminated for the overall well being of the individual. Any new treatment strategy that can help in controlling gingivitis should have a beneficial effect both on oral health and on systemic health.

References


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Diabetes mellitus is a chronic metabolic disorder affecting carbohydrate, fat, and protein metabolism. It is characterized by hyperglycemia (i.e., elevation of blood glucose concentration) caused by the defective secretion of insulin (type I), or impaired insulin action due to tissue resistance (type II). While there is no known cure for diabetes, appropriate measures can be taken to control blood glucose levels and prevent both acute and chronic complications. Poor glycemic control in diabetic patients has several repercussions, including some on oral health. Patients with diabetes are prone to develop oral complications such as gingivitis and periodontal disease, fungal infections (oral candidiasis, lichen planus), dental caries, tooth loss, enlarged parotid glands, xerostomia, taste dysfunction, and burning mouth syndrome.

The most prominent oral symptom associated with diabetes is the increased prevalence and severity of periodontitis; it is recognized as one of the major complications of diabetes. Persistent poor glycemic control has been associated with an increased incidence and more rapid progression of gingivitis and periodontitis with associated alveolar bone loss. The degree of metabolic control and the duration of diabetes are closely associated with the severity of periodontal disease.

The pathogenesis of periodontal disease involves two components: bacterial infection and the host response. Bacteria present in periodontal pockets initiate an oral inflammatory response that can lead to the deterioration of the supporting periodontal tissues. When the host response is comprised of an excess of pro-inflammatory mediators known as cytokines, prostanoids, and enzymes, the destruction of periodontal tissues occurs. This results in increased pocket depths, loss of clinical attachment, and radiographic evidence of bone loss. In patients with poorly controlled diabetes, periodontal destruction is exacerbated due to hyperglycemia.

**Hyperglycemia and Oral Health**

The effects of hyperglycemia on oral health are two-fold. First, it causes an increase in the concentration of glucose in the saliva and the gingival crevicular fluid of the periodontal pocket, contributing to bacterial proliferation and oral inflammation. Second, hyperglycemia increases the formation of advanced glycation end-products (AGEs); the overexposure of proteins (such as collagen) or lipids to aldose sugars induces non-enzymatic glycation and oxidation. These glycosylated products can create complex molecular arrangements, reducing collagen solubility and increasing levels of pro-inflammatory mediators responsible for the degradation of connective tissues throughout the body of the diabetic, including the oral cavity. Changes to collagen metabolism result in accelerated degradation of both non-mineralized connective tissue and mineralized bone. Research has demonstrated the presence of elevated levels of pro-inflammatory mediators in the gingival crevicular fluid of periodontal pockets of poorly controlled diabetics, compared to non-diabetics or well-controlled diabetics, resulting in significant periodontal destruction with an equivalent bacterial challenge. For clinicians and diabetic patients, this means that the oral hygiene of the diabetic must be optimized to prevent further stimulation of an already primed and heightened host response.

The interaction of AGEs with target cells, such as macrophages, via cell-surface polypeptide receptors stimulates the production of cytokines and matrix mediators.
metalloproteinases, including collagenases and other connective tissue-degrading enzymes. This exacerbation of the pro-inflammatory response in diabetes can lead to delayed wound repair and amplify damage to connective tissues. This is important to consider when evaluating the response of poorly controlled diabetic patients to periodontal therapy. The pro-inflammatory response may be further heightened by the chemotactic properties of AGEs for human monocytes which differentiate into the chronic inflammatory macrophage cells.

Degradation of newly synthesized collagen in connective tissues and alterations in the immune response can both contribute to predisposition to periodontal disease and impaired wound healing. The degree of metabolic control and the presence of other complications (e.g., retinopathy and nephropathy) can be predictive of the periodontal status. Concurrent risk factors (plaque, smoking, stress, medications, pregnancy, hormonal variations) are cumulative and should be considered in the assessment of the periodontal status of a patient.

The presence of AGEs has also been linked to thickening of the basement membrane and altered vasculature. These changes may be associated with enlargement of the parotid glands and decreased salivary flow seen in diabetics, which facilitates plaque accumulation and increases the risk for caries, gingivitis, periodontitis, and candidiasis. Degenerative vascular changes may interfere with nutrient and leukocyte migration to gingival tissue, decreasing oxygen diffusion and elimination of metabolic waste, thereby increasing the severity of periodontitis by decreasing dental healing capacity. Collectively, diabetes creates specific conditions leading to enhanced oral inflammation associated with overproduction of inflammatory mediators and degradation enzymes, all of which participate in worsening periodontal disease.

**Oral-Systemic Interactions**

While a systemic condition like diabetes can affect oral health, there is growing evidence that oral infections can also have systemic repercussions. This bi-directional relationship is especially important for the metabolic control of diabetes. Studies of active inflammatory connective tissue disease have shown that inflammation can trigger insulin resistance. Cytokines, such as tumor necrosis factor (TNF)-α, have been reported to interfere with lipid metabolism and to cause insulin resistance, while interleukins (IL)−1β and IL-6 antagonize insulin action. The host-mediated inflammatory response can thus hinder glyemic control in diabetic patients, in turn creating a vicious cycle of events that compounds diabetes control and further stimulates periodontal disease. Poor metabolic control of diabetes can also increase the risk for other complications of diabetes, such as angiopathy, nephropathy, retinopathy, neuropathy, and delayed wound healing. Prevention and control of oral infection and inflammation, i.e., periodontal disease, is essential for appropriate prevention and optimal management of diabetic complications.

It is also thought that elevations of AGEs in gingival tissue increase vascular permeability. An inflamed periodontium is highly vascular and may serve as a portal to the systemic circulation for bacterial products (bacteremias) and host-produced local inflammatory mediators. Other connections between a poor periodontal status and systemic health sequelae have been studied; adverse pregnancy outcomes and cardiovascular disease are both known complications in diabetics. Recent research has shown that pregnant women with severe periodontitis have a higher risk of giving birth to preterm low-birth-weight babies. Other studies have shown that the risk of major cardiovascular events, such as heart attack and stroke, is significantly higher in those with severe periodontal disease. It has become apparent that prevention and treatment of periodontitis are essential to optimal systemic health, including in the diabetic patient.

**Management of Diabetes and Oral Inflammation**

Control of blood glucose is the fundamental aspect of diabetes management to minimize related complications. Adequate glycemic control will not only reduce glucose concentration in serum, gingival crevicular fluid, and saliva, but also reduces AGE formation and limits inflammation. Prevention and control of periodontal disease must be considered an integral aspect of diabetes management, since improved oral health can lead to improvements in the overall health of diabetic patients.

Given the increased susceptibility of diabetic patients for oral inflammation, emphasis should be placed on reduction of bacterial infection and gingivitis. An optimal prevention plan should include twice-daily brushing and flossing to remove bacterial plaque from teeth. A dentifrice containing triclosan/copolymer (Colgate Total® Toothpaste) has been shown to be very effective in controlling bacterial infection, reducing plaque and gingival inflammation, and preventing or slowing the progression of periodontitis. Restriction of oral infection and inflammation as manifested in periodontitis contributes to the maintenance of normal blood glucose levels, which aids in the overall management of diabetic patients.

For the treatment of periodontitis, a two-step process aimed at the two components of the disease can be considered. The first step is reduction and control of bacteria, both supragingival and subgingival, in the tooth pockets and spaces around teeth. Scaling and root planing helps remove bacterial plaque and associated toxins from the tooth and root surfaces, and can help to prevent the bacterial accumulation that is common on rough surfaces. The second step is inhibition of the enzymes that destroy periodontal tissue so that connective tissue degradation is minimized (host modulation therapy). Clinical trials have demonstrated the efficacy of some tetracycline analogs to inhibit a series of host-derived, tissue-destructive enzymes and inflammatory mediators, thereby reducing the connective tissue damage associated with periodontitis.

**Conclusion**

Diabetes is a complex disease with a wide range of potential complications, including effects on oral health. Integrated strategies for the prevention and treatment of periodontal disease involving the reduction of periodontal pathogens and host modulation therapy greatly reduce the risk for severe periodontitis, and can help in the overall management of the diabetic patient. A diabetic patient who maintains rigorous glyemic control and good oral health has the same risk of severe periodontitis as a non-diabetic patient, emphasizing the importance of diabetes and oral health management.

**References**


Visit www.perio.org for more information on periodontal disease and systemic health.
Atherosclerosis, the thickening and hardening of arteries produced by a build-up of plaque, is the underlying cause of cardiovascular disease (CVD). It is essentially an inflammatory disease, whereby an initial lesion, in response to injury to the endothelium of elastic and muscular arterial tissue, leads to a complex chronic inflammatory process. There is accumulating evidence of a role for infectious agents in atherogenesis; by causing endothelial injury, they may, in part, trigger the inflammatory response. The levels of inflammatory mediators in the systemic circulation, such as C-reactive protein (CRP) and fibrinogen, are indicators of a general inflammatory response and atherosclerosis. This link between inflammation and atherosclerosis suggests that chronic infections, such as oral infections from periodontal disease, may predispose to cardiovascular disease. Significant similarities in the pathogenesis of atherosclerosis and periodontitis have suggested a common underlying biological mechanism for the two conditions. Based on this paradigm, several studies have investigated the relationship between periodontitis and cardiovascular disease. 

Indirect Evidence: Epidemiological Studies

Most of the evidence supporting a relationship between periodontal disease and CVD comes from epidemiological studies. In the late 1980s, pioneer work showed that patients who had a history of myocardial infarction (MI) generally had worse oral health than control subjects. Subsequently, cross-sectional data from the Third National Health and Nutrition Survey (NHANES III) indicated that patients with severe clinical attachment loss were at greater risk for MI than subjects with a healthy periodontium (odds ratio: 3.8). Since then, systematic literature reviews have indicated that most studies report a modest association between periodontal disease and CVD, between a 1.3 and 2-fold increase in the risk of CVD in people with periodontitis. Conversely, treatment of periodontitis was shown to decrease serum concentration of CRP, interleukin (IL)-6 and tumor necrosis factor (TNF)-α, indicating that infection of the periodontium can influence systemic conditions. What remains unclear from these studies, however, is whether periodontitis can predispose to atherosclerosis.

Direct Evidence: Experimental Studies

Direct evidence for the role of oral infection in predisposing to atherosclerosis comes from several lines. The presence of predominant oral pathogens such as Porphyromonas gingivalis, Tannerella forsythensis, and Prevotella intermedia was detected in atherosclerotic plaque, suggesting a possible invasion of atheromas by oral pathogens. In addition, P. gingivalis can invade endothelial cells and can also induce platelet aggregation, a key process in atheroma and thrombus formation. Whether these pathogens actively contribute to the development of atheroma, however, remains to be established. Most of the experimental evidence supporting a relationship between CVD and periodontal disease comes from animal model studies. Using apolipoprotein E-deficient mice, research has shown that clinically induced bacteremia or oral infection with P. gingivalis increase atheroma size compared to non-

Figure 1. Mean carotid intima-media thickness (IMT), adjusted for CVD risk factors, as a function of periodontal bacterial burden

- Biologically linked with periodontal disease
- Putatively associated with periodontal disease
- Associated with healthy periodontal conditions

Adapted from Desvarieux et al., 2005.
infected mice. Similarly, pigs exposed orally to *P. gingivalis* had elevated CRP and increased atheroma size compared to control animals, suggesting a role for this particular periodontal pathogen in the development of atherosclerosis.

A recent study in humans reported a positive independent association between periodontal bacterial burden and carotid intima-media thickness (IMT). Results were adjusted for known risk factors for CVD (age, ethnicity, gender, education, body mass index, smoking, diabetes, systolic blood pressure, low-density and high-density lipoprotein cholesterol). A positive relationship between carotid IMT and bacterial burden was especially strong in patients predominantly infected by specific bacteria involved in the etiology of gingival disease, including *P. gingivalis*, *Actinobacillus actinomycetemcomitans*, *Treponema denticola*, and *Tannerella forsythensis* (Figure 1).  

**Biological Mechanism and Pathogenesis**

Gingival inflammation may influence atherosclerosis in three distinct pathways (Figure 2). Oral infection by periodontal pathogens initiates the formation of dental plaque which leads to inflammation of periodontal tissues. The formation of periodontal pockets increases subgingival space, which is conducive for bacterial growth and deposits. Ensuing local inflammation processes produce micro-ulcerations through the pocket epithelium, promoting risks for distant-site infection and transient bacteremia. Moreover, bacteria release a variety of biologically active molecules, including lipopolysaccharides, endotoxins, chemotactic peptides, proteins, and organic acids, that may then enter the systemic circulation. These products can trigger the host inflammatory response and elevate serum concentration of acute-phase reactants and inflammatory mediators (CRP, serum amyloid A, fibrinogen, haptoglobin, TNF-α, IL-6 and IL-8). Increased levels of circulating inflammatory mediators is thought to contribute to the inflammatory processes leading to atherosclerosis.

Immunization against bacterial pathogens may also induce an autoimmune response involved in the development of atherosclerosis. Homology of some bacterial and human proteins (e.g., heat-shock protein HSP60) raises the possibility that antibodies against bacterial versions of the protein may cross-react with the human protein, inducing an autoimmune response. In the case of HSP60, disruption of arterial endothelial cells is thought to stimulate atherosclerosis. Proinflammatory response may also be enhanced by cross-reactive epitopes that stimulate T-cell response reactive with host antigens, enhancing the effects of bacterial pathogens on cardiovascular health.

**Management and Prevention**

Oral inflammation and periodontal disease are generally chronic and can persist asymptomatically for many years in the absence of appropriate treatment. This results in chronic exposure to local and systemic inflammation, which may induce or enhance already existing inflammatory disease, including atherosclerosis. For this reason, oral preventive care is important not only to preserve oral health, but also systemic health. Management and prevention strategies must sensitize both dental care providers and patients to the importance of good oral health on systemic burden and chronic diseases.

Early control of bacterial plaque accumulation is essential for the prevention of oral inflammation and periodontal disease, with daily mechanical removal of bacterial plaque by tooth brushing supplemented with flossing. Utilization of a dentifrice with antibacterial and anti-inflammation properties will help in achieving this goal. Such a dentifrice, that contains the antibacterial agent triclosan in a copolymer to prolong adherence to the tooth (Colgate Total Toothpaste), has been shown to effectively contribute to the control of oral inflammation and to slow the progression of periodontitis. This is due to its 12-hour antibacterial action coupled with its ability to directly inhibit potent inflammatory mediators.

Control of periodontal infection and inflammation will improve the oral health of patients, decrease the systemic chronic inflammation burden caused by oral inflammation, improve general health, and may ultimately contribute to the reduction of cardiovascular disease.

**References**


Periodontal disease has been linked to an increased risk of respiratory diseases, such as pneumonia and chronic obstructive pulmonary disease (COPD). This article briefly describes evidence for this association, and the mechanisms by which oral bacteria may promote colonization of the lungs by pathogens.

Pneumonia

Pneumonia is defined as inflammation of the lungs resulting from infection, usually bacterial or viral. Pneumonia cases can be divided into two major types: community-acquired and hospital-acquired (nosocomial). About 1.1 million cases of community-acquired pneumonia require hospitalization annually in the United States, with a mortality in hospitalized patients of 12%. Bacteria that often colonize the oropharynx and upper airway, such as Streptococcus pneumoniae, Haemophilus influenzae, and Mycoplasma pneumoniae, usually cause community-acquired pneumonia.

Nosocomial pneumonia represents 13-18% of hospital-acquired infections and occurs in 0.4-0.7% of hospitalizations; mortality is about 30%. Nosocomial pneumonia is usually caused by bacteria acquired from the environment, such as Pseudomonas aeruginosa, Staphylococcus aureus, and enteric Gram-negative bacteria. Nosocomial pneumonia has implications for the institutionalized, scientific advisory panel.

For example, uses a copolymer to improve retention of the bactericide triclosan on oral surfaces, providing 12-hour antibacterial action and direct inhibition of potent inflammatory mediators. Although its effects on respiratory disease have not been tested, this dentifrice may provide some protection because it reduces the growth of oral bacteria and formation of plaque.

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including those living in nursing homes or hospitals for extended periods of time. People in these situations have a higher exposure to pathogens, are less likely to pay close attention to oral health, and are more likely to have poor general health. \(^{10}\) In descriptive studies, institutionalized subjects have more dental plaque and are more prone to colonization by respiratory pathogens than controls. \(^{2}\) Therefore, institutionalized people represent a high-risk group for pneumonia related to oral bacteria.

### Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) was the sixth leading cause of death worldwide in 1990. \(^{2}\) COPD includes chronic bronchitis, in which irritation of the bronchial airway causes increased mucous production and persistent cough, and emphysema, in which dilation of small air passages leads to lung damage. \(^{3}\)

Risk factors for COPD include smoking, chronic exposure to atmospheric pollutants, such as second-hand smoke, and genetic conditions. \(^{10}\) COPD patients experience periodic exacerbations for unknown reasons, and bacterial infections caused by *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis* may contribute to these episodes. \(^{9}\)

### Association Between Periodontal Disease and COPD

Epidemiological studies have revealed an association between periodontal disease and COPD. \(^{2}\) For example, among 13,792 participants in a national health survey who received a standardized dental examination, subjects with a history of COPD had a greater mean periodontal attachment loss (p = 0.001). \(^{12}\) Those with a mean attachment loss of at least 2.0 mm were more likely to have COPD than those with a mean attachment loss of less than 2.0 mm (odds ratio 1.35, 95% confidence interval = 1.07-1.71). However, this association has been reported in epidemiological studies only. To date, no prospective studies have investigated the link between periodontal disease and COPD. \(^{2}\)

### Potential Mechanisms by which Oral Bacteria Influence Respiratory Disease

At least four mechanisms have been envisioned \(^{11}\) to explain the role of oral bacteria in the pathogenesis of respiratory disease (see Figure).

**First**, oral pathogens may be directly inhaled. Organisms living in dental plaque are shed into saliva, and small droplets may be aspirated into the lungs. Normally, the defense mechanisms of the lungs prevent infection. However, bacterial colonization of the lower airway can occur if the immune system is suppressed or defective, or if an unusually virulent pathogen is aspirated, or if an overwhelming number of organisms are aspirated simultaneously.

**Second**, the action of bacterial enzymes on oral epithelial cells may promote colonization by respiratory pathogens. Ordinarily, molecules on the surface of epithelial cells protect against bacterial adhesion, but oral bacteria release enzymes that may degrade these molecules. Poor oral health results in high protease activity in saliva that may damage epithelial cell surfaces and cause increased susceptibility to colonization by pathogenic bacteria.

**Third**, bacterial enzymes may reduce the protection against colonization provided by mucosal secretions. Proteins in mucosal secretions appear to bind to invading bacteria, inhibiting their adherence to epithelial cells and promoting their elimination from the host. Enzymes from oral bacteria can modify these protective proteins, preventing them from binding to invading pathogens.

**Fourth**, cytokines may contribute to colonization of the respiratory epithelium. Periodontitis stimulates gum tissue to release cytokines, which may induce changes on the epithelial cell surface. Cytokines also recruit neutrophils to the site of inflammation; neutrophils produce proteases and oxygen radicals that may damage the epithelium. Either of these actions may increase the susceptibility of tissue to bacterial colonization. Contamination of the respiratory epithelium by orally released cytokines, or release of cytokines by the respiratory epithelium itself in response to contact with oral bacteria, may promote respiratory infection.

### Conclusion

Regardless of the mechanism, large numbers of respiratory pathogens in the oral cavity appear to promote respiratory diseases, such as pneumonia and COPD. Although further study is needed to define the relationships between periodontitis and respiratory disease, inhibiting growth of oral bacteria may reduce the risk of pneumonia. Therefore, proper attention to oral hygiene, including brushing with an antibacterial dentifrice such as Colgate® Total® and regular flossing, may help prevent respiratory illness, especially in vulnerable populations, such as hospitalized patients and institutionalized elders.

### References


Visit www.perio.org for more information on periodontal disease and systemic health.
Bone loss is a central, common feature of both periodontal disease and osteoporosis. Osteoporosis, or low bone mineral density (BMD), results when bone metabolism becomes unbalanced, with bone resorption by osteoclast cells occurring at a faster rate than bone production by osteoblast cells. A woman with a BMD 2.5 standard deviations below the mean peak density for young women has osteoporosis, according to the definition of the World Health Organization. Prevalence is higher in women than men and increases with age. About 35% of post-menopausal white women have osteoporosis of the hip, spine, or distal forearm; prevalence in Asian women is similar. Increased risk of fracture associated with osteoporosis is a serious concern. After age 50, 50% of women and 25% of men will have an osteoporosis-related fracture, and the financial implications are significant. In 2002, for example, the direct cost of treating hip fractures was $18 billion in the US alone.

In periodontal disease, oral inflammation due to chronic infection of the tissue around the teeth results in destruction of oral bone and periodontal ligament (Figure 1), ultimately leading to tooth loss. Oral inflammation increases production of cytokines, such as interleukin-6, that stimulate osteoclast activity and promote bone resorption. A similar mechanism may contribute to osteoporosis, raising the question of whether people with low skeletal BMD are at increased risk of oral osteopenia (Figure 1). Several lines of evidence indicate that there is an association between osteoporosis and periodontal disease.

Common Risk Factors
First, there are risk factors common to both conditions. Both osteoporosis and periodontal disease become more prevalent with advancing age, and individuals with a family history are at higher risk. In women, estrogen deficiency increases the risk of both oral and systemic osteopenia. Smoking is a risk factor for, and hastens progression of, both conditions.

Cross-Sectional and Longitudinal Studies
Second, many studies have reported an association between systemic BMD and periodontal disease, regardless of whether the measure of periodontal status is clinical (e.g., attachment loss, probing pocket depth), or radiographic (alveolar crestal height loss). Although studies of osteoporosis and clinical attachment level have produced mixed results, larger cross-sectional studies and at least two prospective studies support an association. For example, in a three-year longitudinal study, 70-year-old subjects were divided into osteopenia and non-osteopenia groups based on BMD of the heel at baseline. The number of sites with at least 3 mm of additional attachment loss after three years was significantly higher in the osteopenia group (p =
This study indicates that, in this older population, systemic BMD may be one factor in predicting periodontal disease progression. A positive association between low BMD and tooth loss has also been reported in many studies, and studies that found no association have generally been in younger populations.

The relationship is not firmly established, however, because some studies report no association, and of those that do, most are cross-sectional, many have small sample sizes, and most do not control adequately for possible confounding factors, such as smoking status, postmenopausal hormone use, or treatment for periodontal disease. More prospective studies are needed.

**Therapies Affecting Both Osteoporosis and Periodontal Disease**

Third, some interventions that improve systemic BMD also improve measures of periodontal disease. Improvement of the two conditions by the same therapies suggests an underlying connection. The three classes of therapy that have been implicated in this regard are 1) hormone replacement therapy (HRT), 2) diet supplementation with calcium and vitamin D, and 3) bisphosphonates.

HRT appears to improve oral bone density, and also leads to less bleeding on probing, less frequent clinical attachment loss, and less tooth loss. These effects are consistent with the benefit of HRT for systemic BMD.

Sufficient dietary calcium is essential for maintaining BMD, and low calcium intake may increase the risk of periodontal disease or hasten disease progression. Vitamin D aids calcium absorption from the intestine and regulates calcium metabolism. A three-year prospective, placebo-controlled trial of calcium and vitamin D supplementation in men and women over age 65 found that fewer subjects who received supplements lost at least one tooth (Figure 2, odds ratio for tooth loss = 0.4, p < 0.05). In a two-year follow-up period, fewer subjects consuming at least 1000 mg of calcium per day lost one or more teeth than those who consumed less calcium (Figure 2, odds ratio for tooth loss = 0.4, p < 0.03). These results support a potential benefit of calcium and vitamin D for improving periodontal disease.

Few studies have examined the impact of bisphosphonate therapy on periodontal outcomes. One prospective, double-blind trial in women aged 55–65 years who were not receiving HRT found greater improvement in probing depth and gingival bleeding in subjects receiving bisphosphonate alendronate than in those receiving placebo. Systemic BMD and alveolar crest height increased in the alendronate group but worsened in the placebo group. More studies of bisphosphonates are needed to confirm their impact on periodontal disease.

**Possible Mechanisms**

The above evidence supports an association between systemic BMD and periodontal disease. The mechanisms underlying this association, however, are unknown. Patients with low systemic BMD may also have low oral BMD, allowing periodontal disease to progress more rapidly because there is simply less oral bone present. A second possibility is that osteoporosis and bone loss due to periodontal disease both proceed by the same cellular mechanism, namely increased production of cytokines, such as interleukin-6, that stimulate osteoclast activity. Genetics may also play a role, in that patients predisposed to BMD loss may also be more likely to suffer periodontal damage. Finally, certain lifestyle factors may increase a patient’s risk of bone loss and periodontal disease.

Regardless of the mechanism, patients with low systemic BMD appear to be at higher risk for progression of periodontal disease. Therefore, it is especially important for patients who have osteoporosis or who are at high risk for systemic bone loss to prevent oral inflammation through good oral hygiene, including daily brushing with an antibacterial dentifrice, such as Colgate® Total® Toothpaste. Colgate® Total® uses a copolymer to improve retention of the antibacterial agent triclosan on oral surfaces, resulting in antibacterial and antiplaque activity for as long as 12 hours after brushing. Colgate® Total® also directly inhibits potent inflammatory mediators, helping to keep oral inflammation under control.

**Conclusion**

Although mechanisms explaining the association between periodontal disease and osteoporosis have been suggested, it is unknown if one of these conditions helps cause the other, if they are independently caused by the same factors, or if the association is coincidental. More prospective longitudinal studies, ideally intervention trials, are needed to understand this relationship. Given the increasing worldwide prevalence of osteopenia and osteoporosis, a full understanding of the precise relationship between these two diseases is necessary. Measures commonly used to prevent and treat systemic bone loss may have a beneficial impact on the oral health of the population as well.

**References**

Oral Inflammation and Patient Management

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The effects of oral inflammation are not limited to oral health. The previous five installments in this series of articles have addressed various aspects of the relationship between oral inflammation and systemic conditions, including cardiovascular disease, respiratory diseases, osteoporosis, and diabetes. In this respect, it is critical to manage oral inflammation not only for oral health, but also to maintain the general health of patients.

Oral Inflammation

Oral inflammation is the basis of gingivitis and periodontitis; it is caused by bacteria that initiate the destruction of gingival tissue and compromise periodontal attachment. Bacteria adhere to oral surfaces and aggregate to produce plaque, or dental biofilm, that are complex and physically structured microbial communities able to support the growth of several pathogenic species in large numbers. Dental biofilm is largely composed of polysaccharides that form a physical barrier which protects bacteria from the effects of antibiotics, antiseptics, and host defense mechanisms.

The pathogenic bacteria in the periodontium have the ability to evade the host defense mechanisms that would routinely control such infections and prevent disease. This breakdown in the host defense mechanism appears as an inflammatory response, which can itself contribute to tissue pathology, promoting the release of tissue-derived enzymes that destroy the extracellular matrix and bone. Antigens released by bacterial cells stimulate the production of antibodies which are not effective at killing bacteria within biofilm, but may form immune complexes that further damage surrounding tissues.

The main underlying concepts for the treatment of oral inflammation are summarized in the figure at right. Therapy is targeted at three interdependent components to prevent initiation or halt progression of oral inflammation. Treatment requirements and effectiveness are modulated by genetic and environmental factors. The first component is to remove dental biofilm and reduce the levels of bacteria, which also changes the composition of the oral microflora. The second component involves the modulation of the host response (inflammation) by limiting the production of antibodies and the release of protease caused by bacterial tissue invasion. The last component involves alteration of the oral microhabitat by modifying the physical features that facilitate the growth and accumulation of bacteria.

Several factors can contribute to oral inflammation (see table overleaf). Some factors can be modified to minimize the risk of oral diseases and improve control of oral inflammation, while others will help to define an individual treatment plan for optimal oral health.

Management of the Patient with Oral Inflammation

The optimal strategy to eliminate dental biofilm from the oral cavity has four dimensions: physical removal of dental biofilm; destruction of the remaining bacteria using antimicrobial agents; routine oral hygiene habits; and patient education.
**Inflammation and Physical Removal of Biofilm**

Dental biofilm offers remarkable resistance to host defense mechanisms and antibacterial agents. The most effective method to disrupt dental biofilm is through mechanical means, such as the use of power and hand instrumentation, and oral physiotherapy aids such as toothbrushes, floss, and other interdental devices. Mechanical alteration of dental biofilm disrupts the bacterial structure and is essential in dislodging bacteria, reducing plaque, preventing dental calculus, and maintaining subgingival bacteria at a level below that which is capable of initiating inflammation.7

**Risk Factors Contributing to Oral Inflammation**

- Aging
- Concomitant use of medication
- Diabetes
- Gender
- Genetics
- HIV infection
- Nutrition
- Pregnancy
- Smoking
- Specific periodontal pathogens
- Stress
- Substance abuse
- Systemic conditions (e.g., immunosuppression)

Alteration of the microenvironment surrounding the subgingival microbiota can affect numbers, proportions, and prevalence of bacterial species present in the oral cavity. Some physical features predisposing to the accumulation of plaque, such as over-contoured crowns, open or overhanging margins, narrow embrasure space, open contacts, caries, or tooth malposition, should be preventively corrected to improve the patient’s ability to remove the biofilm. Gingival deformities hindering biofilm control should be corrected by adequate surgery to reduce the potential for plaque accumulation.12,13 Daily removal of supragingival plaque reduces gingival inflammation and also controls the amount of subgingival plaque. It also can significantly reduce the proportion of known periodontal pathogens such as *B. forsythus*, *P. gingivalis*, and *A. actinomycetemcomitans*.10

**Antibacterial Agents**

Despite frequent mechanical cleaning, the rapid multiplication rates of bacteria warrant consistent efforts to decrease these pathogens to baseline levels.10 Use of topical oral rinses containing antibacterial agents, such as chlorhexidine (Periex®, PerioCard®) or essential oils (Listerine®), or of an antibacterial dentifrice (Colgate® Total®) will help to prevent or delay bacterial accumulation and dental biofilm formation.5 Daily brushing with Colgate Total has been shown to reduce the growth of oral bacteria and the formation of plaque.14 It is the only toothpaste in the United States that contains the antibacterial agent triclosan, and uses a patented copolymer to improve retention of the bactericide triclosan to oral surfaces, providing 12-hour antibacterial action. In addition, it provides direct inhibition of potent inflammatory mediators, thus affecting the inflammation process as well.10,11 Topical agents improve the control of supragingival plaque, which will also have indirect effects on subgingival plaque.7

**Individualized Patient Oral Hygiene Program**

A long-term treatment plan for managing chronic oral inflammation should include regular maintenance care by an oral healthcare professional for thorough elimination of dental biofilm and calculus, and to perform periodic evaluation of the periodontal status.7 Frequency of visits—every three to six months—depends on the patient’s condition and risk factors, and the extent of bacterial infection, oral inflammation, and periodontal disease. Diagnosis of the periodontal condition is based on traditional clinical assessments, including the presence of clinical signs of inflammation (gingival bleeding), probing depth, loss of clinical attachment, radiographic findings and various symptoms such as pain, ulceration, and amount of observable plaque and calculus.15 An accurate diagnosis of periodontal disease severity is essential for selecting an appropriate treatment and maintenance strategy for a given patient. For the patient with gingivitis, a combination of routine personal plaque control in combination with professional removal of plaque, calculus, and local contributing factors may be needed to reduce inflammation. At-home use of an antimicrobial toothpaste containing triclosan/copolymer (Colgate Total) has been shown to improve the outcome of a gingivitis treatment regimen and reduce oral inflammation.10,11

**Self-Care Communication and Education**

Control of oral inflammation essentially relies on preventive measures to inhibit dental biofilm accumulation, and can be achieved by maintaining good oral hygiene involving daily flossing and brushing with an antibacterial antiplaque toothpaste. Patient education and support are essential for successful prevention or treatment of gingivitis and oral inflammation, and personalized oral hygiene instruction should be provided, taking into account each patient’s profile. Patient non-compliance to treatment is a frequent cause of failure to prevent inflammation and periodontal disease.11 Consequences of a lack of attention to the daily treatment regimen should be explained to patients to reinforce their motivation to perform the required daily preventive measures.11

An individualized treatment plan is needed to monitor the maintenance of the oral environment and the progression of oral inflammation. Frequent follow-up evaluation of a patient’s condition to determine the need for further treatment is recommended.11 Communication between practitioners and patients is an essential aspect of oral inflammation management. Oral healthcare professionals should advise patients on how to modify risk factors to reduce oral inflammation. Cessation of smoking, a key risk factor for oral disease, should be advocated.

A good plaque control program, coupled with regular periodontal maintenance by an oral healthcare professional and reduction of risk factors, can effectively manage oral inflammation in the majority of patients.

**References**


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