

# White Papers

## ORAL INFLAMMATION

### Scientific Advisory Panel

Ray Williams, DMD  
Chair, Department of Periodontology  
University of North Carolina  
School of Dentistry  
Chapel Hill, North Carolina

Maria Ryan, DDS, PhD  
Associate Professor, Department of  
Oral Biology and Pathology  
SUNY at Stony Brook  
School of Dental Medicine  
Stony Brook, New York

Sara Grossi, DDS  
Clinical Assistant Professor of Oral  
Biology  
SUNY at Buffalo  
School of Dentistry  
Buffalo, New York

Frank Scannapieco, DMD, PhD  
Professor and Chair, Department of  
Oral Biology  
SUNY at Buffalo  
School of Dentistry  
Buffalo, New York

Michael Reddy, DMD  
Professor and Chair, Department of  
Periodontology  
University of Alabama at  
Birmingham  
School of Dentistry  
Birmingham, Alabama

Rebecca Wilder, RDH, MS  
Director, Graduate Dental Hygiene  
Education Program  
University of North Carolina  
School of Dentistry  
Chapel Hill, North Carolina

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## Overview of Oral Inflammation

Ray C. Williams, DMD, Chair, Department of Periodontology  
University of North Carolina School of Dentistry

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.<sup>1</sup> *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.<sup>1</sup> *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.<sup>1</sup> 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  $\geq 6$  mm).<sup>1</sup> The risk of developing periodontal disease varies among patients based on factors including age, heredity, diabetes, poor oral hygiene, and smoking.<sup>2,3</sup> While previously considered an inevitable consequence of aging, it is now recognized that periodontal disease can be prevented or treated 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.<sup>1</sup> 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.<sup>1</sup> Prostaglandins and cytokines appear to be critically involved in the tissue destruction caused by periodontitis.<sup>4</sup>

### Oral Inflammation → Periodontal Disease

#### Acute and Chronic Phase

- Bacterial invasion of tissue
- Production of toxic substances
- Inflammation, cell death and tissue necrosis
- Inflammatory/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 for the prevention of periodontal disease. Proper dental hygiene, with daily mechanical removal of bacterial plaque by tooth brushing supplemented with flossing, is recommended to control gingivitis.<sup>1</sup>

Antimicrobial agents can also play a role in the prevention and treatment 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*.<sup>5</sup> 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.<sup>4</sup> 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.<sup>6</sup>

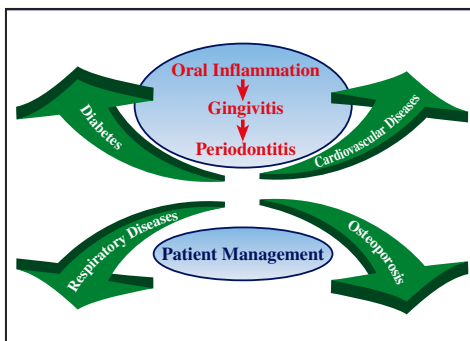
New avenues of treatment explore the use of histatins, histidine-rich proteins that are naturally found within parotid and submandibular secretions, and contain antimicrobial peptides that can effectively inhibit plaque accumulation. Animal studies have shown that topically applied synthetic histatins can significantly reduce bleeding and the progression of gingivitis.<sup>7</sup> 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.<sup>8</sup> Localized antibiotic treatments using novel delivery systems can also be used to control advanced periodontitis and halt acute infection.<sup>4</sup> For example, minocycline topically applied in microspheres (Arestin®) into periodontal pockets has been shown to significantly reduce pocket depth when combined with scaling and root planing.<sup>9</sup>

In parallel, the inflammatory nature of periodontitis suggests that blocking inflamma-

tory pathways and modulating host responses via pharmacological treatment may also attenuate periodontal tissue destruction.<sup>3,4</sup> 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.<sup>4</sup>

### 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.<sup>1</sup> In recent years, increasing evidence has supported the concept that the relationship between systemic and oral health is bi-directional.<sup>10</sup> Much research has documented the association between periodontitis and its effects on preterm delivery and low birth weight newborns.<sup>3,10-12</sup> 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).



The general mechanism behind the systemic effects of periodontitis is thought to involve, in part, a systemic inflammatory response through blood-borne oral lipopolysaccharides and oral bacteria which provoke the release of the cytokines interleukin-6 and tumor necrosis factor  $\alpha$ .<sup>10</sup> These mediators activate a hepatic acute phase response with secretion and systemic release of C-reactive proteins, haptoglobin,  $\alpha_1$ -antitrypsin and fibrinogen.<sup>10</sup> Understanding and managing the impact of oral infection on systemic health is a challenge of periodontal medicine.<sup>10</sup> For example, the identification and validation of systemic markers for periodontitis will provide powerful tools to diagnose, treat, and monitor

patients with periodontitis. These relationships, as well as management of the patient with periodontal disease, will be the topics of future issues of this *Colgate White Papers* series.

### 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.

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