

Nutrition, Inflammation, and Periodontal Disease

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INTRODUCTION

Historically, periodontal disease has been seen as an inflammatory disease with limited associations to nutrition, with the possible exception of scurvy in which teeth are readily lost due to reduced collagen support in the periodontal ligament. However, pathology related to scurvy differs from the pathology of chronic inflammatory periodontal disease. The aim of this article is to provide an overview of the ways in which nutrition can influence the two main subsets of periodontal disease: gingivitis and periodontitis. Recent data have suggested that nutrition has an important role in periodontal disease. Nutrients that can act as antioxidants that may modulate gingival inflammation. Obesity has significant metabolic and systemic immune and inflammatory effects and also may increase the host's susceptibility to periodontal disease through its impact on metabolic and immune parameters.

PERIODONTAL DISEASE

Periodontitis is a disease of the supporting structures of the teeth resulting from the interaction between pathogenic bacteria and the host's immune response. Periodontitis is caused by microbial plaque building up on the tooth margins of susceptible patients. Accumulation of plaque and calculus (plaque that calcifies) produces a low-grade inflammatory response in the gingiva (gums). If the inflammatory process is allowed to progress, reduction in connective tissue support (attachment loss) occurs, and teeth loosen, eventually are extruded, and lost due to loss of bony and connective tissue support. Periodontitis affects 10% to 15% of any population to the extent that these individuals will lose half their teeth by the age of 50 y. With the reduced prevalence of caries and subsequent loss of teeth in the aging population, periodontal disease has become a more significant problem. The microbes involved in chronic periodontitis and aggressive periodontitis are predominantly gram-negative anaerobic bacilli with some anaerobic cocci and a large quantity of anaerobic spirochetes. These bacteria produce a number of molecules, including lipopolysaccharides, proteases, and other cytotoxic molecules.

Among the host's responses, polymorphonuclear leukocytes serve as the initial host defense against these periodontal pathogens. After stimulation by bacterial antigens, polymorphonuclear leukocytes produce singlet oxygen (O_2^-), a reactive oxygen species (ROS), during phagocytosis. In addition to being released into the phagosome, O_2^- is released into the extracellular environment. Hypochlorous acid (HOCl), another ROS, is produced by myeloperoxidase during phagocytic degranulation.¹ These ROS contribute to tissue destruction by damaging DNA and protein, causing lipid peroxidation and oxidation of other important enzymes (such as antiproteases) and stimulating proinflammatory cytokine release by monocytes and macrophages through activation of the tran-

scription factor nuclear factor κ B.² Studies also have suggested that ROS stimulate osteoclast activation.³ Compared with healthy controls, patients with adult periodontitis generate higher levels of many ROS.⁴ In addition, several studies have demonstrated a correlation between ROS and periodontal disease activity.^{5,6}

NUTRIENTS AS MODULATORS OF INFLAMMATION

The damage mediated by ROS can be mitigated by antioxidants through three separate mechanisms: scavenging of free radicals as they form, sequestering transition metal ions, and catalyzing oxidation of other molecules. Major extracellular antioxidants include vitamin C (ascorbate), vitamin E (α -tocopherol), carotenoids, and reduced glutathione. Ascorbate is a powerful scavenger of free radicals and protects against oxidants in cigarette smoke. It also regenerates α -tocopherol from the tocopherol radical that forms at membrane surfaces.⁷ Studies of vitamin C and periodontal disease have produced mixed results. Although studies have not shown a clear relation between plasma ascorbate levels and inflammatory periodontitis, an epidemiologic study of vitamin C intake demonstrated a positive association between low dietary vitamin C intake and periodontal disease, especially among smokers.^{8,9}

Vitamin E terminates the free radical chain reaction and stabilizes membrane structure, but the molecule has limited mobility, which restricts its efficacy.¹⁰ Like vitamin C, no statistically significant differences have been found in plasma vitamin E between individuals with and without periodontal disease, although these studies were not conducted with modern techniques.¹¹ Recent studies of gingival tissue have suggested a mitigating effect of vitamin E on periodontal inflammation and collagen breakdown and lower gingival levels vitamin E among those with periodontal disease compared with healthy controls.¹²⁻¹⁴

Carotenoids function as radical-trapping antioxidants. With the exception of Papillon-Lefevre syndrome, almost no research has been done investigating the role of carotenoids in periodontal disease. In the setting of Papillon-Lefevre syndrome, retinoids had no observed positive influence on periodontal status.¹⁵ Recent genetic research has indicated that defects in polymorphonuclear leukocyte functional enzymes are responsible for the syndrome. The defective enzyme, cathepsin C, is central to the generation of ROS.^{16,17} High levels of oxidative stress have been demonstrated in Papillon-Lefevre syndrome, suggesting a potential role for antioxidants.¹⁸

Reduced glutathione serves as an antioxidant and as a modulator of immune function. Increasing reduced glutathione has been shown to block ROS-mediated activation of nuclear factor κ B and to block proinflammatory cytokine production.¹⁹ Studies of periodontal pathogens have demonstrated that many promote cytokine-related tissue damage by degrading reduced glutathione or preventing formation of reduced glutathione through degradation of cysteine.²⁰ However, few studies have been evaluated the impact of reduced glutathione as mediated through its precursors (such as *N*-acetylcysteine) on periodontal health.

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BODY FAT AS A PROMOTER OF INFLAMMATION

Several decades ago, obesity was noted to contribute to the severity of periodontal disease in rats.²¹ Only recently has obesity been noted to be a risk factor for periodontal disease in human studies. In a study of Japanese adults, Saito et al. associated increasing body mass index and waist-to-hip ratio with increased risk of periodontitis.²² In a study of older adults in New England, increased body mass index was associated with gingival bleeding, and periodontal disease was associated with weight gain.²³ The pathophysiology of this relation has not been clearly elucidated. Although these studies were observational in nature and may be confounded by other health behaviors (such as smoking), recent evidence has demonstrated that adipose tissue secretes a variety of molecules that affect the metabolism of the entire body and contribute to low-grade systemic inflammation. Adipose tissue secretes leptin, interleukin-6, tumor necrosis factor- α , adiponectin, complement factor C3, angiotensinogen, and plasminogen activator inhibitor-1. Many of these molecules are secreted in proportion to the amount of adipose tissue present.²⁴ Interleukin-6 and tumor necrosis factor- α in turn stimulate production of C reactive protein and other acute phase reactions in the liver.²⁵ Thus, increasing body fat may induce a hyperinflammatory response in periodontal disease.²⁶ Obesity, like smoking, may have the potential of modulating the host's immune and inflammatory system, rendering the patient more susceptible to the effects of microbial plaque. Likewise, individuals who are obese may ingest larger quantities of nutrient-poor, calorie- and saturated fat-dense foods that may contribute to poor overall oral health.

In summary, nutrition factors in terms of nutrient intake and adiposity may play an important role in periodontal disease. Additional research is needed to explore these relations at the population and molecular levels. Epidemiologic studies should evaluate relations between antioxidant nutrients and periodontal disease. Given the potentially modulating role of antioxidants on the detrimental effects of smoking, the interaction between smoking and antioxidant status should be carefully addressed. Much of the basic research thus far has tested nutrient mechanisms in chronic disease processes other than in periodontal disease²; there is a need to consider the influence of nutrient mechanisms and inflammation associated with periodontal disease. The impact of adiposity and weight change on inflammation in general and periodontal disease in particular is ripe for investigation.

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