



## Periodontal medicine, part II: the relationship between periodontal disease, atherosclerosis, coronary heart disease, and stroke

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### Introduction

Approximately 20% of all annual deaths are caused by cardiovascular disease (CVD). CVD is the major cause of death in developed countries such as the United States. The classical risk factors of CVD (hypertension, hypercholesterolemia, and smoking) account for 50% to 66% of the total cases of CVD. Consequently other risk factors have yet to be determined and further scientific investigation is needed into the pathogenesis of CVD. Recently, investigators have speculated on the relationship between chronic oral infections and CVD. This clinical update will discuss these possibilities and will expound upon the relationship between periodontal disease and atherosclerosis, coronary heart disease (CHD), and stroke.

### Atherosclerosis

Atherosclerosis, the primary cause of death and disability in the United States, is a chronic condition associated with a hyperinflammatory state. In the scientific literature, direct and indirect evidence exists that suggests there is a causative relationship between periodontal pathogens and atherosclerosis. Direct evidence of the role of periodontal disease in atherosclerosis is supported by the identification of periodontal pathogens (such as *T. Forsythus* and *P. Gingivalis*) in human carotid biopsies and their possible local effects on the vessel lumen (1). Through an indirect mechanism, periodontal disease results in elevated systemic levels of inflammatory mediators such as cytokines, with some of these mediators influencing the endothelial cells of vessels. These cytokines cause the endothelial cells of the circulatory vessels to have an increased expression of adhesion factors for circulating inflammatory cells, specifically monocytes. These hyperactive monocytes attach to the vessel lining, migrate through the subendothelial layer, and become embedded in the intima layer. These monocytes subsequently release more cytokines locally to exacerbate this inflammatory process. They also actively ingest circulating Low Density Lipoproteins (LDL) and then become known as foam cells, due to their histologic appearance. These foam cells (monocytes) increase in number and dimension in the vessel lining causing the intima layer to thicken and bulge into the vessel lumen. This narrowing of the lumen increases the risk of an ischemic event. Mattila examined periodontitis patients with and

without atherosclerosis and found there was a positive association between the severity of periodontal disease and atherosclerosis (2). A recent medical report in the journal *Circulation* detailed the profile of 657 dentate patients with a negative history of stroke and myocardial infarction (MI), but demonstrating an increased incidence of atherosclerosis. Patients were evaluated for cholesterol levels, smoking, blood pressure, and the amount of carotid narrowing, which is an indicator of future stroke. Likewise, comprehensive periodontal exams were completed, including collection of 4,500 subgingival microbial samples for bacterial analysis. After compensating for all risk factors, patients with periodontal pathogens from the subgingival samples were found to have an increased carotid thickness and were more at risk for an atherosclerotic event (3).

### Coronary Heart Disease

Studies have demonstrated an association between inflammatory factors and CHD (4). Arbes found that the risk of having a heart attack increased as the severity of periodontal disease increased, up to 3.8 times that of an individual without periodontal disease (5). For comparison, the risk of having a heart attack in a smoker is approximately 3.5 times greater than a non-smoker. Longitudinal studies have suggested that poor periodontal health precedes adverse cardiovascular events. Individuals <50 years of age with periodontal disease had a 70% increase in the risk of death from a CHD event (6). Beck, in an 18-year study, detected a positive relationship between periodontal bone loss and the incidence of CHD, with the greatest amount of bone loss resulting in a 40% increase for signs of myocardial infarction (MI) (7). Known periodontal pathogens potentially associated with CHD and MI has been investigated. For example, in a study comparing MI patients with and without periodontal pathogens, Genco found an increased odds ratio for MI when periodontal pathogens such as *T. Forsythus* and *P. Gingivalis* were isolated from periodontal pockets (8).

### Stroke

Research has recently shown that periodontal disease is associated with an increased risk of stroke (9). In 2004, a report in the medical journal *Stroke* evaluated 173 stroke patients for traditional risk factors and adverse lifestyles.

After compensating for all risk factors, there was a significant association (up to 79% with *P. Gingivalis*) between periodontal pathogens and stroke, and the presence of these periodontal pathogens could be indicative of a future stroke (10). Similarly, Beck found that bone loss due to periodontal disease had an increased odds ratio for CHD and stroke independent of other known risk factors (11). Grau assessed the dental status of 300 patients with a history of stroke and found an increased odds ratio of 2.6 for the patients with periodontal disease and 3.2 for tobacco use (12). Analysis of data from the National Health and Nutritional Examination Survey I has shown that periodontal disease is a significant risk factor for non-hemorrhagic stroke (13). Non-hemorrhagic stroke, as compared to hemorrhagic stroke, results from atherosclerotic changes and arterial narrowing implicating the systemic influences of periodontal disease.

## Conclusion

Even though periodontal disease may be less of a risk factor when compared to smoking and LDL, the control of this chronic inflammatory disease should be part of the protocol for management of atherosclerosis, CHD, and stroke. Periodontal therapy is another means of potentially modifying a risk factor and reducing the morbidity associated with these cardiovascular disease processes. The evidence of direct and indirect systemic influences of periodontal pathogens on medical conditions continues to emerge through longitudinal studies and will result in an increased emphasis for improving medical health through dental health.

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