Published in final edited form as:

J Dent. 2009 August ; 37(8): S581–S582. doi:10.1016/j.jdent.2009.05.016.

PERIODONTAL DISEASE AND MACROVASCULAR DISEASE: WHAT IS THE EVIDENCE?

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There are several levels of evidence that need to be fulfilled to accept that a putative risk factor is causally associated with a particular disease: These include (i) a biologically plausible scenario by which the exposure contributes to the outcome; (ii) supporting data from epidemiologic studies (cross-sectional, case-control and prospective cohort studies); (iii) evidence from mechanistic, experimental studies; and (iv) ultimately, evidence from intervention studies, ideally randomized controlled trials.

Periodontal infections clearly fulfill the biological plausibility requirement. The ulcerated epithelium of the periodontal pocket has a sizeable surface area and is in constant contact with a highly organized biofilm that is inhabited by several bacteria with significant virulence potential. Bacteria have been shown to enter the circulation after even mild manipulation of the periodontal tissues, resulting in repeated transient bacteremias that may facilitate dissemination of oral microbiota at distant sites. Bacterial products and inflammatory mediators that are produced abundantly, locally within the diseased periodontal tissues may also enter the circulation and result in systemic inflammation which may trigger endothelial activation. Molecular mimicry, i.e. the high degree of homology between prokaryotic and mammalian proteins, redirects anti-bacterial antibodies to act also as auto-antibodies, ultimately resulting in activation of, and damage to the vascular endothelium. The possibility of a certain degree of confounding due to common risk factors for atherosclerosis and periodontitis should not, however, be overlooked.

Over the past two decades, cross-sectional and prospective cohort studies have demonstrated a significant association between radiographically and clinically assessed periodontitis and coronary heart disease (CHD), broadly defined as myocardial infarction, death due to hospitalization due to CHD, or revascularization procedures. Importantly, these positive associations persist after adjustment for established risk factors for CHD, including age, gender, race, poverty, smoking, diabetes, high blood pressure, body mass index and high serum low density lipoprotein cholesterol. With few exceptions, the above associations have been confirmed in several populations with varying race/ethnicity profiles. Positive associations have also been reported between periodontitis, defined by clinical measures or by seropositivity to important periodontal pathogens, and non-hemorrhagic stroke. Finally, limited recent evidence suggests that periodontitis may be associated with peripheral artery disease after adjustment for concomitant exposures.

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Epidemiologic evidence also exists on the association between periodontitis and subclinical markers of CVD, including levels of serum C-reactive protein and seropositivity for interleukin 6. Heavy colonization by specific periodontal pathogens was found to be associated with increased intima-media thickness, while DNA from oral bacteria and, in one report, viable invasive periodontal pathogens were recovered from human endarterectomy specimens.

Data from intervention studies suggest that treatment of periodontitis may result in lower levels of serum inflammatory mediators such as CRP and IL-6, positive alteration of lipid profiles and improved endothelial function, although the degree of variability is substantial. A randomized clinical trial that employed local antibiotics as adjuncts to mechanical periodontal therapy demonstrated improved endothelial function six months after completion of treatment. Finally, a pilot, multicenter randomized secondary prevention trial of 18-months duration compared periodontal therapy to community dental care, but failed to detect any differences in the incidence of cardiovascular adverse events between the treatment arms.

In conclusion, the association between periodontitis and macrovascular disease is biologically plausible; the epidemiologic data and the findings from intervention trials focusing on surrogate markers are supportive; however, the effects of periodontal therapy on clinical macrovascular disease endpoints are largely untested.