Aggressive basic and clinical research during the past decade has produced evidence that inflammation plays a fundamental role in the evolution of atherogenesis. Low-grade systemic inflammation has been widely accepted as contributing to an increased risk for cardiovascular disease.\(^1\) Being distinguished from gingivitis, periodontitis is a chronic and multifactorial inflammatory disease caused by microorganisms and delineated by progressive eradication of the tooth-bearing apparatus, resulting in tooth loss. Because more than 700 microbacteria exist in the oral cavity, poor oral hygiene, including periodontitis and/or gingivitis, could contribute to widespread and frequent dissemination of bacterial pathogens, antigens, endotoxins, and inflammatory cytokines into the systemic circulation. This condition could subsequently promote the process of systemic atherosclerosis and/or a thromboembolic state. Based on a recent meta-analysis\(^2\) and the Joint EFP/AAP Workshop consensus report,\(^3\) it has been concluded that “(I) there is consistent and strong epidemiologic evidence that periodontitis imparts increased risk for future cardiovascular disease, and (II) while in vitro, animal and clinical studies do support the interaction and biological mechanism, intervention trials to date are not adequate to draw further conclusions”,\(^3\) because periodontitis plays a significant role in the entry of bacteria into the blood stream. Generally, bacterial infection...
can activate the host inflammatory response by various mechanisms, so that the host immune response would likely and significantly promote atheroma formation, maturation, and exacerbation, as shown in the Figure. Even if the meta-analysis and consensus report support a relationship between periodontitis and an increased risk of cardiovascular disease, the effect of intervention for periodontitis, such as treatment, on the amelioration of the risk of cardiovascular disease is still controversial. Several studies support that (I) periodontitis treatment reduces systemic inflammation as evidenced by reduction in C-reactive protein (CRP) and improvement of both clinical and surrogate measures of atherosclerotic process, but that (II) limited evidence shows improvements in coagulation, biomarkers of endothelial cell activation, arterial blood pressure and subclinical atherosclerosis after periodontitis treatment.3

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As mentioned, many previous reports and the American Heart Association scientific statement4 highlight that poor oral hygiene is consistently associated with elevated levels of high-sensitivity CRP (hsCRP). However, poor oral hygiene, such as existing periodontitis and/or gingivitis, is not consistently related with worsening biomarkers of elevated inflammatory cytokines and abnormal plasma levels of fibrinogen and leukocyte profiles. Concerning endothelial function, which is considered to have a central role in the connection between clinical atherosclerotic risk factors and cardiovascular disease, the effects of periodontitis treatment are contradictory. On the one hand, the primary outcome of several trials was endothelial function. Although assessed using different methods, those trials showed improvement of endothelial function.5,6 On the other hand, alternative markers of vascular function, such as nitroglycerin-mediated dilatation, brachial-artery diameter, reactive hyperemia ratio,7 forearm blood flow (FBF), sodium-nitroprusside-dependent FBF, acetylcholine-dependent FBF in the presence of a NO synthase-inhibitor, and pulse amplitude tonometry,8 systolic and diastolic blood pressures9 did not change after periodontitis treatment, compared with baseline levels of the periodontitis treatment group and/or the end levels of the no-periodontitis treatment group.

In this issue of the Journal, Kajikawa et al.10 report that poor oral health behavior (reflected by whether oral hygiene was poor or not) is closely related to decreased systemic endothelial dysfunction assessed by the brachial flow-mediated vasodilatation (FMD) technique. The strength of this study is that the authors not only focused on periodontitis, but also examined the more general status of oral hygiene expressed as oral health behavior, and that the study showed a close association between poor oral health behavioral status and impaired endothelial function. The subjects with poor oral health behavior had significantly higher hsCRP levels. This finding is very consistent with many previous reports.1-4 In addition, the authors measured FMD by sophisticated equipment developed in Japan that can measure FMD with an accurate, semi-automatic, online system (UNEXEF18G; UNEX Co, Nagoya, Japan). The authors report excellent inter- and intracoeficients of variation for the brachial artery diameter, which were 1.6% and 1.4%, respectively, in their laboratory. This study will encourage cardiologists and/or other physicians to more carefully monitor the oral health status of their patients who already have cardiovascular disease or patients who have a high risk for cardiovascular disease. From this perspective alone, this study is worth reading.

It is generally recognized that hard clinical outcomes are needed to investigate the effect of periodontal treatment on the prevention of primary and secondary cardiovascular disease in well-designed intervention trials. Two experimental designs of intervention trials can be used: primary cardiovascular disease prevention trials and secondary cardiovascular disease prevention trials. In the future, to clarify whether or not periodontitis treatment or maintaining good oral health behavior has a preventive effect on catastrophic cardiovascular disease events such as stroke or acute coronary syndrome, multicenter, randomized, clinical intervention trials are needed.

**References**