Periodontitis and Cardiovascular Disease: New Findings

The relationship of oral infection/inflammation to diseases and disorders at distant sites (or the relationship of periodontitis to systemic diseases) was first identified in the early 1990s. Since that time, dental professionals and the lay public have shown great interest in these associations. The primary focus has been on the relationship of periodontitis to adverse obstetrical outcomes, cardiovascular disease, cerebrovascular disease, diabetes mellitus and respiratory disease. Other associations have also been identified, including periodontal disease, kidney disease, pancreatic cancer and cognitive impairment.

These associations are believed to be mediated by the inflammatory response to periodontal pathogens. Mechanisms proposed to account for the associations include subgingival microorganisms gaining access to the peripheral circulation, and stimulating production of inflammatory mediators (e.g., in the liver) or directly affecting tissues at distant sites (e.g., atheroma in the carotid arteries). In addition, inflammatory mediators produced in the periodontal tissues can reach the peripheral circulation, contributing to a systemic inflammatory response.

The importance of the association between periodontal disease and cardiovascular disease is illustrated by a consensus paper examining the relationship of periodontitis and atherosclerotic cardiovascular disease published in 2009 in the American Journal of Cardiology and the Journal of Periodontology. The consensus made recommendations for treatment and called for management of periodontitis in patients at risk for or demonstrating cardiovascular disease.

This issue of Periodontics Report reviews studies about the relationship of periodontitis and tooth loss to cardiovascular outcomes. Included are reports examining periodontitis and coronary atherosclerosis, acute coronary syndrome and cerebrovascular accidents, as well as the relationship of the number of teeth to cardiovascular mortality.
Relationship of Periodontitis and Coronary Atherosclerosis

Studies of the relationship of periodontitis and coronary heart disease (CHD) have evaluated CHD in different ways. Often the outcome is myocardial infarction or death. An evaluation of patients at an earlier stage of CHD can assess when this association becomes important. Berent et al from the Center for Cardiovascular Rehabilitation, Austria, examined the periodontal status of patients who had been seen for coronary angiography to identify stenosis of ≥1 coronary arteries.

A total of 466 individuals were evaluated by coronary angiography. The degree of arterial stenosis was determined to be significant if at least 1 vessel demonstrated at least 50% blockage. The extent of the stenosis was also evaluated as to the number of vessels demonstrating varying degrees of blockage in different areas. The oral examination included the following:

- number of missing teeth
- measures of the extent and severity of periodontitis
- presence of remaining root tips
- presence of pericoronitis

Serum analysis included a lipid profile, glycated hemoglobin and fasting blood glucose. Epidemiologic data were also available. Data were analyzed as the mean for different groups, and logistic regression analysis was performed.

A total of 349 individuals (75%) were determined to have CHD. Of those, 56% also had periodontal disease vs 42% of the individuals without CHD (p < .01; Figure 1). In a fully adjusted model, periodontal disease was independently related to CHD (odds ratio 1.9; 95% confidence interval, 1.2–3.1). The authors noted that other risk factors for CHD were evident (male gender, increasing age, lower level of high-density lipoprotein cholesterol and the presence of type 2 diabetes mellitus) but that periodontitis is a modifiable risk factor. While the mechanism to account for periodontitis as a risk factor for CHD was not evaluated in this study, a likely scenario involves periodontal disease contributing to an increase in the systemic inflammatory response, and alterations in endothelial cell function, promoting atheroma development.


Periodontitis and Acute Coronary Syndrome

Acute coronary syndrome (ACS) is a cardiac condition characterized by chest pain, specific changes on an electrocardiogram and elevation in serum cardiac enzymes (e.g., creatinine kinase) that characterize a myocardial infarction. This is a definite outcome of cardiovascular disease, and patients with a history of ACS are at risk for another cardiovascular event. Renvert et al from the University of Kristianstad, Sweden, reviewed the occurrence of ACS as predicted by traditional medical and periodontal variables.
A total of 165 patients with a confirmed history of ACS and 159 matched control patients were followed for 3 years. All ACS patients received a complete medical evaluation and appropriate medical care (including medications). A periodontal examination was performed after the ACS patients had been released from the hospital. All controls were examined to rule out cardiovascular disease, and medical variables were collected. The complete periodontal examination included clinical measures and periapical radiographs. Subgingival plaque samples were collected for microbiological analysis.

During the 3-year observation period, 40% (66 of 165) of the cases experienced an ACS event vs 4.4% (7 of 159) of controls. The variables collected at the beginning of the monitoring period were analyzed to identify important indicators of risk for ACS. Considering the cases and controls separately, periodontitis was found to be a risk factor for both a first ACS event (odds ratio [OR] 10.3; \( p < .001 \)) and a second ACS event (OR 3.6; \( p < .001 \)). Multivariate analysis was used to develop a model to predict an ACS event, and after controlling for age, significant variables included the following:

- white blood cell count (\( p < .001 \))
- presence of periodontitis (\( p < .001 \))
- serum creatinine level (\( p < .05 \))

The levels of periodontal pathogens were generally higher at the initial periodontal examination for the cases vs the controls (27 of 40 species), but levels of these pathogens at baseline did not predict a future ACS event.

This is an important prospective study because it identifies periodontal disease as a risk factor for confirmed ACS. The next logical step would be to treat periodontal disease to see if therapy reduces the risk for a future event.


### Table 1. Age- and gender-adjusted analysis of maximum likelihood risk factors (variables)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Category</th>
<th>Cases</th>
<th>Controls</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>≤1</td>
<td>7</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;1 to ≤1.5</td>
<td>30</td>
<td>32</td>
<td>0.8 (0.1-5.5)</td>
</tr>
<tr>
<td></td>
<td>&gt;1.5 to ≤2</td>
<td>34</td>
<td>28</td>
<td>2.0 (0.2-19.0)</td>
</tr>
<tr>
<td></td>
<td>&gt;2</td>
<td>29</td>
<td>16</td>
<td>2.1 (0.2-22.5)</td>
</tr>
<tr>
<td>GI</td>
<td>≤0.4</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;0.4 to ≤0.8</td>
<td>7</td>
<td>30</td>
<td>0.1 (0.1-2.1)</td>
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<tr>
<td></td>
<td>&gt;0.8 to ≤1.2</td>
<td>39</td>
<td>27</td>
<td>0.5 (0.02-13.4)</td>
</tr>
<tr>
<td></td>
<td>&gt;1.2</td>
<td>52</td>
<td>41</td>
<td>0.1 (0.00-2.8)</td>
</tr>
<tr>
<td>PPD (mm)</td>
<td>≤3.0</td>
<td>10</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0 to ≤4.5</td>
<td>44</td>
<td>59</td>
<td>1.2 (0.3-4.8)</td>
</tr>
<tr>
<td></td>
<td>&gt;4.5</td>
<td>46</td>
<td>16</td>
<td>8.5 (1.1-68.2)*</td>
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<tr>
<td>CAL (mm)</td>
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<td>22</td>
<td>47</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0 to ≤4.5</td>
<td>45</td>
<td>41</td>
<td>1.5 (0.5-4.8)</td>
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<tr>
<td></td>
<td>&gt;4.5</td>
<td>33</td>
<td>12</td>
<td>2.4 (0.3-17.1)</td>
</tr>
</tbody>
</table>

\( \text{CI, confidence interval; PI, plaque index; GI, gingival index. \*Statistically significant.} \)
presence of diabetes and a lipid profile. The periodontal examination measured probing pocket depth (PPD), clinical attachment loss (CAL), gingivitis and plaque. Statistical analysis was performed, including logistic regression analysis to identify risk factors for cerebral ischemia.

All periodontal measures (mean CAL, PPD, gingival index and plaque index) were higher in the patients vs the controls (Table 1). Logistic analysis indicated that in a fully adjusted model, the following 3 variables were significantly associated with the risk for a cerebrovascular accident:

- mean PPD >4.5 mm (odds ratio [OR] 8.5)
- hypertension (OR 7.6)
- current smoking (OR 3.1)

These data support the association of periodontitis and acute cerebral accidents. While these data do not prove causation, and cerebrovascular disease is a complex disorder, the high OR observed for periodontitis suggests the importance of this relationship.


Among the population, 629 individuals died. CVD was the cause of death for 299 individuals (167 from coronary heart disease [CHD], 83 from stroke and 49 from an aortic aneurysm or congestive heart failure).

The dental examination included evaluation of the number of teeth, as well as the severity of periodontal disease, the number of deep periodontal pockets and bleeding following probing. These measures were evaluated relative to death from CVD.

In a model adjusted for age of the patient, gender and current smoking status, the number of teeth was found to predict mortality from all causes, mortality related to CVD and mortality related to CHD (all p < .001). There was a 7-fold increase in risk of death from CHD if there were <10 teeth compared with individuals with >25 teeth. These associations were not seen for the 3 periodontal variables.

These data are noteworthy for the large number of individuals evaluated and the extended period of follow-up. The authors suggested that the reason tooth loss is related to CVD is that the majority of teeth are lost as a consequence of infection (periodontal disease, caries), which in turn is associated with inflammation. It is important to emphasize that all individuals in this study had been seen in the periodontology clinic, suggesting the underlying importance of periodontitis to tooth loss in this population.