

Scientists Report Important Lead in Studying Possible Association Between Periodontal and Cardiovascular Disease

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Scientists have hypothesized that people with chronic gum, or periodontal, disease may be predisposed to heart disease and stroke. However, supporting this hypothesis has been difficult, in part because researchers have yet to identify a molecule or some other telltale biological marker that is somehow linked to these conditions.

Now, a team of scientists reports that it may have found a possible marker. As published online in the journal *Stroke*, the researchers found in a large, racially mixed group of adults that the more teeth a person has lost, the more likely he or she is to have both advanced periodontal infections and potentially clogging plaques in the carotid artery, the vessel that feeds the brain.

"There is no way to look into the mouth and know why a tooth was lost a year or two after the fact," said Moise Desvarieux, M.D., Ph.D., lead author on the study and an assistant professor of Epidemiology at the University of Minnesota School of Public Health. "But, in our study, we could ask: In middle aged and older people with periodontal disease, is there a measurable association between tooth loss, severity of their oral infections, and subclinical cardiovascular disease? In this population at least, the answer was most definitely yes."

Desvarieux said he and his colleagues also found that the association held true in a large subgroup of people with periodontal disease who had never smoked. He said this finding is especially noteworthy, because results from several related studies have been questioned on the grounds that a large percentage of the participants smoked. Smoking is a major risk factor for both periodontal infections and heart disease, raising the possibility that the smoking, not the gum disease, might be responsible for the reported effect in these studies.

The Desvarieux et al. paper builds on the broader idea that disease-causing bacteria shed from periodontal infections, enter the circulatory system, and contribute to disease in other parts of the body, such as the heart or brain. The more chronic and severe a

person's periodontal infections are, the thinking goes, the greater the risk for secondary infections.

What particularly intrigues researchers is, if the theory proves to be correct, it may be possible to help prevent or control the development of vascular disease in some people by treating their periodontal disease. Over the past decade, however, researchers have yielded mixed results to support the theory. According to some, these variable results do not necessarily disprove the hypothesis. Rather, they show how difficult research on complex biological problems can be without the needed specificity of biomarkers and other necessary research tools to simplify the process.

Among the published studies in the scientific literature are a few that have looked at the possible association between tooth loss, periodontal disease, and cardiovascular disease. Most notable is a retrospective analysis of data from a large national health survey, known by the acronym NHANES, that compared the rate of heart disease among people who were edentulous (lost their teeth) and those who had severe periodontal disease. The researchers hypothesized that, because people without teeth do not develop periodontal disease, their rate of heart disease would be lower than those with active periodontal infections. That was not the case, however, as the researchers found the rate of heart disease was similar in both groups.

Desvarieux and colleagues reasoned there might be an alternative explanation. "While one certainly can interpret these results as there is no association between periodontal disease and cardiovascular disease, the other possible explanation is the edentulous patients lost their teeth, in part, because of previous periodontal disease," said Desvarieux, who is also an assistant professor of Medicine at the University of Minnesota Medical School. "The fact that the teeth are gone doesn't necessarily mean that the possible effect of the previous periodontal infections hasn't already occurred."

To begin testing this idea, Desvarieux and colleagues collected baseline data on 711 randomly selected participants enrolled in the Oral Infections and Vascular Disease Epidemiology Study (INVEST). The study, which is supported by NIH's National Institute of Dental and Craniofacial Research and whose principal investigator is Dr. Desvarieux, will monitor the oral and cardiovascular health of a large, racially mixed group of people for at least three years. All people enrolled in the study live in a northern section of Manhattan in New York City and are age 55 or older. Participants also must have no previous history of heart disease or chronic inflammatory conditions, such as Lyme disease. All enrollees are also members of the Northern Manhattan Study (NOMAS), a prospective cohort study supported by NIH's National Institute of Neurological Disorders and Stroke.

During the baseline dental examination, the researchers defined periodontal disease as oral infections that have created a pocket depth between a tooth and the surrounding gum that is 5 millimeters or greater and a loss of a tooth's normal attachment to bone that is 4 millimeters or greater. Both of these values are slightly higher than several previously reported studies, which typically have defined severe periodontal disease using a pocket

depth of 4 millimeters or more and an attachment loss of 3 millimeters or greater. "If we had used the common standards for periodontal disease, about 90 percent of those in the study would have been classified as having serious disease," said Panos Papapanou, D.D.S., Ph.D., an author on the study and professor and director of the Division of Periodontics at Columbia University School of Dental and Oral Surgery. "That wouldn't have given us enough discriminatory power to see differences in disease progression."

Papapanou and his collaborators also counted and categorized the number of missing teeth in their participants. The categories were: 0 to 9 teeth missing, 10 to 19 teeth missing, 20 to 31 teeth missing, and edentulous.

After completing the oral examinations and analyzing the data, the scientists determined that the greater the number of teeth that a person had lost, the greater the proportion of their remaining teeth that were riddled with deep pockets and severe attachment loss. For instance, in the people with 0 to nine missing teeth, on average, 28 percent of their remaining teeth had severe attachment loss and 8 percent had deep pocket depths. For those missing 20 to 31 teeth, the average rates were 60 percent attachment loss and 15 percent deep pocket depths.

This still left open the question of whether tooth loss correlated with cardiovascular disease. To get their answer, clinicians performed high-resolution ultrasound on the carotid arteries of the participants to detect the presence or absence of potentially clogging plaques. Using the standard measures of periodontal disease - attachment loss and pocket depth - the scientists found no relation between those with severe gum disease and the development of carotid plaques. "That was not the case when they compared levels of tooth loss to carotid plaques," said Ralph Sacco, M.D., M.S., senior author on the paper and professor of Neurology and Epidemiology at Columbia University College of Physicians and Surgeons and principal investigator of the companion Northern Manhattan Study. "Among participants who had lost 0 to 9 teeth, 45 percent had plaques, while those who had lost 10 to 19 teeth, 62 percent had plaques. For people who were edentulous, 57 percent had plaques."

Interestingly, when the researchers examined their data in non smokers, the correlation held. Carotid plaques were present in 39 percent of those missing 0 to nine teeth, 52 percent of people missing 10 to 19 teeth, and 58 percent of edentulous volunteers. "We made extensive adjustments for smoking in our data analysis," said David Jacobs, Ph.D., an author on the paper and professor in the Division of Epidemiology at the University of Minnesota School of Public Health. "Irrespective of all of the variables that we factored into our analysis, the relationship remained."

The study is titled, "Relationship between periodontal disease, tooth loss, and carotid artery plaque," and it was published online in the journal *Stroke* on Thursday, July 31, 2003. The authors are: Moise Desvarieux, Ryan T. Demmer, Tatjana Rundek, Bernadette Boden-Albala, David R. Jacobs, Panos Papapanou, and Ralph L. Sacco.

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