Assessing the Relationship Between Dental Disease and Coronary Heart Disease in Elderly U.S. Veterans

ABSTRACT

Several recent studies have shown a link between dental disease and coronary heart disease. The authors studied 320 U.S. veterans in a convenience sample to assess the relationship between oral health and systemic diseases among older people. They present cross-sectional data confirming that a statistically significant association exists between a diagnosis of coronary heart disease and certain oral health parameters, such as the number of missing teeth, plaque benzoyl-DL-arginine-naphthylamide test scores, salivary levels of *Streptococcus sanguis* and complaints of xerostomia. The oral parameters in these subjects were independent of and more strongly associated with coronary heart disease than were recognized risk factors, such as serum cholesterol levels, body mass index, diabetes and smoking status. However, because of the convenience sample studied, these findings cannot be generalized to other populations.

In 1989, Mattila and colleagues[1] reported that poor dental health could be associated with both an acute myocardial infarction and a cerebral vascular accident.[2] The investigators developed two measurements of dental disease, one based on radiographs of the teeth and jaws, called the pantomographic index, and the second, based on clinical examination findings, which they termed the Total Dental Index, or TDI.

In a subsequent seven-year prospective study, the TDI, the number of previous myocardial infarctions and, to a lesser extent, diabetes and the pantomographic index were associated with a risk of developing a new and often fatal myocardial infarction.[3] Traditional risk factors such as hypertension, smoking, total cholesterol levels, high-density lipoprotein cholesterol levels, triglycerides levels, socioeconomic status, sex and age were not significant predictors of a coronary event when included in a model that contained the dental variables.

Other studies have generally confirmed this link between dental disease and coronary heart disease, or CHD. A prospective, cohort-designed study, involving data from 9,760 American men who were examined three times between 1971 and 1987, found a significant relationship between either periodontitis or edentulism and CHD, even after adjusting for 13 known risk factors.[4] A study of 1,384 Finnish men, aged 45 to 64 years, showed that the number of missing teeth, along with hypertension, geographical area and educational level were independent explanatory factors for the presence of ischemic heart disease.[5]

In a longitudinal aging study of U.S. veterans, Beck and colleagues[6] found a significant association between periodontal disease, as measured by the extent of alveolar bone loss, and CHD and stroke after adjusting for various cardiovascular risk factors. In a case-control study of hospitalized patients, people with acute cerebrovascular ischemia had a higher TDI than did age- and sex-matched controls.[7]

WALTER J. LOESCHE, D.M.D., PH.D.; ANTHONY SCHORK, PH.D.; MARGARET S. TERPENNING, M.D.; YIN-MIAO CHEN, M.S.; B. LIZA DOMINGUEZ, D.D.S., M.S.; NATALIE GROSSMAN, R.D.H., M.A.

These associations indicate that there may be some type of linkage between dental disease and cardiovascular disease. Because dental caries and periodontal disease are chronic infections that are often asymptomatic, they could be the source of the increased levels of C-reactive protein that have been suggested as a predictor of myocardial infarction and stroke.[8]

Since 1990, we have been recording information for a large number of oral health variables in a group of elderly veterans to study the relationship between oral health and systemic diseases among older people.[9] We present cross-sectional data confirming that a statistically significant association exists between a diagnosis of CHD and certain oral health parameters, such as the level of gingival bleeding; number of missing teeth; benzoyl-DL-arginine-naphthylamide, or BANA, test scores; and complaints of xerostomia.

SUBJECTS AND METHODS

Subjects. We recruited a convenience sample of 320 veterans who were at least 60 years of age from the dental outpatient clinic of the Veterans Affairs Hospital, Ann Arbor, Mich. (n = 206), and from a long-term care facility (nursing home) associated with the hospital (n = 114). Patients who use the Veterans Affairs medical and dental facilities usually have a service-connected injury or disability, or have met a financial hardship qualification.

There were no age, sex, racial, income or educational differences among the subjects from the dental outpatient clinic (that is, the independent living group) and the long-term care facility (that is, the dependent living group), which led us to initially combine all the subjects into a single group for statistical analysis.[9] The group from the long-term care facility had significantly more edentulous subjects than did the outpatient group[9]; because of this, a separate variable indicating whether the participant entered from the independent living or dependent living situation was included in the multivariate analysis to account for any confounders that might have been introduced as a result of entry site.

Cross-sectional data confirm that a statistically significant association exists between a diagnosis of coronary heart disease and certain oral health parameters.

Dental variables. One of us (B.L.D.) performed a clinical examination to determine the number of teeth and the number of restorations and amount of decay on all tooth surfaces in each subject. The presence and type of dentures and other prosthetic devices were recorded.

We stratified the subjects into two groups: the first was composed of subjects with one to 14 teeth and the second was composed of subjects with 15 to 28 teeth. This division was done because subjects with one to 14 teeth could have been wearing a full denture, whereas subjects with 15 to 28 teeth could not wear a full denture. Third molars, which were rarely present in these older subjects, were omitted from all analyses.

We measured periodontal pocket depths, attachment levels and gingival recession for all teeth with an automated pressure-sensitive periodontal probe (Dental Probe Inc.), and recorded the results electronically. Oral hygiene was assessed with the plaque index, or PlI,[10] and gingivitis was assessed with the papillary bleeding score, or PBS.[11,12] We calculated the mean PlI and PBS for each subject by summing the PlIs and PBSs of the individual teeth, and then dividing the totals by the number of teeth. These mean PlIs and PBSs were then used in the statistical analyses. The subjects were asked how often they brushed and flossed their teeth and how often they visited their dentist or hygienist. A complaint of xerostomia was elicited by asking questions about perceived dryness of the mouth.[13]

Bacteriologic variables. We used stimulated saliva to determine the number of colony-forming units, or CFU, of selected bacterial types. The media used, the dispersal procedures and the culturing conditions have been described elsewhere.[14] A curette was used to obtain plaque samples from the mesial surface of the first molars or, if they were missing, from the most posterior tooth in each quadrant. The four plaque samples were individually applied to the lower reagent strip on the BANA test card. The cards were incubated at chairside for five minutes at 55 C,[15] and the resultant blue color for each plaque sample was scored and the numbers averaged to

give a single BANA score for each subject.

Medical variables. For this study, CHD had to be a medically established diagnosis in the patient's medical record based on the International Classification of Diseases, 9th Revision, coding system used by the Veterans Affairs Hospital for CHD. This diagnosis was supplemented with a review of the patient's medical records and documentation of established myocardial infarction; bypass surgery; clinical angina; electrocardiogram readings; serum enzyme levels, if available; angiography; and a positive response to treatment for heart disease. Systolic and diastolic blood pressures and blood cholesterol values were obtained from the patient's medical records.

We also obtained the subject's diabetic status from the medical records; if diabetes was present, the medical records indicated whether it was controlled by insulin, diet or medication. Two of the authors (B.L.D. and N.G.) obtained the patient's weight and height during the dental examination, and these measurements were used to calculate the body mass index, or BMI. We determined the number of medications used by the subjects through interviews (performed by B.L.D. and N.G.) and by examining a computerized record of medications maintained by the Department of Veteran's Affairs.

Statistical methods. Summary statistics are presented as means (± standard deviations) and frequencies, with percentages as appropriate. Initial statistical tests consisted of χ^2 analyses and/or multiple logistic models with Bonferroni-adjusted ($P < .05$) pairwise comparisons for categorical data. After extensive investigation of transformations of the continuous measures, we concluded that normality was not achievable, so nonparametric Wilcoxon-Rank sum or Kruskal-Wallis tests with Bonferroni-adjusted ($P < .05$) pairwise comparisons were used. Based on these initial analyses, variables with $P < .25$ were entered into multiple logistic analyses. These models consisted of predictors with dental relevance and/or statistical significance. Only significant ($P < .05$) overall models were retained, and significant ($P < .05$) predictors were noted.

Two models were developed, one that included all subjects, but excluded the dental variables (that is, the all-subjects model) and one that was restricted to the dentate subjects, but included the dental variables (that is, the dentate subjects model). In the all-subjects model, we would be able to observe the effect of variables such as salivary flow and swallowing, independent of the tooth-related variables, whereas in the dentate subjects model, any effect of being edentulous and wearing complete dentures would not be considered.

These models consisted of predictors with dental relevance and/or statistical significance, as well as many of the recognized risk factors for CHD (that is, diabetes, smoking history, current use of alcohol, age, BMI, blood pressure and serum cholesterol levels). Based on analyses of these models, variables with $P < .25$ were entered into reduced models until a model was obtained that combined the highest likelihood ratio with the fewest degrees of freedom. In this reduced model, the nonsignificant variables were then added back, one at a time, to the model containing the significant variables, to determine their individual effect on the model.

RESULTS

Demographics and medical history. Data were collected from 320 subjects, 99 percent of whom were male. There were no age or racial differences among the subjects with and without a diagnosis of CHD. Because the relationship between dental status and CHD was the primary parameter under investigation, the results are shown separately for the dentate subjects, the edentulous subjects and all subjects combined. Forty-six percent of the dentate subjects and 53 percent of the edentulous subjects had received a diagnosis of CHD. This stratification of subjects, based on the presence of teeth, was not associated with any difference in age, race or any of the standard risk factors analyzed for CHD (Table 1).

Subjects with and without CHD had similar BMIs, blood pressures and total serum cholesterol levels. The edentulous subjects were more likely to be current smokers than were the dentate subjects. Subjects without CHD were more likely to report that they drank alcoholic beverages on a daily basis. Subjects with CHD received significantly more medications of any type and more xerogenic medications than did subjects without CHD.

Dental findings. The dentate subjects with CHD had significantly fewer teeth than the

TABLE 1

RECOGNIZED RISK FACTORS/INDICATORS FOR CORONARY HEART DISEASE IN OLDER VETERANS.

RISK FACTOR/ INDICATOR	DENTATE SUBJECTS Coronary Heart Disease Status		EDENTULOUS SUBJECTS Coronary Heart Disease Status		ALL SUBJECTS Coronary Heart Disease Status	
	No (n = 112)	Yes (n = 95)	No (n = 53)	Yes (n = 60)	No (n = 165)	Yes (n = 155)
Age (years)	68.3 (5.3)*	68.7 (4.9)*	68.6 (5.4)*	68.7 (7.2)*	68.4 (5.3)*	68.7 (5.9)*
< 70	61%	63%	62%	67%	62%	65%
70-79	36%	34%	36%	25%	36%	30%
> 79	3%	3%	2%	8%	2%	5%
Race						
White	93%	92%	87%	95%	91%	93%
African-American	5%	5%	9%	3%	7%	4%
Other	2%	3%	4%	2%	2%	3%
Cholesterol level (mg/dL)	203 (40)*	190 (38)*†	194 (37)*	191 (44)*	201 (39)*	190 (40)*
Body mass index	26.9 (5.3)*	26.7 (4.9)*	26.8 (8.3)*	26.3 (5.5)*	26.9 (6.4)*	26.5 (5.1)*
No. of xerogenic medications	1.4 (1.3)*	2.0 (1.5)*†	1.4 (1.2)*	2.0 (1.4)*†	1.4 (1.3)*	2.0 (1.5)*†
No. of all medications	5.8 (3.9)*	8.5 (3.9)*†	7.2 (4.2)*	10.1 (4.6)*†	6.3 (4.0)*	9.2 (4.3)*†
Blood pressure						
Systolic (mm Hg)	143 (24)*	140 (19)*	140 (29)*	142 (21)*	142 (26)*	141 (20)*
Diastolic (mm Hg)	71 (10)*	74 (11) *	79 (15)*	76 (14)*	75 (13)*	74 (13)*
Diabetic status						
Insulin dependent	7%	19%‡	19%	15%	11%	17%
Diet controlled	8%	9%	15%	12%	10%	10%
Smoking status						
Never	16%	13%	7%	3%	13%	9%
Quit	64%	72%	57%	65%	62%	70%
Current	20%	15%	36%	32%	25%	21%
Alcohol use						
No	36%	49%	49%	60%	41%	53%‡
Occasionally	45%	43%	32%	30%	41%	38%
Daily	19%	8%	19%	10%	18%	9%

* Data are mean (± standard deviation).
† Value is significantly different from corresponding "no" value with $P < .05$ (Wilcoxon test).
‡ χ^2 or Fisher's Exact Test with $P < .05$ values.

dentate subjects without CHD (Table 2). Significantly more subjects with CHD had from one to 14 teeth, compared with subjects without CHD ($P = .007$). Dentate subjects with CHD were significantly more likely to be wearing at least one full denture than were dentate subjects without CHD. Among the edentulous subjects, there was no relationship between wearing full dentures and CHD status. Most subjects complained of dryness at some time during the day, but the complaint was significantly more frequent in the subjects with CHD, especially in the dentate subjects.

We examined the tooth-related parameters in more detail by comparing the oral health variables in subjects with one to 14 teeth with those in subjects having 15 to 28 teeth (Table 3). We report the findings as a percentage of teeth with decay or periodontal morbidity because subjects with one to 14 teeth would have a smaller number of involved teeth than would subjects with 15 to 28 teeth. Thus, by reporting dental decay and periodontal disease as a percentage of teeth with the given problem, we could compare results between subjects with one to 14 teeth and those with 15 to 28 teeth.

Bacterial findings. Because some of the observed oral conditions might affect certain bacterial species on the tooth/mucosal surfaces, we measured the salivary levels of representative oral and medically important species. Salivary levels of yeast were significantly higher in all subjects with CHD than in all subjects without CHD (2.9 $\log_{10}$/milliliter vs. 2.5 $\log_{10}$/mL, $P < .05$, Wilcoxon test), whereas the levels of *Streptococcus san-*

TABLE 2

DISTRIBUTION OF ORAL VARIABLES IN SUBJECTS WITH AND WITHOUT CORONARY HEART DISEASE.

ORAL VARIABLE	DENTATE SUBJECTS		EDENTULOUS SUBJECTS		ALL SUBJECTS	
	CHD Status		CHD Status		CHD Status	
	No (n = 112)	Yes (n = 95)	No (n = 53)	Yes (n = 60)	No (n = 165)	Yes (n = 155)
Number of teeth	20.2 (6.7)*	17.2 (7.7)*†	0	0	13.7 (11)*	10.5 (10.3)*†
Zero	NA‡	NA‡	100%	100%	32%	39%
One to 14	19%	36%	NA‡	NA‡	13%	22%
> 14	81%	64%	NA‡	NA‡	55%	39%
	$P = .007$§				$P = .01$	
Presence of dentures						
Any type	52%	57%	92%	83%	65%	67%
Full	17%	32%§	92%	83%	42%	52%
Streptococcus sanguis (log_{10}/mL saliva)	4.0 (2.8)*	2.9 (3.0)*†	2.1 (2.9)*	1.2 (2.4)*	3.4 (3.0)*	2.2 (2.9)*†
Mouth complaint						
Dry while eating	11%	13%	11%	8%	11%	11%
Dry any time	65%	81%§	68%	78%	66%	80%§

* Data are mean (± standard deviation).
† Value is significantly different from corresponding "no" value with $P < .05$ (Wilcoxon test).
‡ NA: not applicable.
§ Nonparametric values are significantly different with $P < .05$ using χ^2 or Fisher's Exact Test.

guis were significantly lower in subjects with CHD than in subjects without CHD (Table 2).

The levels of cariogenic organisms, such as *Streptococcus mutans* and the lactobacilli species, did not differ between subjects with or without CHD. *Streptococcus sobrinus*, another cariogenic species, was rarely encountered, but when it was, the levels were elevated in dentate subjects without CHD and in edentulous subjects without CHD.

There were no differences in the salivary levels of certain periodontopathic species such as *Porphyromonas gingivalis, Prevotella intermedia, Fusobacterium nucleatum* and *Capnocytophaga* species, or in levels of medically important species, such as β-hemolytic streptococci, *Bacteroides fragilis* and aerobic gram-negative bacilli. There was no apparent difference in the mean plaque BANA score or in the percentage of subjects with plaque BANA scores of 2 or greater as a function of number of teeth or CHD status. (A BANA score of 2 or greater means that all four plaque samples tested positive.)

Statistical models. We initially evaluated three logistic regression models, one that included all subjects, but omitted the tooth-related variables (Table 4); one that was restricted to the dentate subjects but included all the variables (Table 4); and one that included only edentulous subjects. The edentulous subject model showed that the higher numbers of medications used were positively associated with CHD, but since this variable along with others were significant in the other models, we omitted the edentulous model. Because some of the parameters associated with CHD in the bivariate analyses, such as number of medications taken, presence of dentures, complaints of dry mouth and various oral hygiene parameters, could be a function of the dependent living status, a separate variable for dependent living was added to the model.

As Table 4 shows, dependent living status was not significant in the all-subjects and dentate subjects models. CHD was 2.64 times more likely to be found in subjects with one to 14 teeth than in subjects with either zero teeth or 15 to 28 teeth. A higher salivary level of *S. sanguis* was inversely associated with CHD. A higher number of medications taken and a complaint of xerostomia were significantly associated with CHD. The reported daily consumption of alcoholic beverages had a significant negative association with CHD—that is, an odds ratio, or OR, of less than one.

When the recognized risk factors such as the BMI, age, total serum cholesterol levels, smoking status and diabetic status were added to the model, they

TABLE 3

DISTRIBUTION OF DENTAL RISK INDICATORS AS A FUNCTION OF THE NUMBER OF TEETH.

RISK INDICATOR	ONE-14 TEETH (n = 61)		15-28 TEETH (n = 145)		*P* - VALUE
	Coronary Heart Disease Status		Coronary Heart Disease Status		
	No (n = 23)	Yes (n = 38)	No (n = 89)	Yes (n = 56)	
Number of teeth	8.7 (3.2)*†	8.4 (3.5)*†	22.9 (3.9)*	22.2 (3.6)*	.0001‡
Decayed teeth (% of teeth)	8.5 (15.0)*	4.0 (6.6)*	3.0 (7.8)*	4.2 (6.4)*	.07‡
Pockets > 4 mm (% of teeth)	38 (33)*	47 (27)*	44 (23)*	40 (20)*	.7‡
Attachment > 4 mm (% of teeth)	63 (35)*	81 (25)*†	62 (23)*	59 (23)*	.0006‡
Recession > 4 mm (% of teeth)	24 (30)*	24 (28)*	8.6 (15)*	7.1 (11)*	.01‡
Papillary bleeding score					
< .05	19%	12%	20%	8%	
0.5 to 1.5	29%	47%	53%	56%	.1§
> 1.5	52%	41%	27%	36%	
Plaque BANA score	1.9 (0.9)*	1.9 (0.9)*	1.8 (0.6)*	2.0 (0.7)*	.7
< 2	57%	50%	47%	39%	.4**
≥ 2	43%	50%	53%	61%	
Plaque index					
≤ 1	45%	26%	45%	43%	.04**
> 1	55%	74%	45%	57%	
Brush daily	95%	94%	98%	92%	.3**
Floss daily	24%	28%	42%	33%	.3**
Visit dentist yearly	67%	61%†	87%	82%	.007**

* Data are mean (± standard deviation).
† Value is significantly different from all values in the 15-28 teeth group.
‡ Kruskal-Wallis test with Bonferroni-adjusted pairwise comparisons.
§ χ^2 test.
** Multiple logistic models with Bonferoni-adjusted pairwise comparisons.

were not statistically associated with CHD. They did not affect the significance of the other variables in the model.

As Table 4 shows, CHD was 2.92 times more likely to be found in dentate subjects with one to 14 teeth than in dentate subjects with 15 to 28 teeth. Again, a higher salivary level of *S. sanguis* had a significant negative association with CHD. The mean BANA score was 2.08 times more likely to be higher in subjects with CHD. None of the measured oral hygiene parameters was significant. The complaint of xerostomia was positively associated with CHD, as was the number of medications taken. The daily consumption of alcoholic beverages was not significantly associated with CHD and was dropped from the model. When the recognized risk factors were included in the dentate subjects model, none was found to be significantly associated with CHD.

The prevalence of CHD in residents in the long-term care facility (dependent living) was 62 percent compared with 42 percent in the dental outpatients (independent living) (Table 5). This raised a concern that there may be factors operating in the nursing home subjects that were not detected in our all-subjects models (Table 4). Accordingly, we repeated the modeling procedure using separate models for the independent living group and the dependent living group. In the independent living, all-subjects model, the greater use of medications and daily consumption of alcoholic beverages were significantly associated with CHD, but the presence of one to 14 teeth, a complaint of xerostomia and salivary levels of *S. sanguis* were no longer significantly associated with CHD (Table 5).

In the independent living, dentate subjects model, the presence of one to 14 teeth, a complaint of xerostomia, a greater use of medications and

TABLE 4

MEDICAL RISK FACTORS/INDICATORS IN CORONARY HEART DISEASE—RESULTS OF LOGISTIC REGRESSION ANALYSIS.*

RISK FACTOR/ INDICATOR	ALL SUBJECTS (n = 309)†			DENTATE SUBJECTS (n = 199)‡		
	Odds Ratio	95% Confidence Interval	*P* - Value	Odds Ratio	95% Confidence Interval	*P* - Value
No. of teeth						
Zero	1.00			2.92§	1.39-6.11	.005
One-14	2.64§	1.26-5.56	.01	1.00		
15-28	1.04	0.57-1.90				
Streptococcus sanguis **(log_{10}/mL saliva)**	0.86	0.79-0.94	.0007	0.84§	0.75-0.94	.0017
Plaque BANA score	NA**	NA**	NA**	2.08§	1.08-4.01	.029
No. of medications	1.16	1.08-1.25	.0001	1.17§	1.07-1.29	.001
Complaint of xerostomia	1.82§	1.01-3.28	.05	2.43§	1.12-5.25	.024
Use of alcohol						
None	1.00			NA**	NA**	
Occasionally	0.91	0.53-1.57				
Daily	0.40§	0.18-0.90	.026			
Dependent living (nursing home)	1.18	0.63-2.22	.6	1.33	0.58-3.01	.50
Likelihood ratio	62.71			48.34		
Degrees of freedom	8			6		
***P* - value**	< .0001			< .0001		

* Recognized risk factors for coronary heart disease, such as age, serum cholesterol levels, body mass index, smoking history, diabetes and race, were not significant in this model.
† Of the 309 subjects for whom we had complete data, 156 did not have a diagnosis of coronary heart disease and 153 did, for a prevalence of 49.5 percent.
‡ Of the 199 dentate subjects for whom we had complete data, 104 did not have a diagnosis of coronary heart disease and 95 did, for a prevalence of 47.7 percent.
§ Significant at $P < .05$.
**NA: not applicable. The variable was omitted from the model.

a higher BANA test score had significant positive associations with CHD, and the salivary levels of *S. sanguis* had significant negative associations with CHD. A higher level of gingivitis, as measured by the PBS, was also significantly associated with CHD (Table 5). A higher OR for the PBS paralleled the clinical severity of the condition, as gingivitis that did not involve bleeding had an OR of 2.4, and gingivitis that involved bleeding had an OR of 4.6.

The smaller number of subjects in the dependent living group hampered the modeling procedures, especially in the dentate model, but the presence of one to 14 teeth and salivary levels of *S. sanguis* were significantly associated with CHD in both the all-subjects and dentate subjects models (Table 5). In the all-subjects model, patients who had a complaint of xerostomia were 2.92 times more likely to have CHD. Two variables became significant for the first time: subjects who quit smoking were 11.9 times more likely to have CHD than subjects who never smoked, and subjects who controlled their diabetic condition with diet were almost five times less likely to have CHD than diabetic subjects who did not control their condition with diet.

DISCUSSION

Cross-sectional studies performed with convenience samples, such as this study, cannot be generalized to the entire population. However, they can identify as risk indicators those parameters that are significantly associated with the condition being investigated (in this case, CHD). Whether these risk indicators prove to be risk factors (that is, causally related) remains to be demonstrated in prospective studies performed with a more representative population.

The results of this cross-sectional study confirmed those of previous studies conducted with younger subjects that showed a significant association between dental disease and CHD.[1-6] We found that the subjects with one to 14 teeth were most likely to

TABLE 5

RISK FACTORS/INDICATORS ASSOCIATED WITH CHD IN OLDER VETERANS—RESULTS OF LOGISTIC REGRESSION ANALYSIS.*

RISK FACTOR/ INDICATOR	INDEPENDENT LIVING				DEPENDENT LIVING			
	All Subjects (n = 195)†		Dentate Subjects (n = 147)‡		All Subjects (n = 114)§		Dentate Subjects (n = 52)**	
	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval	Odds Ratio	95% Confidence Interval
Streptococcus sanguis (log_{10}/mL saliva)	0.9	0.8-1.01	0.86††	0.76-0.98	0.74††	0.63-0.87	0.74††	0.59-0.93
No. of teeth								
Zero	1.00				1.00			
One-14	1.8	0.07-4.9	2.83††	1.11-7.2	6.16††	1.60-23.7	3.85††	1.001-14.8
15-28	0.92	0.42-2.0	1.00		1.28	0.39-4.15	1.00	
Complaint of xerostomia	1.94	0.90-4.21	2.6††	1.02-6.62	2.92††	1.02-8.39	NA‡‡	NA‡‡
No. of medications	1.21††	1.09-1.34	1.20††	1.07-1.36	NA‡‡	NA‡‡	NA‡‡	NA‡‡
Plaque BANA score	NA‡‡	NA‡‡	2.46††	1.13-5.38	NA‡‡	NA‡‡	NA‡‡	NA‡‡
PBS* < 0.5 (healthy)	NA‡‡	NA‡‡	1.0		NA‡‡	NA‡‡	NA‡‡	NA‡‡
PBS ≤ 1.5 (nonbleeding)			2.42	0.74-7.6				
PBS > 1.5 (bleeding)			4.6††	1.32-15.97				
Alcohol use								
None	1.0		NA‡‡	NA‡‡	NA‡‡	NA‡‡	NA‡‡	NA‡‡
Occasionally	0.77	0.39-1.5						
Daily	0.21††	0.06-0.69						
Smoking status								
Never	NA‡‡	NA‡‡	NA‡‡	NA‡‡	1.0		NA‡‡	NA‡‡
Quit					11.9††	1.43-99.5		
Current					4.9	0.54-44.8		
Diet-controlled diabetes	NA‡‡	NA‡‡	NA‡‡	NA‡‡	0.21††	0.06-0.7	NA‡‡	NA‡‡
Likelihood ratio	37.7		37.7		32.77		10.45	
Degrees of freedom	7		7		7		2	
P - value	.0001		.0001		.0001		.005	

* CHD: coronary heart disease; PBS: papillary bleeding score.
† Of the 195 subjects for whom we had complete data, 113 did not have a diagnosis of CHD and 82 did, for a prevalence of 42 percent.
‡ Of the 147 subjects for whom we had complete data, 86 did not have a diagnosis of CHD and 61 did, for a prevalence of 41 percent.
§ Of the 114 subjects for whom we had complete data, 71 had a diagnosis of CHD and 45 did not, for a prevalence of 62 percent.
** Of the 52 subjects for whom we had complete data, 34 had a diagnosis of CHD and 18 did not, for a prevalence of 65 percent.
†† Significant values.
‡‡ NA: not applicable. The variable was omitted from the model.

have CHD, and observed this association in subjects in both independent living and dependent living circumstances.

Chronic infection hypothesis. The importance of having only a few teeth in these subjects seems to be related to the greater periodontal morbidity of their teeth—that is, a higher percentage of teeth with attachment loss—to poorer oral hygiene as assessed by higher plaque scores, and to less-frequent visits to the dentist (Table 3). In the multivariate analysis, a high BANA test score was positively associated with CHD in both the all-subjects dentate model (Table 4) and the independent living dentate model (Table 5).

The BANA test detects the presence of an enzyme(s) that hydrolyzes the synthetic trypsinlike substrate benzoyl-DL-arginine-naphthylamide, or BANA, in plaque samples.[16] Of more than 60 plaque bacterial species that have been tested, only *P. gingivalis*, *Treponema denticola* and *Bacteroides forsythus* always exhibit strong BANA activity, although some species, like the *Capnocytophaga* species, occasionally exhibit weak BANA activity.[16] The three strongly BANA-positive species are invariably elevated in plaque samples removed from teeth with periodontal pathology.[17-20] Thus, a higher plaque BANA

score would indirectly indicate that these periodontopathic species are elevated on the tooth surfaces of subjects with CHD. This implies some degree of periodontal pathology, which was documented by the significantly higher PBS in the multivariate model of independent living dentate subjects (Table 5).

These BANA-positive species are gram-negative anaerobes, so that their elevation in the dental plaque would support the various hypotheses linking chronic bacterial infection to CHD via effects mediated by endotoxins or lipopolysaccharides, or LPS.[21-23] The confrontation of the varied host-defense mechanisms with these LPS-containing invaders may lead to the supplementation of serum cytokine levels with inflammatory mediators derived from this confrontation,[24] which could contribute to the chronic inflammatory process that leads to increased levels of C-reactive proteins in the serum.[8] LPS has long been known to promote atherosclerosis and thrombus formation.[25]

An additional factor in this process could be an exaggerated host response to LPS, mediated by the presence of hyperresponsive monocytic cells.[6] Certain patients with early-onset periodontitis, refractory periodontitis or insulin-dependent diabetes have peripheral blood monocytes that secrete threefold to 10-fold greater amounts of PGE_2, IL-1β and TNFα when exposed to LPS in vitro. These people would react to the penetration of gram-negative bacteria, such as the BANA-positive species, from the subgingival plaque into the periodontium by the overproduction of cytokines that could leak from the gingival tissue into the general circulation and have an effect on distant organs.

Other studies have proposed a chronic infection hypothesis involving dental disease as a possible risk factor for the development of a cardiovascular event.[21,22] In their prospective study, Mattila and colleagues[3] were able only to associate dental infections as measured by the TDI and a history of myocardial infarction with a subsequent acute myocardial infarction. They then showed that there are elevated levels of von Willebrand factor antigen in subjects with an elevated TDI,[26] which could reflect increased endothelial cell damage induced by the LPS derived from the gram-negative dental plaque flora. Grau and colleagues[7] have shown that the TDI may be associated with an increased risk of cerebral vascular ischemia.

The results indicate that in these elderly subjects, it is the presence of only a few teeth that is associated with coronary heart disease.

Missing teeth. The number of missing teeth was independently associated with CHD in the two epidemiologic surveys that randomly selected their study populations,[4,5] but these studies did not distinguish between edentulous subjects and dentate subjects with many missing teeth. Our results indicate that in these elderly subjects, it is the presence of only a few teeth that is associated with CHD. When we divided our subjects into groups with one to 14 teeth and 15 to 28 teeth, the presence of one to 14 teeth was significantly associated with CHD in both the all-subjects and dentate subjects models (Table 4).

An indirect confirmation of the importance of having 15 to 28 teeth in protecting against CHD was the relationship between the salivary levels of *S. sanguis* and CHD status. The significant negative association seen in all models (Table 4) can be explained by the fact that this organism is associated with teeth, and is among the best microbial colonizers on the tooth surface.[27] This organism is dominant in early plaque formation, so that people with good oral hygiene would have higher proportions of *S. sanguis* in the mouth. The more teeth in the mouth, the more likely that the salivary levels of *S. sanguis* would be higher.

S. sanguis has been studied for its role in endocarditis,[28,29] and a platelet-aggregation-associated protein has been identified as a virulence factor because it interacts with platelets, promoting coagulation, or it may behave as a heat-shock protein, which, by causing an autoimmune response, could initiate the early atherosclerotic lesion.[30] Our findings do not support a role for *S. sanguis* in CHD in these older subjects, but it is possible that such interactions could have occurred earlier in their lives.

Evidence in the literature suggests that edentulous people with and without dentures and dentate people with missing

teeth change their eating habits after they lose their teeth.[31,32] They may avoid certain nutritious foods because of difficulty in chewing, and select high-calorie, high-fat foods whose consumption is recognized as a risk factor for cardiovascular disease.[33] But an additional feature of this dietary change that could be particularly relevant in those dentate subjects with one to 14 teeth is that dietary-induced elevation of serum low-density lipoprotein levels has been shown to increase monocytic responses to LPS.[34] These subjects would have both the dietary-induced sensitization of the monocytes and the plaque-laden teeth and gingivitis that could provide the LPS challenge to these cells.

The advanced age of our subjects might explain the absence of an association between edentulism and CHD in the logistic regression models, since people most susceptible to the linkage between edentulism and CHD may already be dead. This would be consistent with the National Health and Nutrition Examination Survey, or NHANES, data that showed that in males younger than 50 years of age, edentulism was 2.6 times more likely to be associated with death resulting from any cause.[4]

However, this explanation, as well as the chronic infection hypothesis involving dental infections, would not seem to explain why 53 percent of our edentulous subjects had CHD, unless these patients experienced their first heart attack while they had teeth. It is possible that by having had their teeth extracted, these people coincidentally had the tooth-related microbial challenge removed that had been a major contributor to the events leading to their heart attack. Edentulism in this sense would be protective, although in the younger subjects in the NHANES study, edentulism might have been a marker for rampant dental disease that could have predisposed them to CHD by the mechanisms described above.

Other significant findings. The possible protective role of daily alcohol consumption noted in the all-subjects model in this study has been observed by others.[35] The greater use of all types of medications was significantly associated with CHD in both the all-subjects and dentate subjects models. This was expected, as our subjects were taking many types of medications associated with old age and a diagnosis of cardiovascular and other diseases.[36]

For this group of older veterans, our findings suggest that the oral health parameters may play an important role in the occurrence of coronary heart disease.

It is not clear how a complaint of xerostomia could be such a powerful risk indicator for CHD. Xerostomia is a common complaint of older people,[37] and it has been associated with poor oral hygiene, the inability to chew and involuntary weight loss among both institutionalized[38,39] and independent older adults.[38] We have found that people with complaints of xerostomia avoid crunchy (carrots), dry (bread) and sticky (peanut butter) foods, but not crumbly (cake) or chewy (red meat) foods.[40] This choice of foods could lead to the selection of the high-calorie, high-fat foods that are associated with obesity and CHD.[33]

The use of a convenience sample of older subjects for our analysis may explain why recognized risk factors, such as serum cholesterol levels, BMI, smoking status and diabetes, were not more prominent in the modeling procedure. The use of medications to control blood pressure or cholesterol levels was not included in our analysis; as these subjects were actively receiving treatment for CHD, this could explain why these risk factors were not associated with CHD.

In other studies performed with convenience samples, the dental variables were significantly associated with CHD, whereas the classical risk factors such as cholesterol levels, alcohol consumption, BMI and hypertension were not.[1-3,7] Thus, our investigation, like others performed with convenience samples, cannot be generalized to the entire population, and because of the cross-sectional nature of our study, the oral health variables can at best be considered risk indicators. Despite these limitations, for this group of older veterans, our findings suggest that the oral health parameters may play an important role in the occurrence of CHD. We are following up these subjects to determine whether any of these dental parameters can be shown to be risk factors.

CONCLUSION

Our cross-sectional study of a convenience sample of older U.S. veterans identified several oral health variables—including having one to 14 teeth, low salivary levels of *S. sanguis*, positive plaque BANA scores, gingivitis involving bleeding and a complaint of xerostomia—as risk indicators for CHD. Whether they prove to be risk factors depends on their ability to predict episodes of CHD in a longitudinal study. Certain known risk factors, such as smoking, total cholesterol levels, BMI, diabetes and race, were not significant in this model. This probably reflects the fact that these subjects were older and many were receiving medical treatment directed toward some of these risk factors. ■

Dr. Loesche is a professor, University of Michigan, School of Dentistry, Department of Biologic and Materials Science, 1011 N. University, Ann Arbor, Mich. 48109-1078. Address reprint requests to Dr. Loesche.

Dr. Schork is a professor, University of Michigan, School of Public Health, Department of Biostatistics, Ann Arbor, Mich.

Dr. Terpenning practices at the Veterans Affairs Medical Center, Ann Arbor, Mich., and is an associate professor, University of Michigan, School of Medicine, Department of Internal Medicine, Division of Geriatric Medicine, Ann Arbor, Mich.

Dr. Chen is a graduate research associate, University of Michigan, School of Public Health, Department of Biostatistics, Ann Arbor, Mich.

Dr. Dominguez is a research investigator, the Veterans Affairs Medical Center, Ann Arbor, Mich.

Ms. Grossman is a research associate, University of Michigan, School of Dentistry, Department of Biologic and Materials Science, Ann Arbor, Mich.

This study was supported by Program Project grant DE 09142 from the National Institute of Dental Research. Walter Bretz, Gary Hildebrandt, Connie Kerr, Mario DeMeirelas and Kathryn Curry assisted in the collection of the dental data. Carol Gerlach and George Taylor assisted in the preparation of the manuscript.

1. Mattila KJ, Nieminen MS, Valtonen VV, et al. Association between dental health and acute myocardial infarction. Br Med J 1989; 298:779-81.
2. Syrjänen J, Peltola J, Valtonen V, Iivanainen M, Kaste M, Huttunen JK. Dental infections in association with cerebral infarction in young and middle-aged men. J Intern Med 1989;225:179-84.
3. Mattila KJ, Valtonen VV, Nieminen M, Huttunen JK. Dental infection and the risk of new coronary events: prospective study of patients with documented coronary artery disease. Clin Infect Dis 1995;20(3):588-92.
4. DeStefano F, Anda RF, Kahn HS, Williamson DF, Russell CM. Dental disease and risk of coronary heart disease and mortality. Br Med J 1993;306:688-91.
5. Paunio K, Impivaara O, Tiekso J, Maki J. Missing teeth and ischaemic heart disease in men aged 45-64 years. Eur Heart J 1993;14 (Supplement K):54-6.
6. Beck J, Garcia R, Heiss G, Vokonas PS, Offenbacher S. Periodontal disease and cardiovascular disease. J Periodontol 1996;67:1123-37.
7. Grau AJ, Buggle F, Ziegler C, et al. Association between acute cerebrovascular ischemia and chronic and recurrent infection. Stroke 1997;28:1714-29.
8. Ridker PM, Cushman M, Stampfer MJ, Tracy RP, Hennekens CH. Inflammation, aspirin and the risk of cardiovascular disease in apparently healthy men. N Engl J Med 1997; 336:973-9.
9. Loesche WJ, Abrams J, Terpenning MS, et al. Dental findings in geriatric populations with diverse medical backgrounds. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1995;80:43-54.
10. Löe H, Silness J. Periodontal disease in pregnancy. I. Prevalence and severity. Acta Odontol Scand 1963;21:533-51.
11. Loesche WJ. Clinical and microbiological aspects of chemotherapeutic agents used according to the specific plaque hypothesis. J Dent Res 1979;58:2404-12.
12. Marks RG, Magnusson I, Taylor M, Clouser B, Maruniak J, Clark WB. Evaluation of reliability and reproducibility of dental indices. J Clin Periodontol 1993;20:54-8.
13. Fox PC, Busch KA, Baum BJ. Subjective reports of xerostomia and objective measures of salivary gland performance. JADA 1987; 115:581-4.
14. Loesche WJ, Schork A, Terpenning MS, Chen Y-M, Stoll J. Factors which influence the salivary levels of selected organisms in older individuals. J Clin Microbiol 1995;33:2550-7.
15. Loesche WJ, Kazor CE, Taylor GW. The optimization of the BANA test as a screening instrument for gingivitis among subjects seeking dental treatment. J Clin Periodontol 1997;24:718-26.
16. Loesche WJ, Bretz WA, Kerschensteiner D, et al. Development of a diagnostic test for anaerobic periodontal infections based on plaque hydrolysis of benzoyl-DL-arginine naphthylamide. J Clin Microbiol 1990;28:1551-9.
17. Grossi SG, Genco RJ, Marthei EE, et al. Assessment of risk for periodontal disease. II. Risk indicators for alveolar bone loss. J Periodontol 1995;66:23-9.
18. Loesche WJ, Syed SA, Schmidt E, Morrison EC. Bacterial profiles of subgingival plaques in periodontitis. J Periodontol 1985;56:447-56.
19. Ashimoto A, Chen C, Slots J. Polymerase chain reaction detection of 8 putative periodontal pathogens in subgingival plaque of gingivitis and advanced periodontitis lesions. Oral Microbiol Immunol 1996;11:266-73.
20. Loesche WJ, Lopatin DE, Giordano J, Alcoforado G, Hujoel P. Comparison of the benzoyl-DL-arginine-naphthylamide (BANA) test, DNA probes, and immunological reagents for ability to detect anaerobic periodontal infections due to *Porphyromonas gingivalis*, *Treponema denticola*, and *Bacteroides forsythus*. J Clin Microbiol 1992;30:427-33.
21. Syrjänen J. Vascular diseases and oral infections. J Clin Periodontol 1990;17:497-500.
22. Valtonen VV. Infection as a risk factor for infarction and atherosclerosis. Ann Med 1991;23(5):539-43.
23. Loesche WJ. Periodontal disease as a risk factor for heart disease. Compend Contin Educ Dent 1995;15:976-91.
24. Offenbacher S, Katz VL, Fertik GS, et al. Periodontal infection as a risk factor for preterm low birth weight. J Periodontol 1996;67:1103-13.
25. Morrison DC, Ulevitch RJ. The effects of bacterial endotoxins on host mediation systems. Am J Pathol 1978;93:527-617.
26. Mattila K, Rasi V, Nieminen M, et al. Von Willebrand factor antigen and dental infections. Thromb Res 1989;56:325-9.
27. Syed SA, Loesche WJ. Bacteriology of human experimental gingivitis: effect of plaque age. Infect Immunol 1978;21:821-9.
28. Herzberg MC. Platelet-streptococcal interactions in endocarditis. Crit Rev Oral Biol Med 1996;7(3):222-36.
29. Herzberg MC, Meyer MW. Effects of oral flora on platelets: possible consequences in cardiovascular disease. J Periodontol 1996; 67:1138-42.
30. Xu Q, Willeit J, Marosi M, et al. Association of serum antibodies to heat-shock protein 65 with carotid atherosclerosis. The Lancet 1993;341:255-9.
31. Österberg T, Steen B. Relationship between dental state and dietary intake in 70-year-old males and females in Göteborg, Sweden: a population study. J Oral Rehabil 1982;9:509-21.
32. Sandström B, Lindquist LW. The effect of different prosthetic restorations on the dietary selection in edentulous patients. Acta Odontol Scand 1987;45:423-8.
33. Willett WC. Nutritional epidemiology. New York: Oxford University Press Inc.; 1990.
34. Molvig J. A model of pathogenesis of insulin-dependent diabetics. Dan Med Bull 1992;39:509-41.
35. Gaziano JM, Buring JE, Breslow JL, et al. Moderate alcohol intake, increased levels of high-density lipoprotein and its subfractions, and decreased risk of myocardial infarction. N Engl J Med 1993;329:1829-34.
36. Lamy P. Prescribing for the elderly. Littleton, Mass: PSG Publishing Co.; 1980.
37. Loesche WJ, Bromberg J, Terpenning MS, et al. Xerostomia, xerogenic medications and food avoidances in selected geriatric groups. J Am Geriatr Soc 1996;43:401-7.
38. Rhodus NL, Brown J. The association of xerostomia and inadequate intake in older adults. J Am Diet Assoc 1990;90:1688-92.
39. Sullivan DH, Martin W, Flaxman N, Hagen JE. Oral health problems and involuntary weight loss in a population of frail elderly. J Am Geriatr Soc 1993;41:725-31.
40. Hildebrandt GH, Loesche WJ, Lin C-F, Bretz WA. Comparison of the number and type of dental functional units in geriatric populations with diverse medical backgrounds. J Prosthet Dent 1995;73:253-61.