The Relationship Between Periodontal Disease Attributes and *Helicobacter pylori* Infection Among Adults in the United States

Bruce A. Dye, DDS, MPH, Deanna Kruszon-Moran, MS, and Geraldine McQuillan, PhD

Objectives. We investigated the relationship between *Helicobacter pylori* infection and abnormal periodontal conditions.

Methods. Data from the first phase of the third National Health and Nutrition Examination Survey were used. A total of 4504 participants aged 20 to 59 years who completed a periodontal examination and tested positive for *H. pylori* antibodies were examined.

Results. Periodontal pockets with a depth of 5 mm or more were associated with increased odds of *H. pylori* seropositivity (odds ratio [OR]=1.47; 95% confidence interval [CI]=1.12, 1.94) after adjustment for sociodemographic factors. This association is comparable to the independent effects of poverty on *H. pylori* (OR=1.54; 95% CI=1.10, 2.16).

Conclusions. Poor periodontal health, characterized by advanced periodontal pockets, may be associated with *H. pylori* infection in adults, independent of poverty status. (*Am J Public Health.* 2002;92:1809–1815)

Helicobacter pylori is a gram-negative, spiral-shaped bacterium that infects nearly a third of the total population of the United States and is associated with a variety of socioeconomic indicators.[1] In the developing world, researchers have proposed that the age distribution of *H. pylori* infection resembles a cohort effect, reflecting reduced transmission in younger age groups as sanitary conditions improve.[2] *H. pylori* causes duodenal ulcer disease and has been implicated in the development of gastric ulcers. Moreover, it has been associated with an increased risk for gastric cancer.[3–6] Recently, researchers have suggested that the primary extragastric reservoir for *H. pylori* is the oral cavity.[7] Because human infection by this pathogen appears to involve an oral route, it seems biologically plausible that oral health status directly or indirectly influences the process of *H. pylori* infection or reinfection.

Although *H. pylori* was first isolated nearly 20 years ago, the process of infection or human transmission remains unclear. Because most gastrointestinal microbes have been commonly believed to be transmitted by either oral–oral or fecal–oral pathways, numerous *H. pylori* carriage sources, including dental plaque, saliva, vomit, and feces, have been postulated and explored.[8–25] Some studies have examined plaque and saliva and have produced positive findings of an association with *H. pylori*,[8,10,13–17] whereas others have not.[18–25] Findings of a positive association between poor oral health (undefined periodontal disease) and *H. pylori* have been reported as well.[26] The suggestion has also been made that either *H. pylori* may promote the development of oral mucosal lesions—specifically, recurrent aphthous ulcers—or oral mucosal lesions may function as an intermediary in the route of oral–gastric infection.[27,28] Again, study results have been contradictory.[29–31]

Most of the prior studies that examined an oral condition as a factor in the promotion of extra gastric *H. pylori* activity examined dental plaque as a vehicle for *H. pylori* carriage. Dental plaque is primarily a collection of microorganisms embedded in an intracellular matrix composed of organic compounds (e.g., glycoproteins) and inorganic compounds (e.g., calcium and other minerals) that forms a biofilm. The biofilm matrix promotes and protects bacterial ecology, but not all of the bacteria residing within the biofilm are capable of becoming pathogenic. Dental plaque typically adheres to supragingival and subgingival tooth surfaces, and it will quickly form in the absence of good oral hygiene measures. Over time, undisturbed plaque progresses into calculus, which consists of a mineralized core that is superficially covered by the soft biofilm. Plaque biofilm can enhance the survivability of some bacteria by providing access to urea, which then can be reduced by urease-producing microorganisms to neutralize the effects of acidification.[32] The suggestion has recently been made that bacterial biofilms not only are commonly associated with many chronic infections but also are much more resistant to antibiotics than freely circulating bacteria.[33]

Many previous *H. pylori* studies have randomly acquired plaque samples from unspecified periodontal areas, mucosa, and saliva. Most studies collected plaque with a curette by upwardly scraping along the tooth surface.[13,15,16,20,21,23,24] Some studies used a paper point, a cytology brush, or a toothpick to remove the plaque specimen from periodontal sites.[19,25,29] Although some studies attempted to isolate supragingival plaque from subgingival plaque for separate analyses, others did not.[15,18,20,24,29,34] Moreover, among studies that collected isolates from pocket sites, many failed to describe the depth of the periodontal pocket from which the isolates were obtained.[15,18,19,20,25] Some studies even used periodontal index measures as an indicator of overall oral health status.[15,18,25] Methods used in testing isolates for *H. pylori* also have varied among studies. Cultures, urease activity tests, enzyme-linked immunosorbent assay (ELISA) tests, and polymerase chain reaction amplification tests have all been used. However, these tests are not uniformly sensitive or specific in their ability to identify *H. pylori* activity. Finally, many of these studies failed to

account for sociodemographic factors within the study population, and only 1 study concluded that future investigations should account for race/ethnicity characteristics.[16]

Periodontitis promotes deep-pocket formation and increased loss of clinical attachment of the tooth. More than 300 bacterial species may be associated with periodontal pockets alone, but only half of these have been cultivable.[35] Numerous microorganisms, mostly spirochetes and gram-negative rods, are associated with advanced periodontitis, and about 75% of the subgingival microorganisms that are found in advanced periodontitis are gram-negative anaerobic rods.[36,37] In individuals with a healthy periodontium, gram-negative rods constitute less than 13% of the microflora. The most current epidemiological findings indicate that 53% of Americans aged 30 to 90 years have at least 1 dental site with moderate to severe (≥3 mm) loss of attachment, compared with 9% who have moderate to severe (≥5 mm) pocket depth.[38] We know that periodontal disease increases with age, is consistently more prevalent in males, and is associated with certain socioeconomic indicators.

In this study, we attempted to examine the relationship between *H. pylori* seropositivity and abnormal oral conditions (e.g., recurrent aphthous ulcers) or clinical dental parameters suggestive of poor periodontal health. Our hypothesis was that some attributes indicative of poor periodontal health are associated with *H. pylori* infection. It has been suggested that "well designed, population-based studies that adequately consider confounding" would clarify the process of *H. pylori* transmission.[2] By using a nationally representative sample, we hoped to shed light on the epidemiological relationship between specific abnormal oral conditions and *H. pylori* infection.

METHODS

Study Population

We used data from 4504 subjects who participated in the first phase of the third National Health and Nutritional Examination Survey (NHANES III; 1988–1991). Conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention, NHANES III encompassed two 3-year phases (1988–1991 and 1991–1994), each producing a nationally representative sample of the noninstitutionalized civilian population of the United States. The NHANES sampling frame used a complex, highly stratified, multistage probability design. Details of the sampling design and methods used in obtaining informed consent from the study participants have been described elsewhere.[39] Data from 1988 to 1991 were used for our study, because information on *H. pylori* was measured only in phase 1. We assumed that individuals participating from 1988 to 1991 were less likely to have been exposed to antimicrobial treatments directed toward *H. pylori* eradication. During this period, results of treatment studies yielded unclear recommendations for chemotherapeutic eradication.[40]

A total of 5720 participants aged 20 years or older who had a serological test for *H. pylori* antibodies and who had completed a periodontal examination were eligible for this study. Demographic data for the study were obtained from a home interview questionnaire. Each participant received a standardized dental examination conducted by a trained dentist at a mobile examination center.[41] The serological testing for *H. pylori* antibodies used an ELISA with a reported sensitivity and specificity of 91% and 97%, respectively.[1] Individuals who were aged 60 years or older were excluded from the study because of low participation rates (<50%) in completing the sequence of interviewing, serology testing, and periodontal examination. Participants who were edentulous in at least 1 dental arch were also excluded. The analyzed population of 4504 subjects represented an overall participation rate of 75.9%.

Risk Factor Selection

Race/ethnicity was classified as Mexican American, non-Hispanic Black, non-Hispanic White, and other. Individuals who were identified as "other" were included in the total population estimates but not in the logistic models. Education was categorized as having not completed high school, having graduated from high school, or having attended college or university. We calculated a poverty index ratio by dividing total family income by the federal poverty income threshold, adjusted for family size. Age, sex, and foreign birth status were also analyzed. Potential effects of cigarette smoking were also explored.

Although we did not classify subjects according to their periodontal disease status, we did identify certain clinical characteristics that could constitute disease when used with radiographic assessment in a diagnostic setting. These attributes include supragingival calculus, subgingival calculus, periodontal attachment loss, pocket formation, and the presence of dental root furcations. Periodontal observations and measurements were made at 2 sites on each permanent tooth in 2 randomly selected quadrants (i.e., 1 upper and 1 lower). Detailed information about the NHANES III oral health component protocols, measurement issues, and data quality assurance have been described elsewhere.[39,41]

An extent index was individually established for supragingival calculus, subgingival calculus, and attachment loss. The number of dental sites affected was summed and divided by the total number of dental sites evaluated. This ratio was categorized into 4 groups: 0 to 15% of dentition affected, 16% to 30% of dentition affected, 31% to 45% of dentition affected, and 46% or more of dentition affected. Clinical attachment loss, an indicator of past periodontal disease, was defined as sites that had experienced a minimum of 2 mm of measured loss. This criteria was based on a previously published extent and severity attachment loss index.[42] We used calculus as a proxy for plaque because plaque was not specifically assessed in NHANES III.

Periodontal pocket depth was expressed as a dichotomous variable—either not present or at least 1 dental site with a pocket depth of 5 mm or more—because the distribution of advanced pocketing did not produce a stable variable to support the development of an extent index. Dental practitioners widely accept that even individuals with excellent at-home oral hygiene skills cannot remove debris or maintain a reasonably clean environment within the pocket at this depth. Dental root furcations, which are a condition of alveolar bone loss between the roots of a multirooted tooth, were analyzed by grouping both partial and complete furcal bony defect types to form a dichotomous variable that identified an individual as having either

none or at least 1 dentate site affected by a furcation.

Dental services utilization, defined as any dental visit in the past 12 months, was analyzed as a dichotomous variable. The presence or absence, independent of any particular time frame, of aphthous ulcers was reported by participants during the home interview. Participants were asked to differentiate between canker sores (aphthous ulcers) and cold sores (herpeslike lesions) on this household questionnaire.

Data Analysis

All statistical analyses were performed with SUDAAN, a software package that is specifically designed to accommodate complex sample surveys.[43] Sample weights were used to account for the unequal probability of selection and nonresponse of the study participants to produce prevalence estimates, odds ratio, and related standard errors. Comparisons across subpopulations were made with age-standardized prevalence estimates using direct adjustment over 4 age groups (20–29, 30–39, 40–49, and 50–59 years). We assessed potential age-standardized differences of *H. pylori* seropositivity within the implied risk categories by calculating *t* statistics using a linear contrast procedure in SUDAAN. Statistical significance was set at $P<.05$.

Logistic regression models were used to calculate crude and adjusted odds ratios with 95% confidence intervals. The presence or absence of *H. pylori* antibody was the dependent variable. Age, attachment loss, and supragingival and subgingival calculus were modeled as continuous variables. The remaining independent variables were modeled as categorical variables, as described in the univariate analyses. Multivariate logistic models also were used to assess the potentially strong interrelationships among the dental variables. Forward-selection and backward-elimination modeling assessments, including tests for interactions, were performed. The standard for retaining variables to produce the most parsimonious model was set for a Satterthwaite adjusted F statistic of $P<.05$. We assessed the possibility of interactions using race/ethnicity, age, sex, and periodontal pocket depth as multiple product terms in the multivariate model.

RESULTS

After direct adjustment for age, 25.3% of the 4504 subjects in this study were seropositive for *H. pylori* (Table 1). Age-adjusted differences in *H. pylori* seropositivity were observed among the 3 racial/ethnic groups (17.4% for non-Hispanic Whites, 47.1% for non-Hispanic Blacks, 55.9% for Mexican Americans). Among subjects who had at least 1 periodontal pocket, *H. pylori* seropositivity was greater ($P<.05$) in those with a measurable pocket depth of 5 mm or more (40.9%) than in those with a pocket depth less than 5 mm (23.9%). The differences in *H. pylori* seropositivity between participants with periodontal pocket depths of 5 mm or more compared with those with lesser pocket depths were significant for all 3 racial/ethnic groups ($P<.05$).

The effect of other dental conditions on *H. pylori* seropositivity was smaller than that seen with periodontal pocket depth. Individuals with either supragingival or subgingival calculus displayed an increase in *H. pylori* seropositivity as the extent of calculus coverage increased in the dentition (Table 1). Prevalence ranged from 17.7% to more than 35% when supragingival calculus coverage extended from less than 15% to more than 45% of dentition affected ($P<.05$). When study participants were stratified by race/ethnicity, only the most severe supragingival calculus category (46%–100% of dentition affected) remained significant ($P<.05$). The magnitude and pattern of *H. pylori* seropositivity among individuals with subgingival calculus were remarkably similar to those observed among individuals with supragingival calculus. The similarity between the effects of subgingival calculus and of supragingival calculus on the seropositivity of *H. pylori* remained after stratification by race/ethnicity, with 1 exception: among Mexican Americans, the difference between the least and most severe category of subgingival calculus was not statistically significant ($P>.05$).

In the age-standardized total population, gradual increase in *H. pylori* seropositivity was observed as the extent of attachment loss progressed from less than 15% to more than 45% of dentition affected, but this linear increase was not significant ($P>.05$). In the total population, *H. pylori* seropositivity increased from 23% among individuals with no dental root furcations to 36% among those with at least 1 root furcation ($P<.05$). Increased *H. pylori* seropositivity was associated with the presence of a root furcation for all 3 racial/ethnic groups, but the difference reached statistical significance only among non-Hispanic Whites.

Not having visited a dentist in the past 12 months was a significant indicator of *H. pylori* seropositivity among all 3 racial/ethnic groups ($P<.05$). Individuals who reported a positive history of aphthous ulcers had a lower seropositivity (18%) than did those without a history of ulcers (27%; $P<.05$). Although the results for aphthous ulcers exhibited a similar pattern when examined by race/ethnicity, the stratified findings were not conclusive. Although smoking is a risk factor for periodontal disease, smoking was found not to be associated with *H. pylori* seropositivity, either as a potential confounder or as an effect modifier in this analysis (data not shown).

Table 2 exhibits the relative odds of *H. pylori* infection from logistic regression modeling. Supragingival calculus had the strongest crude association with *H. pylori* seropositivity (odds ratio [OR]=4.95; 95% confidence interval [CI]=3.57, 6.87). The remaining periodontal indicators were crudely associated with *H. pylori*. Among these dental covariates, only a history of aphthous ulcers produced unadjusted estimates that indicated a potential protective effect (OR=0.57; 95% CI=0.40, 0.79). Sex was the only unadjusted demographic risk factor that was not statistically significant in the crude analysis.

In the final multivariate logistic model, the only dental covariate to remain influential was the presence of any moderate or severe periodontal pockets (Table 2, final model). Individuals with periodontal pocket depths of 5 mm or more had nearly a 50% increase in risk of *H. pylori* infection (OR=1.46; 95% CI=1.11, 1.92), an effect comparable to the adjusted effects of poverty (OR=1.54; 95% CI=1.10, 2.16). During the modeling process, periodontal pocket depth and supragingival calculus emerged as the only significant dental cofactors in a multivariate model. However, with the introduction of poverty into the model, supragingival calculus lost significance. Dental

TABLE 1—Age-Standardized *Helicobacter pylori* Seropositivity and Standard Errors for Selected Characteristics for the Total Population and by Race/Ethnicity: Third National Health and Nutritional Examination Survey, 1988–1991

	Total Population		Non-Hispanic Whites		Non-Hispanic Blacks		Mexican Americans	
	n	% (SE)	n	% (SE)	n	% (SE)	n	% (SE)
Total	4504	25.3 (1.8)	1578	17.4 (1.6)	1225	47.1 (2.2)	1528	55.9 (1.7)
Sex								
Male	2285	26.7 (2.3)	810	18.3 (1.9)	608	53.1 (3.0)	775	58.1 (1.6)
Female[a]	2219	23.8 (1.7)	768	16.5 (1.8)	617	42.0 (2.1)*	753	53.0 (2.3)*
Education								
Did not complete high school	1506	43.6 (2.6)*	230	31.5 (4.1)*	318	53.8 (2.9)*	906	64.2 (2.9)*
Completed high school	1464	28.3 (2.7)*	571	20.9 (2.4)*	504	50.3 (3.8)*	346	47.0 (3.0)
Some college[a]	1507	16.3 (1.5)	770	11.8 (2.4)	397	38.5 (2.9)	264	42.6 (4.5)
Birth status								
Not US born	1135	51.6 (3.4)*	90	36.6 (6.3)*	64[b]	69.3 (8.8)*	842	64.7 (1.9)*
US born[a]	3364	20.9 (1.6)	1488	16.3 (1.7)	1157	45.4 (2.3)	685	44.4 (3.6)
Poverty index								
Below poverty line	917	44.4 (2.9)*	116	30.0 (5.2)*	295	50.6 (3.3)*	478	66.8 (2.5)*
Above poverty line[a]	3168	22.4 (2.0)	1397	16.4 (1.7)	804	44.7 (2.1)	836	47.3 (2.2)
Prior history of aphthous ulcers								
Yes	622	18.4 (2.9)*	363	15.4 (2.7)	59[b]	36.9 (7.6)	173	47.1 (3.9)*
No[a]	3876	27.0 (1.6)	1214	18.0 (1.6)	1165	47.5 (2.2)	1352	57.1 (1.6)
Supragingival calculus only								
0–15% of dentition affected[a]	1130	17.7 (1.7)	602	14.7 (1.5)	171	37.1 (3.6)	326	45.9 (3.8)
16%–30% of dentition affected	856	21.0 (2.1)*	340	13.8 (2.2)	203	43.7 (3.7)	280	55.6 (3.6)
31%–45% of dentition affected	617	29.0 (3.5)*	188	19.6 (3.5)	156	46.6 (6.7)	248	59.2 (4.2)
46%–100% of dentition affected	1628	35.4 (2.7)*	354	24.0 (3.2)*	598	51.9 (2.2)*	604	59.8 (3.5)*
Any subgingival calculus								
0–15% of dentition affected[a]	2017	20.3 (2.1)	949	14.9 (1.7)	378	42.9 (2.6)	606	54.0 (1.5)
16%–30% of dentition affected	608	25.9 (2.1)*	190	17.9 (2.7)	170	39.0 (3.7)	225	54.6 (2.4)
31%–45% of dentition affected	440	31.9 (3.8)*	103	20.2 (4.1)	141	52.3 (7.0)	178	58.0 (3.8)
46%–100% of dentition affected	1166	36.4 (3.6)*	242	25.4 (4.3)*	439	53.3 (2.9)*	449	59.2 (5.2)
Periodontal pocket probing depth ≥ 5mm								
Yes	493	40.9 (2.7)*	118	25.1 (3.2)*	190	56.5 (3.8)*	164	69.4 (4.0)*
No[a]	3981	23.9 (1.8)	1448	16.5 (1.5)	1023	46.0 (2.4)	1360	55.4 (1.6)
Periodontal attachment loss								
0–15% of dentition affected[a]	2004	20.4 (1.8)	695	14.8 (1.7)	539	44.3 (3.5)	236	51.3 (2.5)
16%–30% of dentition affected	495	26.1 (3.5)	162	15.7 (3.1)	128	44.3 (4.0)	185	60.1 (5.0)
31%–45% of dentition affected	385	27.2 (3.3)	155	20.2 (4.0)	75[b]	48.1 (5.6)	138	54.8 (5.5)
46%–100% of dentition affected	1208	31.6 (2.8)*	433	19.9 (2.5)	319	56.4 (3.4)*	388	64.9 (3.5)*
Presence of a furcation								
Yes	408	36.9 (4.3)*	123	26.0 (4.1)*	124	52.7 (5.4)	137[b]	61.0 (12)
No[a]	3696	23.7 (1.9)	1338	16.3 (1.6)	930	45.1 (2.3)	1295	55.8 (1.7)
Dental visit in past 12 mo								
Yes[a]	2700	21.8 (1.8)	1157	15.7 (1.6)	669	42.5 (2.3)	763	49.6 (2.4)
No	1778	33.3 (2.2)*	412	22.2 (2.3)*	554	53.0 (2.7)*	750	61.2 (3.2)*

[a]Reference category.
[b]Prevalence estimates and standard errors are unreliable owing to low sample size.
*$P < .05$ compared with reference category.

TABLE 2—Odds Ratios (OR) and 95% Confidence Intervals (CI) for *Helicobacter pylori* Seropositivity in the Total US Population

	Crude Model[a] OR (95% CI)	Final Model[b] OR (95% CI)
Sex		
Male	1.16 (0.97, 1.40)	1.25 (1.02, 1.54)
Female	1.00	1.00
Age, y[c]	1.04 (1.03, 1.05)	1.05 (1.04, 1.06)
Race/ethnicity		
Non-Hispanic Blacks	4.20 (3.23, 5.46)	4.14 (3.09, 5.53)
Mexican Americans	6.01 (4.49, 8.06)	2.97 (1.82, 4.86)
Non-Hispanic Whites	1.00	1.00
Education		
Did not complete high school	3.91 (3.31, 4.61)	2.54 (1.91, 3.37)
Completed high school	1.96 (1.45, 2.65)	2.04 (1.45, 2.86)
Some college	1.00	1.00
Birth status		
Not US born	4.05 (3.09, 5.30)	2.92 (1.67, 5.10)
US born	1.00	1.00
Poverty index		
Below poverty line	2.42 (1.74, 3.38)	1.54 (1.10, 2.16)
Above poverty line	1.00	1.00
Reported history of aphthous ulcers		
Yes	0.57 (0.40, 0.79)	–
No	1.00	
Supragingival calculus only[c]	4.95 (3.57, 6.87)	–
Any subgingival calculus[c]	3.60 (2.35, 5.51)	–
Periodontal attachment loss[c]	3.42 (2.46, 4.77)	–
Probing pocket depth ≥ 5mm		
Yes	2.54 (2.08, 3.10)	1.46 (1.11, 1.92)
No	1.00	1.00
Any furcation present		
Yes	2.39 (1.85, 3.08)	–
No	1.00	
Dental visit in past 12 mo		
No	1.63 (1.35, 1.96)	–
Yes	1.00	

Note. Dashes indicate that variable is not included in the model.
[a]Logistic regression model individually includes only 1 independent variable.
[b]Logistic regression model includes only the statistically relevant predictors.
[c]Modeled as a continuous variable.

services utilization was no longer associated with *H. pylori* when pocket depth was added to the model. No significant interactions were found.

DISCUSSION

In the ongoing debate over human *H. pylori* transmission, the association of moderate to severe periodontal pockets with *H. pylori* seropositivity is an important consideration. Most studies have randomly collected isolates from coronal tooth sites, intra-oral mucosa, and unspecified periodontal pockets, such as from the "deepest" pocket measured.[25] In a study by Riggio and Lennon, when all subgingival plaque specimens were obtained from periodontal pockets at least 5 mm deep, subgingival plaque from 33% of the pocket sites analyzed were *H. pylori* positive, and 38% of the 29 subjects with moderate to severe periodontal pocketing were positive for *H. pylori*.[13] Consequently, Riggio and Lennon concluded that subgingival plaque in individuals afflicted with adult periodontitis may function as a reservoir for *H. pylori*. These results closely parallel our finding that nearly 41% of individuals with periodontal pockets of a measurable depth of 5 mm or more were *H. pylori* seropositive.

The extent of clinically measurable attachment loss was not a significant factor in *H. pylori* seropositivity. Although unadjusted attachment loss indicated more than a threefold increase in the odds of *H. pylori* seropositivity, there were no significant findings in the final multivariate models. Individuals with measurable attachment loss also could have had moderate to deep periodontal pockets, and this could have produced collinear effects in the regression models. There was also no significant association between dental root furcations and *H. pylori* in the multivariate models. Because furcations are often clinically associated with moderate to severe pocketing, these results could also be explained by multicollinearity.

Our results indicate a lack of association between recurrent aphthous ulcers and *H. pylori* seropositivity. One possible source of error in our analysis of aphthous ulcers is recall bias. Not only did we rely on the participant to accurately remember a prior experience with aphthous ulcers, but the participant also was required to differentiate between a canker sore (aphthous ulcer) and a cold sore (herpes lesion) with limited explanation in the questionnaire component.

It is reasonable to hypothesize that *H. pylori* survives in moderate to advanced periodontal pockets because the architecture and the microcosm of these periodontal conditions promote a viable habitat for microaerophilic and anaerobic microorganisms. Because dental biofilms can provide urea, urease-producing bacteria such as *H. pylori* may have improved viability in this periodontal environment. Furthermore, recent research has shown that vomitus is highly capable of producing cultivable samples of *H. pylori*, with post-emetic saliva samples

nearly 3 times as likely to produce *H. pylori* as pre-emetic saliva samples.[11] Given the forcible nature of emesis, plaque biofilm could become impregnated with ejected *H. pylori*. Thus, subgingival plaque within deeper periodontal pockets could promote microbe survival. The same strain of *H. pylori* found in the stomach has been identified in subgingival dental plaque.[44]

This is the first large epidemiological study in the United States that demonstrates a positive association between *H. pylori* seropositivity and a periodontal disease parameter. Identification of a positive association between periodontal pockets 5 mm or more in depth and *H. pylori* seropositivity may have an important impact on the control and eradication of *H. pylori* infection in humans. The success rate for gastric eradication has recently been reported to be significantly related to the prevalence of *H. pylori* in the oral cavity.[45] Thus, a combination of professional medical and dental treatment modalities may be required for some individuals with *H. pylori* infection. Because antibiotics have difficulty penetrating bacterial biofilm structures, periodontal treatment that includes dental scaling and root planing, and possibly periodontal surgery, may be needed to eliminate pathogens from diseased periodontal pockets.

A limitation of our study is its cross-sectional design. Because both *H. pylori* infection and periodontal disease are considered chronic disorders, the design of this study does not effectively address temporal relationships. Another limitation is that the periodontal disease indicators were derived from a partial mouth examination. One half of mouth examinations underestimate periodontal disease sites, particularly the more severe conditions.[46,47] Consequently, the direction of bias produced from underreporting disease may actually have underestimated the strength of the association in our study between periodontal pockets and *H. pylori* seropositivity. A strength of our study is that it used a large, nationally representative sample to explore and control for multiple confounding effects to clarify relationships to a degree not achieved by many prior studies. However, small effects may be more likely to demonstrate statistical significance in a study with a large sample size.

The microbial ecology of the oral cavity is highly complex, richly diverse, and not well understood. Most prior studies have inconclusively described the relationships among the oral cavity, oral health, and *H. pylori*. Our study provides additional evidence toward defining the importance of clinical and demographic risk factors in *H. pylori* infection. Although the idea that the oral cavity is a potential site for *H. pylori* gastric reinfection has been proposed before,[48] our findings indicate that only moderate to severe periodontal pockets may be associated with *H. pylori* infection. To assess causality or reinfection, additional research, principally cohort studies focusing on the culture of *H. pylori* from well-defined periodontal pockets, is needed to further examine mechanistic pathways and describe risk factors for *H. pylori* infection within the oral–pharyngeal–gastric macrocosm. ■

About the Authors

The authors are with the National Center for Health Statistics, Centers for Disease Control and Prevention, Hyattsville, Md.

Requests for reprints should be sent to Bruce Dye, DDS, MPH, CDC/NCHS, 6525 Belcrest Rd, Room 900, Hyattsville, MD 20782 (e-mail: bfd1@cdc.gov).

This article was accepted December 12, 2001.

Contributors

B.A. Dye originated the hypothesis and contributed to the literature review and data analyses. D. Kruszon-Moran contributed to the data analyses. G. McQuillan contributed to refining the hypothesis and reviewing the literature. All authors contributed to writing the article, including review of all revisions.

Human Participant Protection

All subjects or their parents provided written informed consent in compliance with the clinical research guidelines of the author's institution, and the study was approved by the CDC/National Centers for Health Statistics Institutional Review Board.

References

1. Everhart JE, Kruszon-Moran D, Perez-Perez GI, Tralka T, McQuillan G. Seroprevalence and ethnic differences in *Helicobacter pylori* infection among adults in the United States. *J Infect Dis.* 2000;181:1359–1363.

2. Goodman KJ, Correa P. The transmission of *Helicobacter pylori*. A critical review of the evidence. *Int J Epidemiol.* 1995;24:875–887.

3. Forman D, Newell D, Fullerton F, et al. Association between infection with *Helicobacter pylori* and risk of gastric cancer: evidence from a prospective investigation. *BMJ.* 1991;302:1302–1305.

4. Parsonnet J. *Helicobacter pylori* and gastric cancer. *Gastroenterol Clin North Am.* 1993;22:89–104.

5. Parsonnet J, Hansen S, Rodriguez L, et al. *Helicobacter pylori* infection and gastric lymphoma. *N Engl J Med.* 1994;330:1267–1271.

6. Asghar R, Parsonnet J. *Helicobacter pylori* and risk for gastric adenocarcinoma. *Semin Gastrointest Dis.* 2001;12:203–208.

7. Nabwera HM, Logan RP. Epidemiology of Helicobacter pylori: transmission and extragastric reservoirs. *J Physiol Pharmacol.* 1999;50:711–722.

8. Mapstone NP, Lynch DA, Lewis FA, et al. Identification of *Helicobacter pylori* DNA in the mouths and stomachs of patients with gastritis using PCR. *J Clin Pathol.* 1993;46:540–543.

9. Thomas JE, Gibson GR, Darboe MK, Dale A, Weaver LT. Isolation of *Helicobacter pylori* from human feces. *Lancet.* 1992;340:1194–1195.

10. Li C, Ha T, Ferguson DA Jr, et al. A newly developed PCR assay of H. pylori in gastric biopsy, saliva, and feces: evidence of high prevalence of H. pylori in saliva supports oral transmission. *Dig Dis Sci.* 1996;41:2142–2149.

11. Parsonnet J, Shmuely H, Haggerty T. Fecal and oral shedding of *Helicobacter pylori* from healthy infected adults. *JAMA.* 1999;282:2240–2245.

12. Okuda K, Ishihara K, Miura T, Katakura A, Noma H, Ebihara Y. *Helicobacter pylori* may have only a transient presence in the oral cavity and on the surface of oral cancer. *Microbiol Immunol.* 2000;44:385–388.

13. Riggio MP, Lennon A. Identification by PCR of *Helicobacter pylori* in subgingival plaque of adult periodontitis patients. *J Med Microbiol.* 1999;48:317–322.

14. Majmudar P, Shah SM, Dhunjibhoy KR, Desaj HG. Isolation of *Helicobacter pylori* from dental plaques in healthy volunteers. *Indian J Gastroenterol.* 1990;9:271–272.

15. Nguyen AH, Engstrand L, Genta RM, Graham DY, El-Zaatari FAK. Detection of *Helicobacter pylori* in dental plaque by reverse transcription-polymerase chain reaction. *J Clin Microbiol.* 1993;31:783–787.

16. Butt AK, Khan AA, Bedi R. *Helicobacter pylori* in dental plaque of Pakistanis. *J Int Acad Periodontol.* 1999;1(3):78–82.

17. Banatvala N, Lopez CR, Owen R, et al. Helicobacter in dental plaque. *Lancet.* 1993:341:380.

18. Von Recklinghausen G, Weischer T, Ansorg R, Mohr C. No cultural detection of *Helicobacter pylori* in dental plaque. *Zentralbl Bakteriol.* 1994;281:102–106.

19. Asikainen S, Chen C, Slots J. Absence of *Helicobacter pylori* in subgingival samples determined by polymerase chain reaction. *Oral Microbiol Immunol.* 1994;9:318–320.

20. Cheng LHH, Webberley M, Evans M, Hanson N, Brown R. *Helicobacter pylori* in dental plaque and gastric mucosa. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1996;81:421–423.

21. Luman W, Alkout AM, Blackwell CC, Weir DM, Palmer KR. *Helicobacter pylori* in the mouth—negative isolation from dental plaque and saliva. *Eur J Gastroenterol Hepatol.* 1996;8:11–14.

22. Krajden S, Fuksa M, Anderson J, et al. Examination of human stomach biopsies, saliva, and dental

plaque for *Campylobacter pylori*. *J Clin Microbiol.* 1989; 27:1397–1398.

23. Song Q, Lange T, Spahr A, Adler G, Bode G. Characteristic distribution pattern of *Helicobacter pylori* in dental plaque and saliva detected with nested PCR. *J Med Microbiol.* 2000;49:349–353

24. Oshowo A, Tunio M, Gillam D, et al. Oral colonization is unlikely to play an important role in *Helicobacter pylori* infection. *Br J Surg.* 1998;85:850–852.

25. Hardo PG, Tugnait A, Lynch DAF, et al. *Helicobacter pylori* infection and dental care. *Gut.* 1995;37: 44–46.

26. Bielanski W. Epidemiological study on *Helicobacter pylori* infection and extragastoduodenal disorders in Polish population. *J Physiol Pharmacol.* 1999;50: 723–733.

27. Birek C, Grandhi R, McNeil K, Singer D, Ficarra G, Bowden G. Detection of *Helicobacter pylori* in oral aphthous ulcers. *J Oral Pathol Med.* 1999;28:197–203.

28. Leimola-Virtanen R, Happonen RP, Syrjanen S. Cytomegalovirus and *Helicobacter pylori* found in oral mucosal ulcers. *J Oral Pathol Med.* 1995:24:14–17.

29. Mravak-Stipetic M, Gall-Troselj K, Lukac J, Kusic Z, Pavelic K, Pavelic J. Detection of *Helicobacter pylori* in various oral lesions by nested polymerase chain reaction. *J Oral Pathol Med.* 1998;27:1–3.

30. Porter SR, Barker GR, Scully C, Macfarlane G. Serum IgG antibodies to *Helicobacter pylori* in patients with recurrent aphthous stomatitis and other oral disorders. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 1997;83:325–328.

31. Singh K, Kumar S, Jaiswal MSD, Chandra M, Singh M. Absence of *Helicobacter pylori* in oral mucosal lesions. *J Indian Med Assoc.* 1998;96:177–178.

32. Marquis RE. Oxygen metabolism, oxidative stress and acid-base physiology of dental plaque biofilms. *J Ind Microbiol.* 1995;15:198–207.

33. Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. *Science.* 1999;284:1318–1322.

34. Song Q, Haller B, Ulrich D, Wichelhaus A, Adler G, Bode G. Quantitation of *Helicobacter pylori* in dental plaque samples by competitive polymerase chain reaction. *J Clin Pathol.* 2000;53:218–222.

35. Jenkinson HF, Dymock D. The microbiology of periodontal disease. *Dent Update.* 1999;26:191–197.

36. Loesche WJ, Syed SA, Schmidt E, Morrison EC. Bacterial profiles of subgingival plaques in periodontitis. *J Periodontol.* 1985;56:447–456.

37. Slots J. Subgingival microflora and periodontal disease. *J Clin Periodontol.* 1979;6:351–382.

38. Albandar JM, Brunelle JA, Kingman A. Destructive periodontal disease in adults 30 years of age and older in the United States, 1988–1994. *J Periodontol.* 1999;70:13–29.

39. Plan and operation of the third National Health and Nutrition Examination Survey, 1988–94. Series 1: programs and collection procedures. *Vital Health Stat 1.* 1994;No. 32:1–40.

40. Chiba N, Rao BV, Rademaker JW, Hunt RH. Meta-analysis of the efficacy of antibiotic therapy in eradicating Helicobacter pylori. *Am J Gastroenterol.* 1992;87:1716–1727.

41. Drury TF, Winn DM, Snowden CB, Kingman A, Kleinman DV, Lewis B. An overview of the oral health component of the 1988–1991 National Health and Nutrition Examination Survey (NHANES III Phase 1). *J Dent Res.* 1996;75(spec no.):620–630.

42. Carlos JP, Wolfe MD, Kingman A. The extent and severity index: a simple method for use in epidemiologic studies of periodontal disease. *J Clin Periodontol.* 1986;13:500–505.

43. Shah B, Barnwell B, Bieler G. *SUDAAN User's Manual, Release 7.0.* Research Triangle Park, NC: Research Triangle Institute; 1996.

44. Shames B, Krajden S, Fuksa M, Babida C, Penner JL. Evidence for the occurrence of the same strain of Campylobacter pylori in the stomach and dental plaque. *J Clin Microbiol.* 1989;27:2849–2850.

45. Miyabayashi H, Furihata K, Shimizu T, Ueno I, Akamatsu T. Influence of oral *Helicobacter pylori* on the success of eradication therapy against gastric Helicobacter pylori. *Helicobacter.* 2000;5:30–37.

46. Kingman A, Morrison E, Loe H, Smith J. Systematic errors in estimating prevalence and severity of periodontal disease. *J Periodontol.* 1988;59:707–713.

47. Hunt RJ, Fann SJ. Effect of examining half the teeth in a partial periodontal recording of older adults. *J Dent Res.* 1991;70:1380–1385.

48. Pytko-Polonczyk J, Konturek S, Karczewska E, Bielanski W, Kaczmarczyk-Stachowska A. Oral cavity as a permanent reservoir of *Helicobacter pylori* and potential source of reinfection. *J Physiol Pharmacol.* 1996; 47:121–129.