Dyspepsia in the Community Is Linked to Smoking and Aspirin Use but Not to Helicobacter pylori Infection

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Background: The relationship between Helicobacter pylori infection and symptoms remains controversial. We aimed to determine if an association exists between unexplained dyspepsia (pain or discomfort centered in the upper part of the abdomen) and H pylori.

Methods: A validated questionnaire was completed by 592 healthy blood donors. Helicobacter pylori serologic values (via enzyme-linked immunosorbent assay), blood group status, and Rh status were measured; 4.9% of subjects who had a history of peptic ulcer disease were excluded from the analyses.

Results: The prevalence of dyspepsia and no ulcer history was 11% (95% confidence interval [CI], 8.6%-13.8%); 15.4% of subjects with dyspepsia had H pylori while 14.6% of subjects without dyspepsia were infected (P = .90). The mean dyspepsia impact scores (combining frequency and severity) in those with and without H pylori were 4.7 and 5.4, respectively (P = .20). The median H pylori optical density values in dyspepsia vs no dyspepsia were not significantly different (P = .30). Independent risk factors for dyspepsia were the use of aspirin (odds ratio [OR], 2.2; 95% CI, 1.3-3.7) and smoking (OR, 2.1; 95% CI, 1.3-3.6) but not age, sex, marital status, educational level, income, or the use of alcohol, coffee, or nonsteroidal anti-inflammatory drugs. Independent risk factors for H pylori were increasing age (OR, 1.8 per decade; 95% CI, 1.5-2.3), male sex (OR, 2.1; 95% CI, 1.3-3.4), and net family income (OR, 1.8; 95% CI, 1.2-3.3).

Conclusion: Dyspepsia in the community is linked to smoking and aspirin use, but not to H pylori infection.

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SUBJECTS, MATERIALS, AND METHODS

SUBJECTS

A total of 648 consecutive volunteer blood donors presenting to the Nepean Hospital Blood Bank, Sydney, were invited to participate in the study. The Nepean Hospital is the major teaching hospital in the area and serves a relatively stable and geographically localized population of 330,000 in western Sydney. The study was approved by the Wentworth Area Health Service Ethics Committee. All subjects gave written informed consent.

DETERMINATION OF H PYLORI STATUS AND ITS OPTICAL DENSITY

Ten milliliters of blood collected at the time of donation was centrifuged after clotting and the serum was separated. The serum was frozen (−70°C) and batched for further analyses. An enzyme-linked immunosorbent assay was used to determine IgG antibodies against H. pylori. Briefly, a reference strain of H. pylori, NCTC 11637 (National Culture Type Collection, Public Health Laboratory Service, London, England), and a clinical isolate, P10, were subcultured under microaerophilic conditions for 48 to 72 hours. Organisms were harvested using 0.1 M phosphate-buffered saline solution (pH 7.2) containing 0.2% sodium azide and then centrifuged at 1000 g for 10 minutes. After harvesting and washing, the cells were subjected to sonication in a sonifier (model B-30, Branson Ultrasonic Company, Danbury, Conn) at 8 kHz (50% cycle). Following protein determination, sonicated cells of each isolate were diluted to 100 µg/mL mixed in equal proportions and 100 µL of the mixture was added to each well of a microtiter plate. The plates were covered in parafilm (parafilm N, American National Can, Chicago, III) and stored at 4°C for at least 48 hours before use. On the day of use, plates were washed 3 times and any remaining free sites were blocked with 100 µL of the blocking buffer. After incubation for 2 hours at 37°C, plates were again washed and 100 µL of each serum sample at a final dilution of 1:100 was added to duplicate wells. The plate was then incubated at 37°C for 2 hours. Serum samples were absorbed with Campylobacter jejuni prior to enzyme-linked immunosorbent assay testing. Alkaline phosphatase–affinity purified goat antihuman IgG (diluted 1:5000) (Kirkergaard and Perry Laboratories, Gaithersburg, Md) was used as a conjugate, and the substrate solution contained disodium p-nitrophenyl-phosphonate (Sigma Chemicals Co, St Louis, Mo), diethanolamine (Unilab, Ajax Chemicals, Sydney, Australia) and magnesium chloride. Absorbance was read at 405 nm on an enzyme-linked immunosorbent assay reader (Titertek Multiscan MC, Flow Laboratories, NorthRide, New South Wales, Australia) and the results were recorded in optical density units. The absorbance of all serum samples was corrected against the negative and positive controls. The corrected optical density values were obtained using a computer program (Microplate Manager, Bio-Rad Laboratories Pty Ltd, Hercules, Calif). An optical density of 0.9 or greater was defined as seropositive.

This serologic technique has been validated previously in both Australian and Chinese populations, with a sensitivity of 100% in both populations and a specificity of 95% and 94%, respectively.16,17

Blood group antigens (ABO) and Rh factor were determined for all subjects using standard methods (Inverness blood group machine, IBGS Ltd, Shoreham-by-Sea, England).

ASSESSMENT OF DYSPESIA AND OTHER ABDOMINAL SYMPTOMS

A validated questionnaire derived from the Bowel Symptom Questionnaire was filled in by all the subjects. Questions about current (within the prior year) and past (whole lifetime except the last year) symptoms were included. Subjects who reported pain or discomfort centered in the upper part of the abdomen were classified as having dyspepsia.1 In subjects with dyspepsia the frequency of symptoms was graded as follows: (1) less than once per month; (2) once per month; (3) 2 to 3 times per month; (4) once per week; (5) several times per week; or (6) daily. The severity was graded as follows: (1) very mild, can usually be ignored; (2) mild, can usually be ignored; (3) moderate, cannot be ignored, but does not affect lifestyle; (4) severe, affects lifestyle; and (5) very severe, markedly affects lifestyle. The frequency and severity scores were added to compute a combined dyspepsia impact score (score range, 0-11). Subjects were classified as having nonulcer dyspepsia if there was no self-reported history of peptic ulcer disease. The subjects were categorized into 1 of the following dyspepsia symptom subgroups as defined by the Rome criteria, based on their answers to the questionnaire:19

DYSPEPSIA

The prevalence of dyspepsia as defined in this study was 13.2% (n = 78) (95% CI, 10.6%-16.2%). Overall, 29 subjects (4.9%) had peptic ulcer disease; among the subjects with dyspepsia, 13 (2.2%) reported a history of peptic ulcer disease. Subjects with peptic ulcer disease were excluded from further analyses, and the remaining subjects with dyspepsia were clinically classified as having NUD (n = 65); further analyses were conducted on this sample.

The prevalence of NUD was 11% (n = 65) (95% CI, 8.6%-13.8%). Nonulcer dyspepsia was not associated with increasing age (Figure 1) or sex. The mean age of subjects with and without dyspepsia was 40 and 38 years, respectively (OR, 1.2 per decade; 95% CI, 0.95-1.45; P = .12).

RESPONSE RATE

Of the 648 subjects, 592 (91.4%) returned a completed questionnaire and were included in the analyses. There were no significant differences between those completing the questionnaire and those who did not in relation to the prevalence of H. pylori infection or blood group status. The blood donor population evaluated was similar to the Australian population (aged 18-65 years) for sociodemographic factors.

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• Category 1: ulcerlike dyspepsia. Subjects with pain or discomfort in the upper part of the abdomen and at least 3 of the following symptoms: (a) pain or discomfort often relieved by food (>25% of the time); (b) pain or discomfort often relieved by antacids; (c) pain or discomfort before meals or when hungry; (d) periodic pain or discomfort (periods of at least 1 month without pain, with periods in between of weeks to months when there is pain); and/or (e) pain or discomfort at night (waking the subject from sleep).  
• Category 2: dysmotilitylike dyspepsia. Subjects with pain or discomfort in the upper part of the abdomen and at least 3 or more of the following symptoms suggesting gastric stasis or upper intestinal dysmotility: (a) nausea or vomiting once per month or more; (b) abdominal bloating or visible distension often; (c) early satiety; (d) pain or discomfort often aggravated by food or milk; (e) pain or discomfort often after meals; and/or (f) pain or discomfort often relieved by belching.  
• Category 3: refluxlike dyspepsia. Subjects with pain or discomfort in the upper part of the abdomen associated with 1 or both of the following symptoms: (a) heartburn at least once per week or more; and/or (b) acid regurgitation once per week or more.  
• Category 4: nonspecific dyspepsia. Subjects with pain or discomfort in the upper part of the abdomen that did not fit into categories 1, 2, or 3.

**MEASUREMENT OF RISK FACTORS**

The data on aspirin and nonaspirin NSAIDs were coded by subjects on the questionnaire as none, 1 to 2, 3 to 6, 7 to 10, 11 to 20, or more than 20 tablets or capsules taken on average each week in the past 12 months. Coffee ingestion was coded as less than 1, 1 to 2, 3 to 4, 5 to 6, 7 to 8, or more than 8 cups on average each day in the past 12 months. Cigarette smoking was coded as none, less than 5, 5 to 15, 16 to 40, or more than 40 cigarettes smoked on average each day. Alcohol use was coded as none, 1 to 2, 3 to 6, 7 to 10, 11 to 30, or more than 30 standard drinks on average each week (a standard drink was defined as 240 mL of beer, a glass of wine, or a nip [shot] of spirits).  
The gross family income, marital status, and highest level of education were also assessed.  
Subjects were diagnosed as having irritable bowel syndrome if they fulfilled the Rome criteria16: continuous or recurrent pain or discomfort in the lower part of the abdomen (>3 months) that was (a) relieved with defecation; and/or (b) associated with a change in frequency of stool; and/or (c) associated with a change in consistency of stool and an irregular pattern of defecation at least 25% of the time that was characterized by 2 or more of the following criteria: (1) altered stool frequency (<3 bowel movements per week or >3 bowel movements per day); (2) altered stool form (lumpy and/or hard or loose and/or watery); (3) altered stool passage (straining or urgency or a sensation of incomplete evacuation); (4) passage of mucus per rectum; and (5) bloating or a feeling of abdominal distension.

**STATISTICAL ANALYSIS**

The statistical analysis sought to identify risk factors for dyspepsia and H pylori infection in the community and to explore the relationship between H pylori and dyspepsia. Prevalence estimates are reported along with corresponding 95% confidence intervals (CIs). The width of CIs for prevalence estimates was calculated using the exact binomial distribution. Descriptive statistics for numerical scale measures are reported as either mean and SD or median and interquartile range. The latter statistics are reported when the distribution of a given measure is substantially skewed. The interquartile range is defined by the 25th and 75th percentiles.

Assessment of risk factors for dyspepsia and H pylori infection used unconditional logistic regression analysis. Univariate (single independent variable) models are equivalent to Pearson χ² tests when discrete risk factors are included and parallel the Wilcoxon rank sum test when numeric risk factors are fitted. Univariate models were used to obtain crude odds ratios (ORs) and describe the empirical relationships. Ninety-five percent CIs were calculated for all ORs.

The extent to which a priori characteristics represented statistically independent risk factors for dyspepsia and H pylori infection was assessed using multiple logistic regression analysis. In this way, the effect of each risk factor can be assessed holding other characteristics constant. Results are reported in ORs, 95% CIs, and P values.

We performed a power calculation to detect a 20% difference in H pylori prevalence between those with dyspepsia and those without it, with the sample size enrolled. At the 5% level of significance, we calculated that the power was 82% for comparing a rate of 15% in subjects without dyspepsia with a rate of 35% in subjects with dyspepsia.
The prevalence of nonulcer dyspepsia (NUD) was not associated with increasing age.

There was no difference in the severity of dyspepsia in subjects with and without H pylori infection. The mean dyspepsia impact scores in subjects with NUD with and without H pylori infection were 4.7 and 5.4, respectively (OR, 0.8; 95% CI, 0.6-1.1; P = .20) (Figure 3). The median H pylori optical density values for subjects with NUD and those without dyspepsia were 2.20 (25%-75% interquartile range, 1.9-2.4) and 2.44 (25%-75% interquartile range, 2.1-2.6), respectively (P = .30); comparison of the optical density between subjects with and without NUD was performed only in those who were positive for H pylori (optical density, ≥0.9).

RISK FACTORS FOR DYSPEPSIA

Univariate logistic regression analyses of various risk factors for dyspepsia are shown in Table 1. In the final model, based on multivariate logistic regression analyses, only the use of aspirin (OR, 2.2; 95% CI, 1.3-3.8; P = .003) and tobacco smoking (OR, 2.2; 95% CI, 1.3-3.7; P = .005) were independently and significantly associated with NUD. This model explained 4.25% of the log likelihood. A threshold response was noted for smoking with a significant increase in ORs for more than 5 cigarettes smoked per day; the ORs for less than 5 cigarettes, 5 to 15 cigarettes, and more than 15 cigarettes per day were 0.4, 1.7, and 1.5, respectively. We did not detect any dose or threshold response for aspirin use. The attributable risks for aspirin use and smoking in subjects with dyspepsia were 18% and 9.5%, respectively.

In the univariate analysis, coffee consumption (OR, 2.0; 95% CI, 1.1-3.6; P = .03) and marital status (OR, 2.3; 95% CI, 1.0-5.2; P = .05) also appeared to be linked to dyspepsia but were not significant in the final model. Age, sex, educational status, income, alcohol consumption, use of nonaspirin NSAIDs, blood groups, and Rh factor were not linked to NUD (Table 1).

Patients with NUD took significantly more antacids (42.5% vs 8.9%) (OR, 7.6; 95% CI, 3.8-15.1; P < .001), H2-receptor antagonists or proton pump inhibitors (60% vs 9.9%) (OR, 13.6; 95% CI, 4.7-39.6; P < .001), and antispasmodics (40% vs 10.7%) (OR, 5.6; 95% CI, 1.5-20.2; P = .009) than those without dyspepsia.

RISK FACTORS FOR H PYLORI

Univariate logistic regression analyses of various risk factors for H pylori infection are shown in Table 2. Multivariate logistic regression analyses adjusting for age revealed that H pylori infection remained significantly associated with male sex (OR, 2.1; 95% CI, 1.3-3.4; P = .003) and a lower net family income level (OR, 1.7; 95% CI, 1.0-2.7; P = .04). The prevalence of H pylori infection was not associated with marital status; the use of aspirin, NSAIDs, coffee, or alcohol; tobacco smoking; blood groups; or Rh factor (Table 2).
Dyspepsia is a common finding in our community. While researchers have developed guidelines for the management of dyspepsia, the role of *H pylori* therapy in the management of NUD continues to be vigorously debated.

Large variations in the prevalence rates of dyspepsia (7%-41%) have been reported. Such differences probably reflect differences in the subjects studied, the methods used, and, particularly, the definitions applied. The prevalence rate of dyspepsia found in our study (13.2%) is at the lower end of rates reported by other groups. This may be because our sample population, namely, blood donors, is likely to be healthier than the general population. On the other hand, the higher prevalence (38%) reported by Jones and Lydeard in England is most likely explained by the inclusion of subjects with predominant heartburn.

After exclusion of subjects who had reported a history of peptic ulcer disease, the remaining subjects in our study were provisionally classified as having NUD (11.6%). We are cognizant of the potential shortcomings of basing the diagnosis of NUD on questionnaire responses. We accept that a minority of subjects may have had an undiagnosed peptic ulcer or atypical reflux disease and therefore may have been misclassified. Self-reported ulcer disease may also be inaccurate; some patients may have been mislabeled by their physicians as having an ulcer based on symptoms alone or after a barium study of the upper gastrointestinal tract with equivocal results. However, we believe that the error in identifying NUD is likely to be small. Endoscopic investigation of a population-based sample in Norway, for example, showed that most subjects with dyspepsia had no evidence of peptic ulcer disease, reflux esophagitis, or cancer. Moreover, because there is a strong link between ulcer disease and *H pylori* infection, inclusion of misclassified subjects would have tended to bias the results toward finding an association between dyspepsia and *H pylori* infection.

In our study, the prevalence of dyspepsia did not mirror that of *H pylori* infection. Such results would suggest that no association exists between dyspepsia and *H pylori*. The finding in our study of a trend for subjects not infected with *H pylori* to have more severe symptoms, although not reaching statistical significance, also supports the hypothesis that *H pylori* does not play a causal role in NUD. We found no association between *H pylori* optical density values and dyspepsia. Mitchell et al showed that serologic tests and optical density correlate closely with the presence of current infection. Recently, Sheu et al showed that an increased specific absorption coefficient index, derived from the optical density, was associated with a greater severity of gastritis. We have also recently shown that a higher specific absorption coefficient index is associated with greater bacterial density.

These data are consistent with several earlier studies in which no association was observed between NUD and *H pylori* infection. For example, in a study of 180 consecutive blood donors with no evidence of organic disease, Holtmann and colleagues observed no association between *H pylori* and dyspepsia. Similarly, in a population-based study in Sweden, Agreus et al observed no significant difference in the prevalence of *H pylori* infection among subjects with dyspepsia or irritable bowel syndrome and asymptomatic persons who were matched for age and sex. It has been suggested that NUD can be classified into distinct symptom subgroups, namely, ulcerlike, refluxlike, and dysmotilitylike, that should reflect different pathophysiological conditions (eg, ulcerlike dyspepsia and *H pylori* infection). To date there is limited information on the prevalence of *H pylori* infection in various sub-classes of NUD. In our study no significant difference in the prevalence rates of *H pylori* infection in ulcerlike, refluxlike, or dysmotilitylike dyspepsia was found, an observation in agreement with the study by Holtmann et al.

### Table 1. Univariate Analyses of Various Risk Factors for Dyspepsia*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Patients With Ulcer Included</th>
<th>Patients With Ulcer Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per decade</td>
<td>581 1.2 (1.0-1.5) .07</td>
<td>570 1.1 (0.9-1.4) .30</td>
</tr>
<tr>
<td>Sex</td>
<td>586 0.7 (0.4-1.1) .10</td>
<td>573 0.6 (0.4-1.1) .09</td>
</tr>
<tr>
<td>Education level</td>
<td>585 1.5 (0.9-2.5) .08</td>
<td>572 1.5 (0.9-2.5) .10</td>
</tr>
<tr>
<td>Income level</td>
<td>568 1.1 (0.6-1.8) .80</td>
<td>556 0.9 (0.5-1.6) .70</td>
</tr>
<tr>
<td>Marital status</td>
<td>586 2.4 (1.1-5.2) .02</td>
<td>573 2.3 (1.0-5.2) .05</td>
</tr>
<tr>
<td>Blood group O vs other</td>
<td>592 0.6 (0.3-1.1) .30</td>
<td>579 1.0 (0.3-3.4) .40</td>
</tr>
<tr>
<td>Rh factor</td>
<td>592 0.9 (0.5-1.7) .80</td>
<td>579 0.7 (0.4-1.5) .40</td>
</tr>
<tr>
<td>Smoking</td>
<td>588 2.5 (1.5-4.1) &lt;.001</td>
<td>575 2.2 (1.3-3.7) .003</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>587 1.1 (0.6-1.8) .80</td>
<td>574 1.2 (0.7-2.1) .60</td>
</tr>
<tr>
<td>Coffee use</td>
<td>584 1.8 (1.0-3.2) .05</td>
<td>571 2.0 (1.1-3.6) .03</td>
</tr>
<tr>
<td>Aspirin use</td>
<td>586 1.7 (1.1-2.8) .03</td>
<td>573 2.2 (1.3-3.8) .003</td>
</tr>
<tr>
<td>NSAID use</td>
<td>587 1.1 (0.6-1.8) .90</td>
<td>574 1.1 (0.6-2.0) .80</td>
</tr>
</tbody>
</table>

*OR indicates odds ratio; CI, confidence interval; and NSAID, nonsteroidal anti-inflammatory drug.

### Table 2. Univariate Analyses of Various Risk Factors for *Helicobacter pylori* Infection*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Patients With Ulcer Included</th>
<th>Patients With Ulcer Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per decade</td>
<td>581 1.8 (1.3-2.3) &lt;.001</td>
<td>570 1.8 (1.4-2.2) &lt;.001</td>
</tr>
<tr>
<td>Sex</td>
<td>586 2.1 (1.4-3.4) &lt;.001</td>
<td>573 2.1 (1.3-3.4) .003</td>
</tr>
<tr>
<td>Education level</td>
<td>585 2.0 (1.3-3.2) &lt;.002</td>
<td>572 1.7 (1.0-2.7) .04</td>
</tr>
<tr>
<td>Income level</td>
<td>568 1.7 (1.1-2.9) .02</td>
<td>556 1.5 (0.9-2.5) .10</td>
</tr>
<tr>
<td>Marital status</td>
<td>586 1.4 (0.7-2.5) .30</td>
<td>573 1.3 (0.7-2.5) .40</td>
</tr>
<tr>
<td>Blood group O vs other</td>
<td>592 0.9 (0.6-1.5) .90</td>
<td>579 0.3 (0.1-1.2) .80</td>
</tr>
<tr>
<td>Rh factor</td>
<td>592 1.7 (1.0-2.8) .04</td>
<td>579 1.5 (0.9-2.6) .20</td>
</tr>
<tr>
<td>Smoking</td>
<td>588 1.6 (1.0-2.5) .04</td>
<td>575 1.4 (0.9-2.3) .20</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>587 0.9 (0.6-1.5) .80</td>
<td>574 1.0 (0.6-1.7) .90</td>
</tr>
<tr>
<td>Coffee use</td>
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<td>571 1.3 (0.7-2.0) .40</td>
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<tr>
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*OR indicates odds ratio; CI, confidence interval; and NSAID, nonsteroidal anti-inflammatory drug.
In our study we found a significant association (2-fold) between dyspepsia and aspirin use as well as tobacco smoking, although these factors at most explained only a small amount of the disorder. On the other hand, ingestion of non-aspirin NSAIDs did not appear to be associated with NUD. Nonsteroidal anti-inflammatory drugs have been associated with silent peptic ulceration, implying that their analgesic effect may mask the symptoms of dyspepsia. An association between NSAIDs use and NUD has not been consistently found, and population-based study findings generally have been negative. In our study, 37 subjects (48%) with dyspepsia had taken aspirin in the past 12 months, whereas only 19 (25%) had consumed NSAIDs. The low consumption of NSAIDs is not surprising because the study population was young, with a mean age of 39 years. We suspect that the low usage of NSAIDs in this population is the reason we failed to observe an association. Previous studies have suggested that gastrointestinal tract symptoms associated with aspirin use are most likely to be related to dose.

In the Aspirin Myocardial Infarction Study, 23.7% of subjects receiving 1000 mg/d of aspirin complained of dyspeptic symptoms compared with 14.9% who were assigned to placebo treatment. Similarly, in a study of transient ischemia, subjects given 300 mg/d of aspirin experienced less dyspepsia compared with those receiving 1200 mg/d (29.4% and 38.8%, respectively; P<.001). In contrast, in the Physicians Health Study no significant difference was found in the gastrointestinal tract discomfort experienced by subjects randomized to receive 325 mg of aspirin on alternate days or placebo (26.1% vs 25.6%; P = .45). Because we did not note a dose-response relationship between dyspepsia and aspirin use, the association may not be causal.

Two previous community-based studies failed to show an association between smoking and dyspepsia, although cigarette smoking has been shown to cause harmful effects to the gastric mucosa. Nicotine, the primary toxic component of tobacco, potentiates mucosal injury by augmenting acid and pepsin secretion, duodenogastric reflux, and free radical production. Smoking also impairs mucosal defenses by decreasing prostaglandin synthesis, mucous secretion, and epidermal growth factor secretion. Gastric mucosal blood flow promotes repair of tissue damage and maintains mucosal tissue integrity. Localized ischemia makes the mucosa susceptible to noxious factors. Guslandi et al studied the gastric mucosal blood flow and mucosal bicarbonate production in 3 groups of patients with dyspepsia: nonsmokers, light smokers (<10 cigarettes per day), and heavy smokers (≥10 cigarettes per day). They showed that there was a statistically significant decrease in gastric mucosal blood flow and alkali secretion in heavy smokers, but not in the other groups (P<.01). Hence, it is conceivable that smoking induces dyspepsia via its effects on the gastric mucosa. Dodds et al showed that smoking can accentuate gastroesophageal reflux symptoms by relaxing the lower esophageal sphincter, and thus any association may alternatively reflect an atypical manifestation of gastroesophageal reflux disease. However, because we did not observe a dose-response relationship between dyspepsia and smoking, causality is therefore questionable.

There are conflicting reports on the role of coffee in dyspepsia. Elta et al analyzed the effect of coffee consumption on patients with duodenal ulcers, those with NUD, and controls. They concluded that, compared with controls, coffee consumption induced a statistically significant increase (P = .004) in dyspeptic symptoms in patients with NUD but not in patients with duodenal ulcer disease. In our questionnaire, we did not differentiate between caffeinated and decaffeinated coffee consumption since this distinction has been shown to be unimportant. However, in a cross-sectional study of 4558 Australian subjects, Shirlow and Mathers demonstrated that, although there was an association between caffeine intake and indigestion, this association did not hold true after controlling for other variables. We, too, detected a significant association between coffee consumption and dyspepsia (Table 1), but this did not persist after controlling for aspirin use and smoking.

We demonstrated an increasing prevalence of H pylori infection with age. Our results are consistent with several studies in Western countries that have demonstrated a linear age-dependent increase in the prevalence of H pylori. Based on available data, it is likely that our study population had acquired the infection in childhood. Parsonnet et al, for example, studied the prevalence of H pylori infection in a cohort of 341 epidemiologists. They showed that most subjects had acquired infection earlier in life and that the rate of seroconversion later in life was only 0.49% per person-year. We also detected an increased prevalence of H pylori infection in men. While we do not have any satisfactory explanation to account for this association, a few studies also have demonstrated an association between male sex and H pylori infection.

Mendel et al assessed the association of H pylori infection with socioeconomic factors. Childhood socioeconomic status appeared to be the most important predictor. A meta-analysis of H pylori infection studies arrived at the same conclusion. Our study, too, demonstrated an association between H pylori infection and a lower income level, supporting the findings of Mendel et al.

In the past, it was believed that blood group O was a risk factor for duodenal ulcers. Since H pylori infection is linked to peptic ulcer disease, it has been hypothesized that blood group O is linked to the prevalence of H pylori infection. We failed to detect any link between particular blood groups and H pylori infection or dyspepsia. Loffeld and Stobberingh also evaluated blood groups and H pylori status in 402 healthy blood donors and found no association. Levi et al reached a similar conclusion, using rapid urease testing for H pylori detection and blood group data.

We did not collect information on prior antibiotic use in this population. However, the antibiotic use in Australia parallels that of other Western countries. We believe that the use of antibiotics is unlikely to have significantly altered the results because antibiotics, which are usually taken singly, rarely cure H pylori infection.

In conclusion, there appears to be no association between H pylori infection and unexplained dyspepsia. This finding does not exclude the possibility that a small undefined subset of infected subjects have symptoms induced by the infection, but only large randomized controlled trials will establish whether this is the case. Until prospective studies demonstrate a convincing association between NUD and H pylori infection and it is shown that antimicrobial therapy alters the natural history of the dis-
References


