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

Sanjay Nandurkar, FRACP; Nicholas J. Talley, MD, PhD, FRACP; Harry Xia, PhD; Hazel Mitchell, PhD; Stuart Hazel, PhD; Michael Jones, PhD

**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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**YSPEPSIA**, defined as chronic or recurrent pain or discomfort centered in the upper part of the abdomen, is one of the most common reasons why patients seek medical help in family practice.1 Approximately one quarter of persons in the general population have dyspepsia; most have a functional rather than a definite structural cause for their complaints.1,3 Dyspepsia, in the absence of peptic ulceration, usually has no clear anatomical or physiological correlate, and thus the diagnosis is made based purely on the medical history and exclusion of other disease. It has been estimated that there are more than 2 million outpatient consultations for dyspepsia annually in the United States, although only approximately 25% of those with dyspepsia seek medical help; pain severity, anxiety, and fear of an underlying serious disease have been identified as important reasons for consultation.3

*Helicobacter pylori* infection is linked causally to peptic ulcer disease,4 but seropositivity in individuals without an ulcer history is common and of less certain clinical significance. In particular, the role of *H pylori* gastritis in chronic dyspepsia continues to be debated.5,6 While approximately 50% of patients with unexplained dyspepsia in clinical practice are infected,7 the symptoms in infected and uninfected patients are similar8 and *H pylori* eradication therapy is of equivocal efficacy.3,10 Specific antibodies are produced by the host in response to *H pylori* infection and the presence of an antibody usually indicates current infection status.11 A recent report suggests that subjects with higher antibody levels as reflected by optical density had an increased risk (4-fold) of nonulcer dyspepsia (NUD), suggesting that a failure to down-regulate inflammation may be linked to symptoms.12 It is still controversial whether tobacco smoking and the use of alcohol, coffee, aspirin, and nonaspirin nonsteroidal anti-inflammatory drugs (NSAIDs) are linked to dyspepsia in the community, since population-based studies have produced conflicting results.13-15

We performed a cross-sectional study of volunteer blood donors in western Sydney, Australia, to determine the prevalence of chronic dyspepsia and *H pylori* infection and their respective risk factors. In particular, using validated measures, we

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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 mL of the mixture was added to each well of a microtiter plate. The plates were covered in parafilm (parafilm N, American National Can, Chicago, Ill) 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 DYSPEPSIA AND OTHER ABDOMINAL SYMPTOMS

A validated questionnaire derived from the Bowel Symptom Questionnaire was filled in by all the subjects.18 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 questionnaire19:

**RESULTS**

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.

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).

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Of the 592 subjects, 87 (14.7%) were positive for *H pylori* infection as women (20.3% vs 10.6%, respectively) (OR, 2.1; 95% CI, 1.3-3.4; P = .001).

ASSOCIATION BETWEEN NUD AND *H PYLORI*

Overall, *H pylori* infection was detected in 15.4% of subjects with NUD compared with 14.6% of subjects without dyspepsia (OR, 1.0; 95% CI, 0.5-2.2; P = .90). The prevalence of *H pylori* infection among subjects with ulcerlike, dysmotilitylike, and refluxlike dyspepsia and non-specific dyspepsia were 17.9% (95% CI, 7.5%-33.5%), 18.8% (95% CI, 7.2%-36.4%), 13.6% (95% CI, 2.9%-34.9%), and 10% (95% CI, 0.3%-44.5%), respectively. The prevalence of *H pylori* infection was 21% (95% CI, 8.0%-39.7%) in those with symptoms compatible with irritable bowel syndrome. We detected a significant asso-
Association between self-reported ulcer disease and *H pylori* infection \((P=.03)\). Nine subjects with self-reported ulcer disease were positive for *H pylori* compared with 20 subjects who were not infected.

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 \((25\%-75\%\text{ interquartile range, } 1.9-2.4)\) and 2.44 \((25\%-75\%\text{ interquartile range, } 2.1-2.6)\), 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\% \text{ vs } 8.9\%);(OR, 7.6; 95\% CI, 3.8-15.1; P<.001), H2-receptor antagonists or proton pump inhibitors \((60\% \text{ vs } 9.9\%);(OR, 13.6; 95\% CI, 4.7-39.6; P<.001), and antispasmodics \((40\% \text{ vs } 10.7\%);(OR, 5.6; 95\% CI, 1.5-20.2; P=.009)\) than those without dyspepsia.

**RISK FACTORS FOR HYLORI**

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 \((OR, 1.7; 95\% CI, 1.1-2.9; P=.02)\). In the univariate analyses, lower educational status was also linked to *H pylori* infection \((OR, 1.7; 95\% CI, 1.0-2.7; P=.04)\). 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 NUD, whether the role of H pylori therapy in the management of NUD continues to be vigorously debated.1,5,18-21

Large variations in the prevalence rates of dyspepsia (7%-41%) have been reported.3,22-27 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.3,13,22 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 Lydeard22 in England is most likely explained by the inclusion of subgroups 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.28 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 al29 have shown that serologic tests and optical density correlate closely with the presence of current infection. Recently, Sheu et al30 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.30

These data are consistent with several earlier studies in which no association was observed between NUD and H pylori infection.24,31-33 For example, in a study of 180 consecutive blood donors with no evidence of organic disease, Holtmann et al30 observed no association between H pylori and dyspepsia. Similarly, in a population-based study in Sweden, Agreus et al32 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).1 To date there is limited information on the prevalence of H pylori infection in various subclasses 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.24

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

<table>
<thead>
<tr>
<th>Factor</th>
<th>No.</th>
<th>OR (95% CI)</th>
<th>P</th>
<th>No.</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age per decade</td>
<td>581</td>
<td>1.2 (1.0-1.5)</td>
<td>.07</td>
<td>570</td>
<td>1.1 (0.9-1.4)</td>
<td>.30</td>
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<td>Sex</td>
<td>586</td>
<td>0.7 (0.4-1.1)</td>
<td>.10</td>
<td>573</td>
<td>0.6 (0.4-1.1)</td>
<td>.09</td>
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<tr>
<td>Education level</td>
<td>585</td>
<td>1.5 (0.9-2.5)</td>
<td>.08</td>
<td>572</td>
<td>1.5 (0.9-2.5)</td>
<td>.10</td>
</tr>
<tr>
<td>Income level</td>
<td>568</td>
<td>1.1 (0.6-1.6)</td>
<td>.80</td>
<td>556</td>
<td>0.9 (0.5-1.6)</td>
<td>.70</td>
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<td>Marital status</td>
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<td>2.4 (1.1-5.2)</td>
<td>.02</td>
<td>573</td>
<td>2.3 (1.0-5.2)</td>
<td>.05</td>
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<tr>
<td>Blood group O vs other</td>
<td>592</td>
<td>0.6 (0.3-1.1)</td>
<td>.30</td>
<td>579</td>
<td>1.0 (0.3-3.4)</td>
<td>.40</td>
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<tr>
<td>Rh factor</td>
<td>592</td>
<td>0.9 (0.5-1.7)</td>
<td>.80</td>
<td>579</td>
<td>0.7 (0.4-1.5)</td>
<td>.40</td>
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<tr>
<td>Smoking</td>
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<td>2.5 (1.5-4.1)</td>
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<td>575</td>
<td>2.2 (1.3-3.7)</td>
<td>.003</td>
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<td>1.1 (0.6-1.8)</td>
<td>.60</td>
<td>574</td>
<td>1.2 (0.7-2.1)</td>
<td>.60</td>
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<tr>
<td>Coffee use</td>
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<td>1.8 (1.0-3.2)</td>
<td>.05</td>
<td>571</td>
<td>2.0 (1.1-3.6)</td>
<td>.03</td>
</tr>
<tr>
<td>Aspirin use</td>
<td>586</td>
<td>1.7 (1.1-2.8)</td>
<td>.03</td>
<td>573</td>
<td>2.2 (1.3-3.8)</td>
<td>.003</td>
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<tr>
<td>NSAID use</td>
<td>587</td>
<td>1.1 (0.6-1.8)</td>
<td>.90</td>
<td>574</td>
<td>1.1 (0.6-2.0)</td>
<td>.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>No.</th>
<th>OR (95% CI)</th>
<th>P</th>
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<tr>
<td>Age per decade</td>
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<td>Sex</td>
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<td>2.1 (1.4-3.4)</td>
<td>.001</td>
<td>573</td>
<td>2.1 (1.3-3.4)</td>
<td>.003</td>
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<td>Education level</td>
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<td>2.0 (1.3-3.2)</td>
<td>.002</td>
<td>572</td>
<td>1.7 (1.0-2.7)</td>
<td>.04</td>
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<td>Income level</td>
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<td>1.7 (1.1-2.9)</td>
<td>.02</td>
<td>556</td>
<td>1.5 (0.9-2.5)</td>
<td>.10</td>
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<td>1.4 (0.7-2.5)</td>
<td>.30</td>
<td>573</td>
<td>1.3 (0.7-2.5)</td>
<td>.40</td>
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<tr>
<td>Blood group O vs other</td>
<td>592</td>
<td>0.9 (0.6-1.5)</td>
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<td>579</td>
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<td>Rh factor</td>
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<tr>
<td>Smoking</td>
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<td>.04</td>
<td>575</td>
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<td>.20</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>587</td>
<td>0.9 (0.6-1.5)</td>
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</tr>
</tbody>
</table>

*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, duodenal gastric 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 Stobering assessed 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-
ease, expensive and potentially toxic antimicrobial therapy should not be considered for patients with NUD.

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