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Positive Serum Antibody and Negative Tissue Staining for *Helicobacter pylori* in Subjects With Atrophic Body Gastritis

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***Helicobacter pylori* is rarely found in gastric biopsy specimens from individuals with atrophic gastritis of the body mucosa. To determine if subjects with atrophic body gastritis have evidence of previous infection with *H. pylori*, immunoglobulin G antibody to *H. pylori* was measured by enzyme-linked immunosorbent assay in sera of 399 Finnish subjects. In 124 subjects, multiple biopsy specimens from body and antrum had been evaluated for the presence of *H. pylori* by Giemsa staining. Antibody correlated well with *H. pylori* staining except in the subgroup with atrophic body gastritis, in whom the prevalence of seropositivity (86%) was significantly greater than the prevalence of positive staining (33%) ($P < 0.001$). Twenty-five subjects had positive antibody and negative staining. This group had a significantly higher prevalence of atrophic body gastritis (80%), lower maximal acid output, lower serum pepsinogen I levels, and higher serum gastrin concentrations than did seropositive subjects with *H. pylori*. These data suggest that most patients with atrophic body gastritis, despite having a low incidence of current overt infection, have been infected with *H. pylori* at some point in their lives.**

Helicobacter pylori is the probable cause of most cases of superficial gastritis of the antrum and body (1–6). The prevalence of *H. pylori* colonization of the gastric mucosa increases with age, reaching 50% by age 50 in developed countries and nearly 80% by age 30 in underdeveloped parts of the world (7). In a given population, the prevalence of atrophic gastritis among older age groups correlates well with the prevalence of *H. pylori* in younger age groups (1), suggesting that *H. pylori*–associated superficial gastritis may progress over time into atrophic gastritis.

In a longitudinal study examining the natural history of gastritis over three decades in a large Finnish population, Ihamaki et al. (8) found that superficial gastritis affecting the antrum tended to regress with time, whereas superficial gastritis affecting the body tended to progress to atrophic body gastritis. Although their study predated the discovery of *H. pylori*, it is tempting to speculate that the cases of superficial gastritis that progressed to atrophic body gastritis were caused by *H. pylori*. However, because the prevalence of *H. pylori* infection in subjects with atrophic body gastritis is quite low (3), the progression of *H. pylori*–associated superficial gastritis to atrophic body gastritis must be accompanied by disappearance of *H. pylori*.

To determine if atrophic body gastritis is associated with evidence of previous infection with *H. pylori*, we measured *H. pylori* antibody in sera from 399 normal Finnish volunteers in whom histology of the gastric body and antrum were known. The results of Giemsa staining of gastric biopsies for *H. pylori* had been previously determined in 124 subjects. Additional data collected in all 399 subjects included age, sex, maximal acid output, serum pepsinogen I (PGI), PGII, and fasting plasma gastrin concentration. These data allowed us to further characterize the group of subjects who tested positive for antibody but negative for Giemsa stains.

Abbreviations used in this paper: **MAO, maximal acid output; PGI, pepsinogen I.**

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Methods

Subjects

The present study included 399 stored sera collected from members of a control group originally selected from a large Finnish population for comparison with subjects with gastric carcinoma (9). They included 67 control subjects computer matched to 67 probands with gastric carcinoma. The remaining 332 sera were from first-degree relatives of the control subjects. Matching was by age, sex, place of birth, and place of residence. A history of duodenal ulcer was present in 3 subjects, and 1 had a history of gastric ulcer. Most had no upper abdominal complaints. Among the original data collected in all subjects were age, sex, pentagastrin-stimulated acid secretion and fasting serum concentrations of gastrin (10), PGI and PGII (11) concentrations, and histological interpretation of gastric biopsy specimens. Sera from subjects with atrophic body gastritis (determined as described below) were evaluated for vitamin B_{12} levels and antibody to intrinsic factor. Also included were Giemsa staining results for *H. pylori* in 124 subjects as described below. Serum and gastric biopsy specimens were obtained on the same day.

Histology

Gastric biopsy specimens were obtained endoscopically under direct vision in all subjects as described previously (3). Four or more specimens were taken from the middle part of the antrum at least 2 cm from the pylorus, and six or more specimens were obtained from the anterior wall and greater curvature of the midbody. Biopsy specimens were fixed overnight in buffered formalin, embedded in paraffin, sectioned, and stained with Alcian blue, periodic acid–Schiff, and van Gieson for histology.

Histology of the antrum and body was classified according to a modification of previously described criteria (12) as normal mucosa, 1; mild, moderate, and severe superficial gastritis, 2, 3, and 4, respectively, based on the degree of inflammatory infiltration in the setting of normal gastric glands; and mild, moderate, and severe atrophic gastritis, 5, 6, and 7, respectively, based on degree of glandular atrophy, irrespective of inflammatory infiltration. With few exceptions, histological grades in adjacent biopsy samples from the same patient were similar. The biopsy specimen with the highest grade was assigned when histological findings in adjacent biopsy specimens were dissimilar.

Staining for H. pylori

Of the 399 subjects, 124 had adequate tissue blocks available for detection of *H. pylori* using a modified Giemsa technique (13). The selection of these subjects has been previously described (3). On average, 11 biopsy specimens were stained from each patient. Availability of adequate material allowed for staining of both body and antral biopsies in 110 subjects, antrum alone in 9 subjects, and body alone in 5 subjects. Subjects with *H. pylori* present in any section from the antrum, body, or both were considered to be positive.

Enzyme-Linked Immunosorbent Assay

Antibody to *H. pylori* was measured by enzyme-linked immunosorbent assay (ELISA) in all 399 sera. Because of its reported high specificity (14), partially purified *H. pylori* urease was selected as antigen for this study. Using this antigen, our ELISA has a specificity of 100% and a sensitivity of 93%, using [^{14}C]urea breath test results as the "gold standard" (15).

As previously described (15), an *H. pylori* isolate was subjected to French Press (AMINCO, Urbane, IL) disruption followed by centrifugation. The supernatant was separated by Sephacryl S-400 column chromatography, and the fractions with peak urease activity were pooled and diluted to 10 μg/mL in phosphate-buffered saline (PBS) for use as antigen. Test sera and 16 negative control sera were assayed at a dilution of 1:1000 in duplicate. Goat anti-human IgG conjugated with horse-radish peroxidase was used as second antibody. Reaction with substrate (*o*-phenylenediamine and hydrogen peroxide) was stopped after 30 minutes with 10% H_2SO_4, and the absorbance at 492 nm was measured using an ELISA reader (Titertek MkII; Flow Laboratories).

H. pylori seropositivity was defined by an absorbance > 2 standard deviations above the mean absorbance of 16 sera obtained from subjects with negative [^{14}C]urea breath test results.

Campylobacter jejuni *Enzyme-Linked Immunosorbent Assay*

Campylobacter jejuni was kindly provided by Dr. Perez-Perez (Division of Infectious Disease, Vanderbilt University, Nashville, TN). *C. jejuni* was grown on *Campylobacter*-selective blood agar (BBL Microbiology Systems, Cockeysville, MD) in microaerobic atmosphere at 37°C. Colonies were scraped free of the agar, washed twice with 0.2 mol/L PBS (pH 7.4), and subjected to French Press disruption with a cell pressure of 12,000 lb/in^2 (Aminco, Urbana, II). French Press extract was clarified by centrifugation at 5000*g* for 30 minutes, and protein concentration was measured by the BioRad microassay procedure (Bio-Rad Chemical Division, Richmond, CA). The ELISA plates were coated with 10 μg/mL of the *C. jejuni* antigen for use in ELISA by the same method that was used for *H. pylori* ELISA.

Statistics

χ^2 and stepwise logistic regression analysis, and Student's *t* test were used for statistical calculations. Deviations were expressed as standard error (SE). Significance was defined as $P < 0.05$.

Results

Analysis of 399 Subjects

Table 1 compares seropositive and seronegative subjects with respect to mean age, sex, serum PGs, serum gastrin, maximal acid output (MAO), and

Table 1. Comparison of Measured Parameters Between Subjects With Positive Serum Antibody and Negative Serum Antibody to H. pylori

	H. pylori antibody		
	Positive n = 210	Negative n = 189	*P*
Sex (*% male*)	51	46	NS
Age (*yr*)	55.2 (1.0)	41.6 (1.2)	<0.001
PGI (*ng/mL*)	79.3 (2.9)	65.5 (2.3)	<0.001[a]
PGII (*ng/mL*)	23.3 (0.8)	12.7 (0.6)	<0.001
PGI-PGII ratio	3.7 (0.1)	6.0 (0.2)	<0.001[a]
Gastrin (*pg/mL*)	68.4 (4.7)	44.6 (1.1)	<0.001
MAO (*mmol/h*)	20.7 (1.1)	27.2 (1.0)	<0.001
Antral grade (1–7)	3.5 (0.1)	1.8 (0.1)	<0.001[a]
Body grade (1–7)	3.3 (0.1)	1.7 (0.1)	<0.001[a]

NOTE. Results are expressed as mean ± SE.
[a]Significant distinguishing variables ($P < 0.05$) by stepwise logistic regression analysis.

degree of antral and body gastritis. Seropositive subjects were significantly older, had lower maximal acid outputs, greater severity of antral and body gastritis, higher serum concentrations of gastrin, PGI, and PGII, and a significantly lower PGI-PGII ratio. There was no gender predilection in the seropositive group. Stepwise logistic regression analysis showed that the significant ($P < 0.05$) predictors of seropositivity were degree of antral gastritis, degree of body gastritis, and the serological markers of gastritis: PGI-PGII ratio and PGI levels. The remaining parameters, PGII, MAO, gastrin, age, and sex, were not significant predictors of *H. pylori* antibody status.

Seropositivity increased from 19% in the 14–20-year-old age group to 74% in the 71–80-year-old age group (Figure 1). Positive serology was also related to degree of gastritis, increasing abruptly with any degree of superficial gastritis of the body or antrum (Figure 2). Seropositivity rate was highest in subjects with severe superficial gastritis of the body (grade 4)

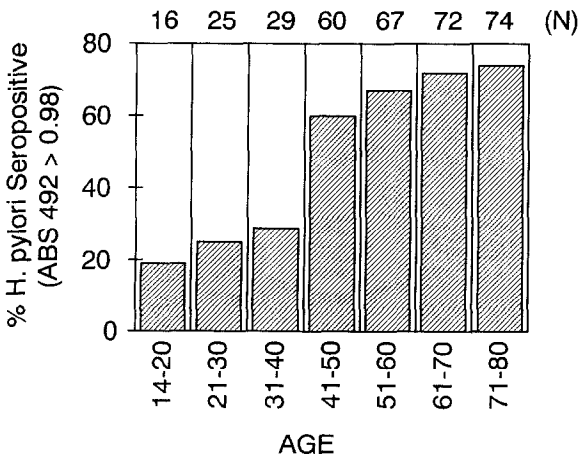

Figure 1. Prevalence of *H. pylori* with increasing age. Numbers of subjects within each age group is shown at top.

and tended to decrease with increasing severity of atrophic gastritis of the body, although the trend downward was not significant by χ^2 trend analysis. Seropositivity remained high in subjects with atrophic antral gastritis. Of the 210 subjects with positive *H. pylori* serology, 207 (99%) had some degree of gastritis affecting either the body or antrum. The prevalence of seropositivity was 13% (20 of 153) in subjects with normal antral histology, and 9% (14 of 152) in subjects with normal body histology. Of the 132 subjects who had normal histology of both the antrum and body only 4 (3.3%) had positive serology for *H. pylori*.

Analysis of 124 Subjects Evaluated for H. pylori *by Giemsa Stain*

Although the group of subjects who were evaluated by Giemsa staining were selected on the basis of availability of tissue blocks, they differed significantly from those whose biopsy specimens were not stained by several measured parameters (Table 2). Compared with the group who were not evaluated for *H. pylori* by Giemsa staining, those who had staining were significantly older, had a significantly higher prevalence of *H. pylori* antibody, lower mean MAO, higher mean PGI concentration, and higher mean histological scores of the antrum and body.

Among the 124 subjects in whom biopsy specimens were evaluated by Giemsa stain, *H. pylori* was found in 67 (54%). Compared with subjects with negative staining results, the group with positive staining was older, contained a higher percentage of women, demonstrated more severe antral gastritis, and had significantly higher concentrations of PGI and PGII II (Table 3).

Table 4 shows subjects distributed within grades of body and antral gastritis according to *H. pylori* staining and antibody status. The group with negative staining and negative antibody contained an overwhelming predominance of subjects with normal antral and body histology. Among those with positive staining and positive antibody, 80% had superficial body gastritis, accompanied by equal proportions of superficial and atrophic antral gastritis. In contrast, of those with negative staining and positive antibody ("false positives"), 80% had atrophic body gastritis accompanied by equal proportions of normal, superficial, and atrophic antral histologies. The prevalence of false positives was significantly higher in the group with atrophic body gastritis (58%, n = 36) than in groups with superficial body gastritis (9%, n = 57), normal body histology (0%, n = 31), or any grade of antral gastritis. Of the 25 subjects with false positive antibody, 20 (80%) had atrophic gastritis affecting the body; of them, 6 (30%) had isolated atrophic body

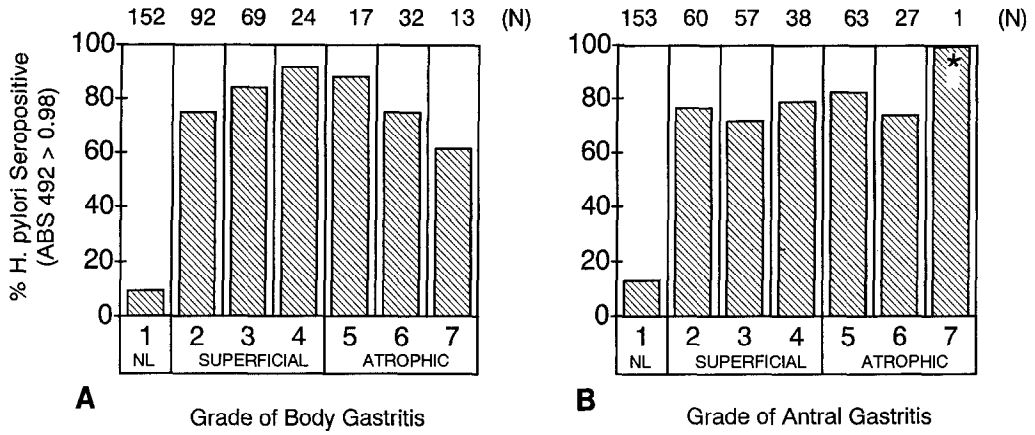

Figure 2. Prevalence of *H. pylori* seropositivity with increasing grades of body (*A*) and antral gastritis (*B*). Numbers of subjects are shown above each category. *The only subject in this group was seropositive.

gastritis (type A gastritis) and 8 (40%) accompanying atrophic antral gastritis (type AB). The remaining 6 (30%) had accompanying superficial antral gastritis. None of these subjects had antibody to intrinsic factor or had abnormal vitamin B_{12} levels.

H. pylori antibody was found in 59 (88%) of subjects with positive staining for *H. pylori* and in 25 (44%) of those with the negative staining. Table 5 shows that among seropositive subjects, those with positive staining did not differ significantly from those with negative staining with respect to age or gender. However, the two groups differed significantly in severity of gastitis and in serological parameters of gastritis. The false-positive group (positive antibody and negative stain) had a higher score for body gastritis, a lower score for antral gastritis, a lower mean MAO, a higher level of serum gastrin, a lower level of serum PGI, and a lower PGI-PGII ratio.

Figure 3 and Table 6 illustrate that the discrepancy between positive serology and positive staining for *H. pylori* is a function of atrophic gastritis of the body mucosa. In subjects with normal mucosa and in those with all grades of superficial gastritis, there was a close correlation between the prevalence of positive serology and positive staining. By contrast, in the subgroup with any degree of atrophic gastritis of the body mucosa, the prevalence of seropositivity was higher than the prevalence of positive staining. This relationship was not evident for the antral mucosa. The secretory and serological parameters of gastric body function, MAO and serum PGI level, which decrease with increasing severity of gastritis, paralleled the histological findings, as did serum gastrin level, which is higher in subjects with atrophic gastritis.

To determine the specificity of the high prevalence of seropositivity in subjects with atrophic body gastritis, antibody to *C. jejuni* was measured by ELISA in all 399 sera. Antiserum to *C. jejuni* is known to cross-react with some *H. pylori* antigens, as well as with antigens expressed by other enteric organisms (16–19). Figure 4 shows the lack of correlation between absorbance readings using our purified *H. pylori* antigen and crude *C. jejuni* antigen among all 399 subjects ($r = 0.02$). Superimposed over these data are seropositive subjects who had negative staining (n = 25) and seropositive subjects who had positive staining (n = 59). No significant difference between

Table 2. Comparison of Measured Parameters Between Subjects Selected for Evaluation of Giemsa Staining for H. pylori *and Those Who Had Inadequate Tissue Blocks for Evaluation*

	Stained n = 124	Not stained n = 275	*P*
Age (*yr*)	52.8 (1.5)	46.9 (1.0)	< 0.001
PGI (*ng/mL*)	64.9 (3.4)	76.3 (2.3)	< 0.01
PGII (*ng/mL*)	18.8 (1.1)	18.0 (0.7)	NS
PGI-PGII ratio	4.4 (0.3)	5.0 (0.1)	< 0.05
Gastrin (*pg/mL*)	65.3 (6.1)	53.5 (3.2)	NS
MAO (*mmol/h*)	19.9 (1.4)	25.6 (0.9)	< 0.001
Antral grade (1–7)	3.3 (0.2)	2.4 (0.1)	< 0.0001
Body grade (1–7)	3.4 (0.2)	2.1 (0.1)	< 0.0001
Positive *H. pylori* antibody (%)	68	46	< 0.0001

NOTE. Results are expressed as mean ± SE.

Table 3. Comparison of Measured Parameters Between Subjects With Positive Tissue Stains and Negative Tissue Stains for H. pylori

	H. pylori stain		
Parameters	Positive n = 67	Negative n = 57	*P*
Sex (*% male*)	45	67	< 0.05
Age (*yr*)	56.6 (1.7)	48.3 (2.5)	< 0.01
PGI (*ng/mL*)	80.6 (4.6)	46.5 (4.0)	< 0.0001
PGII (*ng/mL*)	22.2 (1.4)	14.7 (1.4)	< 0.001
PGI-PGII ratio	4.1 (0.2)	4.7 (0.5)	NS
Gastrin (*pg/mL*)	62.5 (7.5)	68.7 (10.1)	NS
MAO (*mmol/h*)	22.3 (1.8)	17.1 (2.3)	NS
Antral grade (1–7)	4.2 (0.2)	2.3 (0.2)	< 0.0001
Body grade (1–7)	3.3 (0.2)	3.4 (0.3)	NS

NOTE. Results are expressed as mean ± SE.

Table 4. Distribution of Subjects Within Grades of Antral Gastritis and Body Gastritis According to H. pylori *Antibody and Giemsa Stain Results*

		Histological status of the antrum			
AB	ST	Normal; grade 1 (%)	Superficial; grades 2–4 (%)	Atrophic; grades 5–7 (%)	n
–	–	91	3	6	32
–	+	12	50	38	8
+	–	24	36	40	25
+	+	3	46	51	59
		Histological status of the body			
AB	ST	Normal; grade 1 (%)	Superficial; grades 2–4 (%)	Atrophic; grades 5–7 (%)	n
–	–	84	3	13	32
–	+	38	50	1	8
+	–	0	20	80	25
+	+	2	80	19	59

AB, *H. pylori* antibody results; ST, *H. pylori* stain results.

these groups was found with respect to *C. jejuni* ELISA results.

Discussion

Our findings in 399 subjects are consistent with previous reports showing that the prevalence of *H. pylori* antibody increases with age and is associated with gastritis (3–6,16,20–26). *H. pylori* antibody correlated well with gastritis overall; only 3% of subjects with normal histology of the body and antrum were seropositive, whereas 99% of those with some degree of gastritis affecting either the body or antrum were seropositive.

Among the 124 subjects who had gastric biopsy specimens evaluated for *H. pylori* by Giemsa staining, antibody and staining results correlated well except in subjects with atrophic body gastritis. The prevalence of positive staining in those with atrophic body gastritis was 33% (12 of 36 subjects), whereas the prevalence of positive *H. pylori* antibody was 86% (31 of 36 subjects). Furthermore, subjects with atrophic body gastritis accounted for 20 of the 25 false positive *H. pylori* antibody results (positive antibody with negative staining). These observations are consistent with those reported by Fox et al. (27). Analysis of their data showed that 75% (9 of 12) of false positive ELISA results occurred in individuals with atrophic gastritis. However, their results were not reported separately for body and antral atrophic gastritis. To our knowledge, the present study is the first to compare ELISA with *H. pylori* staining of gastric biopsy specimens in individuals with well characterized histology of the antral and body mucosa.

Table 5. Comparison of Measured Parameters Between Subjects With Positive and Negative Giemsa Stain Results Among Subjects With Positive Serum Antibody to H. pylori

	Seropositive subjects (mean ± SE)		
	Negative stain n = 25	Positive stain n = 59	*P*
Sex (*% male*)	65	50	NS
Age (*yr*)	57.3 (3.4)	57.2 (1.8)	NS
PGI (*ng/mL*)	41.1 (7.4)	80.9 (4.8)	<0.0001
PGII (*ng/mL*)	22.5 (2.2)	22.9 (1.4)	NS
PGI-PGII ratio	1.7 (0.2)	3.8 (0.2)	<0.0001
Gastrin (*pg/mL*)	99.3 (18.5)	63.3 (8.0)	<0.05
MAO (*mmol/h*)	5.4 (2.1)	21.6 (1.9)	<0.0001
Antral grade (1–7)	3.5 (0.4)	4.3 (0.2)	<0.05
Body grade (1–7)	5.4 (0.3)	3.4 (0.2)	<0.0001

Among seropositive subjects, the only factor that seemed to differentiate those with negative stain from those with positive stain results was atrophic body gastritis. Other parameters that were significantly different between these two groups were PGI, PGI-PGII ratio, gastrin, and MAO (Table 4). All of these factors are known to be influenced by the histological status of the body mucosa. Interestingly, there was no difference in mean age between these two groups, indicating that the discrepancy between antibody and staining could not be accounted for by age-related increases in *H. pylori* seroprevalence. Analysis of the data in Table 1 by stepwise logistic regression also showed that age was not an important factor for distinguishing seropositive and seronegative subjects. Gastritis and serological markers of gastritis were the important variables.

We believe that the relatively high prevalence of *H. pylori* antibody and low *H. pylori* staining peculiar to subjects with atrophic body gastritis may reflect prior or hidden infection with *H. pylori* in this subgroup. Ordinarily, the presence of serum antibodies to *H. pylori* antigens as determined by ELISA correlates well with measures of active colonization such as staining, culture, and carbon isotope urea breath tests (14,24,28–29). The use of ELISA to detect prior infection with *H. pylori* depends on the persistence of antibody after disappearance of the organism. Preliminary reports suggest that *H. pylori* antibody concentration in serum decreases with time after the organism is eradicated with antibiotics and bismuth-containing compounds (30,31). The length of time required for *H. pylori* antibody concentration to decrease below defined seropositive cutoffs is not known, but, in the absence of evidence of colonization, the presence of antibody to *H. pylori* should reflect previous or current hidden infection.

An important question raised by our findings concerns the possible role of chronic *H. pylori* infection in

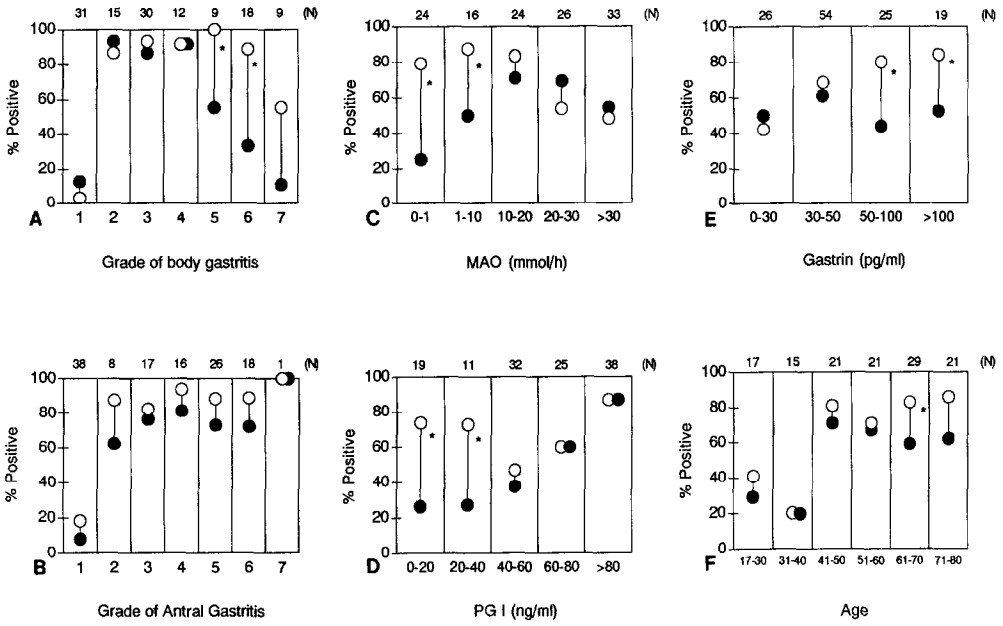

Figure 3. Prevalence of *H. pylori* seropositivity (*open circles*) and positive *H. pylori* stains (*closed circles*) according to histological grade of body gastritis (*A*), histological grade of antral gastritis (*B*), MAO (*C*), serum PGI level (*D*), serum gastrin concentration (*E*) and age (*F*). *Significant differences by χ^2 analysis ($P < 0.05$).

the pathogenesis of atrophic body gastritis. Before the discovery of *H. pylori*, Ihamaki et al. (8) found that in 42% of Finnish subjects with superficial gastritis atrophic gastritis developed over three decades. Specifically, they found that antral mucosa often improved histologically, whereas superficial body gastritis often progressed toward atrophy. These observations, which were corroborated by the same investigators in a cross-sectional study (32), indicate that superficial gastritis may advance over 20–30 years into atrophic body gastritis. It is tempting to speculate that the cases of superficial gastritis that progressed to atophic body gastritis were caused by *H. pylori*.

The hypothesis that atrophic body gastritis represents an end stage of *H. pylori*–associated superficial gastritis has not attracted much attention because of the relatively low prevalence of gastric colonization with *H. pylori* in humans with atrophic body gastritis (3) or pernicious anemia (33–35). As proposed by DeLuca (36), this hypothesis requires that *H. pylori* initiate an irreversible process toward atrophic gastritis accompanied by a dramatic reduction or even demise of the organism. Disappearance of the organism would correlate with the development of intestinal metaplasia and hypochlorhydria, conditions that seem to be inhospitable for *H. pylori* (3,37). Our data are consistent with this hypothesis. However, none of our subjects with atrophic body gastritis had abnormal vitamin B_{12} levels or antibodies to intrinsic factor, indicating that DeLuca's hypothesis may be true for a subgroup of individuals with atrophic body gastritis who do not have pernicious anemia.

An alternative explanation for the high prevalence of positive *H. pylori* antibody in the subgroup with atrophic body gastritis with negative staining is in-

Table 6. Proportion of Subjects With Positive Serum Antibody and Positive Tissue Staining for H. pylori *As a Function of Mucosal Histology*

	Body					
	Normal		Superficial		Atrophic	
	Antibody	Stain	Antibody	Stain	Antibody	Stain
Antrum						
Normal	0/28 (0%)	1/28 (4%)	0/1	0/1	8/9[a] (89%)	2/9 (22%)
Superficial	0/1	1/1	26/29 (90%)	26/29 (90%)	10/11[a] (91%)	4/11 (36%)
Atrophic	1/2	2/2	26/27 (96%)	25/27 (93%)	13/16[a] (81%)	6/16 (38%)
Total	1/31 (3%)	4/31 (13%)	52/56 (93%)	51/56 (91%)	31/36[a] (86%)	12/36 (33%)

[a]Proportion with positive serum antibody is significantly greater than proportion with positive tissue staining in subjects with atrophic body gastritis ($P < 0.05$).

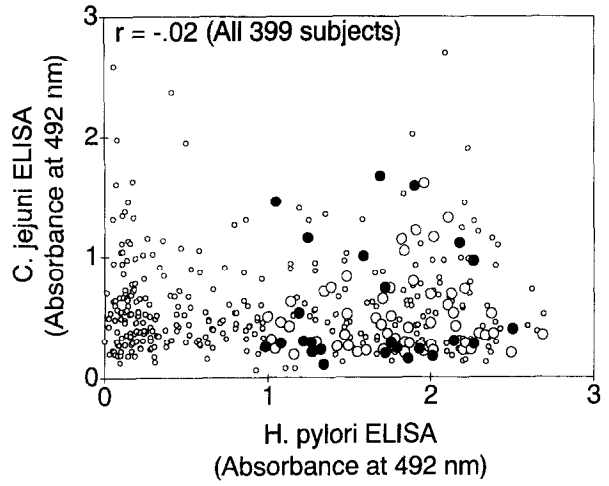

Figure 4. Scatter plot of *C. jejuni* ELISA and *H. pylori* ELISA absorbance readings at 492 nm. *Small open circles* represent all 399 subjects. No significant correlation was seen between *C. jejuni* and *H. pylori* ELISA absorbance readings ($r = -0.02$). *Large open circles* indicate subjects who had positive *H. pylori* stain and positive *H. pylori* ELISA results. *Closed circles* indicate subjects who had negative *H. pylori* stain and positive *H. pylori* ELISA results. No significance difference was seen between these two groups with respect to *C. jejuni* ELISA absorbance results.

creased exposure to antigenically cross-reacting enteric organisms secondary to gastric hypochlorhydria. To explore this possibility, we screened all sera for antibody to *C. jejuni*, a bacteria that shares some antigens with *H. pylori* (16–19). Recently, Perez-Perez et al. showed that their *H. pylori* antigen preparation did not share cross-reactivity with *C. jejuni* antigens (38). Using our *H. pylori* antigen preparation, we also found no evidence for cross-reactivity with a crude preparation of *C. jejuni* antigens ($r = 0.02$). In particular, subjects with false positive *H. pylori* antibody did not have a significantly higher mean *C. jejuni* ELISA absorbance than subjects with true positive *H. pylori* antibody.

Although our data are consistent with the hypothesis that *H. pylori* may cause atrophic body gastritis, proof of this hypothesis would require a longitudinal study in which middle-aged subjects with *H. pylori*–associated superficial gastritis are randomly assigned to have their infections eradicated. Repeated biopsies of the gastric mucosa over a several year follow-up would indicate whether eradication of *H. pylori* reduced or prevented the development of atrophic body gastritis.

In summary, we have shown that subjects with atrophic body gastritis, with or without accompanying antral gastritis, have a high prevalence of *H. pylori* seropositivity and a low prevalence of positive *H. pylori* staining. This observation suggests that most patients with atrophic body gastritis have been infected with *H. pylori* at some point in their life. The marked discrepancy between the prevalence of positive *H. pylori* serology and staining in these subjects is consistent with the hypothesis that *H. pylori* may initiate an irreversible process toward atrophic gastritis that ultimately leads to its demise (36). Proof of this hypothesis awaits the results of longitudinal studies comparing gastric histologies in subjects whose *H. pylori* infections have been eradicated with those whose *H. pylori* infections have been allowed to continue for several years.

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