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Stimulus

What Is the Role of *Helicobacter pylori* in Peptic Ulcer and Gastric Cancer Outside the Big Cities?

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Helicobacter pylori is apparently the etiologic agent of 90% of duodenal ulcers (DUs), 80% of gastric ulcers (GUs) not induced by nonsteroidal anti-inflammatory drugs, and gastric carcinoma (GC). Our community-based investigations and retrospective reviews, however, have been unable to substantiate these associations. A retrospective review of 30 patients with GC revealed only 2 (6.6%) patients with *H. pylori* infection. A retrospective review of all patients with the diagnosis of DU (332) was undertaken. One hundred sixty-six had gastroscopy-confirmed DUs, and 112 had three antral biopsies. Only 36 (32%) of 112 were *H. pylori*-positive. Of bleeding ulcers, 25% were *H. pylori*-positive. These findings differ from the literature, and it provoked us to study prospectively all patients undergoing endoscopy. Biopsy specimens were obtained from the cardia and antrum and were stained for *H. pylori*. Of 272 patients' biopsy specimens, 65 (24%) of 272 were *H. pylori*-positive. Sixteen DUs were diagnosed, and five (31%) were *H. pylori*-positive. There were 36 GUs, and 11 (30%) were *H. pylori*-positive. The prevalence of *H. pylori* in consecutive patients undergoing endoscopy is 24% in Orlando, Florida. This is not significantly different from the prevalence of *H. pylori* in patients with DUs and GUs.
Further community-based studies are needed to determine the widespread applicability of these data in the United States.
Key Words: *Helicobacter pylori*—Duodenal ulcer—Gastric ulcer—Gastric carcinoma.

Thoughts about the pathogenesis of duodenal ulcers have changed during the past decade. Since the association of *Helicobacter pylori* with ulcers by Marshall and Warren, many studies have concluded that 90% of duodenal ulcers (DUs) are caused by these bacteria (1–3). Although it has been demonstrated that the ingestion of *H. pylori* causes acute gastritis, actual proof that *H. pylori* causes DU has been lacking. Most reports of the high association of *H. pylori* with DU has been from the international community (4,5). We present three separate studies in a southeastern, primarily white community population in which we found a low incidence of *H. pylori* associated DU and gastric ulcer (GU) and infrequent incidence of *H. pylori*-associated gastric carcinoma. The disparity between published results and our findings questions the applicability of the international data to the communities in the United States. Personal communications from investigators in other states substantiate our investigations. We describe the data collected in our community, review the implications of our observations, and provide a proposal for the future.

METHODS

All patients were seen in our private clinical practice in Orlando, Florida. Three separate studies were incorporated into this paper.

Study 1: Between January 1990 and December 1995, a retrospective review of all patients seen with gastric cancer was performed. For inclusion, the tumor had to be within the stomach but not extending into the esophagus. Thirty patients were found who had endoscopy and biopsies of the lesions performed. Sixty-eight percent of patients underwent surgery, and that pathology was reviewed for *H. pylori* as well.

Study 2: Between January 1991 and May 1996, a retrospective review of all charts of patients with a diagnosis of duodenal ulcer was undertaken. Although 332 were

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found, only 166 patients had undergone endoscopy. Of those patients, 112 had three antral biopsy specimens examined with Giemsa stain by experienced pathologists. Their charts were reviewed in detail.

Study 3: Between March 1996 and March 1997, a prospective study was set up to examine the prevalence of *H. pylori* in patients undergoing endoscopy for any appropriate indication. All patients had two or three antral and two or three cardia biopsy specimens stained with Giemsa for *H. pylori* examination. Almost 90% of patients were seen for severe or chronic dyspepsia. Endoscopy was performed on 272 patients.

In all of these studies, age, sex, race, presence of aspirin and nonsteroidal anti-inflammatory drugs, and alcohol and cigarette use were tabulated.

RESULTS

Study 1: Gastric cancer and *H. pylori*. Seven percent (2 of 30) of patients with gastric carcinoma had *H. pylori* identified by endoscopic biopsies or after surgical resection. Patient characteristics are listed in Table 1. Types and locations of the cancers are listed in Table 2. Sixty-eight percent of patients underwent palliative surgical resection. The most prevalent signs and symptoms were weight loss, abdominal pain, nausea, and anemia. A review of a local hospital's pathology records from January to March 1996 revealed five cases of gastric adenocarcinoma; all were negative for *H. pylori*.

Study 2: Duodenal ulcer and *H. pylori*. Of the 332 patient charts reviewed with the diagnosis of duodenal ulcer, 166 had DU confirmed by endoscopy, and 112 had three antral biopsies. Thirty-six patients (32%) were *H. pylori*-positive. Seventy-six patients (68%) were *H. pylori*-negative. Five patients had both *H. pylori* revealed by biopsy and aspirin usage. Therefore, only 31 (27%) patients had purely *H. pylori* and DU present. Forty-two (38%) of 112 patients were taking concomitant aspirin or nonsteroidal anti-inflammatory drugs. Twenty-five patients with bleeding DU were examined, eight patients had biopsies performed, and two (25%) had *H. pylori*. The pathologic review of all gastroscopy biopsies done at two local hospitals is detailed in Table 3.

Study 3: *H. pylori* prevalence and association with peptic ulcer disease. Of 272 patients who prospectively had biopsies performed at the time of gastroscopy, 24% were *H. pylori*-positive. The population consisted of 42% men and 58% women. Mean age was 56 years. Ninety percent were white. The characteristics of the DUs and GUs found are detailed in Table 4. Cigarette use was reported in 36 (13%) of 272 patients, with 14 (39%) of these 36 patients being *H. pylori*-positive. Alcohol use (>two drinks per day) was reported in 50 (18%) of 272 patients, with 11 (22%) of these 50 patients being *H. pylori* positive.

TABLE 1. *Patients with gastric cancer (n = 30)*

Patient characteristic	%
Mean age (yr)	65
Male:female	52:48
H. pylori-positive	7 (2/30)
H. pylori-negative	93 (27/30)
Alcohol use	23
Smoking	26
Race	
White	78
Black	10
Hispanic	10
Asian	2

TABLE 2. *Gastric cancer characteristics*

Cancer characteristic	No.	%
Cell type		
Adenocarcinoma	23	77
Signet ring type	8	
Lymphoma	4	14
Melanoma	1	3
Malignant carcinoid	1	3
Leiomyosarcoma	1	3
Location		
Cardia		37
Body		15
Antrum		48

DISCUSSION

There have been a great number of articles written about *H. pylori* with much time, effort, and money invested in its diagnosis and treatment. This has perpetuated the premise that 90% of DUs are caused by *H. pylori* and eradication of this organism will cure DU. Despite the videos, continuing medical education courses, Digestive Disease Institute campaigns, pharmaceutical company investments, and lay press publicity of *H. pylori*, the data we present here deserve attention.

These data are derived from a community-based private practice in Orlando, Florida. The studies reveal a less than 30% association of *H. pylori* with DU, with

TABLE 3. *Prevalence of* H. pylori *at two local hospitals*

Location	No. of gastric biopsies reviewed in pathology	No. of *H. pylori*-positive patients (%)
Hospital 1	791	127 (16)
Hospital 2*	401	91 (23)
Total	1192	218 (18)

*Fifty-two ulcers were detected; 40 were duodenal ulcers. Thirteen (32%) of the 40 duodenal ulcers were *H. pylori*-positive.

TABLE 4. *Prevalence of* H. pylori *in duodenal and gastric ulcers*

Characteristic	*H. pylori*-positive patients (%)	Patients with duodenal ulcers (%)	Patients with gastric ulcers (%)
Prevalence	65/272 (24)	16/272 (5.8)	36/272 (13.2)
NSAID/ASA use	—	8/16 (50)	15/36 (42)
H. pylori-positive	—	5/16 (31)	11/36 (30)
Concomitant ASA use	—	2/5	8/11
H. pylori-positive (not induced by NSAID use)	—	3/16 (19)	3/36 (8.3)

NSAID, nonsteroidal anti-inflammatory drug; ASA, aspirin.

approximately only a 10% association with gastric ulcers and a 7% association with gastric cancers.

The most important limitation of our study is that only one method was used to ascertain exposure to *H. pylori*. A serologic test for exposure to *H. pylori* would have been a useful addition to this study and is currently being used in a separate study of DUs. Nevertheless, the implications of these observations are that duodenal ulcer disease is a multifactorial disease without a single etiology. Like coronary artery disease, in which there are many contributing risk factors, there are many risk factors for duodenal ulcer disease; *H. pylori* is only one of them. Excess acid production, insufficient cytoprotective forces, stress, and direct toxic agents also contribute to DUs. The lure of a single agent etiology, although attractive, does not fulfill Koch's postulates.

We found *H. pylori* in association with DU only slightly more frequently than the community prevalence of *H. pylori* (i.e., when correction is made for concomitant use of aspirin or nonsteroidal anti-inflammatory drugs). This suggests to us that, although *H. pylori* causes gastritis, it is not the sole cause of most DUs. *H. pylori* appears to be a possible etiologic agent for a small percentage of DUs and may be a part of a cascade of events that leads to peptic ulcer disease. The incidence of the different etiologic agents may vary, depending on geographic location, socioeconomic status, race, and the habits and inherent characteristics of a given population. This open view may explain the variances seen between given communities and countries. For the most part, however, *H. pylori* causes gastritis with a benign clinical course that promptly responds to H2 blockers and proton-pump inhibitors with rare exception.

WHAT NEEDS TO BE DONE

1. Do not seek out *H. pylori* or eradicate it unless it is associated with an ulcer (9).
2. Do not empirically test patients with dyspepsia for *H. pylori* or treat them with antibiotics if an ulcer is not documented.
3. Study each community or at least one or more representative communities within each state. If the incidence of *H. pylori*- associated peptic ulcer disease is similarly low, little concern about *H. pylori* is necessary in that location.
4. Avoid any inclination to treat *H. pylori* empirically, because most cases appear to be benign and do not lead to DU, GU, or gastric cancer. Symptomatic treatment is usually all that is required.

REASON FOR DIVERGENT RESULTS

The fact that we found only 30% of DUs to be associated with *H. pylori* differs from the results in the body of published reports. However, it is not that different from what has been recognized in other communities, such as Dayton, Ohio; Ft. Worth, Texas; Sioux Water, Oklahoma; Baltimore, Maryland; and Rochester, New York (10–12). When other investigators collate their data, a large percentage of this country may show a low prevalence of *H. pylori* and *H. pylori*-associated DU. Areas that define a high prevalence will require different guidelines for investigation and therapy than those with low prevalence.

The data on *H. pylori* causing gastric cancer remain speculative (13–15). We found only an infrequent association with gastric carcinoma. Because of the history of low and decreasing incidence of gastric cancer in the United States, treating everyone who has the bacteria in the stomach to prevent gastric cancer appears unfounded.

A logical approach to evaluating and treating *H. pylori* would require community-based studies of patient populations that are representative of the types of patients that many physicians see in this country. This can be reformulated as more data appear to confirm or refute our findings. We hope that other community physicians will report their findings to prove us right or wrong.

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