Case 67

This 60-year-old woman with a past medical history of a gastric ulcer had recently noted symptoms of dyspepsia. She characterized her discomfort as a pressure in the upper abdominal area that radiated to her chest and neck. She underwent an upper gastrointestinal series which showed radiologic findings compatible with a thickened fold within the stomach.

An outpatient esophagogastroduodenoscopy (EGD) was performed. A biopsy of the antral portion of the stomach was consistent with moderate gastritis. No tumor was seen. In addition, the biopsy demonstrated 3+ to 4+ of a bacterial organism (Fig. 1).

1. What bacterium has been associated with chronic gastritis?

2. What clinical syndromes, other than chronic gastritis, have been linked to this organism?

3. Other than by histopathologic examination of a biopsy specimen, how can infection with this organism be diagnosed?

4. What special properties of this organism allow it to live in the rather inhospitable environment of the human stomach?

5. What is the epidemiology of infection with this organism?

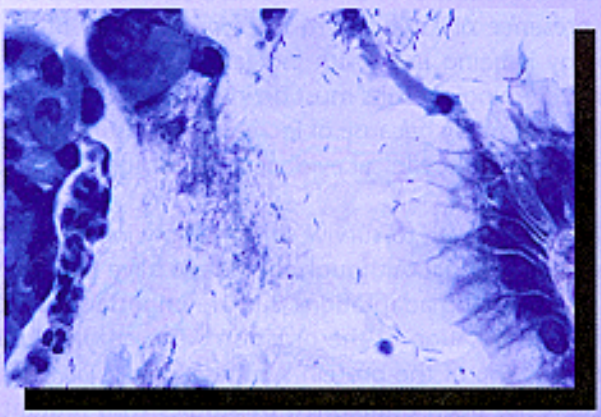

Figure 1

67 Case Discussion

1. The curved or helical gram-negative rod *Helicobacter* (formerly *Campylobacter*) *pylori* has been associated with chronic gastritis. The photomicrograph (Fig. 1) is consistent with *H. pylori* in an area of chronic gastritis.

2. There are data to support links between *H. pylori* and chronic gastritis and peptic ulcer disease. In addition, there is epidemiologic evidence that adenocarcinoma of the stomach is associated with *H. pylori* infection. As you might imagine, it would be difficult to employ Koch's postulates in demonstrating that *H. pylori* is an etiologic agent of adenocarcinoma of the stomach.

3. The isolation of *H. pylori* in a culture of a gastric biopsy specimen is the "gold standard" method of establishing the diagnosis of infection with this organism. Unfortunately, this method requires endoscopic biopsy, and gastric biopsy culture is not routinely performed by all clinical microbiology laboratories. Culture is estimated to be relatively insensitive, with approximately 70% of cultures being positive in patients with *H. pylori*-associated disease. Another method, also requiring endoscopic biopsy, is the campylobacter-like organism (CLO) test, which relies on the presence of the bacterial enzyme urease (see answer **4** below). In this test, gastric biopsy tissue is added to a tube that contains urea agar. The urease activity of tissue containing *H. pylori* is demonstrated by the change in color of the indicator present in the urea agar. Noninvasive tests include the demonstration of urease production following the ingestion of ^{13}C- or ^{14}C-labeled urea and serologic tests to demonstrate the presence of antibody to *H. pylori*. Because of its noninvasive nature, *H. pylori* serology is being used with increasing frequency in an attempt to diagnose this infection. Serologic results must be interpreted cautiously. Seropositivity increases with age presumably because of increased exposure to the organism. Patients can be seropositive without clinical evidence of gastritis or peptic ulcer disease.

4. The ability of *H. pylori* to survive and multiply in the ecologic niche of the acidic stomach is quite unusual. Although the details have not been worked out, there are a number of interesting adaptations that are important in allowing colonization and subsequent multiplication of the organism. The enzyme urease, which may represent as much as 6% of the protein synthesis of *H. pylori*, is active at the low pH of gastric juice. It has been established by studies with mutant *H. pylori* that lack urease that this enzyme is essential for gastric colonization. Urease catalyzes the hydrolysis of urea, resulting in the production of ammonia which is believed to raise the pH of the microenvironment, resulting in improved bacterial survival. It is a subject of active debate whether or not this mechanism is the means by which urease contributes to the colonization of the stomach. Another factor of importance is the presence of flagella, conferring motility to *H. pylori*. The flagella enable *H. pylori* to move through the thick mucus coat that is present in the stomach.

5. *H. pylori* is typically acquired during early childhood in developing countries. In developed countries, such as the United States, the infection is not typically acquired during childhood and the incidence is lower. It is important to recognize that although approximately 50% of Americans have been infected with this organism by age 60, most infections are asymptomatic.

References

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2. **Labigne, A., and H. de Reuse.** 1996. Determinants of *Helicobacter pylori* pathogenicity. *Infect. Agents Dis.* **5:**191–202.