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## Division of Bacterial Diseases (DBD)

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## Helicobacter pylori and Peptic Ulcer Disease

### The Key to Cure



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### What is H. pylori?

*Helicobacter pylori* (*H. pylori*) is a spiral-shaped bacterium that is found in the gastric mucous layer or adherent to the epithelial lining of the stomach. *H. pylori* causes more than 90% of duodenal ulcers and up to 80% of gastric ulcers. Before 1982, when this bacterium was discovered, spicy food, acid, stress, and lifestyle were considered the major causes of ulcers. The majority of patients were given long-term medications, such as H2 blockers, and more recently, proton pump inhibitors, without a chance for permanent cure. These medications relieve ulcer-related symptoms, heal gastric mucosal inflammation, and may heal the ulcer, but they do NOT treat the infection. When acid suppression is removed, the majority of ulcers, particularly those caused by *H. pylori*, recur. Since we now know that most ulcers are caused by *H. pylori*, appropriate antibiotic regimens can successfully eradicate the infection in most patients, with complete resolution of mucosal inflammation and a minimal chance for recurrence of ulcers.

### How common is H. pylori infection?

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Approximately two-thirds of the world's population is infected with *H. pylori*. In the United States, *H. pylori* is more prevalent among older adults, African Americans, Hispanics, and lower socioeconomic groups.

### **What illnesses does *H. pylori* cause?**

Most persons who are infected with *H. pylori* never suffer any symptoms related to the infection; however, *H. pylori* causes chronic active, chronic persistent, and atrophic gastritis in adults and children. Infection with *H. pylori* also causes duodenal and gastric ulcers. Infected persons have a 2- to 6-fold increased risk of developing gastric cancer and mucosal-associated-lymphoid-type (MALT) lymphoma compared with their uninfected counterparts. The role of *H. pylori* in non-ulcer dyspepsia remains unclear.

### **What are the symptoms of ulcers?**

Approximately 25 million Americans suffer from peptic ulcer disease at some point in their lifetime. Each year there are 500,000 to 850,000 new cases of peptic ulcer disease and more than one million ulcer-related hospitalizations. The most common ulcer symptom is gnawing or burning pain in the epigastrium. This pain typically occurs when the stomach is empty, between meals and in the early morning hours, but it can also occur at other times. It may last from minutes to hours and may be relieved by eating or by taking antacids. Less common ulcer symptoms include nausea, vomiting, and loss of appetite. Bleeding can also occur; prolonged bleeding may cause anemia leading to weakness and fatigue. If bleeding is heavy, hematemesis, hematochezia, or melena may occur.

### **Who should be tested and treated for *H. pylori* ?**

Persons with active gastric or duodenal ulcers or documented history of ulcers should be tested for *H. pylori*, and if found to be infected, they should be treated. To date, there has been no conclusive evidence that treatment of *H. pylori* infection in patients with non-ulcer dyspepsia is warranted. Testing for and treatment of *H. pylori* infection are recommended following resection of early gastric cancer and for low-grade gastric MALT lymphoma. Retesting after treatment may be prudent for patients with bleeding or otherwise complicated peptic ulcer disease. Treatment recommendations for children have not been formulated. Pediatric patients who require extensive diagnostic work-ups for abdominal symptoms should be evaluated by a specialist.

### **How is *H. pylori* infection diagnosed?**

Several methods may be used to diagnose *H. pylori* infection. Serological tests that measure specific *H. pylori* IgG antibodies can determine if a person has been infected. The sensitivity and specificity of these assays range from 80% to 95% depending upon the assay used. Another diagnostic method is the breath test. In this test, the patient is given either <sup>13</sup>C- or <sup>14</sup>C-labeled urea to drink. *H. pylori* metabolizes the urea rapidly, and the labeled carbon is absorbed. This labeled carbon can then be measured as CO<sub>2</sub> in the patient's expired breath to determine whether *H. pylori* is present. The sensitivity and specificity of the breath test ranges from 94% to 98%. Upper esophagogastroduodenal endoscopy is considered the reference method of diagnosis. During endoscopy, biopsy specimens of the stomach and duodenum are obtained and the diagnosis of *H. pylori* can be made by several methods: The biopsy urease test - a colorimetric test based on the ability of *H. pylori* to produce urease; it provides rapid testing at the time of biopsy. Histologic identification of organisms - considered the gold

standard of diagnostic tests. Culture of biopsy specimens for *H. pylori*, which requires an experienced laboratory and is necessary when antimicrobial susceptibility testing is desired.

### **What are the treatment regimens used for *H. pylori* eradication?**

Therapy for *H. pylori* infection consists of 10 days to 2 weeks of one or two effective antibiotics, such as amoxicillin, tetracycline (not to be used for children <12 yrs.), metronidazole, or clarithromycin, plus either ranitidine bismuth citrate, bismuth subsalicylate, or a proton pump inhibitor. Acid suppression by the H<sub>2</sub> blocker or proton pump inhibitor in conjunction with the antibiotics helps alleviate ulcer-related symptoms (i.e., abdominal pain, nausea), helps heal gastric mucosal inflammation, and may enhance efficacy of the antibiotics against *H. pylori* at the gastric mucosal surface. Currently, eight *H. pylori* treatment regimens are approved by the Food and Drug Administration (FDA) (Table 1); however, several other combinations have been used successfully. Antibiotic resistance and patient noncompliance are the two major reasons for treatment failure. Eradication rates of the eight FDA-approved regimens range from 61% to 94% depending on the regimen used. Overall, triple therapy regimens have shown better eradication rates than dual therapy. Longer length of treatment (14 days versus 10 days) results in better eradication rates.

### **FDA-Approved Treatment Options**

<b>FDA-approved treatment options</b>
Omeprazole 40 mg QD + clarithromycin 500 mg TID x 2 wks, then omeprazole 20 mg QD x 2 wks
-OR-
Ranitidine bismuth citrate (RBC) 400 mg BID + clarithromycin 500 mg TID x 2 wks, then RBC 400 mg BID x 2 wks
-OR-
Bismuth subsalicylate (Pepto Bismol®) 525 mg QID + metronidazole 250 mg QID + tetracycline 500 mg QID* x 2 wks + H <sub>2</sub> receptor antagonist therapy as directed x 4 wks
-OR-
Lansoprazole 30 mg BID + amoxicillin 1 g BID + clarithromycin 500 mg TID x 10 days
-OR-
Lansoprazole 30 mg TID + amoxicillin 1 g TID x 2 wks**
-OR-
Ranitidine bismuth citrate 400 mg BID + clarithromycin 500 mg BID x 2 wks, then RBC 400 mg BID x 2 wks
-OR-
Omeprazole 20 mg BID + clarithromycin 500 mg BID + amoxicillin 1 g BID x 10 days
-OR-
Lansoprazole 30 mg BID + clarithromycin 500 mg BID + amoxicillin 1 g BID x 10 days

\*Although not FDA approved, amoxicillin has been substituted for tetracycline for patients for whom tetracycline is not recommended.

\*\*This dual therapy regimen has restrictive labeling. It is indicated for patients who are either allergic or intolerant to clarithromycin or for infections with known or suspected resistance to clarithromycin.

### **Are there any long-term consequences of *H. pylori* infection?**

Recent studies have shown an association between long-term infection with *H. pylori* and the development of gastric cancer. Gastric cancer is the second most common cancer worldwide; it is most common in countries such as Colombia and China, where *H. pylori* infects over half the population in early childhood. In the United States, where *H. pylori* is less common in young people, gastric cancer rates have decreased since the 1930s.

### **How do people get infected with *H. pylori*?**

It is not known how *H. pylori* is transmitted or why some patients become symptomatic while others do not. The bacteria are most likely spread from person to person through fecal-oral or oral-oral routes. Possible environmental reservoirs include contaminated water sources. Iatrogenic spread through contaminated endoscopes has been documented but can be prevented by proper cleaning of equipment.

### **What can people do to prevent *H. pylori* infection?**

Since the source of *H. pylori* is not yet known, recommendations for avoiding infection have not been made. In general, it is always wise for persons to wash hands thoroughly, to eat food that has been properly prepared, and to drink water from a safe, clean source.

### **What is the Centers for Disease Control and Prevention (CDC) doing to prevent *H. pylori* infection?**

CDC, with partners in other government agencies, academic institutions, and industry, is conducting a national education campaign to inform health care providers and consumers of the link between *H. pylori* and stomach and duodenal ulcers. CDC is also working with partners to study routes of transmission and possible prevention measures, and to establish an antimicrobial resistance surveillance system to monitor the changes in resistance among *H. pylori* strains in the United States.

### **How can I get more information about *H. pylori*?**

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3. Hunt, RH. *Helicobacter pylori*: from theory to practice. Proceedings of a symposium. *Am J Med* 1996; 100 (5A) supplement.
4. The American Gastroenterological Association, American Digestive Health Foundation, 7910 Woodmont Avenue, 7th floor, Bethesda, MD 20814, (301) 654-2055 telephone, (301) 654-5920 fax.

5. The National Digestive Diseases Information Clearinghouse, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, 2 Information Way, Bethesda, MD 20892-3570, (301) 654-3810 telephone.
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