**Introduction**

Helicobacter pylori, a gram-negative bacterium found on the luminal surface of the gastric epithelium, was first isolated by Warren and Marshall in 1983. Infection with *Helicobacter pylori* has been recognized as a public health problem worldwide. The prevalence of peptic ulcers in patients seropositive for *H. pylori* is seven times greater than in those who are seronegative.

Before the discovery of *H. pylori*, gastroduodenal ulcer healing was achieved with the administration of H2-blockers or proton pump inhibitors (PPIs) for at least four weeks. At present, *H. pylori* eradication therapy is indicated in gastroduodenal ulcer disease. Recent international consensus statements have concluded that *H. pylori* is a causal factor in peptic ulcer disease and a Group 1 carcinogen in humans and all patients with peptic ulcer associated with *H. pylori* infection should receive eradication therapy.

The treatment of *Helicobacter pylori* remains a challenging clinical problem despite extensive research over the last 25 years. PPI-based triple therapy, with a proton pump inhibitor, clarithromycin (CAM), and either amoxicillin (AMPC) or metronidazole, is a widely-recommended eradication therapy. Prevalence of *H. pylori* resistance to metronidazole is approximately 25%. PPI-based triple therapies have shown efficacy in various clinical trials from different geographic areas. Triple therapy using a PPI with clarithromycin and amoxicillin or metronidazole given twice daily remains the recommended first choice treatment.

**Diagnosis**

**Endoscopy.** Endoscopy is performed at baseline, upon completion of ulcer treatment, and one month after completion of ulcer treatment to confirm the state of the ulcer.

**Histologic examination.** All histologic examinations for the diagnosis of *H. pylori* infection should be carried out at baseline and one month after the completion of the ulcer treatment. Biopsies should be obtained from the two sites of the greater curvature of the antrum and the greater curvature of the upper corpus. The biopsies should be fixed in formalin and slides prepared with hematoxylin-eosin and Giemsa stains. The bacterial density should be categorized as none, mild, moderate, marked, or judgment impossible.

**Gastric Ulcer**

The inflammation of the gastric mucosa induced by the infection is most pronounced in the non-acid-secreting antral region of the stomach and stimulates the increased release of gastrin. The increased gastrin levels in turn stimulate excess acid secretion from the more proximal acid-secreting fundic mucosa, which is relatively free of inflammation. The increased duodenal acid load damages the duodenal mucosa, causing ulceration and gastric metaplasia. The metaplastic mucosa then can become
colonized by \textit{H. pylori}, which may contribute to the ulcerative process.

Eradication of the infection provides a long-term cure of duodenal ulcers in more than 80% of patients whose ulcers are not associated with the use of nonsteroidal antiinflammatory drugs (NSAID).\textsuperscript{11} NSAIDs are the main cause of \textit{H. pylori}-negative ulcers. Ulceration of the gastric mucosa is believed to be due to the damage to the mucosa caused by \textit{H. pylori}. As with duodenal ulcers, eradicating the infection usually cures the disease, provided that the gastric ulcer is not due to NSAIDs.\textsuperscript{12}

\textbf{H. pylori Treatment}

Various drug regimens are used to treat \textit{H. pylori} infection. Most include two antibiotics plus a proton-pump inhibitor or a bismuth preparation (or both). The most commonly used initial treatment is triple therapy consisting of a proton-pump inhibitor plus clarithromycin and amoxicillin, each given twice per day for 7 to 14 days. Metronidazole is used in place of amoxicillin in patients with a penicillin allergy.

First-line treatment. Triple eradication therapy is the most commonly used treatment protocol in \textit{H. pylori} eradication. Eradication of \textit{H. pylori} removes the increased risk of developing actual ulcer disease.\textsuperscript{13} General agreement exists in that eradication of \textit{H. pylori} infection with triple therapy including a PPI and two antibiotics for 7–10 days is the gold standard of treatment.\textsuperscript{14} In the recent triple combination studies, the eradication success declines over time.\textsuperscript{15} The preferred regimen internationally is triple therapy with a PPI, clarithromycin, and amoxicillin twice daily for 7–10 days.\textsuperscript{16}

Second-line treatment. Second-line treatment includes bismuth, metronidazole, and tetracycline plus either a PPI or an H2 receptor antagonist (H2RA).\textsuperscript{17} If a PPI is chosen, the regimen can be given for seven days. If an H2RA is used, however, 14 days are recommended. A recent meta-analysis of 93 studies showed a higher rate of eradication with quadruple therapy that included both clarithromycin and metronidazole than with triple therapy that included both these agents in populations with either clarithromycin or metronidazole resistance.\textsuperscript{18}

\textbf{Discussion}

Helicobacter pylori is an important cause of duodenal and gastric ulcers. Greater than 90% of duodenal ulcers and 70% of gastric ulcers are associated with \textit{H. pylori}.\textsuperscript{1} Eradication of \textit{H. pylori} is effective in healing ulcers and drastically reducing the ulcer recurrence, eliminating the need for maintenance therapy.\textsuperscript{19} Treiber et al.\textsuperscript{20} found that successful \textit{H. pylori} eradication induced a better response in peptic ulcer healing, regardless of diagnosis of duodenal or gastric ulcer. Several large-scale clinical trials and meta-analyses have demonstrated that the most common first-line therapies fail in up to 20% of patients.\textsuperscript{21}

Currently-recommended protocols include a 10-14 day treatment with: (1) a proton pump inhibitor (PPI) plus clarithromycin and amoxicillin, (2) a PPI plus clarithromycin and metronidazole, or (3) bismuth subsalicylate plus metronidazole and tetracycline.\textsuperscript{22} The recommended duration of triple therapy is typically 10 to 14 days in the United States and 7 days in Europe.\textsuperscript{23} Triple therapy with a proton pump inhibitor, clarithromycin, and amoxicillin or metronidazole remains an appropriate first-line therapy.

Another possible initial therapy in areas with a high prevalence of clarithromycin-resistant \textit{H. pylori} infection (i.e., >20%) is quadruple therapy comprising the use of a proton-pump inhibitor, tetracycline, metronidazole, and a bismuth salt for 10 to 14 days.\textsuperscript{24}
The choice of second-line treatment is influenced by the initial treatment. Treatment failure often is related to *H. pylori* resistance to clarithromycin or metronidazole (or both agents). Clarithromycin should be avoided as part of second-line therapy unless resistance testing confirms that the *H. pylori* strain is susceptible to the drug. If initial therapy did not include a bismuth salt, bismuth-based quadruple therapy commonly is used as second-line therapy with eradication rates ranging from 57 to 95%. Quadruple therapies, therefore, usually are reserved for patients who have failed one or more courses of triple therapy. Some quadruple therapies are less costly and appropriate for patients in whom cost is a significant factor.

**Conclusions**

Helicobacter pylori is a very common disease with a broad spectrum of clinical symptoms and disorders. A PPI, clarithromycin, and amoxicillin or metronidazole remains an appropriate first-line therapy, provided that there is not a high local rate of clarithromycin resistance. A PPI used in combination with metronidazole and either amoxicillin or tetracycline is recommended in patients previously treated with a PPI, amoxicillin, and clarithromycin. Eradication of *H. pylori* infection has the potential to reduce the risk of gastric cancer development.

**References**


Keywords: Helicobacter pylori, gastrointestinal ulcers, review