Although bismuth compounds and prostaglandin analogues have been shown to provide protective effects on the gastroduodenal mucosa and may have some effect on ulcer healing, these agents are not routinely used in the initial treatment of peptic ulcers.

Treatment of *Helicobacter pylori* Infection

Eradication of *H. pylori* should be attempted in all patients with documented current or past PUD and evidence of infection. Successful therapy requires a combination of drugs that prevents the emergence of resistance and effectively reaches the bacteria, and must be of sufficient duration to ensure eradication. Combinations of two antibiotics, plus either a PPI or ranitidine bismuth citrate, are used to maximize the chance of eradication. Current treatment regimens for *H. pylori* are shown in Table 36-1. Factors such as antibiotic resistance and noncompliance with therapy have been identified as predictors of treatment failure. Metronidazole resistance is most common, and both metronidazole and clarithromycin resistance are increasing in frequency, with rates of 37% and 10%, respectively. Because compliance is essential for treatment success, the current regimens offer simpler dosing than earlier options. A failed initial course of antibiotic therapy suggests antibiotic resistance, and it may be assumed that, if the patient received metronidazole or clarithromycin in the original regimen, resistance to that antibiotic is present. When possible, repeat use of the same antibiotic should be avoided. The recommended duration for repeat treatment courses is 14 days. An alternative initial approach involves a shorter, 10-day treatment course with PPI and sequential dosing of amoxicillin and clarithromycin, but further validation studies are needed before this can be recommended as standard therapy.

Maintenance Therapy

Before embarking on long-term maintenance therapy for PUD, careful attention must be paid to eliminating the most important risk factors for ulcer recurrence: *H. pylori* infection and NSAID use. Moreover, hypersecretory states, including gastrinoma, should be excluded in individuals with recurrent ulcers without *H. pylori* infection. Patients with a history of ulcer complications, frequent ulcer recurrence, continued NSAID use, or *H. pylori*–negative ulcers, and those who fail to clear *H. pylori* infection despite appropriate therapy, should be considered candidates for maintenance antisecretory therapy. However, even patients who have had a complicated ulcer may not require maintenance therapy, provided *H. pylori* infection is cured. Maintenance regimens include an H_2 receptor antagonist at bedtime at one half the dose required for initial healing or a full-dose PPI taken before breakfast.

TABLE 36-1 TREATMENT REGIMENS FOR *HELICOBACTER PYLORI* INFECTION

Triple therapy (cure rate, 85% to >90%)
BMT triple therapy for 14 days
- Bismuth subsalicylate, 524 mg by mouth 4 times daily
- Metronidazole, 250 mg by mouth 4 times daily
- Tetracycline HCl, 500 mg by mouth 4 times daily + H_2-RA for additional 4 weeks

LAC for 10 or 14 days
- Lansoprazole, 30 mg by mouth twice daily
- Amoxicillin, 1 g by mouth twice daily
- Clarithromycin, 500 mg by mouth twice daily

OAC for 10 or 14 days
- Omeprazole, 20 mg by mouth twice daily
- Amoxicillin, 1 g by mouth two times daily
- Clarithromycin, 500 mg by mouth twice daily

RBC-AC (cure rate, >90%)
- Ranitidine bismuth citrate + amoxicillin + clarithromycin

MOC (cure rate, >90% in the absence of metronidazole resistance)
- Metronidazole + omeprazole + clarithromycin

H_2-RA, histamine-2 receptor antagonist; HCl, hydrochloric acid.

Treatment and Prophylaxis of NSAID-Induced Ulceration

The optimal treatment of patients with NSAID-induced gastroduodenal ulcers is the discontinuation of the offending agent. If NSAIDs must be continued, therapy with an antisecretory agent should be instituted. Based on their superior safety profile and their ability to heal gastroduodenal ulcers at an accelerated rate whether or not NSAID use is continued, PPIs are preferred over both H_2 receptor antagonists and misoprostol.

Because of the significant rate of serious complications associated with NSAIDs and the poor correlation between dyspeptic symptoms (e.g., abdominal pain, distention, nausea, heartburn) and the presence of gastroduodenal mucosal injury, prevention of ulceration has become the principal goal in the management of NSAID-related GI toxicity. Risk factors for NSAID-related injury include advanced age (>60 years), prior history of PUD or ulcer hemorrhage, concomitant use of anticoagulants or corticosteroids, significant comorbid conditions, and use of high NSAID doses (Table 36-2). Two strategies have been used to prevent ulcers: (1) the concomitant use of medications such as misoprostol or PPIs, and (2) the development of safer anti-inflammatory agents, such as COX-2–specific inhibitors. Misoprostol, a prostaglandin E_1 analogue, significantly reduces the development of both gastric and duodenal ulcers in patients using NSAIDs. By augmenting prostaglandin-dependent pathways, misoprostol reduces gastric acid secretion and enhances mucosal defenses. However, misoprostol is associated with significant adverse effects and a high frequency of therapy discontinuation as a result of these effects, especially when administered 4 times a day. The most frequent symptom is diarrhea, although symptoms such as abdominal pain, nausea, and bloating may also occur. A lower dose of misoprostol (200 mcg 3 times daily) is nearly as effective as 4 times daily dosing for preventing duodenal and gastric ulcers, with a slight reduction in the occurrence of adverse effects.

The second strategy to prevent NSAID-induced ulcers involves the co-administration of an antisecretory agent, usually a PPI, or the substitution of the traditional NSAID with one of the newer

TABLE 36-2 RISK FACTORS FOR DEVELOPMENT OF NSAID-RELATED ULCERS

DEFINITE	POSSIBLE
Advanced age	Concomitant infection with *Helicobacter pylori*
History of ulcer	Cigarette smoking
Concomitant corticosteroid therapy	Consumption of alcohol
Concomitant anticoagulation therapy	NSAIDs, nonsteroidal anti-inflammatory drugs.
High doses of NSAIDs	
Serious systemic disorders	