Pharmacotherapy of Duodenal and Gastric Ulcerations

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PROLOGUE
Peptic ulcer, an excavation in the mucosal lining penetrating below the muscularis mucosa of the stomach or duodenum (See Figure 1), is a common disorder. The incidence varies with the age, gender, and geographical location with duodenal ulcers occurring in approximately four to ten percent of the United States (U.S.) population and gastric ulcers occurring in less than one percent. Both gastric and duodenal ulcers are associated with severe complications including hemorrhages, perforations, gastrointestinal obstruction, and malignancy.

Peptic ulcer disease and its complications cost the U.S. health care budget greater than three billion dollars annually. Based on the high incidence and the enormous amount of money that is spent on peptic ulcer disease, it is very important for pharmacists and pharmacy students to be educated about this disease and the medication regimens used to treat it. This lecture provides a basic review of the pathophysiology, clinical presentation and evaluation, and medications used to treat uncomplicated duodenal and gastric ulcerations.

ETIOLOGY, PATHOPHYSIOLOGY, AND PATHOGENESIS
Peptic ulcers usually occur as a result of an imbalance between mucosal protective factors and aggressive factors. Significant gastric protective factors include mucus secretion, bicarbonate secretion, mucosal blood flow, cell growth and prostaglandins. By continuously secreting onto the gastric mucosa, mucus which is secreted by goblet cells protects underlying gastric cells and acts as a lubricant layer between the gastric mucosa and its contents. Bicarbonate, which is secreted by the pancreas, biliary system and gastric epithelial cells, protects by neutralizing luminal hydrogen ions in the gastric lumen. Gastrointestinal (GI) blood flow is essential in maintaining mucosal integrity and preventing against vascular insufficiency, whereas, epithelial cell growth plays an important role in restoring damaged epithelium. Endogenous prostaglandins, in particular PGE2 which is secreted by gastric and duodenal mucosal cells, aids in mucosal protection by stimulating mucus and bicarbonate secretion, maintaining blood flow, and participating in epithelial cell growth(1,2).

Peptic ulcers derive their name from pepsin, a digestive enzyme found in gastric juices that hydrolyzes peptide bonds to break down protein. Pepsin is derived from a series of steps involving hydrochloric acid that converts the enzyme pepsinogen, which is secreted from chief cells, to pepsin. In addition to pepsin, there are many other important noxious factors including Helicobacter pylori, nonsteroidal anti-inflammatory drugs (NSAIDs) and gastric acid that play an aggressive role in the development of ulcers (See Figure 2). Evidence is now available that supports that H. pylori and NSAIDs account for the majority of peptic ulcers(3-5).
releasing peptides (12). Although nearly all patients with a defect in controlling acid secretion by increasing gastrin-secreting tumor associated with Zollinger-Ellison syndrome, H. pylori ant-bodies (3). The exact pathophysiologic mechanisms by which H. pylori damages mucosal defense by producing toxins and evoking inflammation. Ammonia, protease, lipase, and cytotoxins have all been indicated as caustic elements. Some studies suggest that H. pylori-infection indirectly produces a defect in controlling acid secretion by increasing gastrin-releasing peptides (12). Although nearly all patients with peptic ulcer disease who are not taking NSAIDs have H. pylori, it is important to note that H. pylori is a very common infection and most infected individuals do not have peptic ulcers. Therefore, it is not known whether the presence of H. pylori within the GI tract is pathologic in and of itself. This lends to the suspicion of the involvement of other factors such as the immune system and H. pylori strain variability playing important roles in the protection or development of peptic ulcers. The importance of the immune system in the formation of peptic ulcers and mechanisms identifying population subsets at risk for ulcer development deserves further investigation. In order to reduce the number of infected individuals, understanding transmission methods of H. pylori is necessary. Transmission of H. pylori is believed to occur primarily by the fecal-oral and oral-oral routes. Prevalence of infection is also related to age and socioeconomic classes with higher incidences reported in the elderly and the lower socioeconomic groups (13). Cases of H. pylori transmission by infected instruments, such as endoscopes, have also been reported (4, 11).

### Peptic Ulcerations and NSAIDs

The second most common form of peptic ulcers is NSAID-associated ulcers (2, 6, 14, 15). Two to four percent of patients who take NSAIDs will have GI damage (3). Chronic NSAID-therapy produces gastric injury by two mechanisms. The first is by a direct caustic action on the mucosa and the second is by a systemic effect whereby endogenous prostaglandin synthesis is inhibited. Individuals that consume large amounts of NSAIDs, such as patients suffering from arthritis and the elderly, are extremely susceptible to the development of ulcers.

### Risk Factors for Ulcer Development

A number of risk factors can predispose an individual to develop peptic ulcers or delay ulcer healing. Of course, the most important risk factors for developing peptic ulcers are the use of NSAIDs and H. pylori infection. Many reports have demonstrated that cigarette smoking impairs ulcer healing and promotes ulcer recurrence. The role of genetic factors, psychological stress, and dietary foods in ulcer formation is controversial and remains uncertain (3).

Many diseases have been associated with peptic ulcer development. Chronic pulmonary disease and rheumatoid arthritis, two common diseases, have been linked to gastric and duodenal ulcers. Using steroids and smoking cigarettes may contribute to the increased rate of peptic ulcers in patients suffering from chronic pulmonary disease, and the use of NSAIDs to reduce pain and inflammation may contribute to the increased rate of peptic ulcerations in rheumatoid arthritis patients.

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**Table I. Drugs that may commonly cause gastrointestinal mucosal injury**

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>Aspirin</td>
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<tr>
<td>Chemotherapeutic agents</td>
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<tr>
<td>Corticosteroids</td>
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<tr>
<td>Ethacrylic acid</td>
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<tr>
<td>Ethanol</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory agents</td>
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<td>Pancrease supplementation</td>
</tr>
<tr>
<td>Potassium chloride</td>
</tr>
<tr>
<td>Reserpine</td>
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<tr>
<td>Warfarin</td>
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</tbody>
</table>

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**Fig. 2. Parietal cell and acid secretion.** The release of histamine from the mast cells activates the proton pump of the parietal cell by increasing intracellular cyclic adenosine monophosphate (cAMP). Gastrin and acetylcholine contribute to acid release by increasing intracellular calcium. Through a series of intracellular events, the net result is a 1:1 exchange of an intracellular hydrogen ion for a luminal potassium ion.
CLINICAL PRESENTATION

Patients with duodenal and gastric ulcers often present with dyspeptic symptoms such as abdominal pain, nausea, and vomiting. Epigastric pain typically described as burning, gnawing, and aching is the most common complaint. Non-specific dyspeptic complaints such as belching, bloating, abdominal distention, and food intolerance occur in approximately 40 to 70 percent of peptic ulcer disease patients. The intensity of the pain and other symptoms vary from patient to patient. Food may alleviate the pain of duodenal ulcers or, conversely, intensify the pain of gastric ulcers. Therefore, epigastric pain that occurs when the stomach is empty (e.g., pain during the night or between meals) and is relieved by food is typical of duodenal ulcers. Because of this, weight loss is common in individuals suffering with duodenal ulcerations and weight gain may occur in individuals suffering with duodenal ulcerations. It is equally important to recognize that pain does not necessarily correlate with the presence of an ulcer. In fact, many patients may be asymptomatic. The elderly, individuals taking analgesics, and people who have a high pain tolerance often experience a “silent ulcer,” meaning that they are symptom free until an ulcer related complication appears such as gastrointestinal bleeding (often suggested by hematoemesis or melena), perforation and obstruction.

CLINICAL EVALUATION

A comprehensive patient history is critical when evaluating patients with peptic ulcer disease complaints. The clinician should ask the patient questions to ascertain the account of the gastrointestinal problem including the setting in which it developed, intensifies, and alleviates. A complete drug history to identify medications that may contribute to the development of gastritis or ulcerations is also imperative(17). See Table I.

More than 95 percent of duodenal ulcers occur in the first portion of the duodenum and approximately 90 percent of these are located within 3 cm of the junction of the pyloric and duodenal mucosa. Duodenal ulcers are usually round or oval, but may be irregular or elliptic and are usually less than 1 cm in diameter (see Figure 3). Most all benign gastric ulcers are found immediately distal to the junction of the antral mucosa. Diagnosis of peptic ulcers depends on visualizing ulcers by radiologic or endoscopic methods. Barium contrast radiology can detect 30 to 80 percent of peptic ulcers, whereas, endoscopy can detect more than 90 percent of peptic ulcers. Although a 24-hour pH study may be valuable in some patients in whom acid secretion is questionable, pH tests are not commonly used and are thought to provide little additional information in evaluating uncomplicated GI ulcerations where acid hypersecretion is not suspected. Tests to measure pH are frequently used to evaluate patients with suspected gastroesophageal reflux disease (the passage of gastric contents from the stomach into the esophagus) or Zollinger-Ellison syndrome (a severe form of peptic ulcer disease in which intractable ulcers are accompanied by extreme gastric hyperacidity and at least one gastroma).

Radiologic procedures are used in visualizing craters of peptic ulcers. An “upper gastrointestinal series,” a common procedure used to evaluate the presence of peptic ulcers, refers to the radiographic visualization of the esophagus, stomach, and small intestine. To enhance the visualization of structures, barium sulfate, a contrast agent, is usually administered orally to patients at the beginning of upper gastrointestinal radiographic procedures (see Figure 4).

An endoscope is an illuminated optical, tube-like instrument designed to inspect the interior of the GI tract.
In order to prevent absorption interactions, antacids should avoid use in patients with renal dysfunction. Due to frequent administration and adverse effects, antacids are primarily used for relieving ulcer pain and are often used in combination with other antulcer agents.

**Histamine2-Receptor Antagonists**

Currently, there are four H2-receptor antagonists (cimetidine, famotidine, nizatidine, and ranitidine) that are commercially available in the U.S. These agents bind to H2-receptors on the parietal cell, thereby diminishing cyclic AMP production and the secretion of gastric acid (see Figure 2). Cimetidine, famotidine, nizatidine, and ranitidine are fairly effective and have similar duodenal ulcer healing rates, 82 to 95 percent healing within eight weeks of therapy(18,19). Numerous drug interactions have been reported with cimetidine due to its effects on inhibiting the hepatic cytochrome P-450 system CYP IIIA4, IID6, IIE1, IA2, and IIC9 isoenzymes, thereby decreasing hepatic clearance of many drugs such as warfarin, theophylline, and propranolol. Cimetidine has also been associated with confusion, gynecomastia, and impotence. Generally, H2-receptor antagonists are safe and well tolerated. Side effects associated with H2-receptor antagonists include thrombocytopenia, drowsiness, nausea, vomiting, skin rash, and headache. All H2-receptor antagonists should be adjusted in patients with renal dysfunction. See Table II for dosages of specific agents.

**Proton Pump Inhibitors**

Currently, there are two proton pump inhibitors, omeprazole and lansoprazole, available in the U.S. Proton pump inhibitors suppress gastric acid secretion by inhibiting the parietal cell H/K-ATPase pump (see Figure 2) and are more effective in healing ulcers than H2-receptor antagonists(20,21). Although omeprazole is relatively well tolerated, it is a hepatic cytochrome P-450 IIC enzyme inhibitor and a cytochrome P-450 1A2 enzyme inducer. When used together, omeprazole has been reported to increase concentrations of phenytoin and warfarin. Because of profound and long lasting inhibition of gastric acid secretion, proton pump inhibitors may interfere with absorption of drugs where pH is a determinant of bioavailability such as with ketoconazole, itraconazole, ampicillin esters, and iron salts. Omeprazole and lansoprazole are most effective when taken in the morning before meals, and omeprazole capsules should be swallowed whole, not chewed, crushed, or opened. For patients who have difficulty swallowing capsules, lansoprazole can be opened and the intact granules within can be sprinkled on a medium such as one tablespoon of applesauce and swallowed immediately (do not chew or crush the granules). See Table II for recommended dosages.

**Sucralfate**

In the presence of acid, sucralfate forms an adhesive that binds electrostatically to ulcer craters forming a protective barrier that covers the ulcer site and protects it against further attack by acid, pepsin, and bile salts. Studies have demonstrated that sucralfate is comparable to the effectiveness of H2-receptor antagonists in healing ulcers. To prevent adverse effects associated with aluminum toxicity, sucralfate should be used in caution with chronic renal failure patients who have impaired excretion of absorbed aluminum. Because of the potential for sucralfate to alter the absorption of some drugs, separate administration (two hours before or after) of...
**Table II. Dosing and laboratory monitoring of histamine2-receptor antagonists, sucralfate, and proton pump inhibitors**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indications</th>
<th>Oral dose</th>
<th>Intravenous dose</th>
<th>Dose adjustment in renal dysfunction</th>
<th>Medication laboratory monitoring parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H2-Receptor inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cimetidine (Tagamet®)</td>
<td>Duodenal ulcer Active</td>
<td>800 mg HS</td>
<td>300 mg Q 6-8 hr</td>
<td>CrCl &lt;30 mL/min - 300mg q 12 h</td>
<td>SCr, AST, ALT BUN, RBC, Platelets, WBC</td>
</tr>
<tr>
<td></td>
<td>Duodenal ulcer Active</td>
<td>400 mg BID or 300 mg QID</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>400 mg HS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric ulcer Maintenance</td>
<td>300 mg QID or 800 mg HS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>400 mg HS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Famotidine (Pepcid®)</td>
<td>Duodenal ulcer Active</td>
<td>20 mg BID or 40 mg HS</td>
<td>20 mg Q 12 hr</td>
<td>CrCl &lt;10 mL/min - 20mghs</td>
<td>SCr, AST, ALT BUN, RBC, Platelets, WBC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20 gm HS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric ulcer Maintenance</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>40 mg HS</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Nizatidine (Axid®)</td>
<td>Duodenal ulcer Active</td>
<td>150 mg BID or 300 mg HS</td>
<td>CrCl 20-50mL/min - 150 mg qd</td>
<td>Scr, AST, ALT BUN, RBC, Platelets, WBC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>150 HS</td>
<td>CrCl &lt;20 mL/min - 150 mg qod</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric ulcer Maintenance</td>
<td>150 mg BID or 300 mg HS</td>
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<tr>
<td>Ranitidine (Zantac®)</td>
<td>Duodenal ulcer Active</td>
<td>150 mg BID or 300 mg HS</td>
<td>50 mg Q 6-8 hr</td>
<td>CrCl &lt;50mL/min - 150 mg qd</td>
<td>Scr, AST, ALT BUN, RBC, Platelets, WBC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>150 mg HS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric ulcer Maintenance</td>
<td>150 mg BID</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Mucosal Defense Enhancer</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Sucralfate (Carafate®)</td>
<td>Duodenal ulcer Active</td>
<td>1 gm QID or 2 gm BID</td>
<td>No adjustment recommended</td>
<td>Aluminum, BUN, SCr</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 gm BID</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Proton Pump Inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omeprazole (Prilosec®)</td>
<td>Duodenal ulcer</td>
<td>20-40 mg QD</td>
<td>No adjustment recommended</td>
<td>SCr, BUN, WBC, ALT, AST, CBC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric ulcer</td>
<td>20-40 mg QD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lansoprazole (Prevacid®)</td>
<td>Duodenal ulcer</td>
<td>15 mg QD</td>
<td>No adjustment recommended</td>
<td>SCr, BUN, WBC, ALT, AST, CBC</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastric ulcer</td>
<td>15 mg QD</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*ALT=alanine transamine, AST=aspartate transaminase, BUN=blood urea nitrogen, CBC=complete blood count, RBC=red blood cell count, SCr=serum creatinine, WBC=white blood cell count

Medications should be considered when alterations of bioavailability are believed to be critical. For treating active peptic ulceration, sucralfate should be taken on an empty stomach at least one hour before meals and at bedtime. See Table II for recommended dosages. Sucralfate is generally safe with the most common adverse effect being constipation.

**Misoprostol**

Discontinuing medications that can induce gastritis or ulcerations is extremely important in the therapeutic treatment and prevention of peptic ulcers. Misoprostol, a synthetic PGE1 analogue, is FDA approved for the prevention of NSAID-induced gastric ulcers and should be considered for those patients who absolutely need to use NSAIDs and are at a high risk for developing peptic ulcers. At doses above 200 mcg daily, misoprostol has both antisecretory and mucosal protective factors. Protective properties of misoprostol are due to its ability to increase bicarbonate and mucus production. The recommended dose of misoprostol approved for the prevention of NSAID-induced gastric ulcers is 200 mcg four times daily. Misoprostol does not interfere with the beneficial effects of NSAIDs. The most frequent side effects associated with misoprostol are abdominal pain and diarrhea. Approximately 25 to 40 percent of patients receiving
misoprostol develop diarrhea within two weeks of therapy and reduction of the dose may help to decrease the frequency and severity of the diarrhea. Other adverse effects associated with misoprostol include nausea, vomiting, and headache. Misoprostol can cause uterine contractions and subsequently belongs to Pregnancy Category X; therefore, it is contraindicated in pregnant women. Because of misoprostol abortifacient properties, it should not be initiated in women of childbearing potential until the possibility of pregnancy has been excluded and an effective method of contraception has been started within two weeks of starting the drug.

**Eradication of Helicobacter pylori**

Although H₂-receptor antagonists, proton pump inhibitors, antacids, and sucralfate have impressive healing rates, ulcer recurrence is common. Clinical trials have demonstrated that eradication of *H. pylori* not only results in healing of ulcers, but greatly reduces the risk of recurrence(22). Studies have suggested that the one-year recurrence rates of duodenal ulcer decreases from 70 to 90 percent with antisecretory agents to less than 15 percent after eradication of *H. pylori* infection(23,24). Furthermore, therapy for the eradication of *H. pylori* appears to be more cost effective than acid suppression therapy for treating duodenal and gastric ulcers(24).

Currently, the American College of Gastroenterology recommends that all patients diagnosed with *H. pylori* associated peptic ulcers receive antimicrobial therapy effective against this organism(22). The FDA has approved several regimens for the treatment of peptic ulcer disease. These include clarithromycin for two weeks plus concurrent omeprazole therapy for four weeks, clarithromycin for two weeks plus concurrent ranitidine bismuth citrate (Tritec®) therapy for four weeks, and concurrent bismuth, metronidazole, tetracycline for two weeks plus an antisecretory agent for four weeks. Eradication rates for these regimens are 70 to 80, 80 to 85 and 73 to 84 percent, respectively(22). Helidac®, a new product approved for *H. pylori* associated duodenal disease, is used in combination with an antisecretory agent. Helidac® is a 14-day blister kit containing bismuth subsalicylate and generic metronidazole and tetracycline. Each blister card contains a one day supply of medication (eight tablets of bismuth 262.4 mg, four tablets of metronidazole 250 mg, and four capsules of tetracycline 500 mg).

Examples of selected regimens which have undergone investigation can be found in Table III. The optimal therapy for eradication or duration of therapy is not known. Thus far, no single agent given as monotherapy for eradication has been proven efficacious. Because of poor results with monotherapy and the emergence of resistance to antimicrobials, combination antimicrobial regimens are more effective than single agents. Due to synergistic antimicrobial effects, therapies including proton pump inhibitors tend to have higher efficacy rates than those with H₂-receptor antagonists.

Reasons for treatment failures with antimicrobial therapy include the development of antibiotic resistance by the organism, adverse drug reactions and poor compliance to medication therapy. The use of multiple agents often results in the patient experiencing a greater number of side effects which may adversely affect compliance(25). Fortunately, most side effects are mild with only five percent of patients actually having to discontinue therapy(26). Severe side effects from *H. pylori* eradication therapies such as pseudomembranous colitis are infrequent; however, minor adverse effects may occur in up to 40 percent of patients. Reactions include diarrhea and candidiasis with amoxicillin; nausea, diarrhea and photosensitivity with tetracycline; nausea, diarrhea, metallic taste and a disulfiram-like reaction with metronidazole; metallic taste, diarrhea, nausea and headache with clarithromycin; and black stools and discoloration of the tongue with bismuth. In addition to adverse effects, many *H. pylori* eradication regimens require patients to take numerous tablets daily, thus making therapy cumbersome and often resulting in a decrease in patient compliance. This demonstrates the important role that pharmacists can play in treating patients with peptic ulcers. Pharmacists should encourage patients to comply with therapy and should educate patients as to what adverse effects are to be expected. Practitioners should take an individualized approach in treating patients with duodenal and gastric ulcers (see Appendix A and Figure 5). When designing eradication therapy, it is extremely important to consider the efficacy and safety profiles of the medications, patient compliance, patients prior exposure to antibiotics, and cost- effectiveness.

**PATIENT EDUCATION**

To promote efficacy and prevent adverse effects, patient counseling is necessary. The patient should be advised to take the medication as prescribed and for the entire duration of therapy. If the patient smokes cigarettes, it is important to counsel the patient on the adverse effects that smoking has on ulcer healing and advice patients that smoking should be

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**Table III. Common regimens used for *H. pylori* eradication and cure rates**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Cure rates (95% CI*)</th>
</tr>
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<tbody>
<tr>
<td>Amoxicillin 1 gm QD + Omeprazole 20 mg BID + Clarithromycin 500 mg BID for 7 days</td>
<td>86-91</td>
</tr>
<tr>
<td>Bismuth subsalicylate 2 tablets QID + Metronidazole 250 mg QID + Amoxicillin 500 mg QID for 7 days</td>
<td>75-81</td>
</tr>
<tr>
<td>Bismuth subsalicylate 2 tablets QID + Metronidazole 250 mg QID + Amoxicillin 500 mg QID for 14 days</td>
<td>80-86</td>
</tr>
<tr>
<td>Bismuth subsalicylate 2 tablets QID + Metronidazole 250 mg QID + Tetracycline 500 mg QID for 7 days</td>
<td>86-90</td>
</tr>
<tr>
<td>Bismuth subsalicylate 2 tablets QID + Metronidazole 250 mg QID + Tetracycline 500 mg QID for 14 days</td>
<td>88-90</td>
</tr>
<tr>
<td>Bismuth subsalicylate 2 tablets QID + Metronidazole 250 mg QID + Tetracycline 500 mg QID + Omeprazole 20 mg BID for 7 days</td>
<td>94-98</td>
</tr>
<tr>
<td>Clarithromycin 500 mg BID + Amoxicillin 1 gm BID + Lansoprazole 30 mg BID for 14 days</td>
<td>86-91</td>
</tr>
<tr>
<td>Clarithromycin 500 mg TID for 14 days + Omeprazole 20 mg BID for 14 days + then Omeprazole 20 mg qd for 14 days</td>
<td>83-90</td>
</tr>
<tr>
<td>Metronidazole 500 mg BID + Omeprazole 20 mg BID + Clarithromycin 500 mg BID for 7 days</td>
<td>87-91</td>
</tr>
<tr>
<td>Metronidazole 250 mg QID + Omeprazole 20 mg BID + Amoxicillin 1 gm QD for 7-14 days</td>
<td>77-83</td>
</tr>
<tr>
<td>Ranitidine Bismuth Citrate (Tritec®) 400 mg BID for 28 days + Clarithromycin 500 mg TID for 14 days</td>
<td>82-94</td>
</tr>
</tbody>
</table>

*CI= Confidence Interval*
The occurrence of duodenal and gastric ulcerations are common. Although agents such as H₂-receptor antagonists, proton pump inhibitors, antacids, and sucralfate have been used successfully to manage peptic ulcers, the recognition of H. pylori as a major culprit in the pathogenesis of peptic ulcers has significantly revolutionized the treatment of peptic ulcers. Eradication of this organism not only aids in ulcer healing but reduces ulcer recurrence. By eradicating H. pylori, many peptic ulcers can now be cured.


References
(24) Taylor, J.L., Zagari, M., Murphy, K. and Freson, J.M., “Pharmacoeconomic comparison of treatments for the eradication of...
APPENDIX A. PATIENT CASE STUDY

CC: "My stomach is killing me."
HPI: JB is a 63 y o man who presents to the clinic with a three week history of epigastric pain, a two day history of melena stools, and constipation. Several weeks ago, he noticed the gradual onset of a localized epigastric pain that has occurred daily, wavered in intensity, and increased at night. JB states that eating food or ingesting Titralac Plus® seems to decrease the pain. He denies any past history of peptic ulcer disease and GI bleeding.

PMH: Not significant
FH: Both parents are deceased. He has two siblings that are alive and well.
SH: He works as a carpenter, smokes approximately 1 pack of cigarettes per day, and is married with one child.

Meds: Titralac Plus® prn abdominal pain (several times daily)

Allergies: NKA
ROS: Unremarkable except for complaints noted above
PE:
GEN: BP136/80; P72; RR14 reg; Temp 37.2°C; Ht 180 cm, Wt 95 kg (84 kg 4 months ago)
HEENT: PERRLA; EOMI; discs flat; no AV nicking, hemor-rhages, or exudates
COR: S1 and S2 normal; no murmurs, rubs, or gallops
CHEST: Clear to auscultation and percussion
ABD: Normal bowel sounds and mild epigastric tenderness
RECT: Non-tender; black melenic stool found in rectal vault

LABS: sodium 140 mEq/L (135-147 mEq/L), potassium 4.2 Eq/L (3.5-5 mEq/L), chloride 104 mEq/L (95-105 mEq/L), carbon dioxide 26 mEq/L (22-28 mEq/L), BUN 10 mg/dL (8-18 mg/dL), serum creatinine 1.0 mg/dL (0.6-1.2 mg/dL), glucose 100 mg/dL (70-110 mg/dL), calcium 9.6 mg/dL (8.8-10 mg/dL), magnesium 2.0 mEq/L (1.6-2.4 meq/L), phosphorus 4.0 mg/dL (2.5-5.0 mg/dL), albumin 5.0 g/dL (4.6 g/dL), hemoglobin 15.2 g/dL (14-18 g/dL), hematocrit 48% (39%-49%), MCV 91 cuu (76-100 cuu), platelets 310,000 (150,000-450,000), WBC 7,500 (5,000-10,000), serum iron 95 mcg/dL (80-180 mcg/dL).

EGD: Two days after the initial clinic visit an EGD was performed and revealed a 4-mm ulcer in the wall of the duodenum (Figure 3). The ulcer base was clear and free of blood. Mild inflammation of the antrum and the stomach was noted and biopsied.

CLO-Test: Abundant Helicobacter pylori-like organisms.

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QUESTIONS AND ANSWERS:

1. What signs, symptoms, and tests indicate the presence of peptic ulcer disease?
   - Localized epigastric pain that appears to worsen at night and decreases by ingesting food or Titralac Plus®.
   - Melenic stools and blood detected in rectal vault.
   - EGD revealing a 4-mm ulcer in the duodenum.

2. Could any of JB’s problems be caused by drug therapy?
   - JB has a history of aspirin use for back pain. Aspirin may cause mucosal erosions and ulcerations of the gastrointestinal tract, especially the stomach and duodenum.
   - JB has also been using an antacid (Titralac Plus®) with a high calcium content, which may contribute to his constipation.

3. By reviewing JB’s past and current medical history, list the two most likely causes of his ulcer.
   - Aspirin use
   - Infection with Helicobacter pylori

4. What are the goals for treating JB’s peptic ulcer disease?
   - Relieve pain and discomfort associated with peptic ulcer.
   - Promote ulcer healing.
   - Prevent or treat complications of peptic ulcerations.
   - Eradicate Helicobacter pylori.
   - Prevent ulcer recurrences.
   - Educate JB about peptic ulcer disease to improve compliance and successful therapy.
   - Avoid adverse effects of medications.

5. Considering JB’s presentation, what non-pharmacologic alternatives are available to treat his peptic ulcer?
   - Since smoking is strongly correlated with delayed ulcer healing and recurrent disease, JB should be advised to stop smoking.
   - Ingestion of foods and liquids that contribute to epigastric pain should be limited or avoided.
   - Since mucosal damage has been reported with the use of aspirin, JB should be advised to stop taking aspirin therapy. If a medication for pain relief is needed, acetaminophen could be recommended.
   - Consider discontinuing Titralac Plus® because of its possible contribution to his constipation. If an antacid is desired, a product containing both magnesium and aluminum to minimize bowel function changes may be recommended.

6. What pharmacotherapeutic alternatives are available to treat JB?
   - Helicobacter pylori eradication therapy is needed. Selection of specific regimen should be based on cost effectiveness and JB’s compliance to medication therapy. See Tables II and III and Figure 5.

7. Design a pharmacotherapeutic regimen for JB.
   - Since JB is not allergic to any medications, an effective combination antibiotic regimen with an antisecretory agent is preferred (See Table III and Figure 5). It is also important to ascertain information from the patient concerning prior antibiotic use and adherence to medication therapy.
   - Discontinue aspirin use. If pain relief is needed, acetaminophen may be an appropriate alternative.
   - Please include the non-pharmacologic recommendations suggested earlier (see answer to Question 5). The need to be compliant to medication therapy should also be reinforced to JB.

8. In reference to JB’s duodenal ulcer, list the two major monitoring parameters.
   - Relief of epigastric pain
   - Resolution of complications (i.e., blood in stools).
   - For other possible monitoring parameters, refer back to goals of treatment (see answer to Question 4).