REVIEW

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Diagnosis and Treatment of Peptic Ulcer Disease

Robert T. Kavitt, MD, MPH,[a] Anna M. Lipowska, MD,[b] Adjoa Anyane-Yeboa, MD,[a] Ian M. Gralnek, MD, MSHS, FASGE[c,d]

[a]Section of Gastroenterology, Hepatology, and Nutrition, University of Chicago, Ill; [b]Division of Gastroenterology and Hepatology, University of Illinois at Chicago; [c]Institute of Gastroenterology, Hepatology, and Nutrition, Emek Medical Center, Afula, Israel; [d]Rappaport Faculty of Medicine, Technion—Israel Institute of Technology, Haifa, Israel.

ABSTRACT

Peptic ulcer disease continues to be a source of significant morbidity and mortality worldwide. Approximately two-thirds of patients found to have peptic ulcer disease are asymptomatic. In symptomatic patients, the most common presenting symptom of peptic ulcer disease is epigastric pain, which may be associated with dyspepsia, bloating, abdominal fullness, nausea, or early satiety. Most cases of peptic ulcer disease are associated with *Helicobacter pylori* infection or the use of nonsteroidal anti-inflammatory drugs (NSAIDs), or both. In this review, we discuss the role of proton pump inhibitors in the management of peptic ulcer disease, highlight the latest guidelines about the diagnosis and management of *H. pylori*, and discuss the latest evidence in the management of complications related to peptic ulcer disease, including endoscopic intervention for peptic ulcer-related bleeding. Timely diagnosis and treatment of peptic ulcer disease and its sequelae are crucial in order to minimize associated morbidity and mortality, as is prevention of peptic ulcer disease among patients at high risk, including those infected with *H. pylori* and users of NSAIDs.
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KEYWORDS: *Helicobacter pylori*; Peptic ulcer disease

INTRODUCTION

It was previously accepted as dogma that stress was the etiology of peptic ulcer disease, mediated via increased gastric acid production.[1] Until the late 1970s, peptic ulcers in the United States were treated with antacids and anticholinergics, and surgery was frequently necessary for the treatment of ulcer disease.[1] Histamine-2-receptor antagonists (H_2RAs) were introduced in 1976. Dr. J. Robin Warren had observed *Helicobacter pylori* (originally named *Campylobacter pyloridis*) in gastric biopsies,[2] and in 1982 Dr. Barry Marshall cultured *H. pylori* from patients with ulcers and gastritis.[3] However, it was not until 1994 that National Institutes of Health guidelines recommended the use of antibiotics in the treatment of patients with peptic ulcer disease attributed to *H. pylori*.[4] By the end of the 20th century, a decrease in the occurrence of peptic ulcer disease was observed.[5] The decrease in *H. pylori* infection rate in the population is assumed to have resulted from increasing hygiene standards.[5]

In this review we focus on an update about the diagnosis of peptic ulcer disease and highlight advances in treatment strategies in recent years.

EPIDEMIOLOGY AND ETIOLOGIC FACTORS

Peptic ulcer disease is a source of significant morbidity and mortality worldwide. Sequelae may range from abdominal pain and gastrointestinal bleeding to gastric outlet obstruction and perforation.

The prevalence of peptic ulcer disease in the United States is estimated to be 8.4%.[6] Higher peptic ulcer disease incidence has been found to be associated with male sex, smoking, and chronic medical conditions.[6,7] Peptic ulcer disease has also been found to be associated with increasing age.[8] Over time, a significant decrease in peptic ulcer disease diagnoses, as well as its associated complications, has been observed in both the United States and elsewhere in the world.[9-12]

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Requests for reprints should be addressed to Ian M. Gralnek, MD, MSHS, Institute of Gastroenterology, Hepatology, and Nutrition, Emek Medical Center, 21 Izhak Rabin Blvd., Afula 1834111, Israel.

E-mail address: ian_gr@clalit.org.il

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The majority of peptic ulcer disease cases are now known to be associated with *H. pylori* infection or the use of nonsteroidal antiinflammatory drugs (NSAIDs), or both.[13] *H. pylori* is a Gram-negative bacterium that colonizes the gastric mucosa, progressing to gastritis and potentially peptic ulcer disease and gastric cancer.[14,15] *H. pylori* affects a large segment of the population; however, only a small subset will develop clinical disease.[15] NSAID use, including aspirin, is common and leads to an increased risk of gastrointestinal adverse events, including peptic ulcer disease. The relative risk of developing a symptomatic ulcer is 4.0 for nonaspirin NSAID users and 2.9 for patients taking aspirin.[16]

While *H. pylori* and NSAID use are the cause of the vast majority of peptic ulcers, other less common causes have been identified, including gastrinoma (eg, Zollinger-Ellison syndrome), other medications, and other etiologies, as detailed in Table 1.[17-19]

CLINICAL SIGNIFICANCE

- Two-thirds of patients with peptic ulcer disease are asymptomatic; those with symptoms most commonly experience epigastric pain.
- Most cases of peptic ulcer disease are associated with *Helicobacter pylori* infection or nonsteroidal antiinflammatory drug use.
- Timely diagnosis and treatment of peptic ulcer disease is crucial.

CLINICAL MANIFESTATIONS AND DIAGNOSIS

A prospective study of patients in Taiwan undergoing a screening upper endoscopy as part of routine health maintenance determined that approximately two-thirds of those found to have peptic ulcer disease are asymptomatic.[20]

Among symptomatic patients with peptic ulcer disease, the most common presenting symptom is epigastric pain, which may be associated with dyspepsia, bloating, abdominal fullness, nausea, and early satiety.[21] In many patients, symptoms may be intermittent in nature.

It is imperative to obtain a detailed clinical history about NSAID use and any documented prior *H. pylori* infection. Upper endoscopy can be used to diagnose peptic ulcer disease and is of particular urgency in those with dyspepsia and concurrent alarm symptoms (eg, age >60 years, family history of upper gastrointestinal tract malignancy, weight loss, early satiety, dysphagia, gastrointestinal bleeding, iron deficiency anemia, or vomiting) (Figure 1).[22,23] Endoscopy with biopsy of peptic ulcers allows for characterization of a benign vs malignant etiology (Figure 2).

Diagnostic testing for *H. pylori* infection includes urea breath testing, stool antigen testing, rapid urease testing or histology of gastric biopsies taken at the time of upper endoscopy, and serologic testing (Table 2). In most circumstances, tests for active infection (urea breath testing, stool antigen testing, rapid urease testing, or histology) are preferable compared with serologic antibody testing due to low pretest probability of infection.[24] In those with documented peptic ulcer disease, serologic testing for *H. pylori* immunoglobulin G antibody is appropriate due to a higher pretest probability.[24] Those with a peptic ulcer disease history who have been treated for *H. pylori* in the past are advised to undergo testing for eradication with either stool antigen testing or urea breath testing.[24] Due to the possibility of false negative testing, testing to confirm eradication of *H. pylori* infection should be performed no sooner than 1 month after completing antibiotic treatment.[24]

ADVANCES IN TREATMENT

Role of Proton Pump Inhibitors in the Treatment of Peptic Ulcer Disease

Since their introduction into medical practice in the late 1980s, proton pump inhibitors (PPIs) have substantially changed the approach to peptic ulcer disease management. PPIs remain the mainstay of medical therapy for peptic ulcer-related gastrointestinal bleeding. Well-performed systematic reviews support the initiation of PPIs prior to endoscopic evaluation for acute upper gastrointestinal bleeding, although a clear mortality benefit has not been demonstrated.[25,26] The length of PPI administration following the diagnosis of a peptic ulcer depends on the underlying ulcer etiology, location, and associated complications. The ultimate goal of PPI therapy is to promote ulcer healing

Table 1 Risk Factors for Peptic Ulcer Disease

Helicobacter pylori infection	Significantly more common in developing nations May lead to both gastric and duodenal ulcers
Nonsteroidal antiinflammatory drugs	Includes acetylsalicylic acid (ASA) More commonly associated with gastric ulcers
Other medications	Co-administration of corticosteroids and bisphosphonates with NSAIDs; Sirolimus, selective serotonin reuptake inhibitors (SSRIs), 5-fluorouracil (5-FU)
Smoking	Synergistic effect between tobacco use and *H. pylori* infection
Neoplasms	Gastrinoma, gastric adenocarcinoma, carcinoid syndrome
Idiopathic	No cause identified despite thorough investigation

NSAID = nonsteroidal antiinflammatory drug.

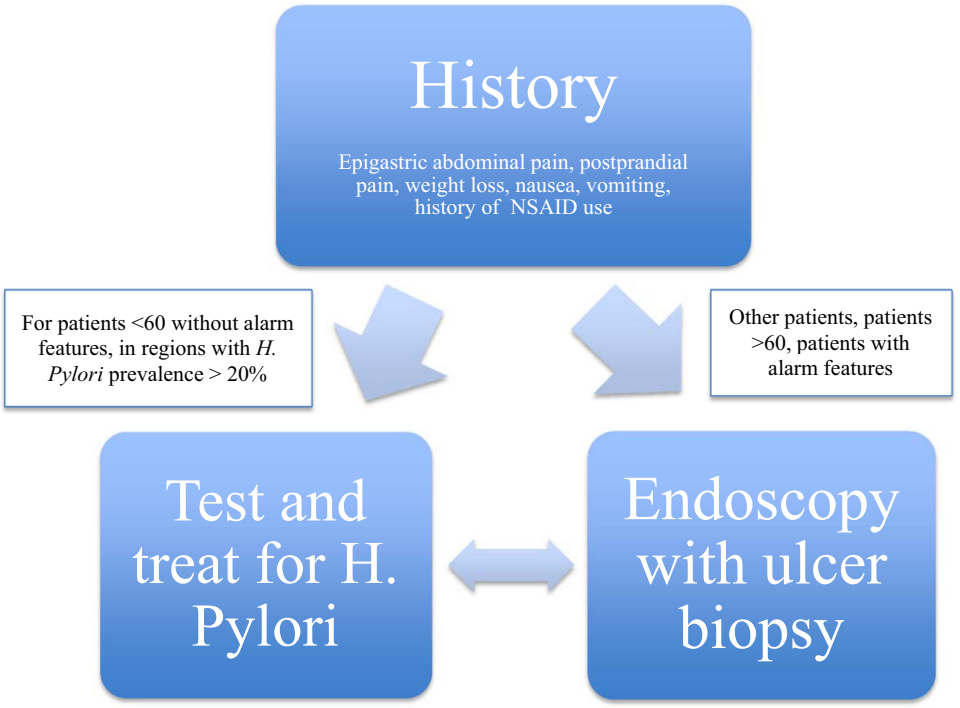

Figure 1 Diagnosis of peptic ulcer disease.

through acid suppression, while the underlying etiology of the ulcer(s) is addressed. Positive *H. pylori* testing prompts treatment of the infection, while patients with NSAID-induced ulcers are counseled to avoid the aggravating agents.[27] Patients with peptic ulcer disease who require ongoing NSAID therapy are recommended to remain on PPI co-therapy while on treatment.[28-30]

Concern over the long-term safety profile of PPI use has triggered changes in prescribing patterns and patient reluctance to pursue treatment.[31,32] Long-term PPI use inducing gastric hypochlorhydria and hypergastrinemia may have an adverse effect on absorption of calcium, iron, magnesium, and vitamin B12, and may predispose to infection.[33,34] Some studies have suggested an association between PPI use and community-acquired pneumonia, *Clostridium difficile* infection, and chronic kidney disease, among other conditions.[35-37] However, causality remains unclear, with low quality of evidence to date.[34] Physicians are advised to evaluate each patient individually, confirming the appropriate treatment indication and the lowest appropriate PPI dose for an appropriate duration of therapy.

Role of H_2 Receptor Antagonists in Peptic Ulcer Disease

In the era of PPI therapy, there is only a limited role for H_2RAs in the treatment of peptic ulcer disease. As early as the 1980s, as compared with H_2RAs, PPIs were demonstrated to improve rates of peptic ulcer healing.[38] A recent randomized controlled trial showed that famotidine failed to significantly reduce the incidence of peptic ulcers or bleeding from peptic ulcers in patients with a history of both atherosclerotic and peptic ulcer disease and who take a thienopyridine.[39]

When patients who are found to have an *H. pylori*-related ulcer undergo testing after antibiotic treatment to confirm *H. pylori* eradication, PPI use can lead to false negative test results. Therefore, it is recommended that patients switch to treatment with an H_2RA rather than a PPI for the 2 weeks prior to *H. pylori* eradication testing.

H. Pylori Treatment

The Maastricht V/Florence Consensus Report, released in 2017, presented evidence-based, consensus guidelines on the diagnosis and management of *H. pylori* infection.[40] This consensus report cites several meta-analyses illustrating increased *H. pylori* cure rates for 14-day triple therapy over 10-day triple therapy.[40] The authors advocate a 14-day *H. pylori* treatment course for bismuth- and non-bismuth-containing quadruple therapy as well as clarithromycin-based triple therapy (unless 10-day therapies are proven effective locally). Data supporting extending quadruple therapy from 10 to 14 days is not as robust, however, the guideline recommends a longer duration of antibiotic therapy, particularly in known areas of high resistance to metronidazole.

The American College of Gastroenterology (ACG) also published guidelines in 2017 about the diagnosis and treatment of *H. pylori* infection.[24] These guidelines also note that prior antibiotic exposure should be taken into account when choosing an *H. pylori* treatment regimen. The

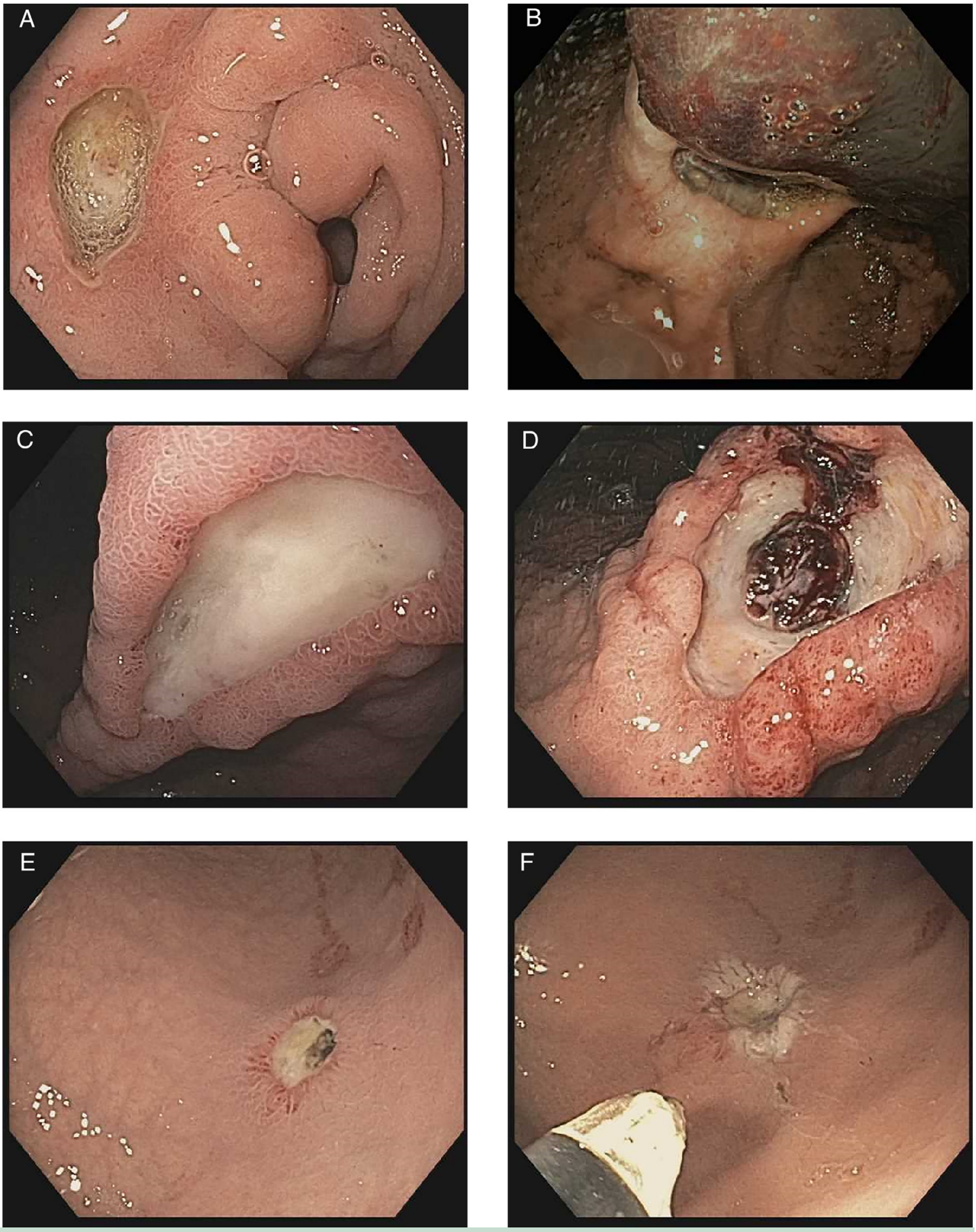

Figure 2 Endoscopic images of peptic ulcer disease. **(A)** Clean-based ulcer of gastric antrum. **(B)** Ulcer of incisura with adherent clot. **(C)** Large ulcer of incisura. **(D)** Gastric ulcer with adherent clot. **(E)** Gastric ulcer with nonbleeding visible vessel. **(F)** Gastric ulcer with nonbleeding visible vessel after thermal coagulation therapy.

Table 2 *Helicobacter Pylori* Diagnostic Tests

	Test	Mechanism	Efficacy	Notes
Nonendoscopic diagnostic tests				
	Urea breath test	Ingestion of urea in presence of isotope C13 or C14 causes CO_2 production, which is detected in expired breath	>95% sensitivity and specificity	Most expensive test, not widely available, can be used to test for eradication
	Stool antigen testing	*Helicobacter pylori* antigen detected in the stool by enzyme immunoassay using anti-*H. pylori* antibody	91%-96% sensitivity, 93%-97% specificity	Can be used to test for eradication, decreased sensitivity in bleeding peptic ulcer disease
	Antibody testing	Detects *H. pylori* immunoglobulin G antibodies in serum, blood, or urine	85% sensitivity, 79% specificity (if no prior exposure to *H. pylori*)	Stays positive for years after successful cure of the infection
Endoscopic biopsy-based tests				
	Rapid urease test	Gastric biopsies are placed in medium containing urea with a pH-sensitive indicator. In the presence of *H. pylori* urease, urea is metabolized and there is an increase in pH	>90% sensitivity, >95% specificity	Decreased sensitivity by acute ulcer bleeding, recommended that biopsies are taken from 2 sites in the stomach, decreased sensitivity with the use of bismuth-containing compounds, antibiotics, PPIs
	Histology	Detects pathologic changes associated with *H. pylori*	>95% sensitivity and specificity	

PPI = proton pump inhibitor.

guidelines recommend clarithromycin triple therapy with a PPI, clarithromycin, and amoxicillin or metronidazole for 14 days in areas of low (<15%) clarithromycin resistance and in those patients with no prior history of macrolide exposure. The guidelines further suggest bismuth quadruple therapy (PPI, bismuth, tetracycline, and a nitroimidazole) for 10-14 days as an additional first-line treatment option, particularly among patients with any prior macrolide exposure or those with a penicillin allergy.[24] Tables 3 and 4 highlight common first-line and salvage therapies for the treatment of *H. pylori* recommended by the ACG guidelines.[24]

Only limited data about modern *H. pylori* treatment regimen efficacy and *H. pylori* antibiotic resistance rates are available in the United States; thus, the majority of guideline recommendations are based on data from studies performed elsewhere in the world. First-line therapies offer the greatest likelihood of treatment success; however, it is unlikely that most regimens ever achieve >90% eradication success.[24] There are no organized efforts in the United States to track *H. pylori* antibiotic resistance patterns.[24]

Management of Complications of Peptic Ulcer Disease

Complications of peptic ulcer disease include bleeding, perforation, penetration, and gastric outlet obstruction.[41,42] Patient-specific risk factors associated with complicated peptic ulcer disease include use of NSAIDs including aspirin, *H. pylori* infection, smoking, and acid hypersecretory states (eg, Zollinger-Ellison syndrome). In addition, ulcer-specific characteristics such as chronicity/refractory type ulcers, large size (≥1 cm), and location (eg, pyloric channel) are associated with an increased risk of developing an ulcer complication. Factors associated with poor outcome in patients with complicated peptic ulcer disease include concomitant comorbid disease, older age, poor physiological status at the time of presentation (eg, hypotensive shock, metabolic acidosis, acute renal failure, hypoalbuminemia), and delayed treatment.[41]

Acute upper gastrointestinal hemorrhage is the most common complication of peptic ulcer disease and is associated with morbidity (mortality up to 10%) and high medical costs.[41,42] Upper endoscopy is the best initial test in suspected peptic ulcer bleeding because it is both diagnostic and, if required, therapeutic. Table 5[24] highlights the treatment of peptic ulcer disease prior to, during, and after endoscopy. Modern-day endoscopic hemostasis therapies include injection, thermal, mechanical, or a combination of these modalities.[43-45] Endoscopic hemostasis has been shown to be effective in achieving primary hemostasis and to significantly reduce ulcer re-bleeding, need for blood transfusion, urgent surgery, length of hospitalization, and mortality.[46] High-dose intravenous PPIs should be used for 72 hours post endoscopic hemostasis followed by oral PPI therapy.[43-45] Patients with recurrent bleeding should undergo repeat endoscopy with repeat endoscopic

Table 3 Common First-Line Therapies for Treating *Helicobacter Pylori* Infection

Treatment Regimen	Medication (Dose)	Dosing Frequency	Duration of Treatment
Clarithromycin-based triple (if clarithromycin resistance <15%)	PPI (standard or double dose)	Twice daily	14 days
	Clarithromycin (500 mg)	Twice daily	
	Amoxicillin (1 gm)	Twice daily	
Clarithromycin-based triple (if clarithromycin resistance <15%, penicillin allergy)	PPI (standard or double dose)	Twice daily	14 days
	Clarithromycin (500 mg)	Twice daily	
	Metronidazole (500 mg)	Three times daily	
Bismuth-based quadruple	PPI (standard dose)	Twice daily	10-14 days
	Bismuth subcitrate (120—300 mg) or subsalicylate (300 mg)	Four times daily	
	Tetracycline (50 0mg)	Four times daily	
	Metronidazole (250 mg-500 mg)	250 mg 4 times daily or 500 mg 3 times daily	
Concomitant (non-bismuth-based quadruple)	PPI (standard dose)	Twice daily	10-14 days
	Clarithromycin (500 mg)	Twice daily	
	Amoxicillin (1 gm)	Twice daily	
	Metronidazole (500 mg) or Tinidazole (500 mg)	Twice daily	
Sequential	PPI (standard dose) + Amoxicillin (1 gm)	Twice daily	5-7 days
	PPI (standard dose) + Clarithromycin (500 mg) + Metronidazole (500 mg) or Tinidazole (500 mg)	Twice daily	5-7 days

PPI = proton pump inhibitor.

Note: Adapted from the American College of Gastroenterology Clinical Guideline: Treatment of *Helicobacter pylori* Infection.[24] Note that the only FDA-approved regimens are clarithromycin triple-therapy with amoxicillin and Pylera (Allergan USA, Inc, Madison, NJ), a combination product containing bismuth-based quadruple therapy.

hemostasis.[43-45] Those patients who again fail endoscopic hemostasis should be referred for interventional radiology evaluation (eg, multi-detector computed tomography angiography ± transcatheter angiography) and treatment.[47] The role of surgery in the treatment of peptic ulcer bleeding has significantly diminished over the past 2 decades and is now used when interventional radiology services are unavailable or other therapeutic interventions have failed. Comprehensive, evidence-based guidelines for the evaluation and treatment of peptic ulcer bleeding are widely available.[43-45]

Perforated peptic ulcer is a medical emergency with associated mortality of up to 30%.[48-50] Perforated peptic

Table 4 Common Salvage Therapies for Treating *Helicobacter Pylori* Infection

Treatment Regimen	Medication (Dose)	Dosing Frequency	Duration of Treatment
Bismuth-based quadruple	PPI (standard dose)	Twice daily	14 days
	Bismuth subcitrate (120—300 mg) or subsalicylate (300 mg)	Four times daily	
	Tetracycline (500 mg)	Four times daily	
	Metronidazole (500 mg)	Three times daily or 4 times daily	
Fluoroquinolone-based triple	PPI (standard dose)	Twice daily	14 days
	Levofloxacin (500 mg)	Once daily	
	Amoxicillin (1 gm)	Twice daily	
Concomitant (non-bismuth-based quadruple)	PPI (standard dose)	Twice daily	10-14 days
	Clarithromycin (500 mg)	Twice daily	
	Amoxicillin (1 gm)	Twice daily	
	Metronidazole (500 mg) or tinidazole (500 mg)	Twice daily or 3 times daily	
Rifabutin-based triple	PPI (standard dose)	Twice daily	10 days
	Rifabutin (300 mg)	Once daily	
	Amoxicillin (1 gm)	Twice daily	

PPI = proton pump inhibitor.

Note: Adapted from American College of Gastroenterology Clinical Guideline: Treatment of *Helicobacter pylori* Infection.[24] After failure of second-line treatment, culture with susceptibility testing to guide treatment. Note that the only US Food and Drug Administration-approved regimen is Pylera (Allergan USA, Inc, Madison, NJ), a combination product containing bismuth-based quadruple therapy.

Table 5 Treatment for Peptic Ulcer Disease

Treatment for Peptic Ulcer Disease		
Prior to Endoscopy	During Endoscopy	After Endoscopy
Assess hemodynamic stability and provide resuscitation	Perform endoscopic procedure within 24 hours of presentation following resuscitation and optimization of other medical problems	If high-risk stigmata is present on endoscopy, treat with high-dose intravenous PPI for 72 hours
Administer blood transfusion to target hemoglobin ≥7 g/dL	Assess for high-risk peptic ulcer stigmata including active bleeding, visible vessel, or adherent clot	Repeat endoscopy if there is evidence of recurrent bleeding
Utilize the Glasgow-Blatchford Score for risk stratification. If the score is zero, consider early discharge without intervention	Carry out endoscopic therapy if active bleeding or visible vessel are identified	Avoid routine second-look endoscopy after initial endoscopic therapy
Evaluate for coagulopathy and consider discontinuation of blood-thinning medications if evidence of bleeding is present	Add a second modality of treatment, such as thermal therapy or clipping, to epinephrine injection	Refer to surgery or interventional radiology if there is rebleeding after second endoscopic therapy
Stop NSAID drugs		Closely assess need for NSAIDs in those with NSAID-associated ulcers
Consider use of prokinetic drugs to aid in visualization and decrease need for repeat endoscopy		Treat for *Helicobacter pylori* infection if applicable
Initiate PPI intravenous therapy prior to endoscopic intervention to decrease likelihood of high-risk stigmata presence during endoscopy		Continue long-term PPI therapy in those with idiopathic peptic ulcers

NSAID = nonsteroidal antiinflammatory drugs; PPI = proton pump inhibitor.
From Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of *Helicobacter pylori* Infection. *Am J Gastroenterol.* 2017;112 (2):212-239.

ulcer should be suspected in patients presenting with acute, diffuse, severe, abdominal pain.[48,49] The classic triad of sudden onset of abdominal pain, tachycardia, and abdominal rigidity is the hallmark of peptic ulcer perforation.[48] Physical examination can demonstrate abdominal distension, tenderness to palpation, guarding, and rebound when peritonitis is present. Leukocytosis and fever may be present. Plain film chest x-ray studies (upright) may miss sub-diaphragmatic free air in up to 15% of cases in patients with bowel perforation.[49] Abdominal computed tomography is more sensitive (98% sensitivity) in detecting small amounts of free air and has thus become the imaging modality of choice in suspected perforated peptic ulcer.[48] Initial management includes nil per os status, nasogastric suction, fluid resuscitation, PPI, broad-spectrum antibiotics, and immediate surgical consultation. Early diagnosis, prompt hemodynamic resuscitation, and urgent surgical intervention are imperative to improve patient outcomes. Delay to surgery has consistently been shown to be associated with increased mortality.[48-50]

Peptic ulcer penetration is defined as the penetration of an ulcer through the bowel wall into an adjacent organ or anatomic structure without free air perforation or leakage of bowel contents into the peritoneal cavity. Penetration occurs most commonly with gastric antral ulcers and duodenal ulcers. Penetration may occur into the pancreas, biliary tract, omentum, liver, vascular structures (eg, aorto-enteric fistula), and the colon. Pyloric channel or prepyloric peptic ulcers may penetrate directly into the duodenal bulb, creating a gastroduodenal fistula, creating an acquired "double" pylorus.[51] Complications of ulcer penetration into adjacent anatomic structures include abscess formation, exsanguinating hemorrhage, hemobilia, hyperamylasemia, and rarely, pancreatitis.

Gastric outlet obstruction is the least common complication of peptic ulcer disease, yet when it does occur, is most often associated with a duodenal or pyloric channel ulcer. However, with the decreasing incidence of peptic ulcer disease, upper gastrointestinal tract malignancy may now be a more common cause of gastric outlet obstruction. Clinical manifestations include bloating, nausea, vomiting, early satiety, anorexia, epigastric distress, and weight loss.[52,53] The diagnosis is usually made with upper endoscopy and biopsy, especially to exclude malignancy.[52] In selected cases, computed tomography or surgical evaluation may be necessary to obtain a definitive diagnosis when malignancy is suspected and endoscopic biopsies are unrevealing. Treatment of patients with gastric outlet obstruction due to a benign cause, and who are thought to have reversible factors, may be achieved with medical therapy (eg, intensive antisecretory therapy initially using high-dose intravenous PPI, and then oral PPI if responsive). Patients not responding to medical therapy should be considered for endoscopic therapy (eg, balloon dilatation or biodegradable stent).[52,53] However, in patients with fibrosis and scarring, endoscopic

therapy may be inadequate and thus, elective surgery (eg, pyloroplasty or gastrojejunostomy drainage procedures) may be preferred.

Prevention of Peptic Ulcer Disease

NSAID use increases the risk of rebleeding in patients with prior peptic ulcer disease. The ACG 2012 guideline about the management of patients with ulcer bleeding advises careful assessment of the need for ongoing NSAID use in patients with a history of peptic ulcer and permanent NSAID discontinuation if possible.[44] If a patient is unable to discontinue NSAIDs, it is recommended that a cyclooxygenase (COX)-2 selective NSAID be used at the lowest effective dose in conjunction with a PPI.[44] The risk of rebleeding is decreased by the use of a COX-2 selective NSAID in conjunction with a proton pump inhibitor, and this is thought to be due to decreased effects of COX-1 on the gastrointestinal mucosa.[54,55]

Furthermore, the risk of rebleeding with concomitant NSAID use and *H. pylori* infection is higher than the risk of bleeding with NSAID use alone.[56] For patients with *H. pylori* infection who cannot discontinue NSAIDs, rebleeding rates are reduced with eradication of *H. pylori* infection in combination with long-term PPI therapy.[57] For patients with peptic ulcer disease due to *H. pylori* alone, treatment of *H. pylori* is sufficient and these patients do not require long-term PPI therapy.[44]

Aspirin is also significantly associated with peptic ulcer disease and bleeding. In one study, the relative risk of bleeding with low-dose aspirin was 1.80 (95% confidence interval, 1.59-2.03) as compared with placebo.[58] However, in patients who take aspirin for the secondary prevention of cardiovascular and cerebrovascular disease, there is a significant decrease in mortality for those who restart aspirin soon after hospital discharge. One study found a significant increase in the risk of death and cardiovascular events within the first 6 months in patients with cardiovascular comorbidities who discontinued aspirin after hospitalization for peptic ulcer bleeding, in comparison with those who reinitiated aspirin at hospital discharge (31% vs 8%).[59] A 2011 randomized controlled trial found that among patients taking low-dose aspirin who underwent endoscopic hemostatic therapy for peptic ulcer disease bleeding, continuous aspirin therapy may increase the risk of recurrent peptic ulcer disease bleeding but potentially may reduce mortality rates.[60] For this reason, the ACG guidelines advise that aspirin be restarted as soon as possible in patients who take aspirin for secondary prevention. Ideally, aspirin should be restarted within 1-3 days, and no later than 7 days, in these patients[43,61] Aspirin therapy should be given in conjunction with a PPI. In most cases, aspirin taken for primary prevention should not be resumed unless clearly indicated, and ongoing need should be assessed on a case-by-case basis.[44]

The management of idiopathic ulcers (eg, *H. pylori* negative, non-NSAID, non-aspirin-associated ulcers) is less clear. The relative risk of rebleeding and mortality is higher in patients with *H. pylori*-negative idiopathic ulcers than in *H. pylori*-positive controls.[62] The ACG guidelines conditionally recommend daily PPI therapy for these patients, however, data are quite limited.[44]

CONCLUSIONS

Timely diagnosis and management of peptic ulcer disease and its sequelae are crucial, as is prevention of peptic ulcer disease among patients at high risk. Prompt diagnosis of *H. pylori* and initiation of appropriate therapy is important, as is cautious use of NSAIDs.

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