Peptic ulcer disease: Clinical manifestations and diagnosis

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INTRODUCTION

A peptic ulcer is a defect in the gastric or duodenal mucosa that extends through the muscularis mucosa into the deeper layers of the wall. Peptic ulcers may present with dyspeptic or other gastrointestinal symptoms, or may be initially asymptomatic and then present with complications such as hemorrhage or perforation. This topic will review the clinical manifestations and diagnosis of peptic ulcer disease. The etiology, complications, and management of peptic ulcer disease are discussed in detail, separately. (See "Peptic ulcer disease: Epidemiology, etiology, and pathogenesis" and "Overview of complications of peptic ulcer disease" and "Peptic ulcer disease: Treatment and secondary prevention" and "Approach to refractory peptic ulcer disease" and "Surgical management of peptic ulcer disease".)

CLINICAL MANIFESTATIONS

Asymptomatic — Approximately 70 percent of peptic ulcers are asymptomatic [1]. Patients with silent peptic ulcers may later present with ulcer-related complications such as hemorrhage or perforation. Between 43 and 87 percent of patients with bleeding peptic ulcers present without antecedent dyspepsia or other heralding gastrointestinal symptoms [2-4]. Older adults and individuals on nonsteroidal anti-inflammatory drugs are more likely to be asymptomatic

from their ulcers and later present with ulcer complications [3,5-7]. (See 'Ulcer complications' below.)

Symptomatic

Abdominal pain — Upper abdominal pain or discomfort is the most prominent symptom in patients with peptic ulcers. Approximately 80 percent of patients with endoscopically diagnosed ulcers have epigastric pain [5]. Occasionally the discomfort localizes to the right or left upper quadrants of the hypochondrium [8]. Radiation of pain to the back may occur, but back pain as the primary symptom is atypical. In untreated patients, pain can last a few weeks followed by symptom-free periods of weeks or months. The "classic" pain of duodenal ulcers occurs two to five hours after a meal when acid is secreted in the absence of a food buffer, and at night (between about 11 PM and 2 AM) when the circadian pattern of acid secretion is maximal [9].

Patients with peptic ulcers, and particularly pyloric channel ulcers, may have food-provoked symptoms due to visceral sensitization and gastroduodenal dysmotility [2]. These symptoms include epigastric pain that worsens with eating, postprandial belching and epigastric fullness, early satiety, fatty food intolerance, nausea, and occasional vomiting [2,5].

Associated symptoms — Patients may have associated symptoms of bloating, abdominal fullness, nausea, and early satiety that may be provoked by eating. Gastroesophageal reflux may coexist but may or may not be related to the peptic ulcers. In one systematic review that included 33 studies of patients with endoscopically diagnosed peptic ulcer disease, the average prevalence of heartburn or acid regurgitation was 46 percent [5].

Ulcer complications — Complications may be heralded by new ulcer symptoms or a change in symptoms or may occur in the absence of typical symptoms. (See "Overview of complications of peptic ulcer disease", section on 'Clinical presentation'.)

Bleeding — Acute upper gastrointestinal hemorrhage is the most common complication of peptic ulcer disease. Patients with bleeding from a peptic ulcer may present with nausea, hematemesis (either red blood or coffee-ground emesis), or melena (black, tarry stool). In rare cases, patients have massive bleeding and present with hematochezia (red or maroon blood in the stool) and orthostatic hypotension (picture 1). (See "Causes of upper gastrointestinal bleeding in adults", section on 'Peptic ulcer disease'.)

Gastric outlet obstruction — Ulcers located in the pyloric channel or duodenum may cause gastric outlet obstruction. Symptoms include early satiety, bloating, indigestion, anorexia, nausea, vomiting, epigastric pain shortly after eating, and weight loss. (See "Gastric outlet obstruction in adults", section on 'Clinical manifestations'.)

Penetration and fistulization — Peptic ulcers may penetrate through the bowel wall without a free perforation or leakage of luminal contents into the peritoneal cavity. Pyloric channel or prepyloric peptic ulcers may penetrate directly into the duodenal bulb, creating a gastroduodenal fistula, resulting in an acquired "double" pylorus.

The pain of penetration typically becomes more intense, of longer duration, and is frequently referred to the lower thoracic or upper lumbar spine region. Penetrating posterior ulcers classically present with a shift from the typical vague visceral discomfort to a more localized and intense pain that is felt in the back and is not relieved by food or antacids. This change in symptom pattern may be gradual or sudden.

Patients with penetrating ulcers often present with a change in symptoms due to symptomatic involvement of adjacent structures.

- Gastrocolic or duodenocolic fistulas can present with halitosis, feculent vomiting, postprandial diarrhea, dyspepsia, and weight loss.
- Penetration into a surrounding organ can result in an abscess.
- Penetration into vascular structures can result in exsanguinating hemorrhage (eg, aortoenteric fistula or penetration into the cystic artery) [10-12].
- Penetration into the biliary tree can result in a choledochoduodenal fistula, extrahepatic biliary obstruction, or hemobilia [13,14].
- Fistulization into the pancreatic duct has also been reported with penetrating duodenal ulcers [15]. Mild hyperamylasemia can develop with posterior penetration of either a gastric or duodenal ulcer, but clinical pancreatitis is uncommon.

Perforation — Perforations complicate 2 to 10 percent of patients with peptic ulcer disease [16]. Ulcer perforation should be suspected in patients who suddenly develop severe, diffuse abdominal pain. A classic triad of sudden onset of abdominal pain, tachycardia, and abdominal rigidity is the hallmark of peptic ulcer perforation. Prepyloric gastric ulcerations account for most perforations followed by duodenal bulb ulcers [17]. (See "Overview of gastrointestinal tract perforation", section on 'Presentations'.)

Laboratory findings — Most patients with uncomplicated peptic ulcers have a normal complete blood count. Patients may have iron deficiency anemia due to recurrent gastrointestinal blood loss. Patients with acute gastrointestinal perforation may have leukocytosis.

Imaging findings — The two direct signs of peptic ulcer disease on abdominal computed tomography scan include focal discontinuity of the mucosal hyperenhancement, which reflects disease reaching the muscularis mucosa, and identification of luminal outpouching. Luminal outpouching corresponds to the ulcer crater which extends through and beyond the gastroduodenal wall [18]. Other non-specific signs include gastric wall thickening, perigastric or periduodenal inflammation, and mucosal enhancement in a focal area [19]. Abdominal CT is not sensitive for uncomplicated peptic ulcer disease and superficial ulcers may be missed [20].

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of peptic ulcer disease consists of other causes of dyspepsia and includes drug-induced dyspepsia, biliary disease, gastric malignancy, and less commonly, chronic pancreatitis. These conditions can be excluded from peptic ulcer disease by upper endoscopy. The diagnostic evaluation of a patient with upper abdominal pain and dyspepsia are discussed in detail, separately. (See "Approach to the adult with dyspepsia" and "Evaluation of the adult with abdominal pain", section on 'Epigastric pain'.)

DIAGNOSIS

The diagnosis of peptic ulcer disease is suspected in patients with dyspepsia, especially in the setting of nonsteroidal anti-inflammatory drug (NSAID) use or a history of *Helicobacter pylori* (*H. pylori*) infection. Occasionally peptic ulcers may be suspected based on imaging performed for evaluation of abdominal pain. The diagnosis of peptic ulcer disease is definitively established by direct visualization of the ulcer on upper endoscopy.

Upper endoscopy — Endoscopy is the most accurate diagnostic test for peptic ulcer disease (picture 2). The sensitivity of upper endoscopy in the detection of gastroduodenal lesions is approximately 90 percent but varies based on the location of the ulcer and the experience of the endoscopist [21,22].

Indications for ulcer biopsy

Malignant appearing ulcers — All ulcers with malignant features should be biopsied. Endoscopic features that suggest that an ulcer may be malignant include:

- An ulcerated mass protruding into the lumen
- Folds surrounding the ulcer crater that are nodular, clubbed, fused, or stop short of the ulcer margin

- Overhanging, irregular, or thickened ulcer margins

Selected benign appearing ulcers — On upper endoscopy, benign ulcers have smooth, regular, rounded edges, with a flat, smooth ulcer base often filled with exudate. Routine biopsy of benign-appearing duodenal ulcers is not recommended, as they are unlikely to harbor malignancy.

However, in areas with high gastric cancer incidence, all gastric ulcers should be biopsied. Whether to biopsy benign-appearing gastric ulcers in areas of low gastric cancer incidence is controversial. While we generally biopsy benign-appearing gastric ulcers at the index upper endoscopy as they may harbor malignancy; other experts do not biopsy gastric ulcers if the patient's history and demographic features suggest a low-risk of gastric cancer (eg, a young patient in the United States with a history of NSAID use and a shallow, flat antral ulcer) [23]. (See "Clinical features, diagnosis, and staging of gastric cancer".)

Specific etiology suspected — In patients with some systemic infiltrative or inflammatory conditions (eg, sarcoidosis, Crohn disease, eosinophilic gastroenteritis), peptic ulcers may be due to gastric or duodenal involvement by these conditions. In such cases, biopsies of the peptic ulcer and surrounding mucosa may be helpful to confirm the suspected etiology. (See "Unusual causes of peptic ulcer disease", section on 'Inflammatory and infiltrating disease'.)

Ulcer biopsy technique — If biopsies of an ulcer are indicated, we obtain samples from all four quadrants of the ulcer. If there are endoscopic features suspicious for malignancy, we obtain biopsies using jumbo forceps with more extensive sampling along the edges of the ulcer. We do not routinely perform cytology as this adds little to the diagnostic yield.

Biopsy for H. pylori — Gastric mucosal biopsy from the gastric antrum and body should be obtained to exclude *H. pylori* in patients undergoing upper endoscopy for peptic ulcer disease unless it is impractical or difficult, such as with a blood-filled stomach. In such cases, testing should be performed when possible to exclude *H. pylori*. Serology may also be used in this setting to make a diagnosis of *H. pylori* infection. (See 'Exclude Helicobacter pylori (H. pylori) infection' below and "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Patient undergoing upper endoscopy'.)

ESTABLISHING THE ETIOLOGY

Exclude Helicobacter pylori (H. pylori) infection — All patients diagnosed with peptic ulcer disease should undergo testing for *H. pylori* infection.

- Patients with evidence of *H. pylori* on biopsy should receive eradication therapy. However, in patients with active bleeding, a negative biopsy result does not exclude *H. pylori*, and another test (ideally a urea breath test or a stool antigen test for *H. pylori*) should be performed to confirm a negative result, but these tests may be difficult to perform in the setting of gastrointestinal bleeding. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Urea breath testing'.)

- If a gastric mucosal biopsy is not obtained at the time of endoscopy, in the absence of active GI bleeding we perform a urea breath test or stool antigen assay to diagnose *H. pylori.* (See "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Noninvasive testing'.)

- In patients who receive treatment for *H. pylori,* eradication of infection should be confirmed four or more weeks after the completion of therapy [24]. (See "Indications and diagnostic tests for Helicobacter pylori infection in adults", section on 'Confirm eradication in all patients'.)

Evaluate for nonsteroidal anti-inflammatory drug (NSAID) and corticosteroid use — A history of NSAID use should be sought. Urine salicylate levels are not helpful for the detection of low-dose aspirin use or other widely used NSAIDs. Testing for individual agents is possible but is not practical and is limited by its expense.

A large retrospective study that included 8894 patients found that 7 to 28 days of exposure to moderate or high doses of corticosteroids increased the risk of ulcer disease in a dose-dependent manner and that the risk was higher when non-selective NSAIDs or aspirin were used concurrently. Corticosteroids may contribute to a refractory ulcer state [25].

Additional evaluation in selected patients — Other causes of peptic ulcer disease should be considered when *H. pylori* and use of NSAIDs have been excluded. Unusual causes for peptic ulcer disease and the evaluation for *H. pylori* and NSAID negative ulcers is discussed in detail, separately. (See "Unusual causes of peptic ulcer disease", section on 'Evaluation of H. pylori and NSAID negative ulcers'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Peptic ulcer disease".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Peptic ulcers (The Basics)" and "Patient education: H. pylori infection (The Basics)" and "Patient education: Gastritis (The Basics)")
- Beyond the Basics topics (see "Patient education: Peptic ulcer disease (Beyond the Basics)" and "Patient education: Helicobacter pylori infection and treatment (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Clinical manifestations** – Peptic ulcers are commonly asymptomatic. Symptomatic peptic ulcers most commonly present with epigastric pain or food-provoked epigastric discomfort and fullness, early satiety, and nausea. (See 'Clinical manifestations' above.)
- **Complications** – Complications may be heralded by new ulcer symptoms or a change in symptoms, or may occur in the absence of typical symptoms. Complications of peptic ulcers include bleeding, gastric outlet obstruction, penetration into a solid organ or fistulization into a hollow viscus, and free perforation. (See 'Ulcer complications' above.)
- **Imaging findings** – The two direct signs of peptic ulcer disease on abdominal computed tomography scan include focal discontinuity of the mucosal hyperenhancement and luminal outpouching. (See 'Imaging findings' above.)
- **Diagnosis** – The diagnosis of peptic ulcer disease is suspected in patients with dyspepsia, especially in the setting of nonsteroidal anti-inflammatory drug (NSAID) use or a history of *Helicobacter pylori* (*H. pylori*) infection. Occasionally peptic ulcers may be diagnosed or

suspected based on contrast imaging performed for evaluation of abdominal pain. The diagnosis of peptic ulcer disease is definitively established by direct visualization of the ulcer on upper endoscopy. On upper endoscopy, benign ulcers have smooth, regular, rounded edges, with a flat, smooth ulcer base often filled with exudate (picture 2).

- **Endoscopic features of malignant ulcers** – All ulcers with malignant features should be biopsied. Endoscopic features that suggest that an ulcer may be malignant include:
  - An ulcerated mass protruding into the lumen
  - Folds surrounding the ulcer crater that are nodular, clubbed, fused, or stop short of the ulcer margin
  - Overhanging, irregular, or thickened ulcer margins
- **Indications for biopsy of peptic ulcers** – Routine biopsy of benign-appearing duodenal ulcers is not recommended as they are unlikely to be malignant. In areas with high gastric cancer incidence, gastric ulcers should be biopsied. The decision to biopsy benign-appearing gastric ulcers in areas of low gastric cancer incidence is controversial. Although we biopsy benign-appearing gastric ulcers at the index upper endoscopy as they may harbor malignancy, other experts do not biopsy gastric ulcers if the patient's history and demographic features suggest a low risk of gastric cancer (eg, young patient with a history of NSAID use and a shallow flat antral ulcer). (See 'Diagnosis' above.)
- **Determining the underlying etiology** – All patients diagnosed with peptic ulcer disease should undergo testing for *H. pylori* infection. Additional evaluation to determine the underlying etiology should be considered when *H. pylori* and NSAID use have been excluded. (See 'Establishing the etiology' above.)

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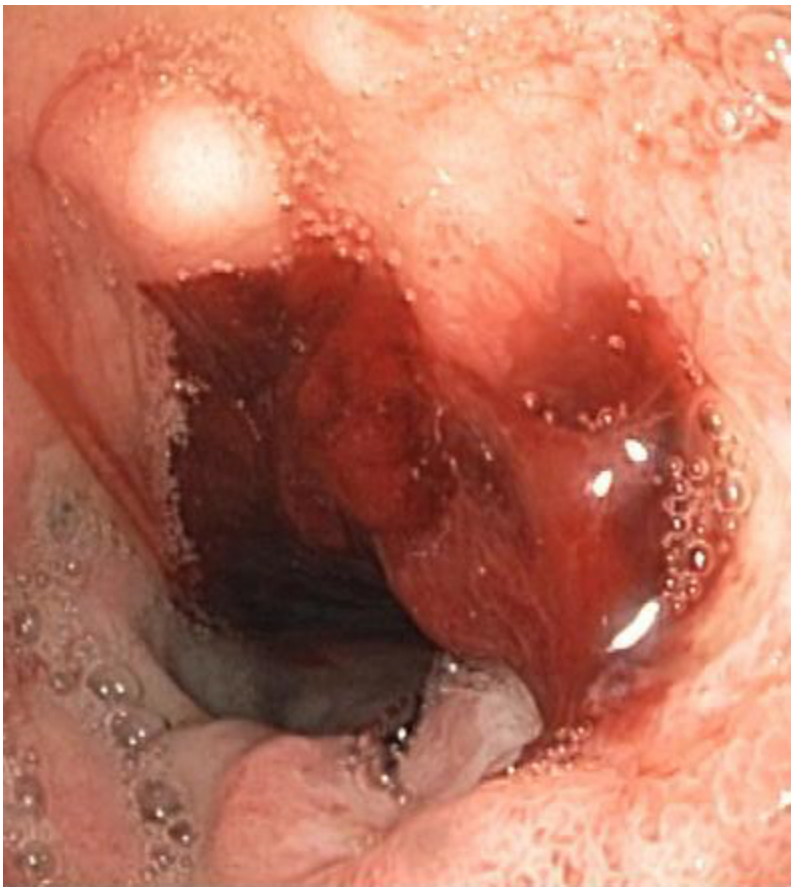
GRAPHICS

Duodenal ulcer

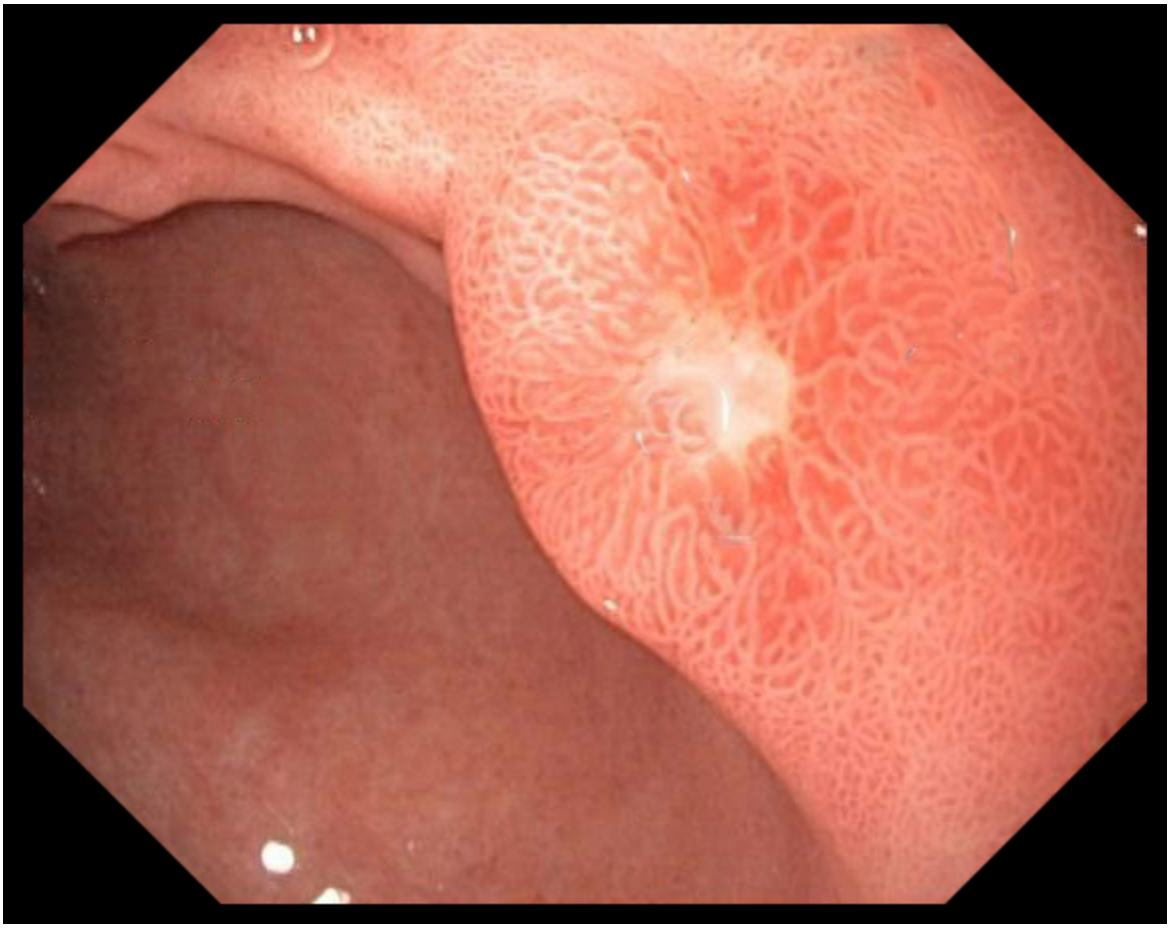


Duodenal ulcer with a small amount of fresh blood oozing from the edge.

Courtesy of Nimish Vakil, MD.

Graphic 63114 Version 4.0

Gastric ulcer



Note the clean white base in the ulcer crater with no evidence of active bleeding.

Courtesy of Nimish Vakil, MD.

Graphic 103830 Version 1.0

Contributor Disclosures

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