

TABLE 348-1 CAUSES OF ULCERS NOT CAUSED BY *HELICOBACTER PYLORI* AND NSAIDs

Pathogenesis of Non-Hp and Non-NSAID Ulcer Disease	
Infection	
	Cytomegalovirus
	Herpes simplex virus
	<i>Helicobacter heilmannii</i>
Drug/Toxin	
	Bisphosphonates
	Chemotherapy
	Clopidogrel
	Crack cocaine
	Glucocorticoids (when combined with NSAIDs)
	Mycophenolate mofetil
	Potassium chloride
Miscellaneous	
	Basophilia in myeloproliferative disease
	Duodenal obstruction (e.g., annular pancreas)
	Infiltrating disease
	Ischemia
	Radiation therapy
	Eosinophilic infiltration
	Sarcoidosis
	Crohn's disease
	Idiopathic hypersecretory state

Abbreviations: Hp, *H. pylori*; NSAIDs, nonsteroidal anti-inflammatory drugs.

not related to *H. pylori* or NSAIDs is increasing. Other less common causes of PUD are shown in **Table 348-1**. These etiologic agents should be considered as the incidence of *H. pylori* is decreasing. Independent of the inciting or injurious agent, peptic ulcers develop as a result of an imbalance between mucosal protection/repair and aggressive factors. Gastric acid plays an important role in mucosal injury.

CLINICAL FEATURES

History Abdominal pain is common to many GI disorders, including DU and GU, but has a poor predictive value for the presence of either DU or GU. Up to 10% of patients with NSAID-induced mucosal disease can present with a complication (bleeding, perforation, and obstruction) without antecedent symptoms. Despite this poor correlation, a careful history and physical examination are essential components of the approach to a patient suspected of having peptic ulcers.

Epigastric pain described as a burning or gnawing discomfort can be present in both DU and GU. The discomfort is also described as an ill-defined, aching sensation or as hunger pain. The typical pain pattern in DU occurs 90 minutes to 3 hours after a meal and is frequently relieved by antacids or food. Pain that awakes the patient from sleep (between midnight and 3 A.M.) is the most discriminating symptom, with two-thirds of DU patients describing this complaint. Unfortunately, this symptom is also present in one-third of patients with NUD (see below). Elderly patients are less likely to have abdominal pain as a manifestation of PUD and may instead present with a complication such as ulcer bleeding or perforation. The pain pattern in GU patients may be different from that in DU patients, where discomfort may actually be precipitated by food. Nausea and weight loss occur more commonly in GU patients. Endoscopy detects ulcers in <30% of patients who have dyspepsia.

The mechanism for development of abdominal pain in ulcer patients is unknown. Several possible explanations include acid-induced activation of chemical receptors in the duodenum, enhanced duodenal sensitivity to bile acids and pepsin, or altered gastroduodenal motility.

Variation in the intensity or distribution of the abdominal pain, as well as the onset of associated symptoms such as nausea and/or

vomiting, may be indicative of an ulcer complication. Dyspepsia that becomes constant, is no longer relieved by food or antacids, or radiates to the back may indicate a penetrating ulcer (pancreas). Sudden onset of severe, generalized abdominal pain may indicate perforation. Pain worsening with meals, nausea, and vomiting of undigested food suggest gastric outlet obstruction. Tarry stools or coffee-ground emesis indicate bleeding.

Physical examination Epigastric tenderness is the most frequent finding in patients with GU or DU. Pain may be found to the right of the midline in 20% of patients. Unfortunately, the predictive value of this finding is rather low. Physical examination is critically important for discovering evidence of ulcer complication. Tachycardia and orthostasis suggest dehydration secondary to vomiting or active GI blood loss. A severely tender, board-like abdomen suggests a perforation. Presence of a succussion splash indicates retained fluid in the stomach, suggesting gastric outlet obstruction.

PUD-Related Complications • GASTROINTESTINAL BLEEDING GI bleeding is the most common complication observed in PUD. Bleeding is estimated to occur in 19.4–57 per 100,000 individuals in a general population or in approximately 15% of patients. Bleeding and complications of ulcer disease occur more often in individuals >60 years of age. The 30-day mortality rate is as high as 5–10%. The higher incidence in the elderly is likely due to the increased use of NSAIDs in this group. In addition, up to 80% of the mortality in PUD-related bleeding is due to nonbleeding causes such as multiorgan failure (24%), pulmonary complications (24%), and malignancy (34%).

Up to 20% of patients with ulcer-related hemorrhage bleed without any preceding warning signs or symptoms.

PERFORATION The second most common ulcer-related complication is perforation, being reported in as many as 6–7% of PUD patients with an estimated 30-day mortality of over 20%. As in the case of bleeding, the incidence of perforation in the elderly appears to be increasing secondary to increased use of NSAIDs. *Penetration* is a form of perforation in which the ulcer bed tunnels into an adjacent organ. DUs tend to penetrate posteriorly into the pancreas, leading to pancreatitis, whereas GUs tend to penetrate into the left hepatic lobe. Gastrocolic fistulas associated with GUs have also been described.

GASTRIC OUTLET OBSTRUCTION Gastric outlet obstruction is the least common ulcer-related complication, occurring in 1–2% of patients. A patient may have relative obstruction secondary to ulcer-related inflammation and edema in the peripyloric region. This process often resolves with ulcer healing. A fixed, mechanical obstruction secondary to scar formation in the peripyloric areas is also possible. The latter requires endoscopic (balloon dilation) or surgical intervention. Signs and symptoms relative to mechanical obstruction may develop insidiously. New onset of early satiety, nausea, vomiting, increase of postprandial abdominal pain, and weight loss should make gastric outlet obstruction a possible diagnosis.

Differential Diagnosis The list of GI and non-GI disorders that can mimic ulceration of the stomach or duodenum is quite extensive. The most commonly encountered diagnosis among patients seen for upper abdominal discomfort is NUD. NUD, also known as *functional dyspepsia* or *essential dyspepsia*, refers to a group of heterogeneous disorders typified by upper abdominal pain without the presence of an ulcer. Dyspepsia has been reported to occur in up to 30% of the U.S. population. Up to 60% of patients seeking medical care for dyspepsia have a negative diagnostic evaluation. The etiology of NUD is not established, and the potential role of *H. pylori* in NUD remains controversial.

Several additional disease processes that may present with “ulcer-like” symptoms include proximal GI tumors, gastroesophageal reflux, vascular disease, pancreaticobiliary disease (biliary colic, chronic pancreatitis), and gastroduodenal Crohn's disease.

Diagnostic Evaluation In view of the poor predictive value of abdominal pain for the presence of a gastroduodenal ulcer and the multiple disease