

Peptic ulcer disease (PUD) is characterized by discontinuation in the inner lining of the gastrointestinal (GI) tract because of gastric acid secretion or pepsin. It usually occurs in the stomach and proximal duodenum. It may involve the lower esophagus, distal duodenum, or jejunum. Epigastric pain usually occurs within 15-30 minutes following a meal in patients with a gastric ulcer; on the other hand, the pain with a duodenal ulcer tends to occur 2-3 hours after a meal.

Today, testing for *Helicobacter pylori* is recommended in all patients with peptic ulcer disease. Endoscopy may be required in some patients to confirm the diagnosis, especially in those patients with sinister symptoms. Today, most patients can be managed with a proton pump inhibitor (PPI) based triple-drug therapy.

## Causes

Peptic ulcer disease (PUD) has various causes; however, *Helicobacter pylori*-associated PUD and NSAID-associated PUD account for the majority of the disease etiology, along with other medications. Other rare causes of the disease include: Zollinger-Ellison syndrome, Malignancy (gastric/lung cancer, lymphomas), Stress (Acute illness, burns, head injury), Viral infection, Vascular insufficiency, Radiation therapy, Crohn disease and Chemotherapy.

***Helicobacter Pylori*-Associated PUD:** *H. pylorus* is a gram-negative bacillus that is found within the gastric epithelial cells. This bacterium is responsible for 90% of duodenal ulcers and 70% to 90% of gastric ulcers. *H. pylori* infection is more prevalent among those with lower socioeconomic status and is commonly acquired during childhood. The organism has a wide spectrum of virulence factors allowing it to adhere to and inflame the gastric mucosa. This results in hypochlorhydria or achlorhydria, leading to gastric ulceration.

The *Virulence Factors* of *Helicobacter Pylori* are:

**Urease:** The secretion of urease breaks down urea into ammonia and protects the organism by neutralizing the acidic gastric environment.

**Toxins:** CagA/VacA is associated with stomach mucosal inflammation and host tissue

damage.

*Flagella*: Provides motility and allows movement toward the gastric epithelium.

**NSAID-associated PUD:** Nonsteroidal anti-inflammatory drugs use is the second most common cause of PUD after *H. pylori* infection. These drugs include: aspirin, ibuprofen, naproxen, diclofenac, celecoxib. The secretion of prostaglandin normally protects the gastric mucosa. NSAIDs block prostaglandin synthesis by inhibiting the COX-1 enzyme, resulting in decreased gastric mucus and bicarbonate production and a decrease in mucosal blood flow.

**Medications:** Apart from NSAIDs, corticosteroids, bisphosphonates, potassium chloride, and fluorouracil have been implicated in the etiology of PUD. Smoking also appears to play a role in duodenal ulcers, but the correlation is not linear. Alcohol can irritate the gastric mucosa and induce acidity.

## Epidemiology

Peptic ulcer disease (PUD) is a global problem with a lifetime risk of development ranging from 5% to 10%. Overall, there is a decrease in the incidence of PUD worldwide due to improved hygienic and sanitary conditions combined with effective treatment and judicious use of NSAIDs. Duodenal ulcers are four times more common than gastric ulcers. Also, duodenal ulcers are more common in men than in women.

The peptic ulcer disease (PUD) mechanism results from an imbalance between gastric mucosal protective and destructive factors. Risk factors predisposing to the development of PUD:

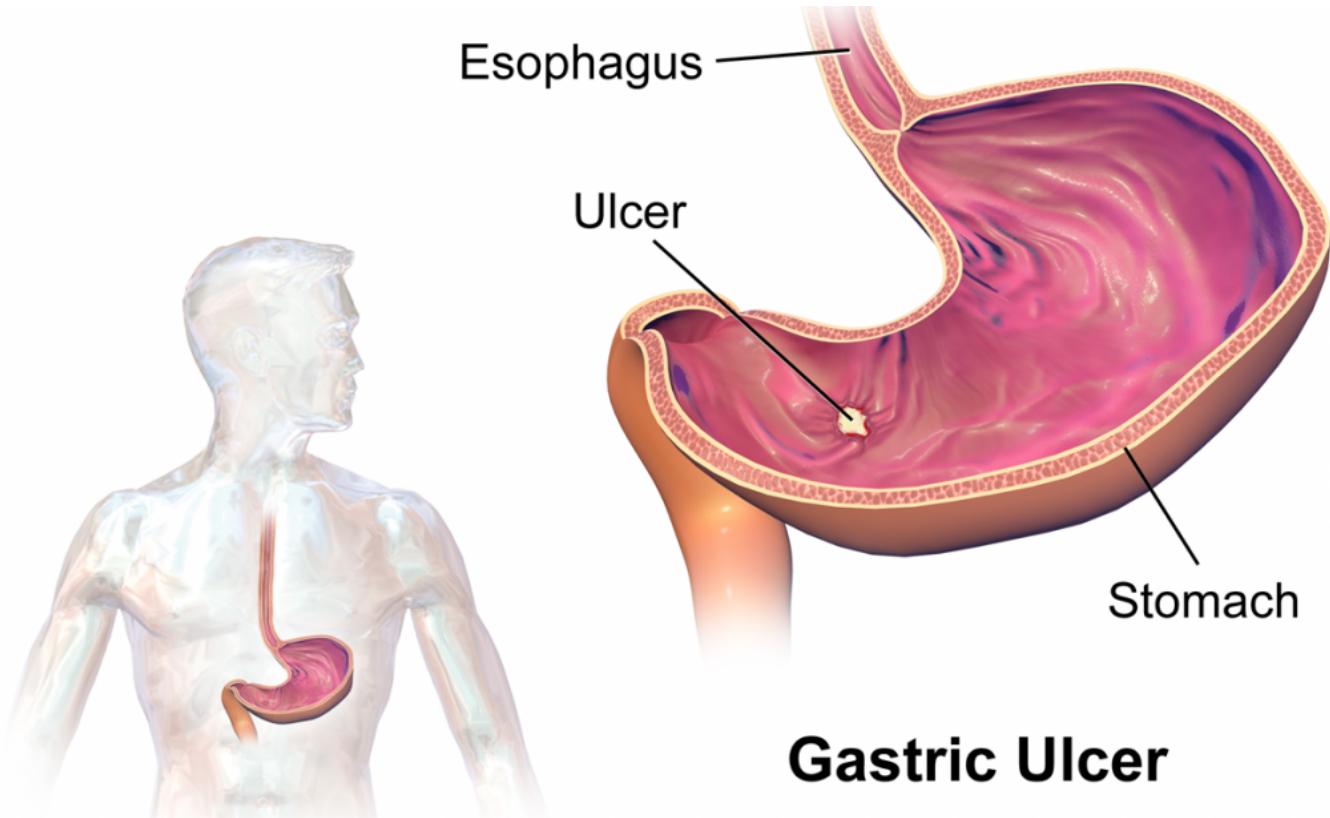
*H. pylori* infection

NSAID use

First-degree relative with PUD

Emigrant from a developed nation

African American/Hispanic ethnicity



## Symptoms

With peptic ulcers, there is usually a defect in the mucosa that extends to the muscularis mucosa. Once the protective superficial mucosal layer is damaged, the inner layers are susceptible to acidity. Further, the ability of the mucosal cells to secrete bicarbonate is compromised.

*H. pylori* is known to colonize the gastric mucosa and causes inflammation. The *H. pylori* also impairs the secretion of bicarbonate, promoting the development of acidity and gastric metaplasia. Gastric ulcers are most commonly located on the lesser curvature, whereas duodenal ulcers are most common at the duodenal bulb. The ulcer is round to oval with a smooth base. Acute ulcers have regular borders, while chronic ulcers have elevated borders with inflammation. An ulcer extends beyond the muscularis mucosa.

Signs and symptoms of peptic ulcer disease may vary depending upon the location of the

disease and age. Gastric and duodenal ulcers can be differentiated from the timing of their symptoms in relation to meals. Nocturnal pain is common with duodenal ulcers. Those with gastric outlet obstruction commonly report a history of abdomen bloating and or fullness.

Common signs and symptoms include: Epigastric abdominal pain, Bloating, Abdominal fullness, Nausea and vomiting, Weight loss/weight gain, Hematemesis and Melena. Warning symptoms or alarm symptoms that should prompt urgent referral include: Unintentional weight loss, Progressive dysphagia, Overt gastrointestinal bleeding, Iron deficiency anemia, Recurrent emesis and Family history of upper gastrointestinal malignancy

## **Evaluation and Diagnosis**

Diagnosis of PUD requires history taking, physical examination, and invasive/non-invasive medical tests. A careful history should be obtained and noted for the presence of any complications. Patient reporting of epigastric abdominal pain, early satiety, and fullness following a meal raise suspicion of PUD. The pain of gastric ulcers increases 2 to 3 hours after a meal and may result in weight loss, whereas the pain of duodenal ulcers decreases with a meal which can result in weight gain. Any patient presenting with anemia, melena, hematemesis, or weight loss should be further investigated for complications of PUD, predominantly bleeding, perforation, or cancer. A physical exam may reveal epigastric abdominal tenderness and signs of anemia. Investigations that could be carried out include:

***Esophagogastroduodenoscopy (EGD):*** Gold standard and most accurate diagnostic test with sensitivity and specificity up to 90% in diagnosing gastric and duodenal ulcers. The American Society of Gastrointestinal Endoscopy has published guidelines on the role of endoscopy in patients presenting with upper abdominal pain or dyspeptic symptoms suggestive of PUD. Patients over 50 years of age and new onset of dyspeptic symptoms should get evaluated by an EGD. Anyone with the presence of alarm symptoms should undergo EGD irrespective of age.

***Barium swallow:*** It is indicated when EGD is contraindicated.

Complete blood work, liver function, and levels of amylase and lipase.

Serum gastric is ordered if Zollinger Ellison syndrome is suspected.

*Helicobacter pylori* testing:

*Serologic testing*

*Urea breath test*: High sensitivity and specificity. It may be used to confirm eradication after 4 to 6 weeks of stopping treatment. In the presence of urease, an enzyme produced by *H.pylori*, the radiolabeled carbon dioxide produced by the stomach is exhaled by the lungs.

Antibodies to *H.pylori* can also be measured.

*Stool antigen test*

*Urine-based ELISA and rapid urine test*

*Endoscopic biopsy*: Culture is not generally recommended as it is expensive, time-consuming, and invasive. It is indicated if eradication treatment fails or there is suspicion about antibiotic resistance. Biopsies from at least 4-6 sites are necessary to increase sensitivity. Gastric ulcers are commonly located on the lesser curvature between the antrum and fundus. The majority of duodenal ulcers are located in the first part of the duodenum.

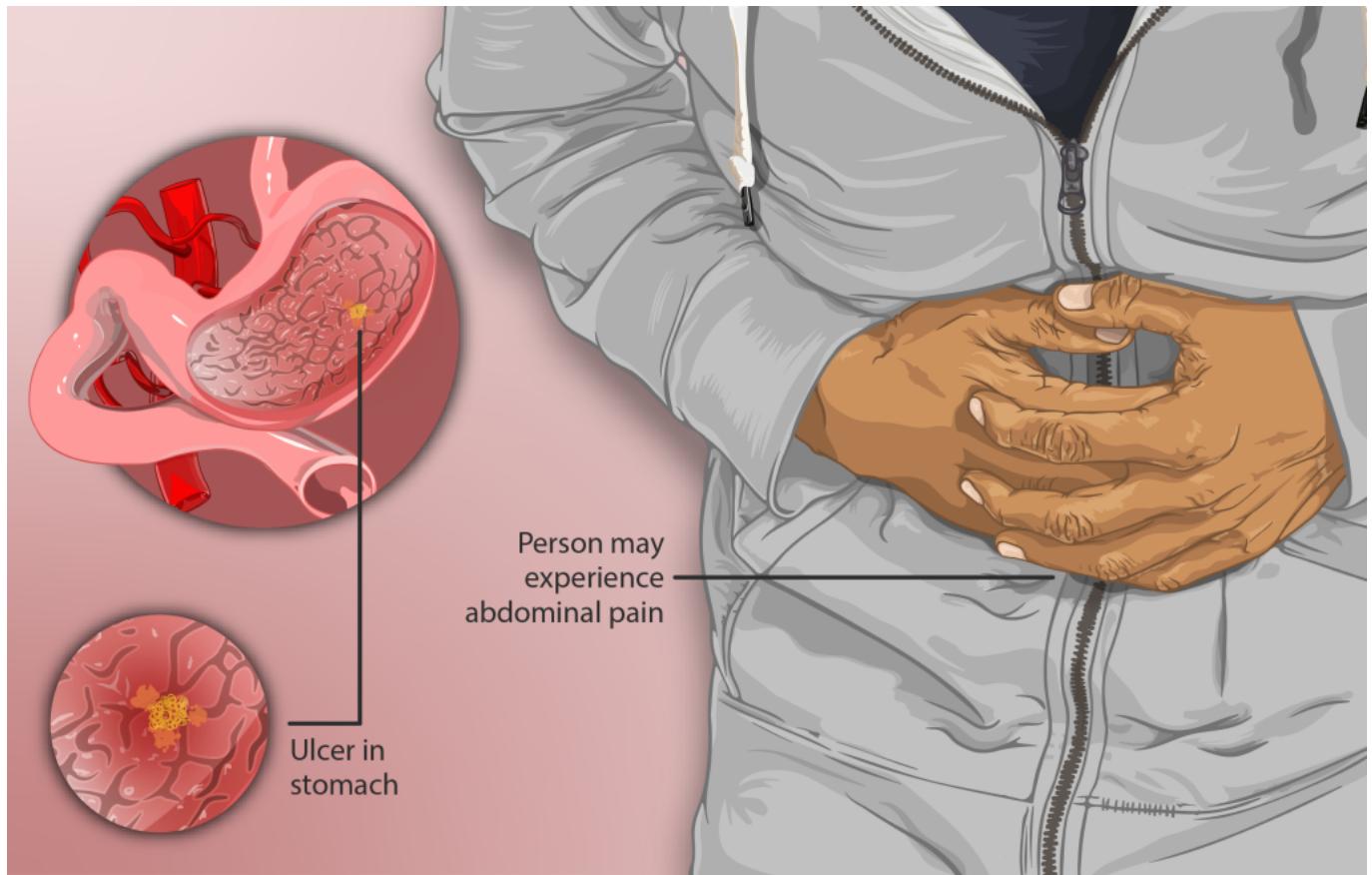
Computerized tomography of the abdomen with contrast is of limited value in the diagnosis of PUD itself but is helpful in the diagnosis of its complications like perforation and gastric outlet obstruction.

## Treatment and Management

**Medical Treatment:** Antisecretory drugs used for peptic ulcer disease (PUD) include H2-receptor antagonists and the proton pump inhibitor (PPIs). PPIs have largely replaced H2 receptor blockers due to their superior healing and efficacy. PPIs block acid production in the stomach, providing relief of symptoms and promote healing. Treatment may be incorporated with calcium supplements as long-term use of the PPIs can increase the risk of bone fractures. NSAIDs induced PUD can be treated by stopping the use of NSAIDs or switching to a lower dose. Corticosteroids, bisphosphonates, and anticoagulants should also be discontinued if possible. Prostaglandin analogs (misoprostol) are sometimes used as

prophylaxis for NSAID-induced peptic ulcers. First-line treatment for *H. pylori*-induced PUD is a triple regimen comprising two antibiotics and a proton pump inhibitor. Pantoprazole, clarithromycin, and metronidazole, or amoxicillin are used for 7 to 14 days. Antibiotics and PPIs work synergistically to eradicate *H. pylori*. The antibiotic selected should take into consideration the presence of antibiotic resistance in the environment. If first-line therapy fails, quadruple therapy with bismuth and different antibiotics is used.

**Refractory Disease and Surgical Treatment:** Surgical treatment is indicated if the patient is unresponsive to medical treatment, noncompliant, or at high risk of complications. A refractory peptic ulcer is one over 5 mm in diameter that does not heal despite 8-12 weeks of PPI therapy. The common causes are persistent *H. pylori* infection, continued use of NSAIDs, or significant comorbidities that impair ulcer healing or other conditions like gastrinoma or gastric cancer. If the ulcer persists despite addressing the above risk factors, patients can be candidates for surgical treatment. Surgical options include vagotomy or partial gastrectomy.



## Differential Diagnosis

The following conditions can present with symptoms similar to peptic ulcer disease and it is important to be familiar with their clinical presentation in order to make the correct diagnosis.

Gastritis – an inflammatory process of the gastric mucosa from immune-mediated or infectious etiology presenting with upper abdominal pain and nausea. Clinical presentation is very similar to that of peptic ulcer disease.

Gastroesophageal reflux disease (GERD) – patients usually describe a burning sensation in the epigastrium and lower retrosternal area, excessive salivation, or intermittent regurgitation of food material.

Gastric cancer – apart from abdominal pain, patients usually describe alarm symptoms like

weight loss, melena, recurrent vomiting, or evidence of malignancy elsewhere in case of metastasis.

Pancreatitis – epigastric or right upper quadrant pain that is more persistent and severe, worse in the supine position, and patients usually have a history of alcoholism or gallstones.

Elevated serum amylase and lipase are useful in the diagnosis.

Biliary colic – intermittent, severe deep pain in the right upper quadrant or epigastrium precipitated by fatty meals.

Cholecystitis – right upper quadrant or epigastric pain that usually lasts for hours and is exacerbated by fatty meals and is associated with nausea and vomiting. Fever, tachycardia, positive Murphy sign, leukocytosis, and abnormal liver functions help further distinguish this from biliary colic.

These are some potentially life-threatening conditions that can also have similar presentations.

Myocardial infarction – especially in the inferior wall and right ventricular involvement, sometimes patients can present with epigastric pain with nausea and vomiting. The presence of other symptoms like dizziness, shortness of breath, and abnormal vital signs in a high-risk patient should alert the clinician to look for this.

Mesenteric ischemia – while acute mesenteric ischemia presents with severe, acute onset abdominal pain; the chronic variant usually presents with ongoing post-prandial epigastric pain and can be mistaken for peptic ulcer disease. Older age, presence of risk factors for atherosclerosis, and weight loss should prompt a workup for the same.

Mesenteric vasculitis – unexplained abdominal symptoms with or without lower gastrointestinal bleeding in a patient with other features from underlying systemic vasculitis should raise the suspicion of mesenteric vasculitis.

## Complications

The prognosis of peptic ulcer disease (PUD) is excellent after the underlying cause is successfully treated. Recurrence of the ulcer may be prevented by maintaining good hygiene

and avoiding alcohol, smoking, and NSAIDs. Unfortunately, recurrence is common with rates exceeding 60% in most series. NSAID-induced gastric perforation occurs at a rate of 0.3% per patient per year. However, unlike in the past, mortality rates for peptic ulcer disease have decreased significantly.

Peptic ulcer disease (PUD) if not diagnosed and treated promptly can lead to serious complications. Following complications can occur in PUD: Upper gastrointestinal bleeding, Gastric outlet obstruction, Perforation, Penetration, and Gastric cancer. Patients with peptic ulcer disease (PUD) should be counseled about potentially injurious agents like nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, alcohol, tobacco, and caffeine. If it is necessary to use NSAIDs use the lowest possible dose and also consider prophylaxis for patients who use NSAIDs. Obesity has a strong association with peptic ulcer disease, and patients should be asked to lose weight. Stress reduction counseling can be helpful in some cases.

An evidence-based approach to peptic ulcer disease is recommended. PUD is a very common disorder that affects millions of people. When left untreated, it has significant morbidity. The majority of patients with PUD present to their primary caregiver, but others may present to the emergency department, urgent care clinic, or an outpatient clinic. Because the presentation of PUD is often vague, healthcare workers, including nurses, need to be aware of this diagnosis. The abdominal pain can mimic a number of other pathologies and consequently lead to a delay in treatment.

Once the diagnosis is made, the key is to educate the patient on lifestyle changes, which include discontinuation of smoking, abstaining from alcohol and caffeinated beverages, and avoid consumption of too many NSAIDs. Gastroenterology nurses monitor patients, provide education, and keep the team updated on the patient's condition. The pharmacist should educate the patient on medication compliance to obtain symptom relief and a cure. A dietary consult should be sought as there is evidence that obesity may be a trigger factor for peptic ulcer disease. Only through a team approach can the morbidity of peptic ulcer disease be decreased. For most patients with PUD who are treated with the triple regimen or PPI, the

outcomes are excellent, but recurrence of symptoms is not uncommon.

### **Source**

*Malik TF, Gnanapandithan K, Singh K. Peptic Ulcer Disease. [Updated 2023 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK534792/>*

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