PEPTIC ULCER

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Definition

- *Peptic ulcer disease (PUD) refers to a group of ulcerative disorders of the upper* GI tract that require acid and pepsin for their formation.
- Ulcers differ from gastritis and erosions in that they extend deeper into the muscularis mucosa.

CLASSIFICATION OF PEPTIC ULCERS

- Acute or stress ulcers : Multiple, Small mucosal erosions.

  Stress ulcers or “stress-related mucosal damage” (SRMD)

- Chronic ulcers: Gastric or Duodenal ulcers.

ETIOLOGY AND RISK FACTORS

- Most peptic ulcers occur in the presence of acid and pepsin when *H. pylori, NSAIDs, or other factors disrupt normal* mucosal defense and healing mechanisms.

- Common causes
  - *Helicobacter pylori* infection
  - Nonsteroidal anti-inflammatory drugs
  - Critical illness (stress-related mucosal damage)
- Uncommon causes
  - Hypersecretion of gastric acid (e.g., Zollinger-Ellison syndrome)
  - Viral infections (e.g., cytomegalovirus)
  - Vascular insufficiency (crack cocaine–associated)
  - Radiation
  - Chemotherapy (e.g., hepatic artery infusions)
  - Rare genetic subtypes
  - Idiopathic

Helicobacter pylori infection

- *H. pylori infection causes chronic gastritis in all infected individuals* and is causally linked to PUD, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma , However, only a small number of infected individuals will develop symptomatic PUD (approximately 20%) or gastric cancer (less than 1%).1,7

- Evidence for PUD is based on the fact that most non-NSAID ulcers are infected with *H. pylori, and that H. pylori eradication markedly* decreases ulcer recurrence.

- *H. pylori is transmitted person-to-person by three possible pathways :*

1. fecal–oral
2. oral–oral
3. gastro–oral

- Transmission of the organism most likely is by the fecal–oral route, either directly from an infected person, or indirectly from fecal-contaminated water or food.
- Members of the same household are likely to become infected when someone in the same household is infected.

NONSTEROIDAL ANTIINFLAMMATORY DRUGS

- There is overwhelming evidence linking chronic nonselective NSAID (including aspirin) use to a variety of GI tract injuries .
- Gastroduodenal ulcers occur in 15% to 30% of regular NSAID users and may develop within a week or with continued treatment (6 months or longer).

Risk Factors for Non steroidal Anti inflammatory Drug (NSAID)-Induced Ulcers and Upper Gastrointestinal Complications

- Established risk factors
  - Older than 60 years of age
  - Previous peptic ulcer
  - Previous ulcer-related upper GI complication
  - Concomitant use of corticosteroid
  - High-dose NSAIDs
  - Multiple NSAID use or NSAID plus aspirin use
  - Choice of NSAID
  - Aspirin (including cardioprotective dosages)
  - Concomitant use of anticoagulant or coagulopathy
  - Concomitant use of antiplatelet drug such as clopidogrel
  - Concomitant use of oral bisphosphonates
  - Concomitant use of selective serotonin reuptake inhibitor
  - Chronic illness (e.g., cardiovascular disease)
- Possible risk factors
  - NSAID-related dyspepsia
  - *Helicobacter pylori* infection
  - Rheumatoid arthritis (extent of disability)
  - Alcohol consumption
- Questionable risk factors
  - Cigarette smoking

Other causes may include

- CIGARETTE SMOKING
- PSYCHOLOGICAL STRESS
- DIETARY FACTORS

PATHOPHYSIOLOGY

- A physiologic imbalance between aggressive factors (gastric acid and pepsin) and protective mucosal defense and repair (mucus and bicarbonate secretion, intrinsic epithelial cell defense, and mucosal blood flow.) remain important issues in the pathophysiology of gastric and duodenal ulcers.

PHATOPHYSIOLOGY OF HELICOBACTER PYLORI INDUCED ULCER

- *H. pylori is a spiral-shaped, pH-sensitive, gram-negative, microaerophilic* bacterium that resides between the mucus layer and surface epithelial cells in the stomach, or any location where gastric-type epithelium is found.

- The acute infection is accompanied by transient hypochlorhydria, which permits the organism to survive in the acidic gastric juice.

- The exact method by which *H. pylori initially induces hypochlorhydria is* unclear.

Pathogenic mechanisms include

(a) Direct mucosal damage

(b) Alterations in the host immune or inflammatory response

(c) Hypergastrinemia leading to increased acid secretion

Nonselective NSAIDs INDUCED ULCER

- Nonselective NSAIDs (including aspirin) cause gastric mucosal damage by
- two mechanisms:

  (1) A direct or topical irritation of the gastric epithelium.

  (2) systemic inhibition of the cyclooxygenase-1 (COX-1) enzyme which results in decreased synthesis of protective prostaglandins.

COMPLICATIONS OF PEPTIC ULCER

Upper GI bleeding

perforation

obstruction

- occur with *H. pylori associated* and NSAID-induced ulcers and constitute the most serious, life-threatening complications of chronic PUD.

Upper GI bleeding

- Bleeding is caused by the erosion of an ulcer into an artery and occurs in approximately 10% to 15% of patients.
- The bleeding may be

i. occult (hidden) and insidious.

ii. may present as melena (black-colored stools) .

iii. hematemesis (vomiting of blood).

Perforation

- Ulcer-related perforation into the peritoneal cavity occurs in approximately 7% of patients with PUD.
- perforation occurs when an ulcer burrows into an adjacent structure (pancreas, biliary tract, or liver) rather than opening freely into a cavity.

Perforation

- The pain of perforation is usually sudden, sharp, and severe, beginning first in the epigastrium, but quickly spreading over the entire abdomen.
- The incidence of perforation is increasing with the increased use of NSAIDs.
- Mortality is usually higher for perforated gastric ulcer than duodenal ulcer.

Obstruction

- Gastric outlet obstruction occurs in approximately 2% of patients with peptic ulcers.
- Mechanical obstruction is caused by scarring or edema of the duodenal bulb or pyloric channel and can lead to gastric retention.
- Symptoms usually occur over several months and include early satiety, bloating, anorexia, nausea, vomiting, and weight loss.

CLINICAL PRESENTATION

Signs

- Weight loss associated with nausea, vomiting, and anorexia.
- Complications, including ulcer bleeding, perforation, penetration, or obstruction

Symptoms

- Abdominal pain that is often epigastric and described as burning, but may present as vague discomfort, abdominal fullness, or cramping.
- A typical nocturnal pain that awakens the patient from sleep (especially between 12 AM and 3 AM)
- Heartburn, belching, and bloating often accompany the pain.
- Nausea, vomiting, and anorexia, are more common in patients with gastric ulcer than with duodenal ulcer, but may also be signs of an ulcer-related complication.

DIAGNOSIS

- Routine laboratory tests are not helpful in establishing a diagnosis of uncomplicated PUD.
- The hematocrit, hemoglobin, and stool hemoccult tests are used to detect bleeding.

TESTS FOR *HELICOBACTER PYLORI*

- The diagnosis of HP infection can be made using endoscopic or nonendoscopic tests.
- The tests that require upper endoscopy are invasive, more expensive, uncomfortable, and usually require a mucosal biopsy for histology, culture, or detection of urease activity.

The non endoscopic tests include :

- Serologic antibody detection tests
- The urea breath test (UBT)
- The stool antigen test

Serologic antibody detection tests

- Serologic tests detect circulating immunoglobulin G directed against HP but are of limited value in evaluating post treatment eradication.
- serology should not be used to confirm *H. pylori eradication and is unreliable in young children.*

The urea breath test (UBT)

- tests require that the patient ingest radiolabeled urea, which is then hydrolyzed by HP (if present in the stomach) to ammonia and radiolabeled bicarbonate.
- The radiolabeled bicarbonate is absorbed in the blood and excreted in the breath.

The stool antigen test

- The stool antigen test is less expensive and easier to perform than the UBT, and may be useful in children.
- Although comparable to the UBT in the initial detection of *H. pylori, the stool antigen test is less accurate when* used to confirm *H. pylori eradication post treatment.*

GENERALLY

- Testing for *H. pylori is only recommended if eradication therapy* is considered.

- The UBT is the preferred non endoscopic method to verify HP eradication after treatment.

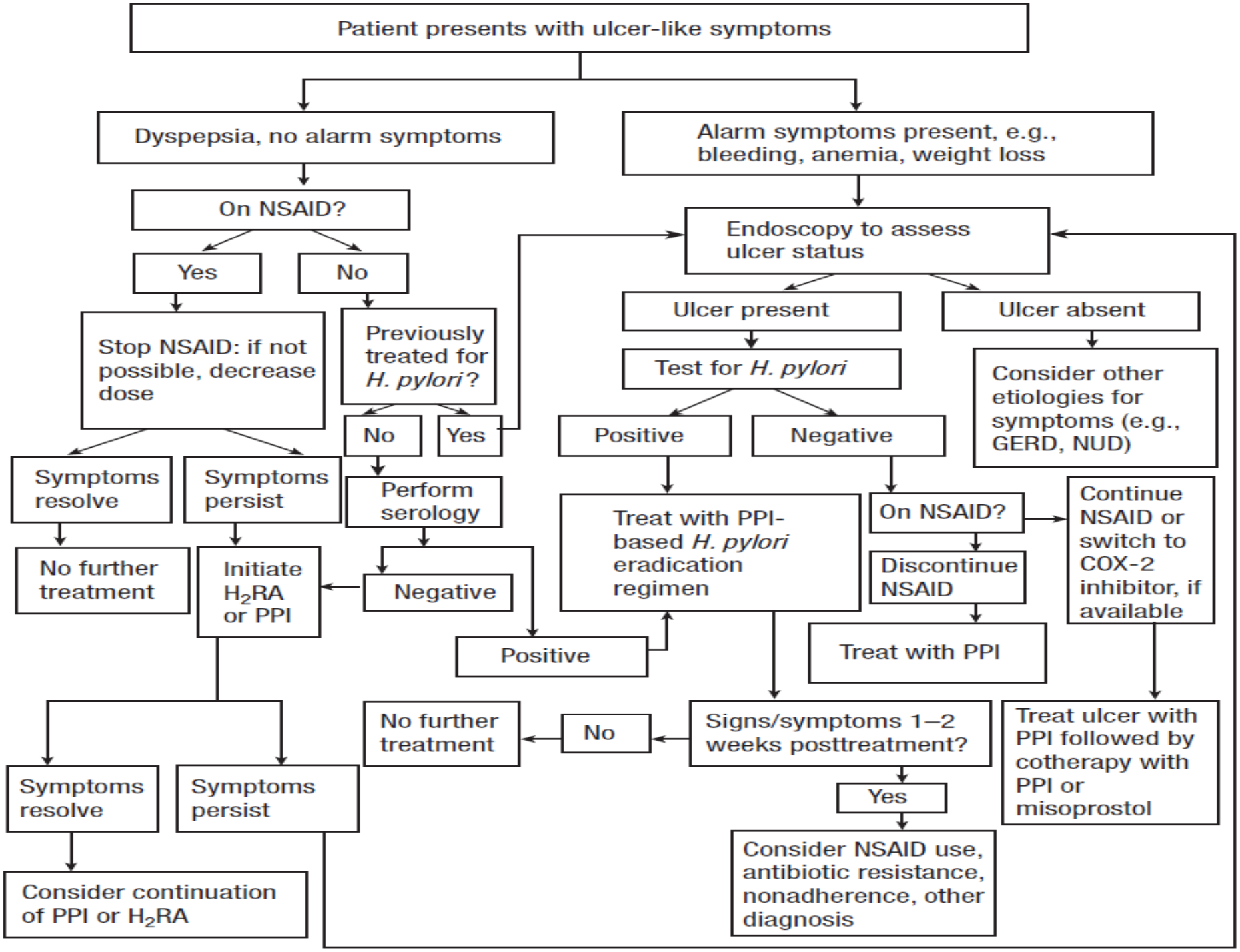
Treatment

- The treatment of chronic PUD varies depending on the etiology of the ulcer (HP or NSAID), whether the ulcer is initial or recurrent.
- Overall treatment is aimed at relieving ulcer pain, healing the ulcer, preventing ulcer recurrence, and reducing ulcer-related complications.

Non Pharmacological

- Eliminate or reduce psychological stress, cigarette smoking, and the use of nonselective NSAIDs (including aspirin).
- Although there is no “antiulcer diet,” the patient should avoid foods and beverages (e.g., spicy foods, caffeine, and alcohol) that cause dyspepsia or that exacerbate ulcer symptoms.

PHARMACOLOGICAL TREATMENT


Patient presents with ulcer-like symptoms
Dyspepsia, no alarm symptoms
Alarm symptoms present, e.g., bleeding, anemia, weight loss
On NSAID?
Yes
No
Endoscopy to assess ulcer status
Ulcer present
Ulcer absent
Stop NSAID: if not possible, decrease dose
Previously treated for H. pylori?
Test for H. pylori
Consider other etiologies for symptoms (e.g., GERD, NUD)
No
Yes
Positive
Negative
Symptoms resolve
Symptoms persist
Perform serology
Treat with PPI-based H. pylori eradication regimen
On NSAID?
Continue NSAID or switch to COX-2 inhibitor, if available
No further treatment
Initiate H2RA or PPI
Negative
Discontinue NSAID
Positive
Treat with PPI
Symptoms resolve
Symptoms persist
No further treatment
No
Signs/symptoms 1–2 weeks posttreatment?
Treat ulcer with PPI followed by cotherapy with PPI or misoprostol
Yes
Consider continuation of PPI or H2RA
Consider NSAID use, antibiotic resistance, nonadherence, other diagnosis

Drug Regimens to Eradicate *Helicobacter pylori*

Drug 1	Drug 2	Drug 3
Proton pump inhibitor–based three-drug regimens		
Omeprazole 20 mg twice daily **or** lansoprazole 30 mg twice daily **or** pantoprazole 40 mg twice daily **or** esomeprazole 40 mg daily **or** rabeprazole 20 mg daily	Clarithromycin 500 mg twice daily	Amoxicillin 1 g twice daily **or** metronidazole 500 mg twice daily

Bismuth-based four-drug regimens[b]

Omeprazole 40 mg twice daily **or** lansoprazole 30 mg twice daily **or** pantoprazole 40 mg twice daily **or** esomeprazole 40 mg daily **or** rabeprazole 20 mg daily **or** standard ulcer-healing dosages of an histamine-2 receptor antagonist taken for 4–6	Bismuth subsalicylate 525 mg four times daily	Metronidazole 250–500 mg four times daily	Tetracycline 500 mg four times daily **or** amoxicillin 500 mg four times daily, **or** clarithromycin 250–500 mg four times daily

PHARMACOLOGIC THERAPY

- For HP
- First-line therapy should be initiated with a PPI-based three-drug regimen for a minimum of 7 days, but preferably 10 to 14 days.
- If a second course of treatment is required, the PPI-based three-drug regimen should contain different antibiotics or
- A four-drug regimen with bismuth subsalicylate, metronidazole, tetracycline, and a PPI should be used.

PHARMACOLOGIC THERAPY

- Eradication regimens that combine two antibiotics and one antisecretory drug (triple therapy) or

- A bismuth salt, two antibiotics, and an antisecretory drug (quadruple therapy) increase eradication rates to an acceptable level and reduce the risk of antimicrobial resistance

PHARMACOLOGIC THERAPY

- Amoxicillin should not be used in penicillin-allergic patients and metronidazole should be avoided if alcohol is consumed.
- When metronidazole resistance is suspected, metronidazole may be replaced by furazolidone (100 mg four times a day) in either the proton pump inhibitor-based three-drug regimen or the bismuth-based four-drugregimen.

- When furazolidone is used, patients should be counseled not to ingest alcohol or monoamine oxidase inhibitors.

- If HP-negative, the NSAID should be discontinued and the patient treated with either a PPI, H2RA, or sucralfate.
- If the NSAID must be continued, treatment should be initiated with a PPI (if HP-negative) or with a PPI-based three-drug eradication regimen (if HP-positive).
- Prophylactic cotherapy with a PPI or misoprostol or switching to a selective COX-2 inhibitor is recommended for patients at risk of developing ulcer-related upper GI complications

- PPI cotherapy should be considered in high-risk patients taking a COX-2 inhibitor.
- Misoprostol(a synthetic prostaglandin E1 analog, moderately inhibits acid secretion and enhances mucosal defense)
- 200 mcg four times a day, reduces the risk of NSAID-induced gastric ulcer, duodenal ulcer, and ulcer-related GI complications, but diarrhea and abdominal cramping limit its use.

- StandardH2-receptor antagonist dosages (e.g., famotidine 40 mg/day) are effective in reducing the risk of NSAID-induced duodenal ulcer, but not gastric ulcer.
- Standard PPI dosages (e.g., omeprazole 20 mg/day and lansoprazole 30 mg/day) reduce the risk of NSAID-induced gastric ulcer and duodenal ulcer.

THANK YOU