Peptic ulcer disease

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Objectives

- Definition of peptic ulcer
- Comparison of duodenal & gastric ulcers
- Aetiology
- Clinical presentation
- Management

Introduction

Erosion of GI mucosa resulting from digestive action of HCl and pepsin

Site

- Lower esophagus
- Stomach
- Duodenum
- 10% of men, 4% of women

Types

Acute

- Superficial erosion
- Minimal erosion

Chronic

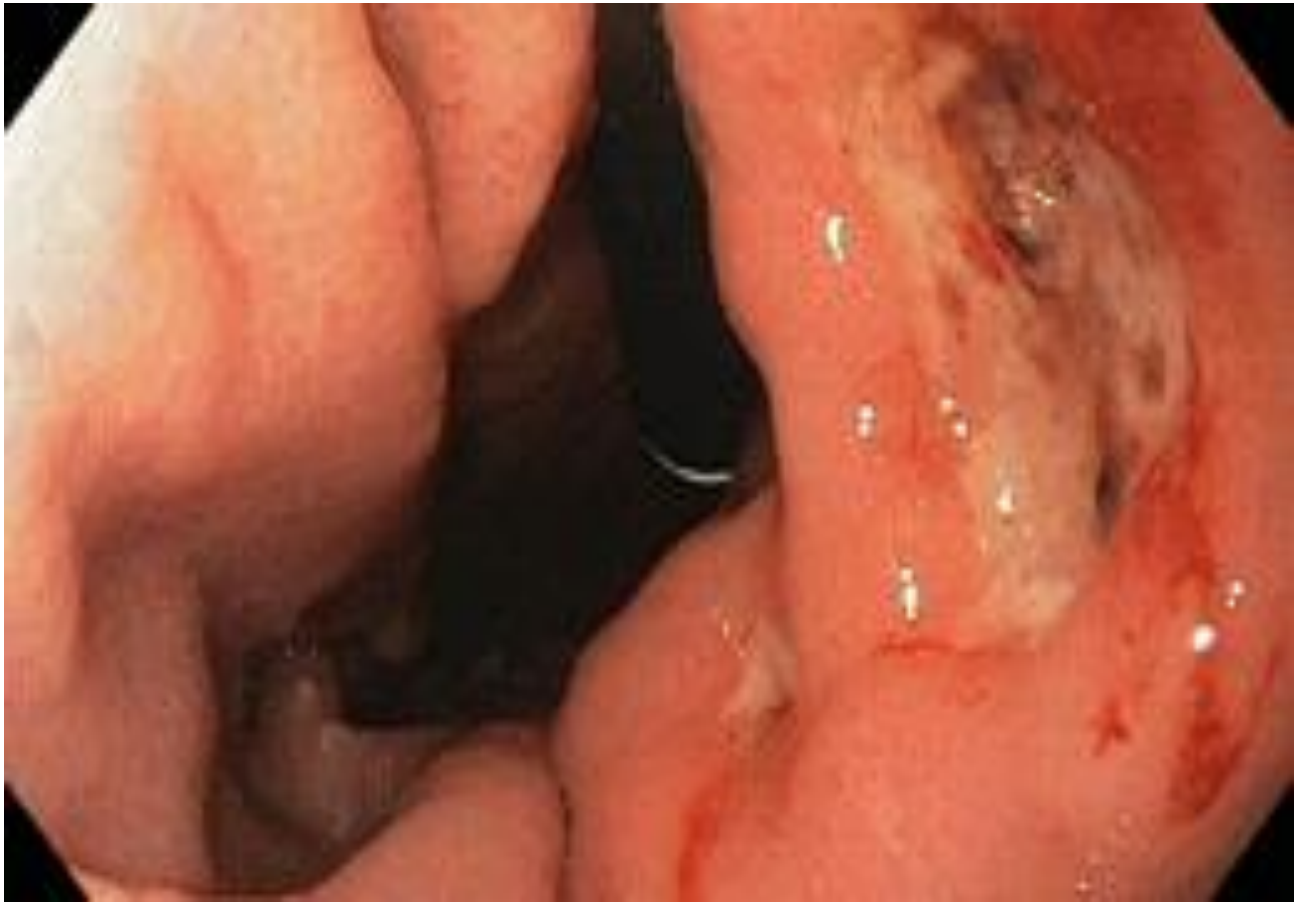
- Muscular wall erosion with formation of fibrous tissue
- Present continuously for many months or intermittently

Etiology and Pathophysiology

- Develop only in presence of acid environment
- Excess of gastric acid not necessary for ulcer development
- Person with a gastric ulcer has normal to less than normal gastric acidity compared with person with a duodenal ulcer
- Some intraluminal acid does seem to be essential for a gastric ulcer to occur
- Pepsinogen is activated to pepsin in presence of HCl
- Secretion of HCl by parietal cells has a pH of 0.8
- pH reaches 2 to 3 after mixing with stomach contents

- At pH level 3. 5 or more, stomach acid is neutralized
- Surface mucosa of stomach is renewed about every 3 days
- Mucosa can continually repair itself except in extreme instances
- Mucosal barrier prevents back diffusion of acid from gastric lumen through mucosal layers to underlying tissue
- Mucosal barrier can be impaired and back diffusion can occur

What is a peptic ulcer?



Peptic ulcer

- A peptic ulcer is a mucosal breach of the stomach or duodenum that penetrates the muscularis mucosa, while erosions are smaller and superficial to the muscularis mucosa.
- Gastric acid and pepsin secretion are important components in the pathogenesis of gastric and duodenal ulcers. However, while some persons with DUs secrete excessive amounts of gastric acid, most DU patients are not hyper-secretors of acid, and most gastric ulcer patients actually have normal-to-low secretion.
- Gastric acid is required for peptic ulcer formation, but acid alone does not commonly cause ulcers. The most common causes of PUD are infection with the bacterium Helicobacter pylori (HP) or the use of NSAIDs.
- Epidemiologic studies indicate that smokers are at moderately increased risk for both DU and GU, and this risk is proportional to the amount smoked.

Higher prevalence in developing countries

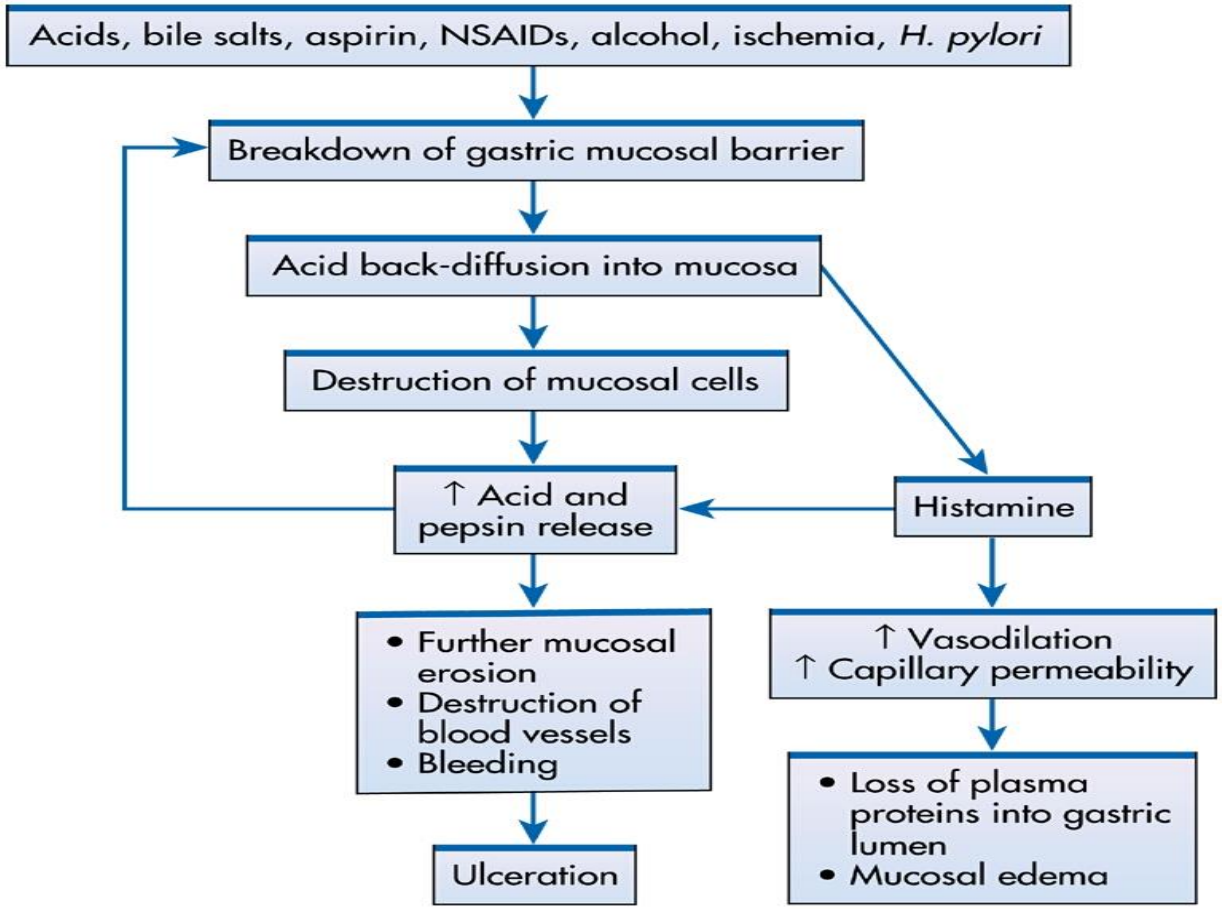
- H. Pylori is sometimes associated with socioeconomic status and poor hygiene

In the US:

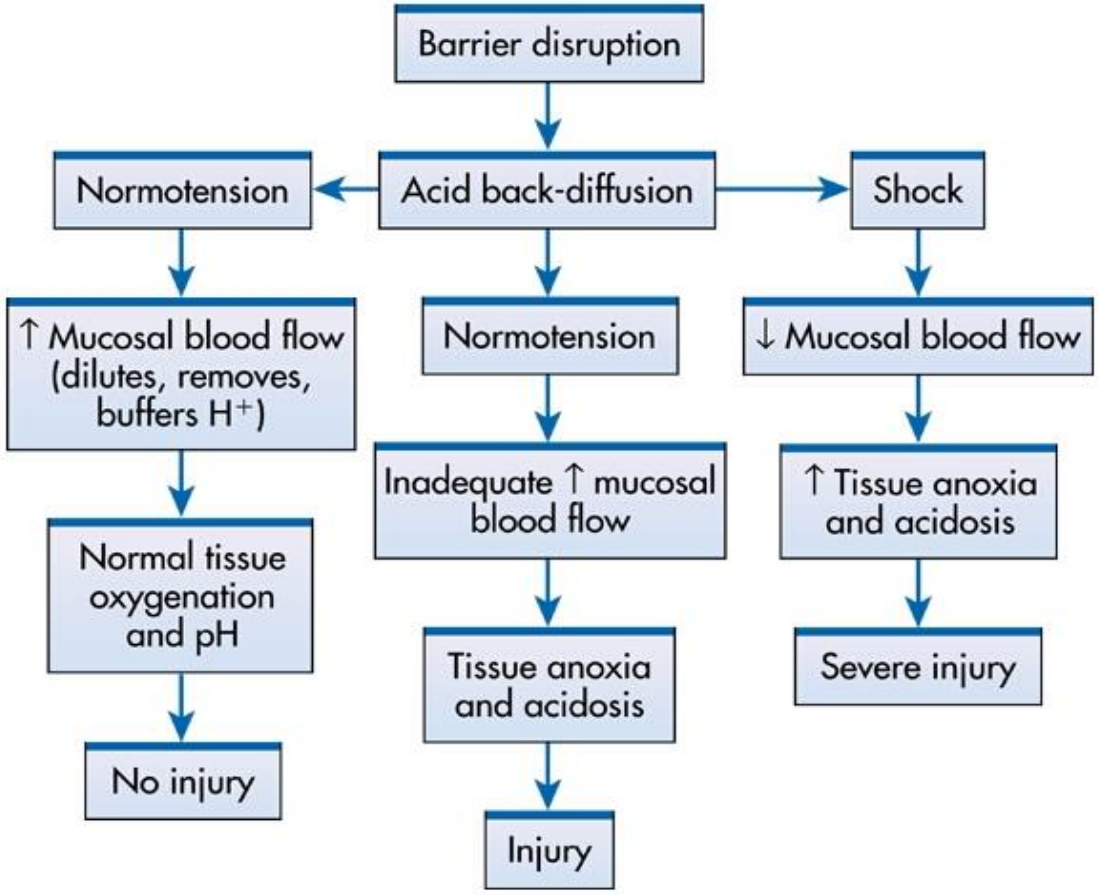
- Lifetime prevalence is ~10%.
- PUD affects ~4.5 million annually.
- Hospitalization rate is ~30 pts per 100,000 cases.
- Mortality rate has decreased dramatically in the past 20 years
  - approximately 1 death per 100,000 cases

PUD Demographics

Diffusion of Acid



Disruption of Gastric Mucosal Barrier



Protective Mechanism

- Mucus forms a layer that entraps or slows diffusion of hydrogen ions across mucosal barrier
- Bicarbonate secreted Neutralizes HCl acid in lumen of GI tract

Clinical Presentation

- Uncomplicated peptic ulcer disease most commonly presents as upper abdominal pain that is often described as burning, sharp, or gnawing and typically does not radiate. However, it may also be characterized as vague abdominal discomfort, nausea, aching, or be perceived as an abdominal pressure, fullness, or hunger sensation.

Symptoms of PUD

- Asymptomatic
- Epigastric pain
- Oral flatulence, bloating, distension and intolerance of fatty food
- Heartburn
- Pain radiating to the back
- Pain—"gnawing", "aching", or "burning"
  - Duodenal ulcers: occurs 1-3 hours after a meal and may awaken patient from sleep. Pain is relieved by food, antacids, or vomiting.
  - Gastric ulcers: food may exacerbate the pain while vomiting relieves it.
- Nausea, vomiting, belching, dyspepsia, bloating, chest discomfort, anorexia, hematemesis, &/or melena may also occur.
  - nausea, vomiting, & weight loss more common with Gastric ulcers

Differential diagnoses for epigastric pain

- Surgical
  - Biliary colic, acute cholecystitis
  - Pancreatitis
  - Perforation of viscus
  - Acute appendicitis
  - Malignancy
- Medical
  - GORD
  - MI
  - PE
  - Pneumonia

ALARM signs for epigastric pain

- Chronic GI bleeding
- Iron-deficiency anaemia
- Progressive unintentional weight loss
- Progressive dysphagia
- Persistent vomiting
- Epigastric mass
- Patients aged 55 years and older with unexplained and persistent recent- onset dyspepsia alone

Duodenal Ulcers

- The pain of duodenal ulceration typically occurs two to three hours after meals, at night or when the stomach is empty, and can awaken the patient from sleep.
- Food and antacids relieve the pain for a short time; however, discomfort usually returns in 30–60 minutes.
- Symptoms may persist for several days, weeks, or months, and patients frequently have a history of self-treatment with antacids or antisecretory therapy.
- Patients may even describe weight gain due to their hyperphagia in attempting to prevent the pain from duodenal ulceration.

	DUODENAL	GASTRIC
INCIDENCE	More common	Less common
ANATOMY	First part of duodenum – anterior wall	Lesser curvature of stomach
DURATION	Acute or chronic	Chronic
MALIGNANCY	Rare	Benign or malignant

Duodenal vs Gastric

Etiology

- The most important contributing factors are H pylori, NSAIDs, acid, and pepsin.
- Additional aggressive factors include smoking, ethanol, bile acids, aspirin, steroids, and stress.
- Important protective factors are mucus, bicarbonate, mucosal blood flow, prostaglandins, hydrophobic layer, and epithelial renewal.
- Increased risk when older than 50 d/t decrease protection
- When an imbalance occurs, PUD might develop.

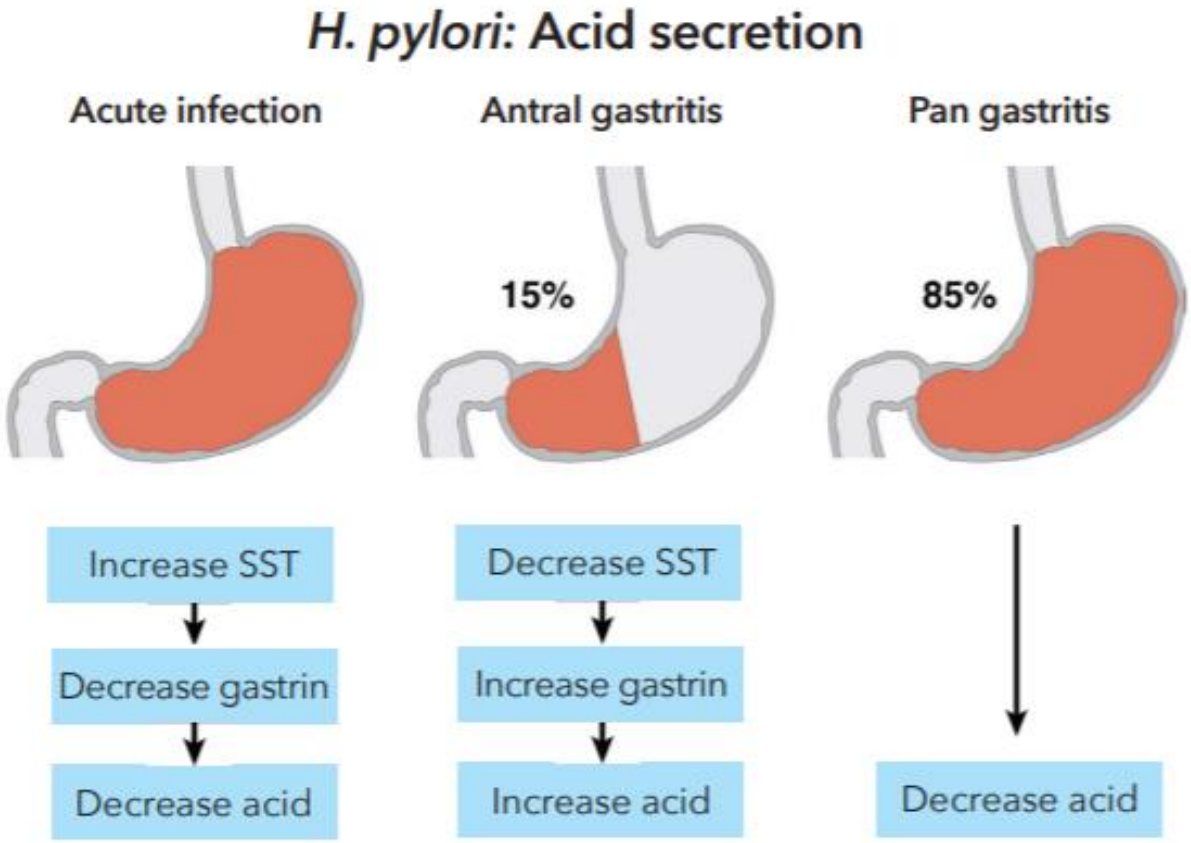
Etiology

- H. pylori colonizes the stomachs of at least half of the world's population and is a strong risk factor for both PUD and gastric malignancy
- HP infection is also associated with iron deficiency anemia and idiopathic thrombocytopenic purpura. Infection is usually acquired in childhood and persists for the lifetime of the host. The prevalence of HP is higher in developing than in developed countries.
- In the U.S., HP is present in 10–15 percent of children under age 12 compared with 50–60 percent of people over age 60.
- After early childhood, the rate of acquisition of new HP infection in developed countries is less than one percent per year.
- Over the past half-century, however, there has been a progressive decline in the prevalence of H. pylori in the U.S. at all ages.
- Risk factors for HP acquisition include lower socioeconomic status and household crowding. Colonization rates reflect country of origin and ethnicity

H Pylori

- The inflammatory response induced by HP consists of neutrophils, lymphocytes, plasma cells, and macrophages, along with epithelial cell degeneration and injury; the most distinctive feature of HP infection is infiltration of the gastric epithelium by neutrophils . This pathology (chronic active gastritis) is the hallmark of H. pylori infection.
- H. pylori colonization also induces an exuberant systemic and mucosal humoral response; however, antibody production does not result in eradication.
- In the majority of infected persons residing in developed countries, gastritis is most severe in the antrum, with little or no inflammation in the gastric body.
- Persons who progress to gastric ulcer disease and gastric adenocarcinoma have a different pattern of gastritis that not only involves the antrum but also the acid-secreting corpus.

Differing effects of *H. pylori* on acid secretion, depending on the extent and intensity of gastric inflammation



Diagnosis of H. pylori

- The presence of H. pylori should only be sought if such results will affect clinical decisions.
- HP should be sought and eradicated in cases of PUD, patients with uninvestigated dyspepsia without alarm symptoms, in non-ulcer dyspepsia, in cases of unexplained iron deficiency anemia, in adults with idiopathic thrombocytopenia purpura, after mucosal resection of an early gastric cancer, and in patients who have developed a low-grade MALT lymphoma.
- Up to 80 percent of low-grade MALT lymphomas will regress with anti-HP therapy alone. It is uncertain whether testing for and treating HP is beneficial in patients taking long term aspirin or NSAIDs, in subjects with a family history of gastric cancer, and in patients on long-term PPI's

H. pylori diagnostic tests

Test	Sensitivity	Specificity	Advantage	Disadvantage
Invasive				
Histology	60-85 percent	greater than 95 percent	Provides additional information on gastric mucosa	Adding immunohistochemistry increases cost
Rapid urease testing	70-95 percent	greater than 95 percent	Inexpensive, works well if not on PPI	High inter-observer variability. Can give equivocal result
Culture	70 percent	100 percent	Can test for antibiotic sensitivity too	Limited availability. Sensitivity low
Noninvasive				
Urea breath testing	greater than 95 percent	greater than 95 percent	High positive & negative predictive value. Can use also to test eradication success	Patients should be off PPI/bismuth and antibiotics to avoid false negatives
Stool antigen tests	+ greater than 95 percent	greater than 95 percent	-High positive & negative predictive value. Can use also to test eradication success	PPI/bismuth and antibiotics to avoid false negatives. Patients may not comply with stool collection
Serology (IgG)	75-85 percent	80-90 percent	Inexpensive	Poor performance characteristics. Cannot be used for test of cure. No longer recommended

Management

Lifestyle modification:

- **Discontinue NSAIDs and use Acetaminophen for pain control if possible.**
- **Acid suppression--Antacids**
- **Smoking cessation**
- **No dietary restrictions unless certain foods are associated with problems.**
- **Alcohol in moderation**
  - **Men under 65: 2 drinks/day**
  - **Men over 65 and all women: 1 drink/day**
- **Stress reduction**

H Pylori Treatment

Treatment regimens for *H. pylori*

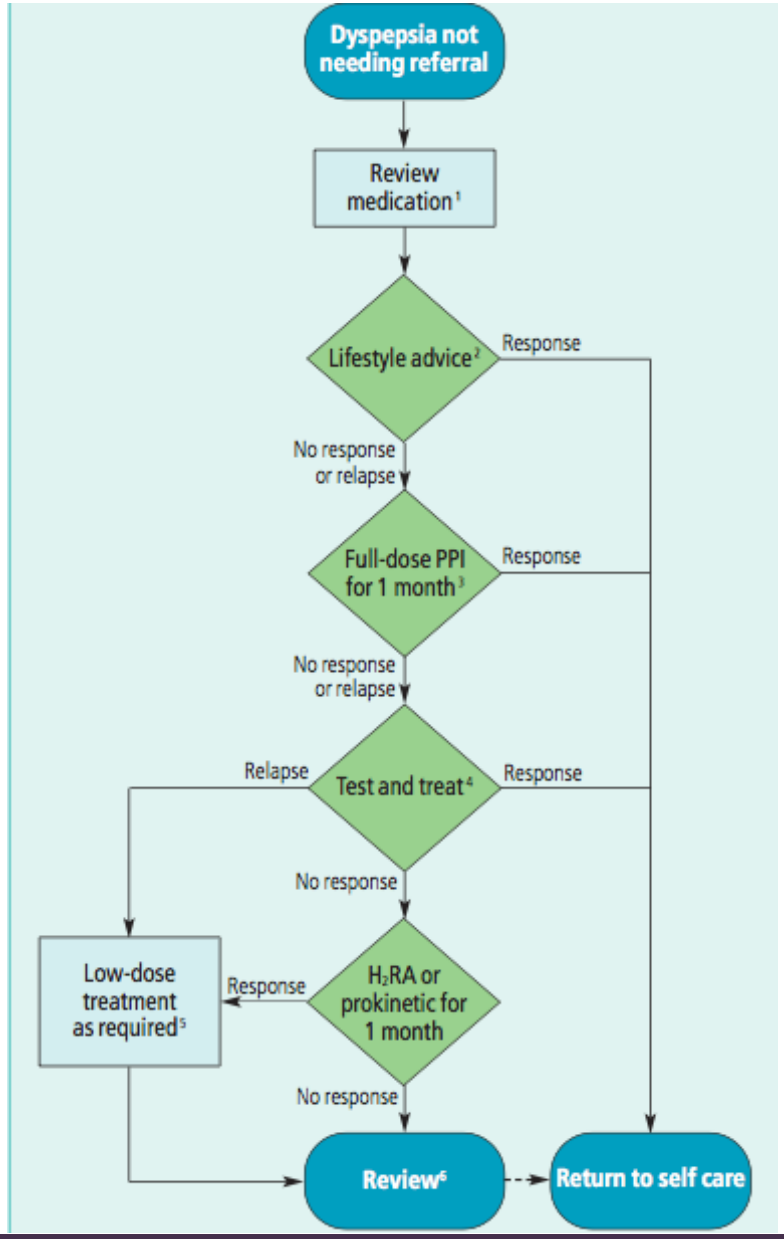
Therapy	Drug	Dosage	Duration (days)
Bismuth-based quadruple	Proton pump inhibitor (PPI)* & Bismuth subsalicylate & Tetracycline & Metronidazole	Twice a day† 120 mg four times a day 500 mg four times a day 500 mg three times a day	**14**
Concomitant	Proton pump inhibitor (PPI)* & Clarithromycin & Amoxicillin & Metronidazole	Twice a day† 500 mg twice a day 1000 mg twice a day 500 mg twice a day	**14**
Standard triple	Proton pump inhibitor (PPI)* & Clarithromycin & Amoxicillin (Or Metronidazole^)	Twice a day† 500 mg twice a day 1000 mg twice a day (500 mg twice a day)	**14**
Levofloxacin triple	Proton pump inhibitor (PPI)* & Levofloxacin & Amoxicillin	Twice a day† 500 mg once a day 1000 mg twice a day	**14**
Rifabutin triple	Proton pump inhibitor (PPI)* & Rifabutin & Amoxicillin	Twice a day† 300 mg once a day 1000 mg twice a day	**10**
High-dose dual	Proton pump inhibitor (PPI)* & Amoxicillin	Twice a day† 750 mg four times a day	**14**

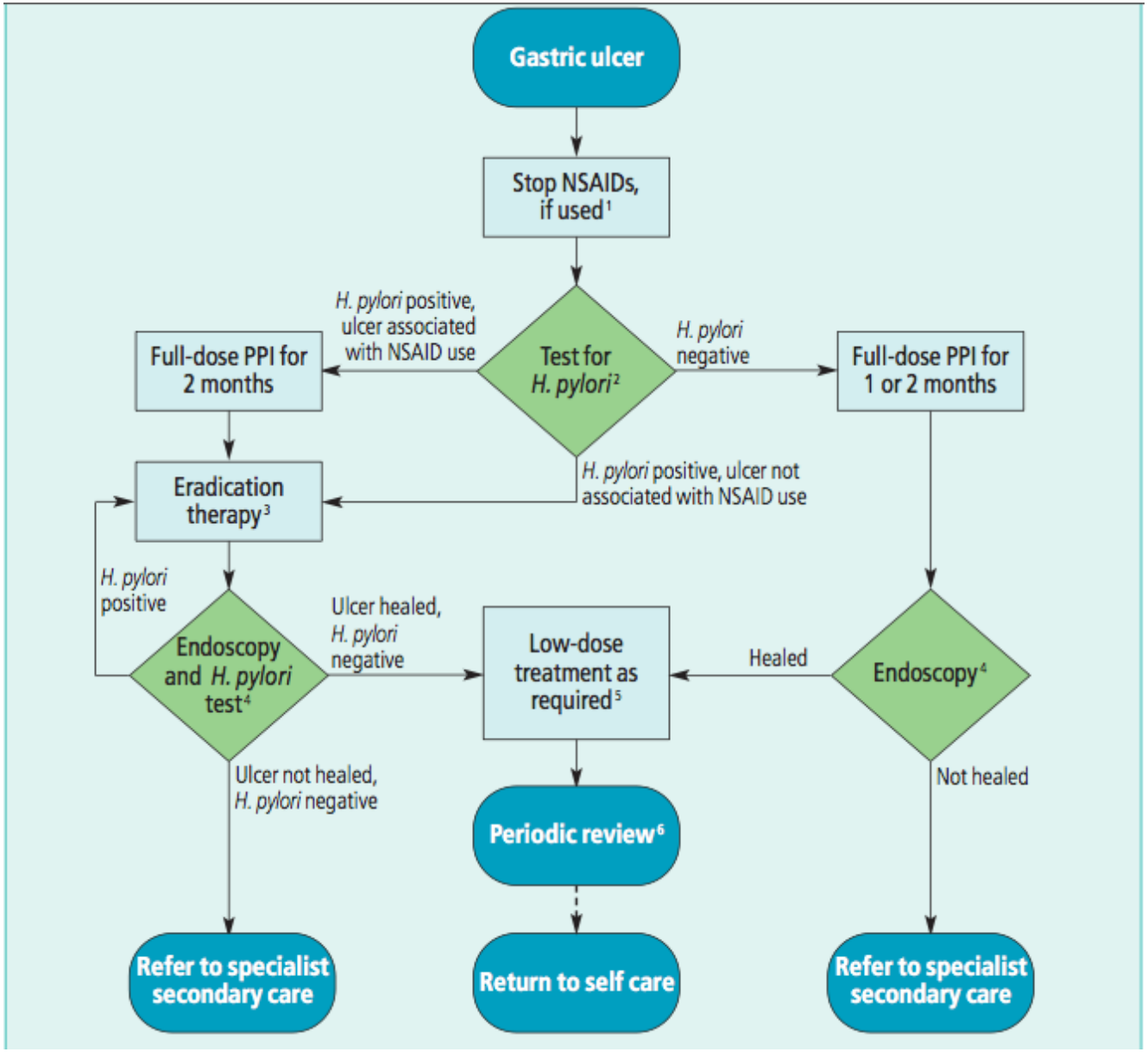
Prevention

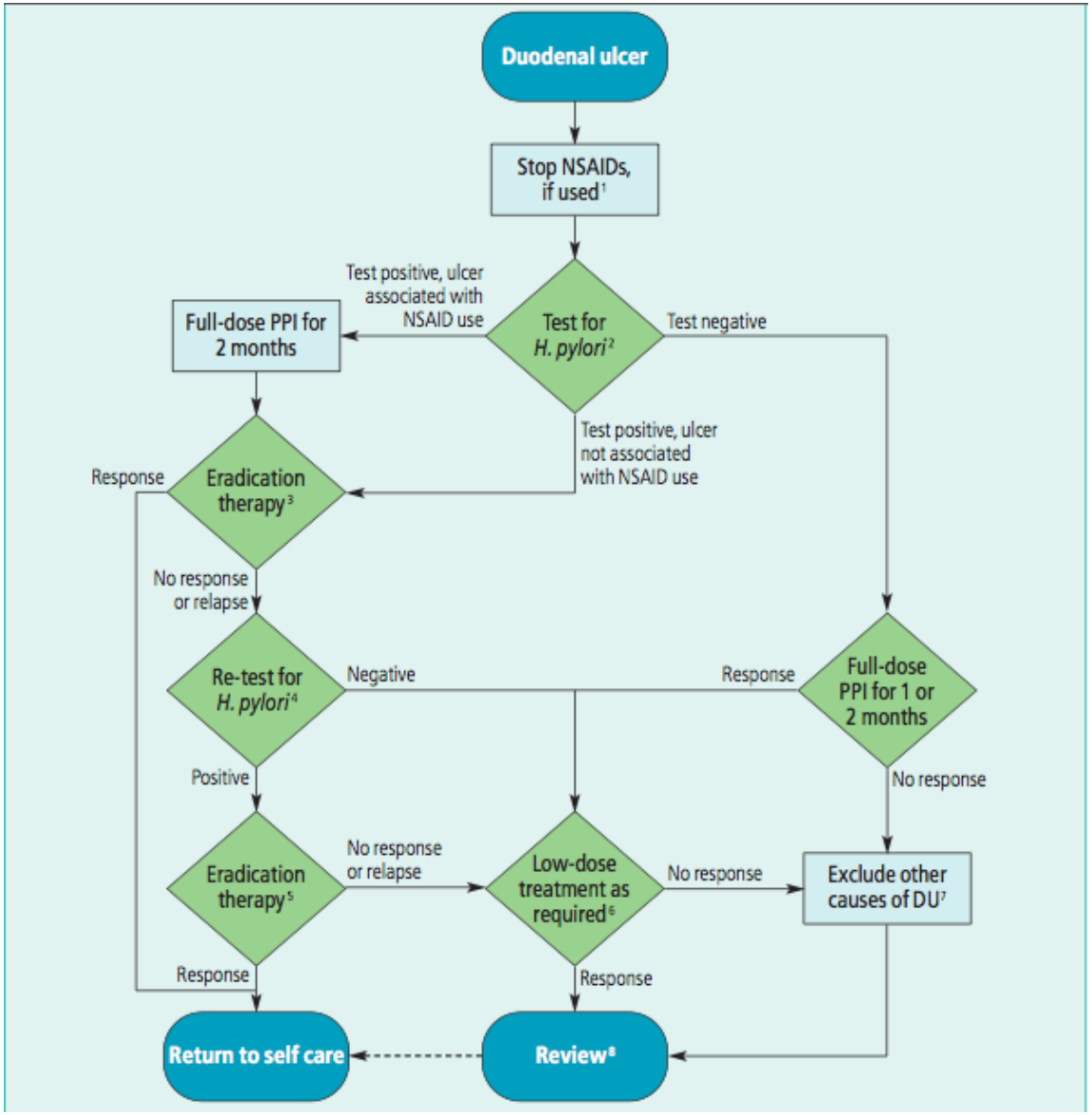
- Consider prophylactic therapy for the following patients:
  - Pts with NSAID-induced ulcers who require daily NSAID therapy
  - Pts older than 60 years
  - Pts with a history of PUD or a complication such as GI bleeding
  - Pts taking steroids or anticoagulants or patients with significant comorbid medical illnesses
- Prophylactic regimens that have been shown to dramatically reduce the risk of NSAID-induced gastric and duodenal ulcers include the use of a prostaglandin analogue or a proton pump inhibitor.
  - Omeprazole 20-40 mg PO every day
  - Lansoprazole 15-30 mg PO every day

Complications

- **Perforation & Penetration—into pancreas, liver and retroperitoneal space**
- **Peritonitis**
- **Bowel obstruction, Gastric outflow obstruction, & Pyloric stenosis**
- **Bleeding--occurs in 25% to 33% of cases and accounts for 25% of ulcer deaths.**
- **Gastric CA**


Dyspepsia not needing referral
Review medication[1]
Lifestyle advice[2]
Response
No response or relapse
Full-dose PPI for 1 month[3]
Response
No response or relapse
Relapse
Test and treat[4]
Response
No response
Low-dose treatment as required[5]
Response
H2RA or prokinetic for 1 month
No response
Review[6]
Return to self care


Gastric ulcer
Stop NSAIDs, if used[1]
Test for H. pylori[2]
H. pylori positive, ulcer associated with NSAID use
H. pylori negative
Full-dose PPI for 2 months
Full-dose PPI for 1 or 2 months
H. pylori positive, ulcer not associated with NSAID use
Eradication therapy[3]
H. pylori positive
Endoscopy and H. pylori test[4]
Ulcer healed, H. pylori negative
Low-dose treatment as required[5]
Healed
Endoscopy[4]
Ulcer not healed, H. pylori negative
Not healed
Periodic review[6]
Refer to specialist secondary care
Return to self care
Refer to specialist secondary care


Duodenal ulcer
Stop NSAIDs, if used[1]
Test for H. pylori[2]
Test positive, ulcer associated with NSAID use
Test negative
Full-dose PPI for 2 months
Test positive, ulcer not associated with NSAID use
Response
Eradication therapy[3]
No response or relapse
Re-test for H. pylori[4]
Negative
Response
Full-dose PPI for 1 or 2 months
Positive
No response
Eradication therapy[5]
No response or relapse
Low-dose treatment as required[6]
No response
Exclude other causes of DU[7]
Response
Response
Return to self care
Review[8]

Summary

- A peptic ulcer is a break in superficial epithelial cells penetrating down to muscularis mucosa
- Duodenal > gastric ulcers
- Can be asymptomatic
- H pylori is a predominant risk factor
- H pylori resistance to treatment is now rising
- Complications of PUD can lead to acute emergency of upper GI bleed