Peptic ulcer

Dr Peltec Angela

Definition

Definition

- Peptic ulcers are defects in the gastric or duodenal mucosa that extend through the muscularis mucosa
- Peptic ulcers occur in those portions of the GI tract that could be exposed to gastric secretions containing pepsin
- That is a disease that have possibility to recurrence

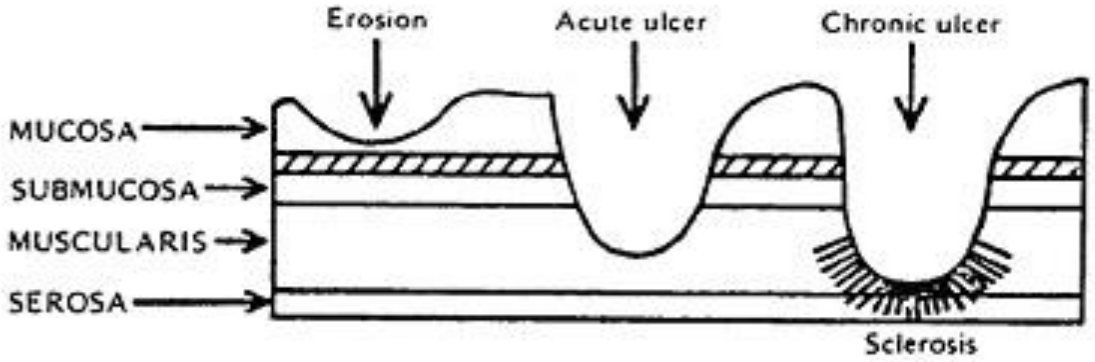


Figure 31.1. Diagrammatic illustration of acute and chronic gastric mucosal lesions. (From Brooks, F.P. (ed.): Gastrointestinal Pathophysiology. New York, Oxford University Press, 1978, p. 101).

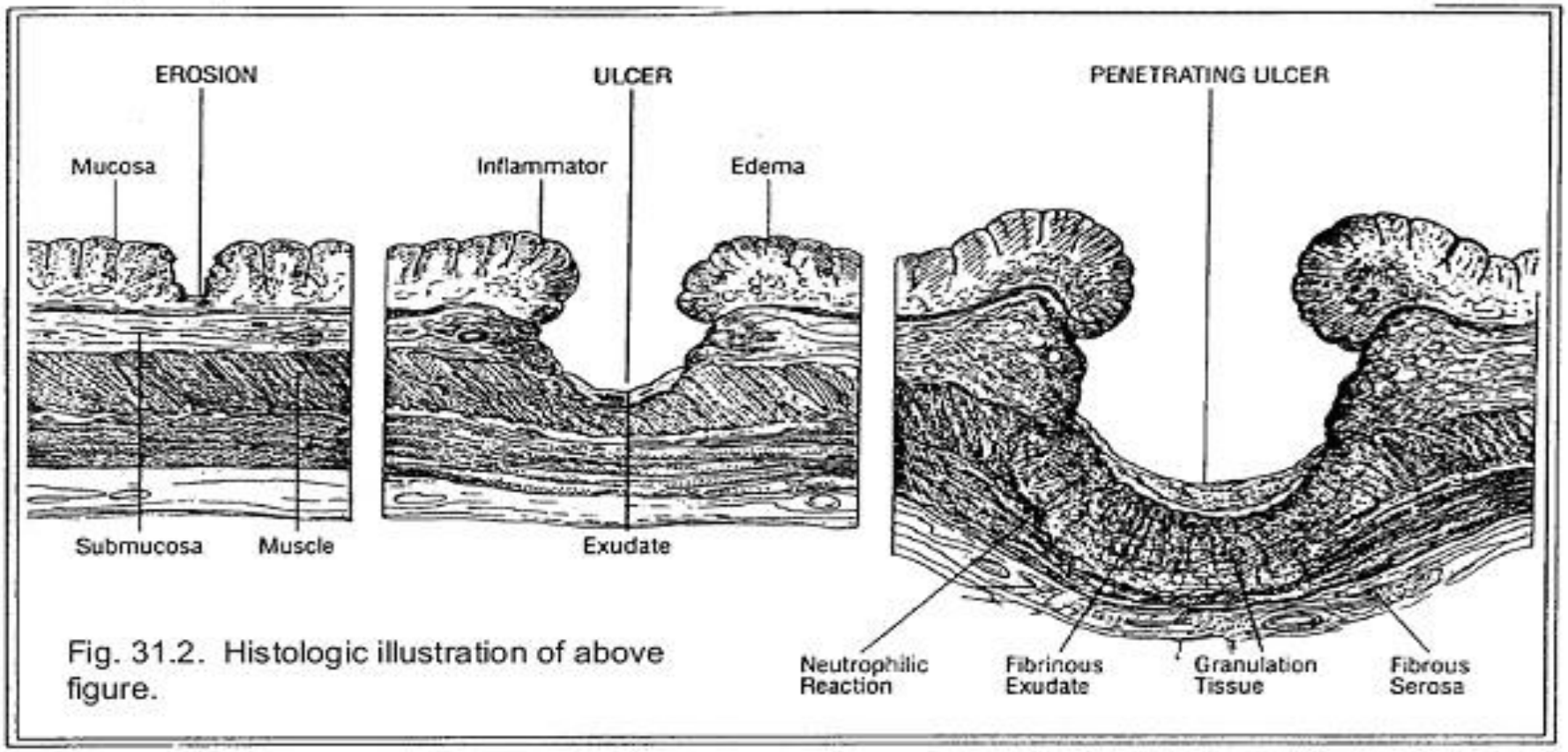


Fig. 31.2. Histologic illustration of above figure.

Epidemiology

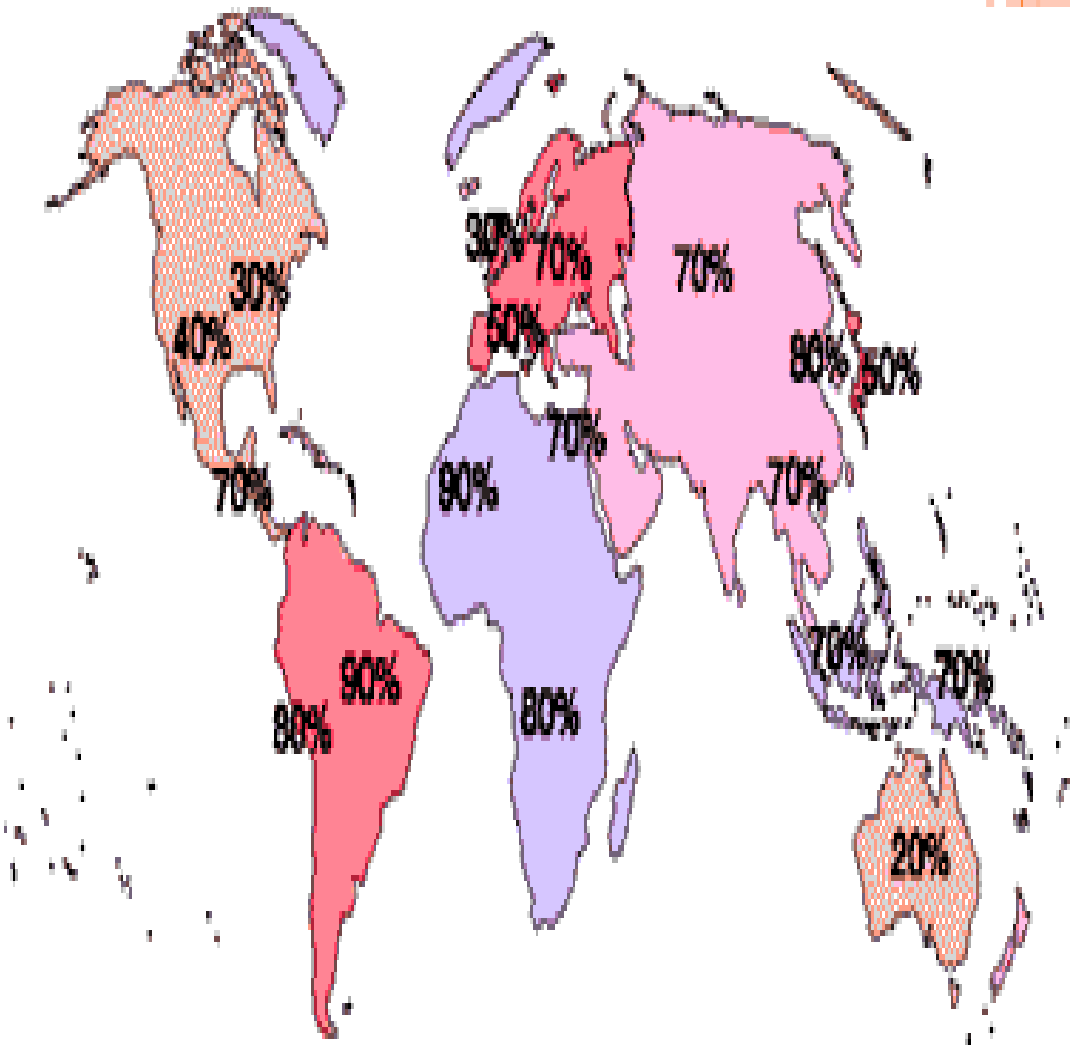
Epidemiology

- The incidence of duodenal ulcers has been decreasing over the past 3-4 decades (the rate of simple gastric ulcer is in decline)
- The incidence of complicated gastric ulcer and hospitalization has remained stable, partly due to the concomitant use of aspirin in an aging population
- The prevalence of PUD has shifted from predominance in males to similar occurrences in males and females (11-14% in men and 8-11% in women)

Epidemiology

- Age trends for ulcer occurrence reveal declining rates in younger men, particularly for duodenal ulcer, and increasing rates in older women
- Trends reflect complex changes in risk factors for PUD, including age-cohort phenomena with the prevalence of *H pylori* infection and the use of NSAIDs in older populations
- The frequency of PUD in other countries is variable and is determined primarily by association with the major causes of PUD: *H pylori* and NSAIDs

Epidemiologic studies reflect the widespread incidence of Hp positive gastritis



Etiology

Etiology

Peptic ulcer disease (PUD) may be due to any of the following:

- ***H pylori* infection**
- **Drugs**
- **Lifestyle factors**
- **Severe physiologic stress**
- **Hypersecretory states (uncommon)**
- **Genetic factors**

Etiology

H pylori infection

- The rate of *H pylori* infection for duodenal ulcers is less than 75% for patients who do not use NSAIDs
- Prevalence of *H pylori* infection in complicated ulcers (ie, bleeding, perforation) is significantly lower than that found in uncomplicated ulcer disease

Drugs

- NSAID use is a common cause of PUD
- As many as 30% of adults taking NSAIDs have GI adverse effects

Etiology
Lifestyle factors - smoking

- However, smoking in the setting of *H pylori* infection may increase the risk of relapse of PUD
- Smoking is harmful to the gastroduodenal mucosa, and *H pylori* infiltration is denser in the gastric antrum of smokers

Lifestyle factors – Ethanol

- **Ethanol** is known to cause gastric mucosal irritation and nonspecific gastritis
- Little evidence suggests that **caffeine intake** is associated with an increased risk of duodenal ulcers

Etiology
Lifestyle factors
Severe physiologic stress

Stressful conditions that may cause PUD include:

- burns
- CNS trauma
- surgery
- severe medical illness (serious systemic illness, sepsis, hypotension, respiratory failure, multiple traumatic injuries)

Etiology
Hypersecretory states (uncommon)

The following are among hypersecretory states that may, uncommonly, cause PUD:

- Gastrinoma (Zollinger-Ellison syndrome) or multiple endocrine neoplasia type I (MEN-I)
- Antral G cell hyperplasia
- Systemic mastocytosis
- Basophilic leukemias
- Cystic fibrosis
- Short bowel syndrome
- Hyperparathyroidism

Etiology
Genetics

- More than 20% of patients have a family history of duodenal ulcers, compared with only 5-10% in the control groups
- In addition, weak associations have been observed between duodenal ulcers and blood type O (patients who do not secrete ABO antigens in their saliva and gastric juices)
- A rare genetic association exists between **familial hyperpepsinogenemia type I** (a genetic phenotype leading to enhanced secretion of pepsin) and duodenal ulcers

Table 1. Etiology of Peptic Ulcer Disease

Common
Helicobacter pylori infection
Nonsteroidal anti-inflammatory drugs (NSAIDs)
Stress-related mucosal damage
Uncommon
Zollinger-Ellison syndrome and other hypersecretory acid states
Tumors (cancer, lymphoma)
Viral infections
Radiation/chemotherapy
Illicit-drug use causing vascular insufficiency
Rare
Crohn's disease of the stomach/duodenum
Colonization of stomach with *Helicobacter heilmannii*
Idiopathic

Source: References 3, 4.

Berardi RR, Welage LS. Peptic ulcer disease. In: DiPiro JT, Talbert RL, Yee GC, et al, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 7th ed. New York, NY: McGraw-Hill; 2008:569-587.
4. Malfertheiner P, Chan FK, McColl KE. Peptic ulcer disease. *Lancet*. 2009;374:1449-1461. - See more at: http://www.uspharmacist.com/content/d/feature/c/24725/#sthash.pfWd6oKi.dpuf

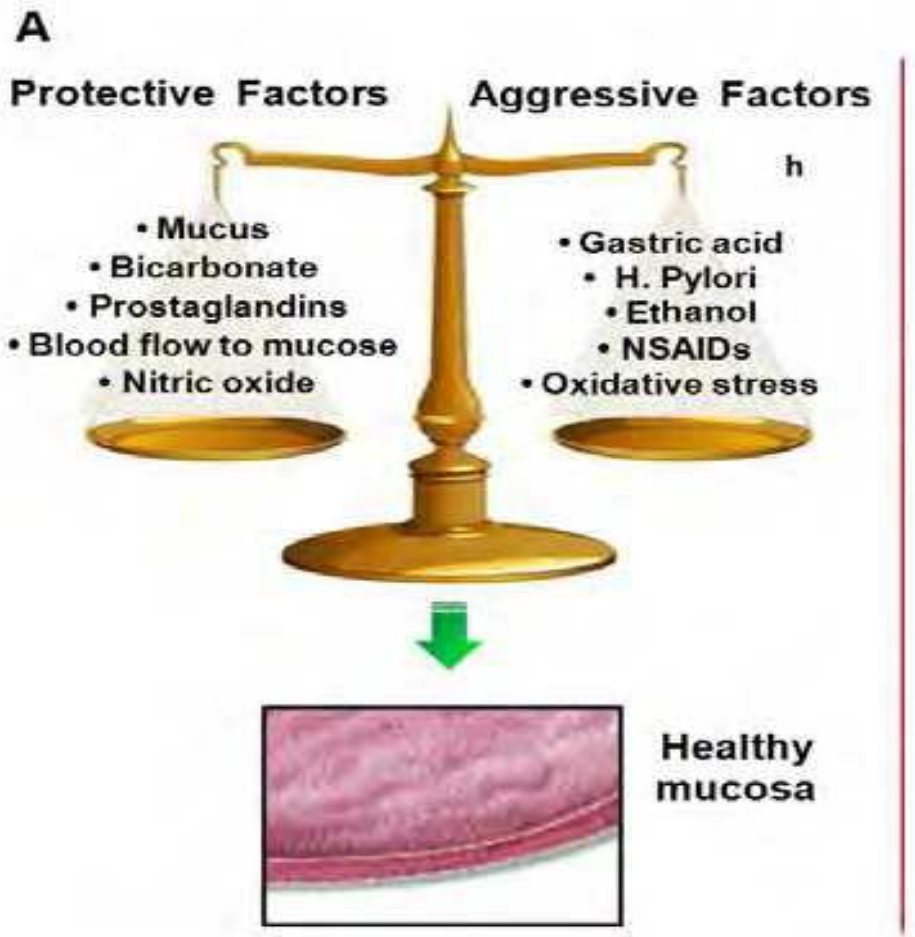
Table 1. Etiology of Peptic Ulcer Disease

Common
Helicobacter pylori infection
Nonsteroidal anti-inflammatory drugs (NSAIDs)
Stress-related mucosal damage
Uncommon
Zollinger-Ellison syndrome and other hypersecretory acid states
Tumors (cancer, lymphoma)
Viral infections
Radiation/chemotherapy
Illicit-drug use causing vascular insufficiency
Rare
Crohn's disease of the stomach/duodenum
Colonization of stomach with *Helicobacter heilmannii*
Idiopathic

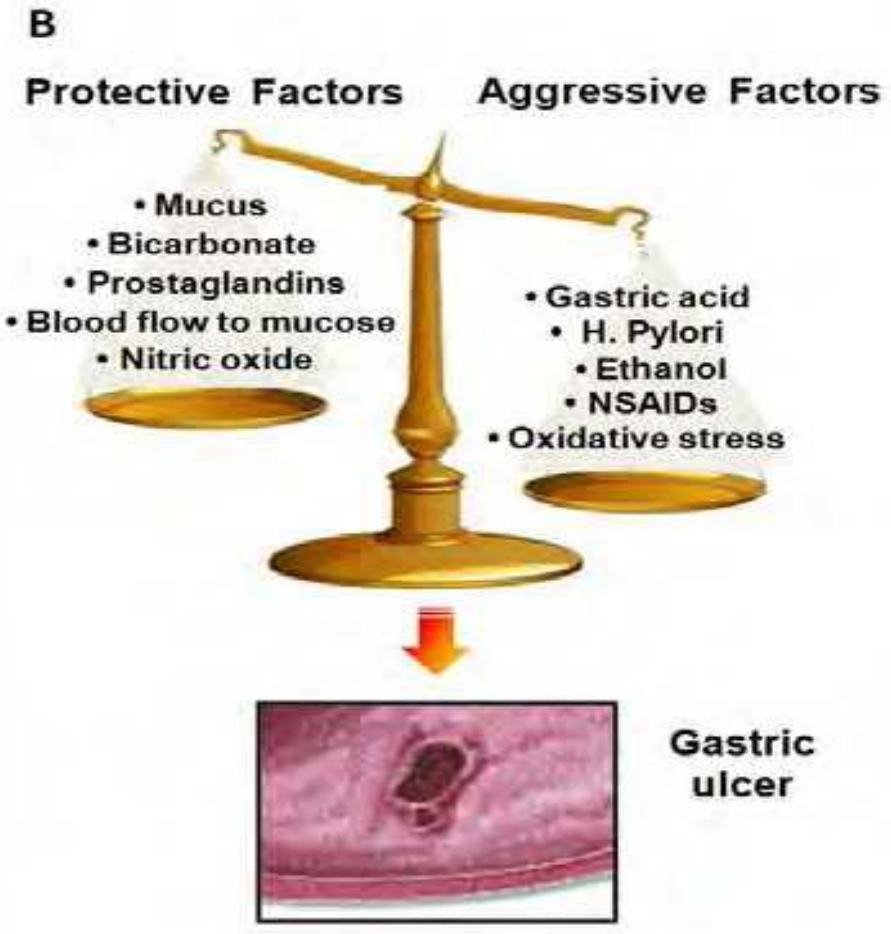
Berardi RR, Welage LS. Peptic ulcer disease. In: DiPiro JT, Talbert RL, Yee GC, et al, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 7th ed. New York, NY: McGraw-Hill; 2008:569-587.
4. Malfertheiner P, Chan FK, McColl KE. Peptic ulcer disease. *Lancet*. 2009;374:1449-1461. - See more at: http://www.uspharmacist.com/content/d/feature/c/24725/#sthash.pfWd6oKi.dpuf

Pathophysiology

PATHOPHYSIOLOGY



(A) HEALTHY GASTRIC MUCOSA: BALANCE BETWEEN MUCOSAL AGGRESSIVE AND PROTECTIVE FACTORS



(B) GASTRIC ULCER FORMATION: IMBALANCE BETWEEN MUCOSAL AGGRESSIVE AND PROTECTIVE FACTORS.

Pathophysiology Protective Factors

The defensive mechanisms include

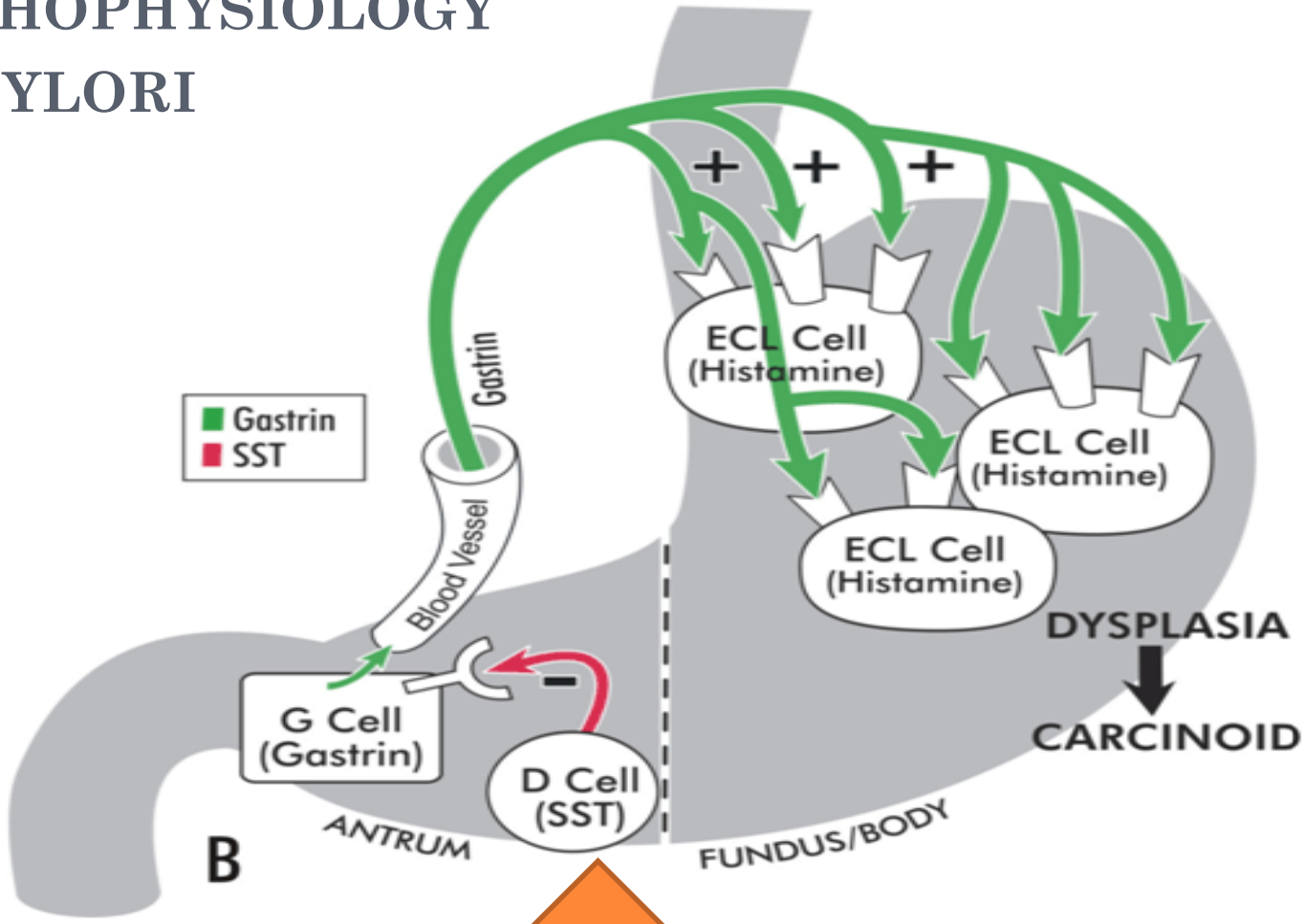
- mucus
- tight intercellular junctions
- cellular restitution
- epithelial renewal
- mucosal blood flow

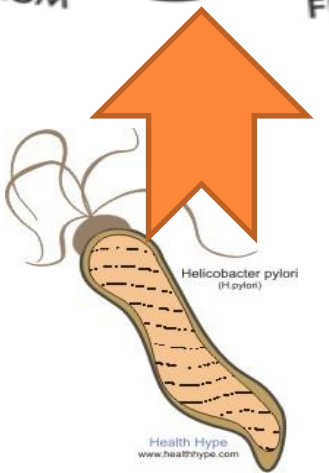
Pathophysiology
Aggressive factors

- NSAIDs
- *H pylori* infection
- Alcohol
- bile salts
- Acid
- Pepsin

can alter the mucosal defense by allowing back diffusion of hydrogen ions and subsequent epithelial cell injury

Pathophysiology H. pylori





inhibiting the D-cell (somatostatin-secreting cells) activity

Type OF Gastric/Duodenal Ulcers

A. *GU-I*

Characteristics, In body of stomach, especially the inner curvature.

- Chief problem - inadequate protective ability
- Acid hyposecretion: parietal cell mass
- Gastrin secretion: normal or increased
- Age: onset at 60-70 years
- Exogenous aggressive factors: aspirin, NSAIDS (PG synthesis and mucosal permeability)
- Duodeno-gastric reflux: low pyloric sphincter pressure; low pyloric contractile response to acid in duodenum; disruption of gastric mucosal barrier
- Genetic factors
- *Helicobacter pylori and NH3 production*

Type of Gastric/Duodenal Ulcers

B. *GU-II/DU*

Characteristics, In pyloric gland region of stomach/duodenum

- Chief problem - excess acid and pepsin
- Acid hypersecretion: parietal cell mass; parietal cell sensitivity to secretagogues
- Nocturnal acid hypersecretion
- Gastrin hypersecretion with meals
- Accelerated gastric emptying
- Impaired inhibition of acid secretion
- Impaired bicarbonate secretion
- Impaired duodenal mucosal defense
- *Helicobacter pylori and NH3 production*

Modified Johnson Classification of peptic ulcers

Type I: Ulcer along the lesser curve of stomach

Type II: Two ulcers present - one gastric, one duodenal/prepyloric

Type III: Prepyloric ulcer

Type IV: Proximal gastroesophageal ulcer

Type V: Anywhere (associated with chronic NSAID use)

Clinical Presentation

History
Pain

- **Epigastric pain** is the most common symptom of both gastric and duodenal ulcers
- It is characterized by a gnawing or burning sensation and occurs after meals—classically, **shortly after meals** with **gastric** ulcer and **2-3 hours afterward** with **duodenal** ulcer
- Food or antacids relieve the pain of duodenal ulcers but provide minimal relief of gastric ulcer pain

History
Pain

- Duodenal ulcer pain often awakens the patient at night
- About 50-80% of patients with duodenal ulcers experience nightly pain, as opposed to only 30-40% of patients with gastric ulcers and 20-40% of patients with nonulcer dyspepsia (NUD)
- Pain typically follows a daily pattern specific to the patient
- Pain with radiation to the back is suggestive of a posterior penetrating gastric ulcer complicated by pancreatitis

History

Other possible manifestations include the following:

- Dyspepsia, including belching, bloating, distention, and fatty food intolerance
- Heartburn
- Chest discomfort
- Hematemesis or melena resulting from gastrointestinal bleeding
- Melena may be intermittent over several days or multiple episodes in a single day

History

Alarm features that warrant prompt gastroenterology referral include the following:

- Bleeding or anemia
- Early satiety
- Unexplained weight loss
- Progressive dysphagia or odynophagia
- Recurrent vomiting
- Family history of GI cancer

Physical Examination

In uncomplicated PUD, the clinical findings are few and nonspecific and include the following:

- **Epigastric tenderness** (usually mild)
- **Right upper quadrant tenderness** may suggest a biliary etiology or, less frequently, PUD
- **Guaiac-positive stool** resulting from occult blood loss
- **Melena** resulting from acute or subacute gastrointestinal bleeding
- **Succussion splash** resulting from partial or complete gastric outlet obstruction

Differential Diagnoses

- Acute Coronary Syndrome
- Aneurysm, Abdominal
- Cholangitis
- Cholecystitis
- Cholecystitis and Biliary Colic in Emergency Medicine
- Cholelithiasis
- Diverticular Disease
- Esophageal Perforation, Rupture and Tears
- Esophagitis
- Gastritis, Acute
- Gastritis, Chronic
- Gastroenteritis
- Gastroesophageal Reflux Disease
- Inflammatory Bowel Disease
- Viral Hepatitis

Workup

Approach Considerations

If the diagnosis of PUD is suspected, obtaining

- CBC count
- liver function tests (LFTs)
- Amylase
- lipase may be useful

- CBC count and iron studies can help detect anemia, which is an alarm signal that mandates early endoscopy to rule out other sources of chronic GI blood loss

H PYLORI TESTING

Testing for *H pylori* infection is essential in all patients with peptic ulcers

Endoscopic or invasive tests for *H pylori* include

- a rapid urease test
- histopathology
- culture

Noninvasive tests for *H pylori* include

- **Urea breath tests**
- **Antibodies (immunoglobulin G [IgG]) to *H pylori***
- **Fecal antigen testing**

Endoscopy

- Upper GI endoscopy is the preferred diagnostic test in the evaluation of patients with suspected PUD
- It is **highly sensitive** for the diagnosis of gastric and duodenal ulcers, allows for **biopsies and cytologic brushings** in the setting of a gastric ulcer to differentiate a **benign ulcer from a malignant lesion**, and allows for the detection of ***H pylori* infection** with antral biopsies for a **rapid urease test and/or histopathology** in patients with PUD

Radiography

- In patients presenting acutely, a chest radiograph may be useful to detect **free abdominal air** when perforation is suspected
- On upper GI contrast study with water-soluble contrast, the extravasation of contrast indicates **gastric perforation**
- **Double-contrast radiography** performed by an experienced radiologist may approach the diagnostic accuracy of upper GI endoscopy
- An upper GI series is **not as sensitive** as endoscopy for establishing a diagnosis of **small ulcers** (< 0.5 cm)

Biopsy

- A single biopsy offers 70% accuracy in diagnosing gastric cancer, but 7 biopsy samples obtained from the base and ulcer margins increase the sensitivity to 99%
- Brush cytology has been shown to increase the biopsy yield, and this method may be useful particularly when bleeding is a concern in a patient with coagulopathy

Stage Classification of Gastric Ulcer by Sakita-Miwa

Stages	Manifestation
Active stage	
A1	The surrounding mucosa is edematously swollen and no regenerating epithelium is seen endoscopically
A2	The surrounding edema has decreased, the ulcer margin is clear, a red halo in the marginal zone
Healing stage	
H1	The ulcer crater is still evident and the margin of the ulcer is sharp. The diameter of the mucosal defect is about one-half to two thirds that of A1
H2	The defect is smaller than in H1 and the regenerating epithelium covers most of the ulcer floor. The area of white coating is about a quarter to one-third that of A1
Scarring stage	
S1	The regenerating epithelium completely covers the floor of ulcer. The white coating has disappeared. Initially, the regenerating region is markedly red. This is called “red scar”
S2	In several months to a few years, the redness is reduced to the color of the surrounding mucosa. This is called “white scar”

Complications of Peptic Ulcer Disease

Complications of Peptic Ulcer Disease

- **Refractory, symptomatic peptic ulcers**, though rare after eradication of *H pylori* infection and the appropriate use of antisecretory therapy, are a potential complication of PUD
- **Obstruction** is particularly likely to complicate PUD in cases refractory to aggressive antisecretory therapy, *H pylori* eradication, or avoidance of NSAIDs
- Obstruction may persist or recur despite endoscopic balloon dilation

Complications of Peptic Ulcer Disease

- **Perforation** is also a possibility
- **Penetration**, particularly if not walled off or if a gastrocolic fistula develops, is a potential complication
- In addition, **ulcer bleeding**, particularly in patients with a history of massive hemorrhage and hemodynamic instability, recurrent bleeding on medical therapy, and failure of therapeutic endoscopy to control bleeding is a serious complication

Complications of Peptic Ulcer Disease

- Patients with gastric ulcers are also at risk of developing **gastric malignancy**
- The risk is approximately 2% in the initial 3 years
- One of the important risk factors is related to ***H pylori* infection**
- *H pylori* is associated with atrophic gastritis, which, in turn, predisposes to **gastric cancer**
- *H pylori* infection is associated with **gastric lymphoma or mucosa-associated lymphoid tissue (MALT) lymphoma**
- Normal gastric mucosa is devoid of organized lymphoid tissue
- *H pylori* infection promotes acquisition of lymphocytic infiltration and often the formation of lymphocytic aggregates and follicles from which MALT lymphoma develops
- Eradication of *H pylori* is very important in this group of patients because **eradication of *H pylori* has been shown to cause a remission of MALT lymphoma**

Prognosis

- **Eradication of *H pylori* infection changes the natural history of the disease**, with a decrease in the ulcer recurrence rate from 60-90% to approximately 10-20%
- With regard to NSAID-related ulcers, the incidence of perforation is approximately 0.3% per patient year, and the incidence of obstruction is approximately 0.1% per patient year

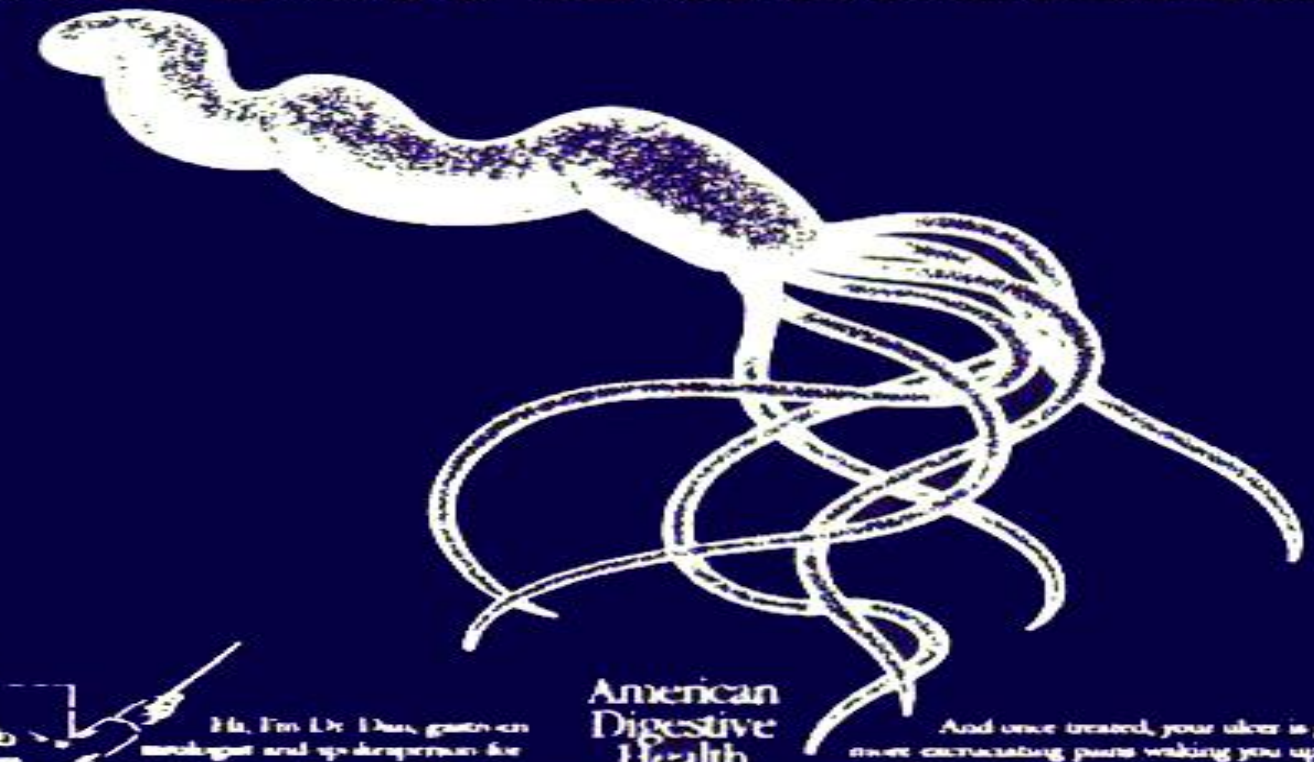
Prognosis

Emergency operations for peptic ulcer perforation carry a mortality risk of 6-30%.

Factors associated with higher mortality in this setting include the following:

- Shock at the time of admission
- Renal insufficiency
- Delaying the initiation of surgery for more than 12 hours after presentation
- Concurrent medical illness (eg, cardiovascular disease, diabetes mellitus
- Age older than 70 years
- Cirrhosis
- Immunocompromised state
- Location of ulcer (mortality associated with perforated gastric ulcer is twice that associated with perforated duodenal ulcer)

Contrary to popular belief, most ulcers are not caused by your boss. Unless, of course, your boss is a bacterium.



Hi. I'm Dr. Dan, gastroenterologist and spokesperson for the American Digestive Health Foundation.™

Research has discovered that nearly all ulcers are caused by this guy, the bacteria, *H. pylori* – not stress or spicy foods as previously thought. More importantly, *H. pylori* can be treated using common medications.

American Digestive Health Foundation

Digestive Health Institute

And once treated, your ulcer is gone! Just think, no more excruciating pains waking you up in the middle of the night. That's got to be worth looking into!

If you've been diagnosed with an ulcer, experience sharp or burning stomach pain, or frequent indigestion, ask your doctor about *H. pylori* and call for more information.

1-800-NO-ULCER. No more ulcer, no more pain.

1-800-466-1237