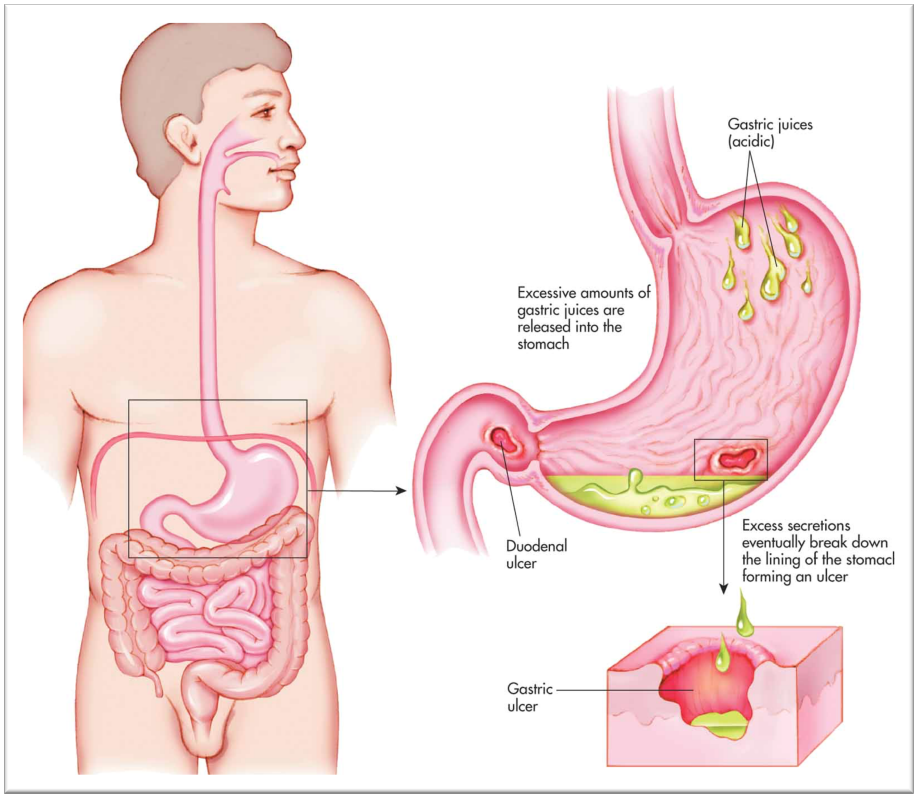
Lecture 2
Peptic Ulcer Disease

{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلَّ الجهل طوال حياتهِ }

Revised by
خولة العماري & هشام الغفيلي

Red: Important. Grey: Extra Notes Doctors Notes will be in text boxes



Objectives:

Upon completion of this lecture the students will:

- **Understand the Pathophysiology of acute and chronic peptic ulcer**
  - Increase Aggressive Factors or decrease Defensive Factors
  - Acute ulcers (acute gastritis, severe stress response, extreme hyperacidity)
  - Chronic ulcer
- **Know the possible causes of gastric and duodenal ulcers with emphasis on most common causes (H pylori and drugs)**
- **Recognize the gross and microscopic features of peptic ulcer:**
  - The classic peptic ulcer is a round to oval, sharply punched-out defect
  - Necrotic tissue and polymorph exudate overlying inflamed granulation tissue which merges with mature fibrous (scar) tissue.
- **Recognize the clinical features and consequences of acute and chronic peptic ulcer:**
  - Epigastric pain Gnawing or burning sensation.
  - Some present with complications such as iron deficiency anemia, frank hemorrhage, or perforation.

Sources: Doctor's slides, Robbins and First aid

Ulcers:

A breach in the mucosa of the alimentary tract that may extend through muscularis mucosa into submucosa or deeper.

What's the difference between an ulcer and erosion?
They both are defects in the lining epithelium. If it was superficial, that makes it erosion. But if it was deep that makes it an ulcer

Types of ulcers:

1. **Peptic ulcers:**

   Peptic ulcer is ulcer in the lining of the stomach or first part of the small intestine, the duodenum. It can be acute or chronic.

   Occurs secondary to gastric acidity.
   Gastric ulcer it's limited to the stomach.
   Peptic ulcer is not limited to the stomach.

2. **Stress ulcers (acute gastric ulcers):**

   Acutely developing gastric mucosal defects that may appear after severe stress.

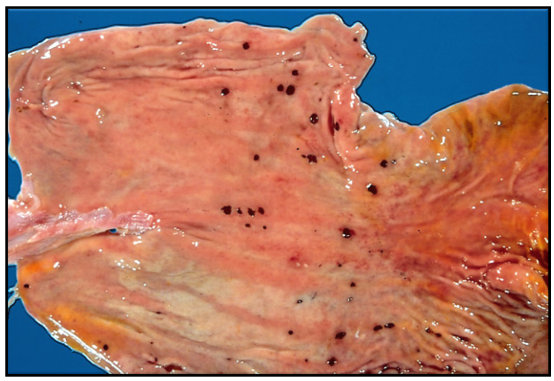
Pathophysiology of ulcers:

Imbalance

Aggressive Factors	Defensive Factors
• H. pylori • Drugs (NSAIDs) • Acid • Pepsin • Bile salts	• Mucus • Bicarbonate • Blood flow • Cell renewal • Prostaglandins • Phospholipid

Aggressive Factors → | ← **Defensive Factors**

Acute Peptic Ulcers: (Stress Ulcers):



Grossly: Acute ulcers are small and multiple, while Chronic are bigger and presents with only 1 or 2 lesions.

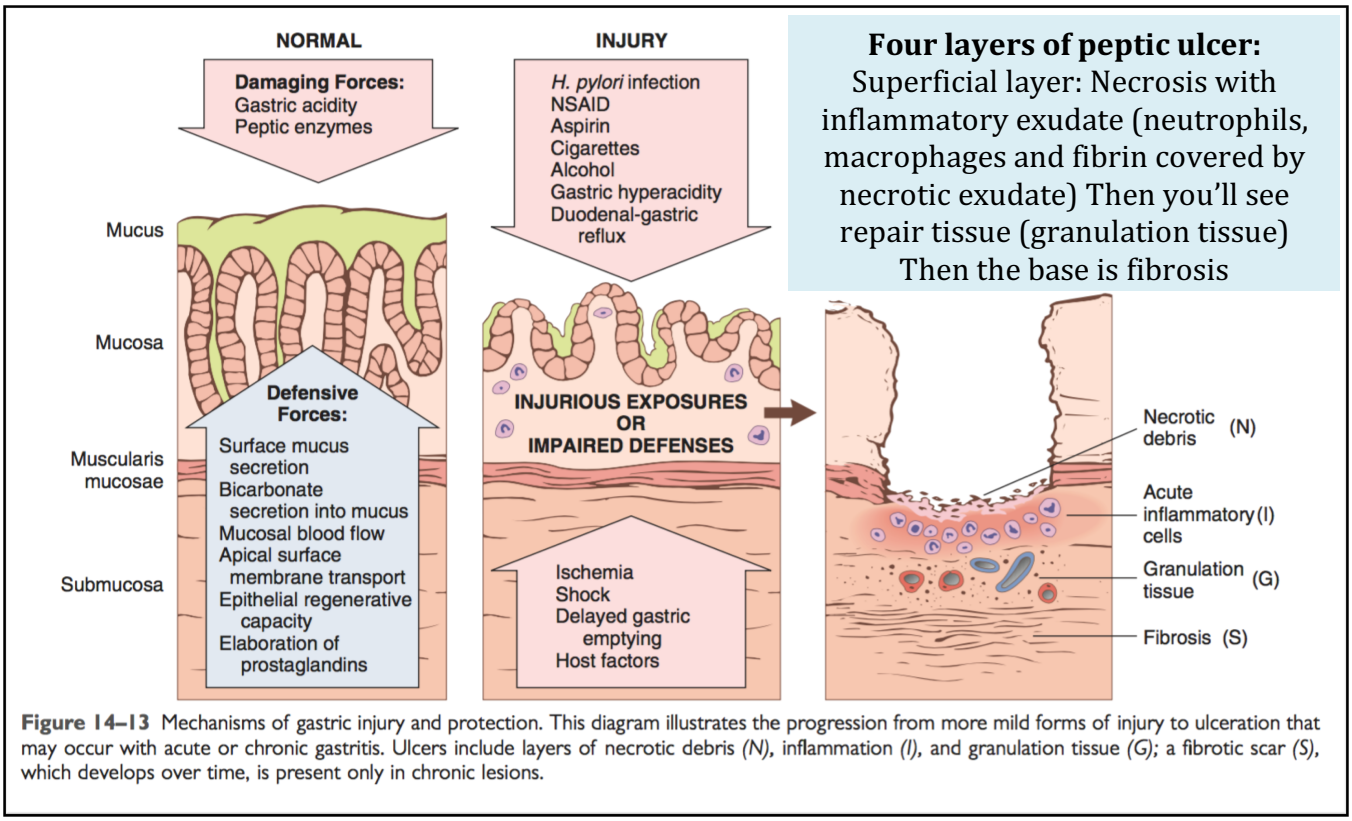
Pathophysiology:

- **As part of an acute gastritis:**

  Acute gastritis: Disruption of mucosal barrier → inflammation

  Due to:

  - Excessive alcohol consumption
  - NSAIDs (↓ PGE2 → ↓ gastric mucosa protection)
  - Radiation therapy
  - Chemotherapy.



Four layers of peptic ulcer:
Superficial layer: Necrosis with inflammatory exudate (neutrophils, macrophages and fibrin covered by necrotic exudate) Then you'll see repair tissue (granulation tissue) Then the base is fibrosis

Figure 14–13 Mechanisms of gastric injury and protection. This diagram illustrates the progression from more mild forms of injury to ulceration that may occur with acute or chronic gastritis. Ulcers include layers of necrotic debris *(N)*, inflammation *(I)*, and granulation tissue *(G)*; a fibrotic scar *(S)*, which develops over time, is present only in chronic lesions.

- **As a complication of a severe stress response:**
  - Curling ulcers: occurring in the proximal duodenum and associated with severe burns. (Burns → ↓ plasma volume → sloughing of gastric mucosa)
  - Cushing ulcers (Major Trauma). (↑ vagal stimulation → ↑ ACh → ↑ H+ production)
  - Cerebrovascular accidents. (Brain hemorrhage).

- **As a result of extreme hyperacidity:**

Zollinger-Ellison syndrome: Gastrin-secreting tumor (gastrinoma) of pancreas or duodenum. Acid hypersecretion causes recurrent ulcers in duodenum and jejunum.

A tumor of neuroendocrine cells producing gastrin

Morphology:

- Acute stress ulcers are found anywhere in the stomach.
- They range in depth from very superficial lesions (erosion) to deeper lesions that involve the entire mucosal thickness (true ulceration).

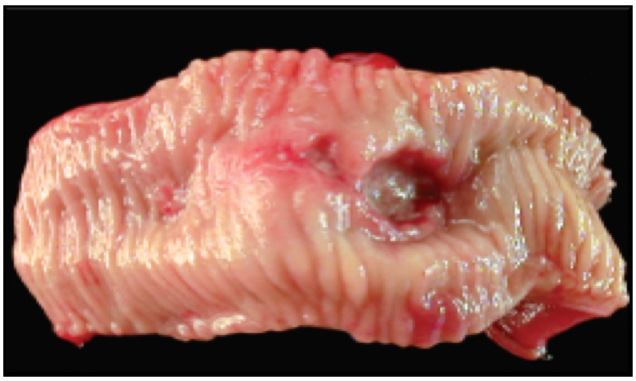
- **Prognosis:**

The gastric mucosa can recover completely if the person does not die from the primary disease.

Prognosis depends on the underlying cause

Chronic Peptic Ulcers:

- Peptic ulcers are chronic, recurring lesions that occur most often in middle-aged to older adults **without** obvious precipitating conditions, other than chronic gastritis.
- The most common cause of chronic gastritis is infection with the bacillus Helicobacter pylori.
- Chronic Peptic Ulcers are, most often solitary.
- H. Pylori infection is a major factor in the pathogenesis of peptic ulcer.



Pathophysiology:

Good regeneration power will be reduced when stopping prostaglandin synthesis

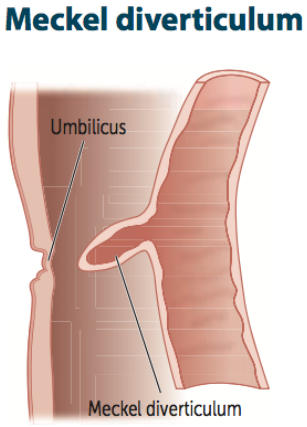
- NSAIDs and aspirin stop prostaglandin synthesis.
- The protective effects of prostaglandins: enhanced bicarbonate secretion and increased vascular perfusion.
- Cigarette smoking: impairs mucosal blood flow and healing.
- Chronic renal failure, and hyperparathyroidism are associated with hypercalcemia: stimulates gastrin production and therefore increases acid secretion.
- Psychological stress (can increase gastric acid secretion).

Locations:

- May occur in any portion of the GI tract exposed to acidic gastric juices.
- 98% located in first portion of duodenum or stomach, ratio = 4:1.
- Esophagus: as a result of GERD or acid secretion by ectopic gastric mucosa.
- Gastric mucosa within a Meckel diverticulum[1] can result in peptic ulceration of adjacent mucosa.
- In **Zollinger-Ellison syndrome:** multiple peptic ulcerations in the stomach, duodenum, and even the jejunum.

Meckel diverticulum[1]: Persistence of the vitelline duct. May contain ectopic acid–secreting gastric mucosa and/or pancreatic tissue.

Congenital and found in the distal end of the ileum.
Usually the Vitelline ducts are completely closed, but if it wasn't completely closed that part is called Meckel diverticulum.
Some of them are lined by gastric type epithelium, so they have the power to produce pepsin and HCL



Gastric ulcers: 70% related to H. Pylori

The mucosal defences against acid attack consist of:

- **Mucus-bicarbonate barrier:**

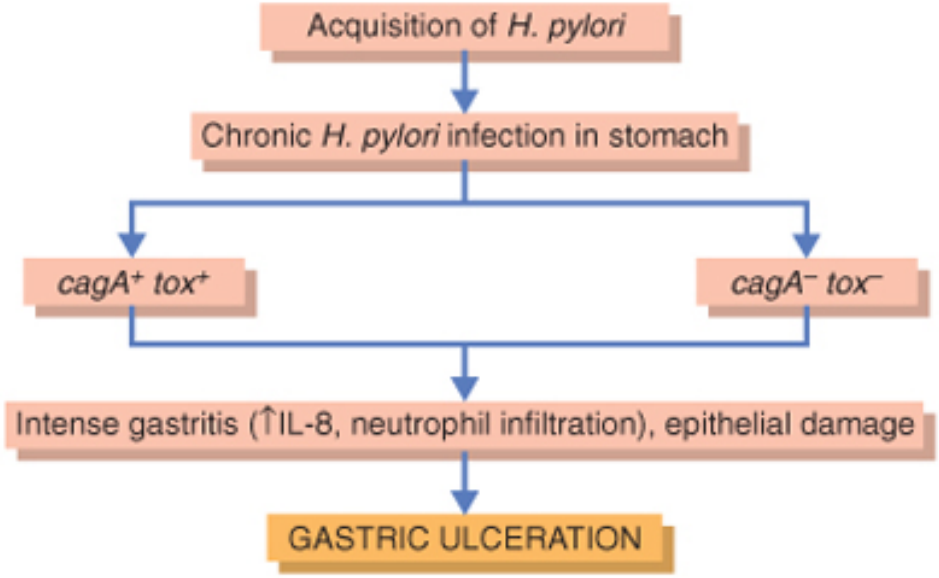
  When Duodeno-gastric reflux (bile) occurs → Ulcer.

- **The surface epithelium:**
  - NSAIDs (blocking the synthesis of the prostaglandins).
  - H. pylori infection, (cytotoxins and ammonia).

Thus peptic ulcers in the stomach caused by breakdown of mucosal defense more than excessive acid production.

Gastric ulcers are caused by mucosal erosion **not** excessive acid production

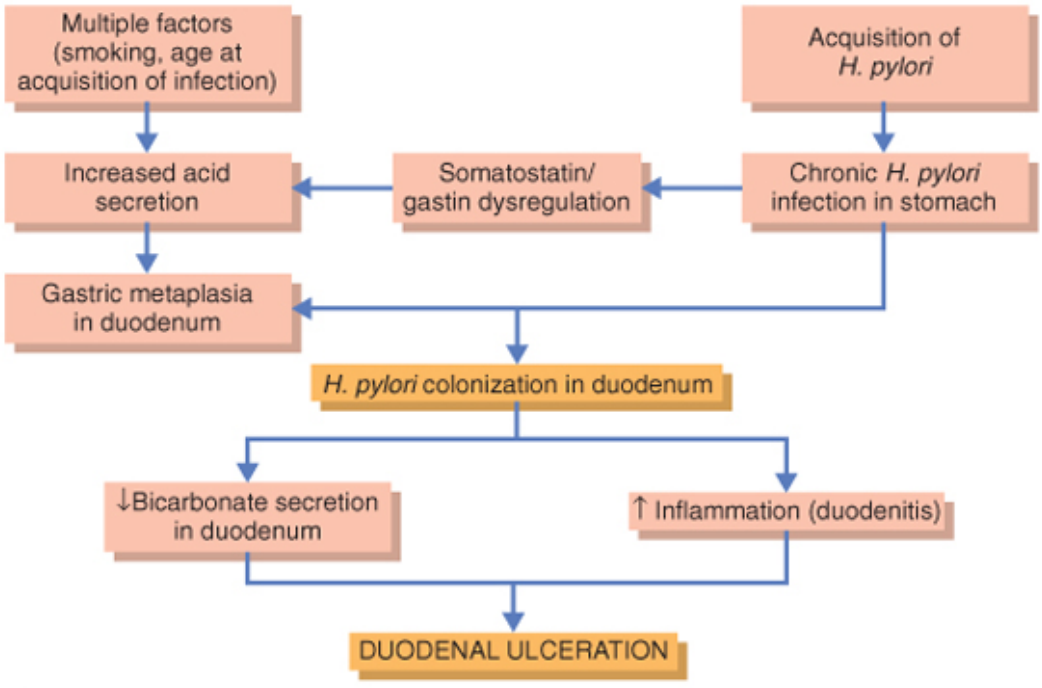
Pathophysiology:

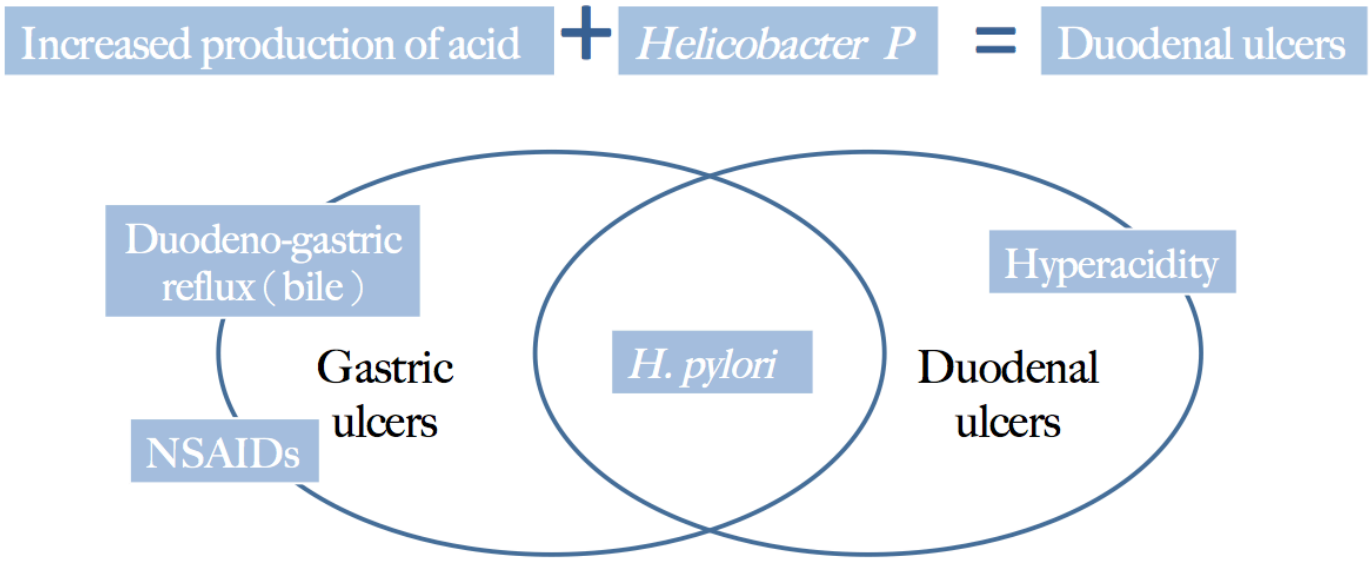


Duodenal ulcers:

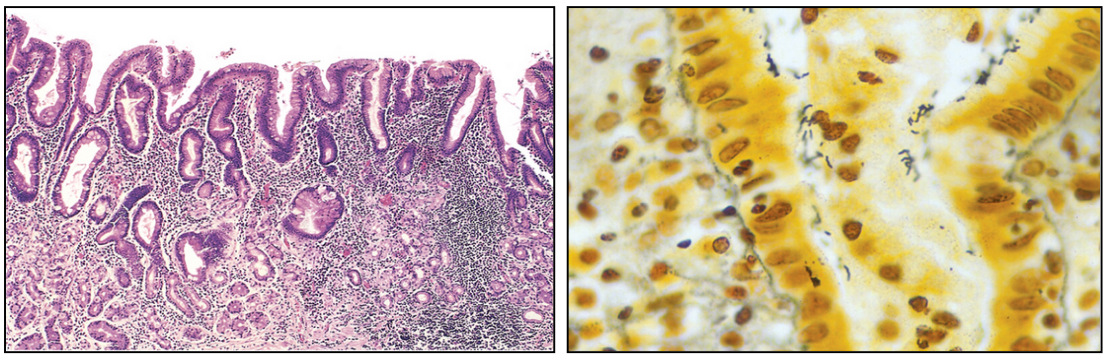
100% related to H. Pylori.

- Increased production of acid assumes more importance in the pathogenesis of duodenal ulceration
- *H. pylori*-infected individuals secrete 2-6 times as much acid as non-infected persons.
- *Helicobacter* Pylori does not colonize normal duodenal epithelium. *Helicobacter* colonizes areas of gastric metaplasia in duodenal ulceration because there is gastric metaplasia in response to excess acid. Gastric metaplasia paves the way for colonization by *Helicobacter.*





- Although more than 70% of individuals with PUD are infected by *H. pylori*, fewer than 20% of *H. pylori*–infected individuals develop peptic ulcer.
- *H pylori* infection of the pyloric antrum is present in nearly all patients with chronic duodenal ulcer and approximately 75% of patients with chronic gastric ulcer.



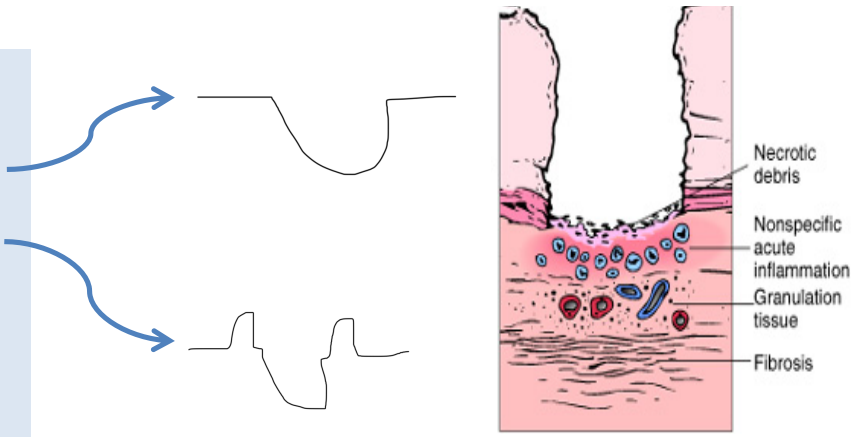
H. pylori chronic active gastritis

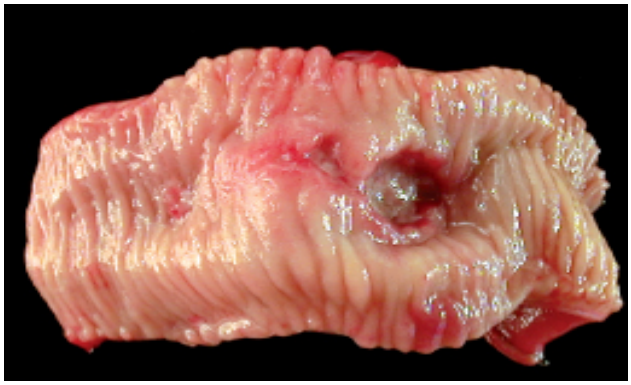
Morphology:

Gross:

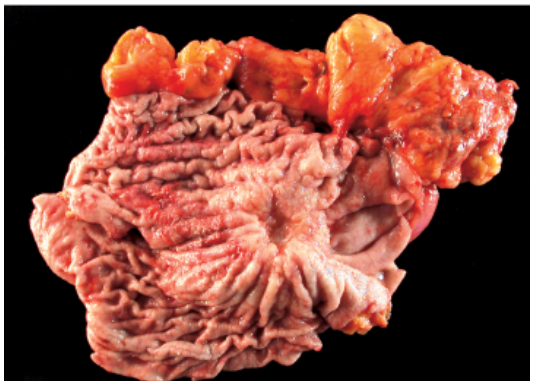
- Usually less than 20 mm in diameter but they may > 100 mm in diameter.
- The classic peptic ulcer is a round to oval, sharply punched-out defect
- Malignant lesions have heaped-up margins.
- Duodenal ulcers usually occur within a few centimeters of the pyloric valve at the anterior duodenal wall.
- Gastric peptic ulcers are predominantly located near the interface of the body and antrum.

Difference between benign & malignant peptic ulcers:
Benign have sharp borders, punched out defect.
In malignant, it has raised, averted and irregular edges.
Benign location: junction between body and antrum in stomach and first part of duodenum a few centimeters away from the pyloric valve.

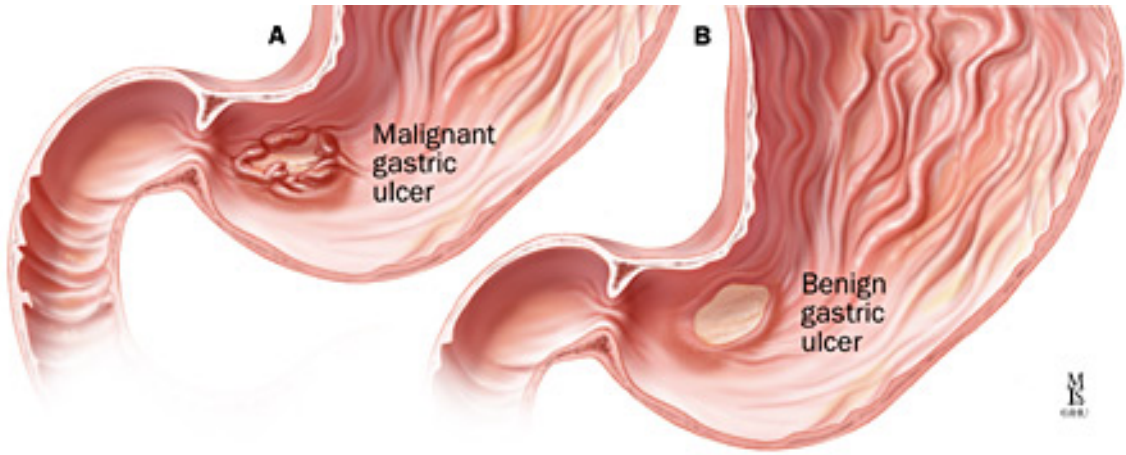




Benign Peptic Ulcer

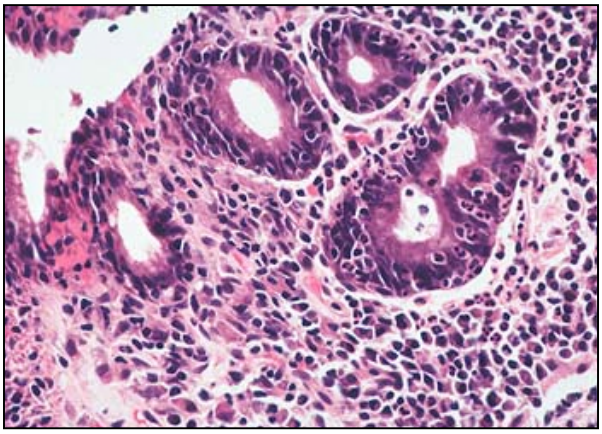


Malignant Peptic Ulcer



Microscopy:

The base consists of necrotic tissue and polymorph exudate overlying inflamed granulation tissue, which merges with mature fibrous (scar) tissue.



The presence of neutrophils within the gastric glands signifies active inflammation and, most of the time, the presence of *H pylori.*

Clinical features:

Symptoms of Gastric Ulcers:

- Epigastric pain (the most common symptom)
  - Gnawing or burning sensation
  - Occurs 2-3 hours after meals
  - Relieved by antacids.
  - Patient awakens with pain at night.
- Gastric ulcers include nausea, vomiting, and coffee-ground hematemesis.
- Some present with complications such as *iron deficiency anemia*, *frank hemorrhage*, or *perforation*.

The symptoms associated with chronic gastritis typically are less severe but more persistent than those of acute gastritis.

Gastric Ulcers: **Food ↑ Pain**
Duodenal Ulcers: **Food ↓ Pain**

For duodenal ulcers, the reason of the pain relief is the release of HCO3 by Brunner glands when food enters that area. So, people eat more. Hence, you see hypertrophy of the glands in these patients.

For gastric ulcers by eating you release more acid that increases the symptoms so people eat less. Hence, they present as people with decreased weight and pain on eating.

Complications:

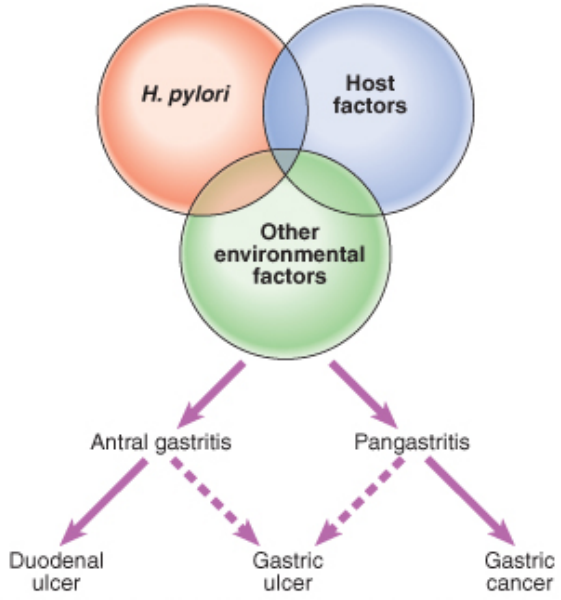
- Hemorrhage.
- Iron deficiency anemia
- Penetration: The ulcer penetrates the full thickness of the stomach or duodenal wall.
- Perforation: leads to peritonitis.
- Fibrous stricture: This is seen in peptic ulcer of the esophagus and the stomach (pyloric stenosis)
- Malignant change: This is extremely uncommon.

Therapy:

Current therapies for PUD are aimed at:

1. *H. pylori* eradication.
2. Neutralization of gastric acid and acid suppression.

Primarily with proton pump inhibitors and H2 blockers.



Acute and Chronic Gastritis Summary:

- The spectrum of *acute gastritis* ranges from asymptomatic disease to mild epigastric pain, nausea, and vomiting. Causative factors include any agent or disease that interferes with gastric mucosal protection. Acute gastritis can progress to *acute gastric ulceration.*

- The most common cause of chronic gastritis is *H. pylori infection*; most remaining cases are caused by *autoimmune gastritis.*

- *H. pylori* gastritis typically affects the antrum and is associated with increased gastric acid production. The induced mucosa-associated lymphoid tissue (MALT) can transform into lymphoma.

- *Autoimmune gastritis* causes atrophy of the gastric body oxyntic glands, which results in decreased gastric acid production, antral G cell hyperplasia, achlorhydria, and vitamin B12 deficiency. Anti-parietal cell and anti–intrinsic factor antibodies typically are present.

- *Intestinal metaplasia* develops in both forms of chronic gastritis and is a risk factor for development of gastric adenocarcinoma.

- Peptic ulcer disease can be caused by *H. pylori* chronic gastritis and the resultant hyperchlorhydria or NSAID use. Ulcers can develop in the stomach or duodenum and usually heal after suppression of gastric acid production and, if present, eradication of the *H. pylori.*

Check Your Understanding

MCQs:

1- Which of the following causes duodenal ulcers:

A. Increased acid production
B. H.pylori
C. Break down of mucosal defense
D. A + B

2- Meckel diverticulum is found in which location:

A. 2nd part of the Stomach
B. Lower part of the esophagus
C. Ileum
D. None of the above

3- H.Pylori generates its effect by:

A. Blocking Prostaglandins
B. Producing cytotoxins
C. Damaging Mucosal lining
D. Producing ammonia
E. B + D

4- If a patient with a gastric ulcer eats a meal, that will lead to which of the following:

A. No effect
B. Increase the risk of another ulcer
C. His pain will be increased
D. His pain will be decreased

5- A 55-year-old man presents with upper gastrointestinal bleeding and is found to have multiple ulcers in the duodenum. Workup finds his serum gastrin levels to be markedly elevated, and an abdominal CT scan finds a large mass in the tail of the pancreas. A biopsy from this pancreatic mass finds an islet-cell adenoma that secretes gastrin. Which of the following is the best diagnosis?

A. Hypertrophic-hypersecretory gastropathy
B. Linitis plastica
C. Verner-Morrison syndrome
D. Zollinger-Ellison syndrome

1:D 2:C 3:E 4:C 5:D

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قال صلى الله عليه وسلم: {من سلك طريقًا يلتمس فيه علمًا سهَّل الله له بهِ طريقًا إلى الجنة}

دعواتنا لكم بالتوفيق
