King Saud University
College of Medicine
Second year – GIT block

Peptic Ulcer Disease

Lecture 2

430 Pathology Team

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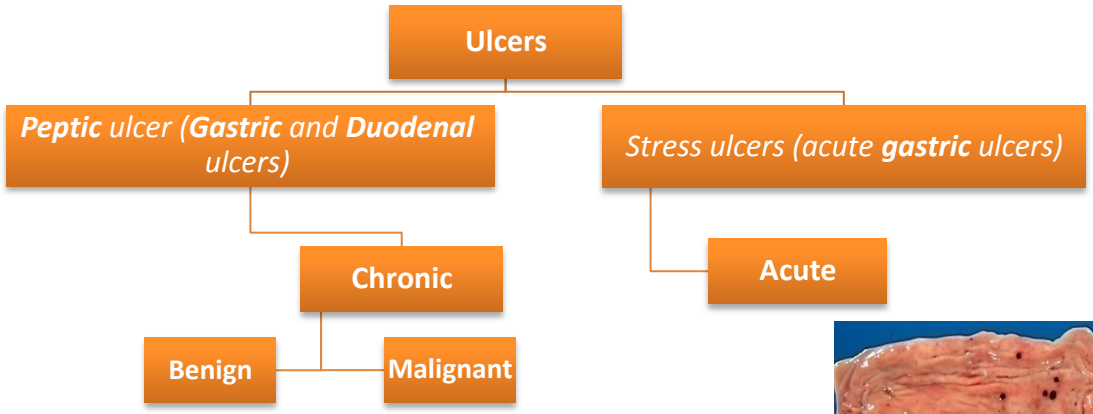
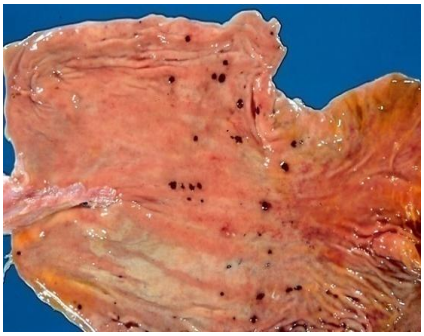
What is the difference between ulcers and erosions?

Ulcers	*Erosions*
- Defined histologically as a breach (break) in the mucosa that extends through the muscularis mucosae into the submucosa or deeper. - Takes much longer time to heal.	- A breach in the epithelium of the mucosa only (superficial). - May heal within days.





Peptic ulcer:

1. Acute peptic ulcers (acute gastric ulcer):

Pathophysiology:

1. As part of an *acute gastritis* (acute response to an irritant 'chemical' injury by drugs like NSAIDs – ibuprofen, vulturine, aspirin - or alcohol)
2. As a complication of a severe *stress response* (severe external burns -leading to Curling's ulcer-, major trauma or cerebrovascular accidents after stroke, shock or operation to the brain). The body reacts to it by hyperacidity, which leads to ulceration. These factors also cause sever pain and subsequent vasoconstriction that reduces blood flow to the stomach, which also helps in the formation of the ulcer.

> Curling's ulcer is a type of ulcer that happens in the proximal duodenum, resulting from the reduced blood flow that occurs with sever burns

3. As a result of *extreme hyperacidity* – resulting from increase the levels of Gastrin- e.g: (Zollinger-Ellison syndrome,).

> Zollinger-Ellison syndrome is a condition in which there is increased production of the hormone gastrin, hence hyperacidity. This is syndrome is caused by tumors in certain locations of the GIT, that cause multiple peptic ulcerations in the stomach, duodenum, and even the jejunum.

Characteristics:

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

Prognosis:

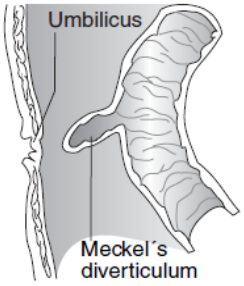
The gastric mucosa can recover completely if the person does not die from the primary disease (e.g. Zollinger-Ellison syndrome, sever trauma …etc).

Treatment: antacids and treatment of the underlying cause.

2. Chronic peptic ulcer:

Locations:

- Usually single (solitary) and involve the full thickness, submucosa or deeper, of the mucosa.
- May occur in any portion of the GI tract exposed to acidic gastric juices (usually limited to the lesser curvature and pyloric).
- 98% located in first portion of duodenum or distal end of the stomach
- The ratio of duodenal ulcers to gastric ulcers is 4:1
- Esophagus can be involved as a result of GERD or acid secretion by ectopic gastric mucosa.
- Gastric mucosa within a Meckel diverticulum can result in peptic ulceration of adjacent mucosa.



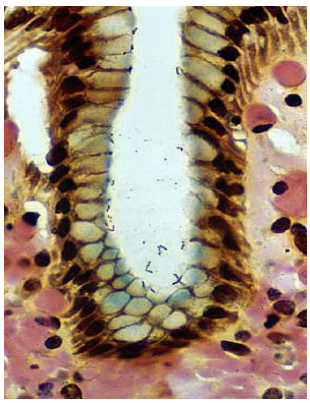
What is Meckel diverticulum?

It is the most common congenital anomaly of the GI tract. It Can cause bleeding and obstruction of the terminal ileum and its wall is covered by ectopic location of gastric type of epithelium (containing parietal cells) which is abnormal and may cause ulcers.

- Zollinger-Ellison syndrome: multiple peptic ulcerations in the stomach, duodenum, and even the jejunum.

Pathophysiology:

1. Gastric ulcers:



The mucosal defences against acid attack consist of:

1. Mucus-bicarbonate barrier: can be damaged by Duodeno-gastric reflux (bile)
2. The surface epithelium: can be damaged by NSAIDs (blocking the synthesis of the prostaglandins), *Helicobacter pylori* infection (producing cytotoxins and ammonia that lead to ulceration).

3. Blood supply.

4. Cell renewal.

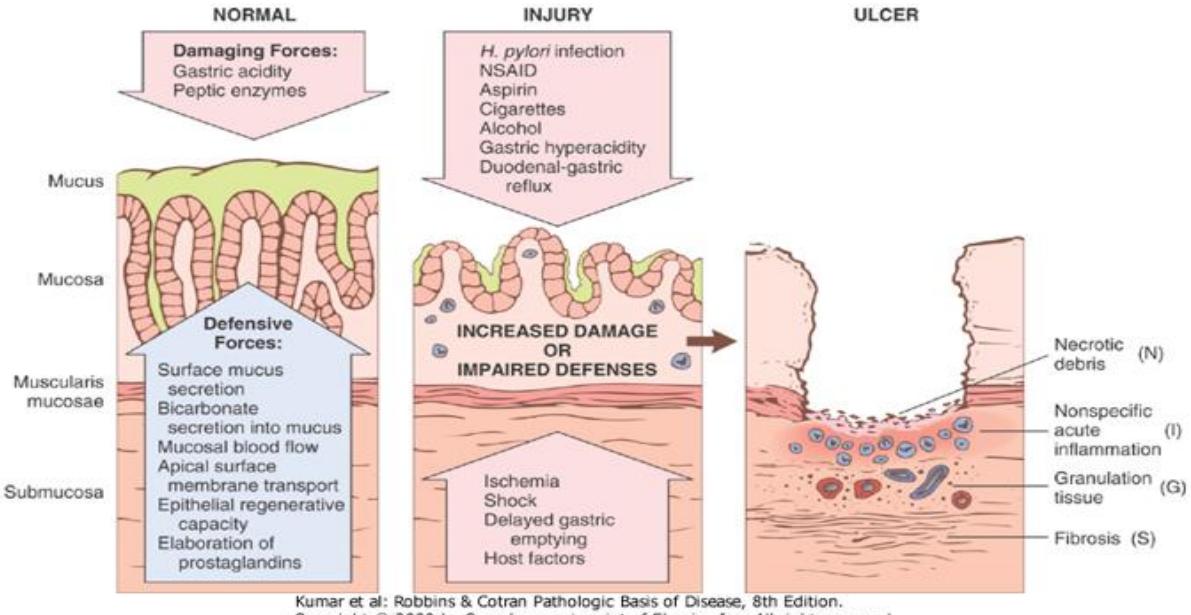
In over all, peptic ulcers in the stomach due to breakdown of mucosal defence is much more important than excessive acid production.

Aggressive Factors
H. pylori
Drugs (NSAIDs)
Acid
pepsin
Bile salts

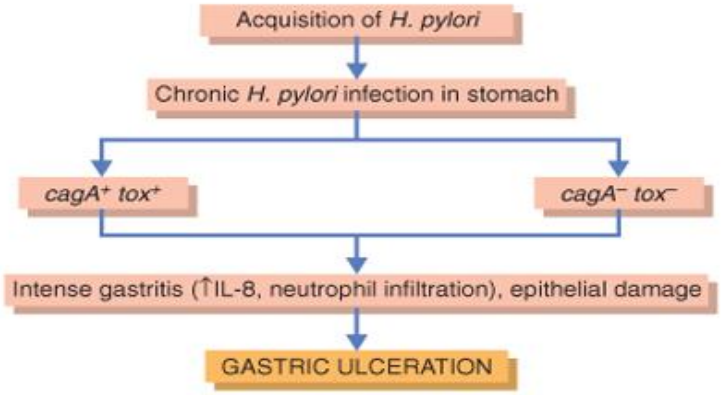
imbalance

Aggressive Factors ⟷ Defensive Factors

Defensive Factors
Mucus
bicarbonate
Blood flow,
cell renewal
Prostaglandins
Phospholipid



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 necrosis (N), inflammation (I), and granulation tissue (G), but a fibrotic scar (S), which takes time to develop, is only present in chronic lesions.

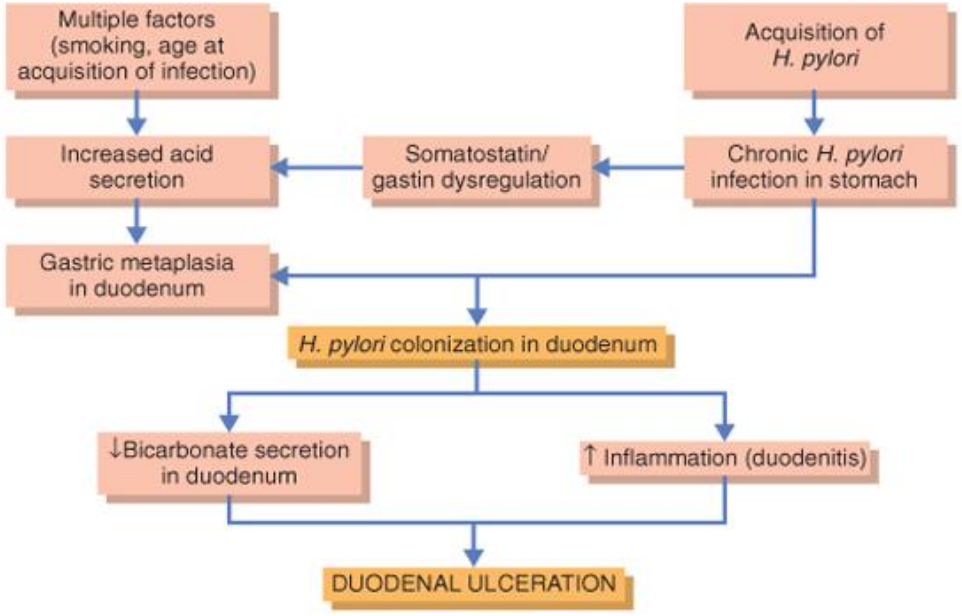


cagA⁺ and cagA⁻ are toxins produced by *Helicobacter pylori*

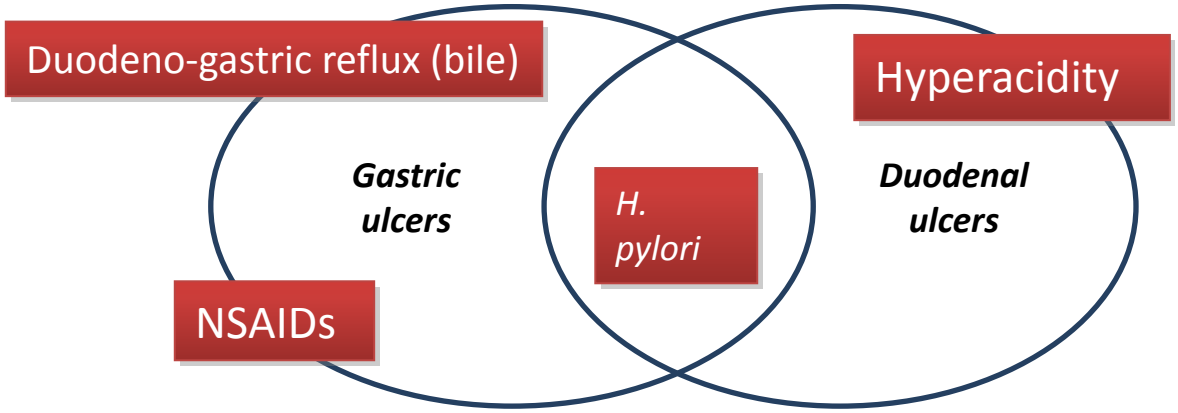
2. Duodenal ulcers:

- Increased production of acid (Hypersecreation) assumes more importance in the pathogenesis of duodenal ulceration.
- *H. pylori*-infected individuals secrete 2-6 times as much acid (HCL) as non-infected indviduals.
- *Helicobacter Pylori* does NOT colonise normal duodenal epithelium.
- *Helicobacter Pylori* is involved in duodenal ulceration because there is gastric metaplasia in response to excess acid. Gastric metaplasia paves the way for colonisation by *H. Pylori.*

Hypersecreation (Hyperacidity) + *H. Pylori* = Duodenal ulcers



Pathophysiology of Peptic Ulcer Disease :



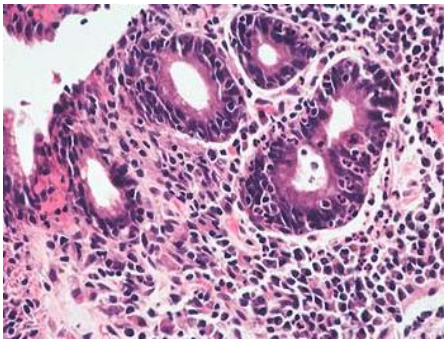
- *H. pylori* infection of the pyloric antrum is present in nearly all patients (almost 100%) with chronic duodenal ulcer and approximately 75% of patients with chronic gastric ulcer.
- Although more than 70% of individuals with PUD are infected by *H. pylori*, fewer than 20% of *H. pylori*–infected individuals develop peptic ulcer.

Morphology:

Grossly:

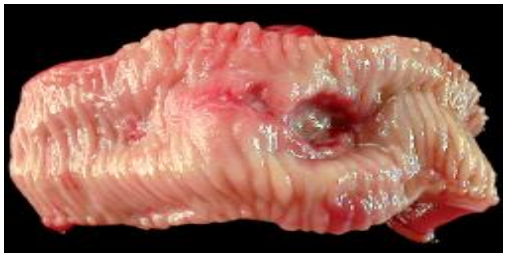
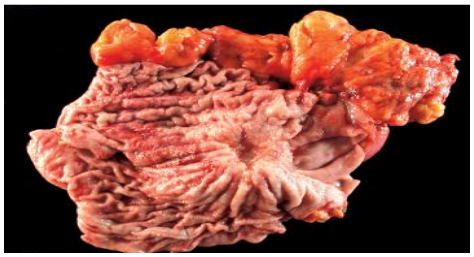
- Usually they are single.
- Usually less than 20 mm in diameter but they may > 100 mm in diameter.
- The classic peptic ulcer is a round to oval, sharply punched-out defect (that's how we can differentiate between benign and malignant peptic ulcer).
- In contrast, heaped-up margins are more characteristic of cancers (malignancy).

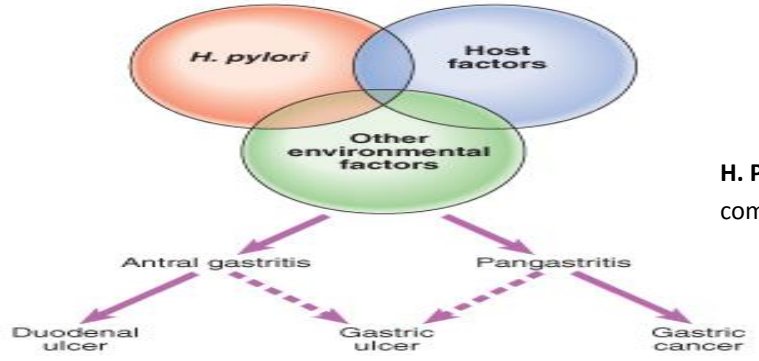
Microscopically: *you should know the layers*



- The base consists of necrotic tissue and polymorph exudates 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.*

What is the difference between benign and malignant peptic ulcer?

Benign Peptic Ulcer	Malignant Peptic Ulcer
- Solitary and < 20 mm - Well defined margins (shallow edge), rounded in shape and the surrounding area are usually edematous and inflamed. 	- Solitary and larger in size (up to 5 cm) - The margins are raised and inverted with a necrotic center. - For better diagnosis we take the biopsy from the edges of the lesion not the necrotic center. 



H. Pylori infection can be complicated by **lymphoma** as well.

Clinical features:

- Epigastric pain (the most common symptom)
- Gnawing or burning sensation.
- Occurs 2-3 hours after meals (due to increased acid secretion)
- Relieved by food or antacids (dudonal ulcers).
- Patient awakens with pain at night.
- Some present with complications: such as *iron deficiency anemia*, *frank hemorrhage* (bright in color) and it's usually seen in acute peptic ulcer, or *perforation* (can cause serious infections e.g. peritonitis).
- Melena (which is *black feces* that are associated with gastrointestinal hemorrhage. The black color is caused by oxidation of the iron in hemoglobin during its passage through the ileum and colon) and it's usually seen in chronic peptic ulcer.
- If hemorrhage is present in chronic cases it'll be coffee like (granular and brown).

Therapy:

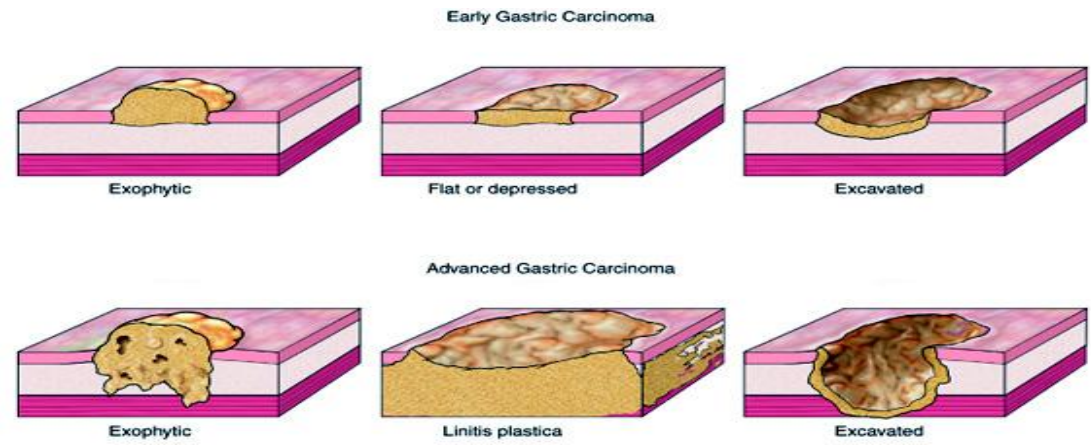
1. *H. pylori* eradication by antibiotics.
2. Acid suppression:
    a. Proton pump inhibitors (PPIs)
    b. H_2 blockers

Gastric cancers:

It has two main malignant types:

- Diffuse Adenocarcinoma:
    - NOT associated with *H. pylori* infection
    - "Linitis Plastica" Diffuse stomach cancer is characterized by the presence of poorly differentiated tumor cells. The appearance of the stomach is like a "*leather bottle*". This cancer (and most other stomach cancers) is more common in Asian countries, particularly Japan.
- Intestinal-Type Adenocarcinoma:
    - Poorly related to *H. pylori* infection and nitrate.
    - Usually localized and well differentiated.

Prognosis: the survival rate for gastric cancers is less than one year.



CASE:

- A 30-year-old male banker complains of mid-epigastric burning and pain for the last week. The pain is worse at night and is somewhat better immediately after he eats. He has not had any fever, nausea, or vomiting. He takes approximately one 500-mg acetaminophen tablet a week for headaches but does not take any other medications. Upper endoscopy reveals a 2-cm mucosal defect in the antrum of the stomach. There is mild edema in the adjacent mucosa, but there is no thickening of the edges of the ulcer.
    - What is the most likely diagnosis?
    - What are complications from this condition?
    - What is the most likely mechanism of this disorder?

ANSWERS: *PEPTIC ULCER DISEASE*

Summary: A 30-year-old man has acute onset of mid-epigastric pain somewhat relieved by eating. Upper endoscopy reveals a 2-cm gastric ulcer.

◆ Most likely diagnosis: Peptic ulcer disease.
◆ Long-term complications: Erosion or perforation with bleeding; gastric carcinoma in patients with chronic gastritis.
◆ Most likely mechanism: Most often associated with *Helicobacter pylori* organisms that produce bacterial urease and protease, damaging the mucus layer and exposing the underlying epithelium to acid-peptic in

Summary

- Ulcers are defined histologically as a breach (break) in the mucosa that extends through the submucosa or deeper, while erosions only breach the lining epithelium.
- Peptic ulcers can affect the duodenum or the stomach and can either be acute or chronic (most common).
- **Acute peptic ulcers are not associated with H.pylori and are caused by:**
  1. As part of an *acute gastritis* drugs that are caused by drugs like NSAIDs – ibuprofen, vulturine, aspirin or alcohol)
  2. As a complication of a severe *stress response* like in Curling's ulcer, major trauma stroke, shock or operation to the brain.
  3. As a result of *extreme hyperacidity* – resulting from increase the levels of Gastrin- e.g. (Zollinger-Ellison syndrome
- Acute stress ulcers are found in multiple of the GIT and patients with kind may present with hematemesis.
- Peptic ulcers can happen any place where in the GIT, but happen mostly in the lesser curvature and pyloric areas. Ulcers are 4 times more likely to happen in the duodenum than in the stomach.
- **Special cases of peptic ulceration:**
  - in the esophagus: with GERD
  - In the small intestine (terminal ileum) in a case of Meckel diverticulum
  - Multiple ulcerations in the GIT tract: Zollinger-Ellison syndrome
- **Clinical features include:** epigastric pain (most common), burning sensation, *iron deficiency anemia*, *frank hemorrhage* (blood bright in color), perforation (causing peritonitis), and Melena.
- Most gastric malignancies are adenocarcinoma

Dudodonal ulcers	Stomach ulcers
• Hypersecreation of acid assumes more importance in the pathogenesis • Not colonized by H.pylori normally, but can only be colonized in cases of gastric metaplasia. • Pain from Duodenal ulcers decreases with food	• Breakdone of protective bariers assumes more importance in the pathogenesis • Readly colonized by H.pylori. • Pain from gastric ulcers increases with food.

Aggressive Factors	Protective Factors
H. pylori Drugs (NSAIDs) Acid pepsin Bile salts	Mucus bicarbonate Blood flow, cell renewal Prostaglandins Phospholipid