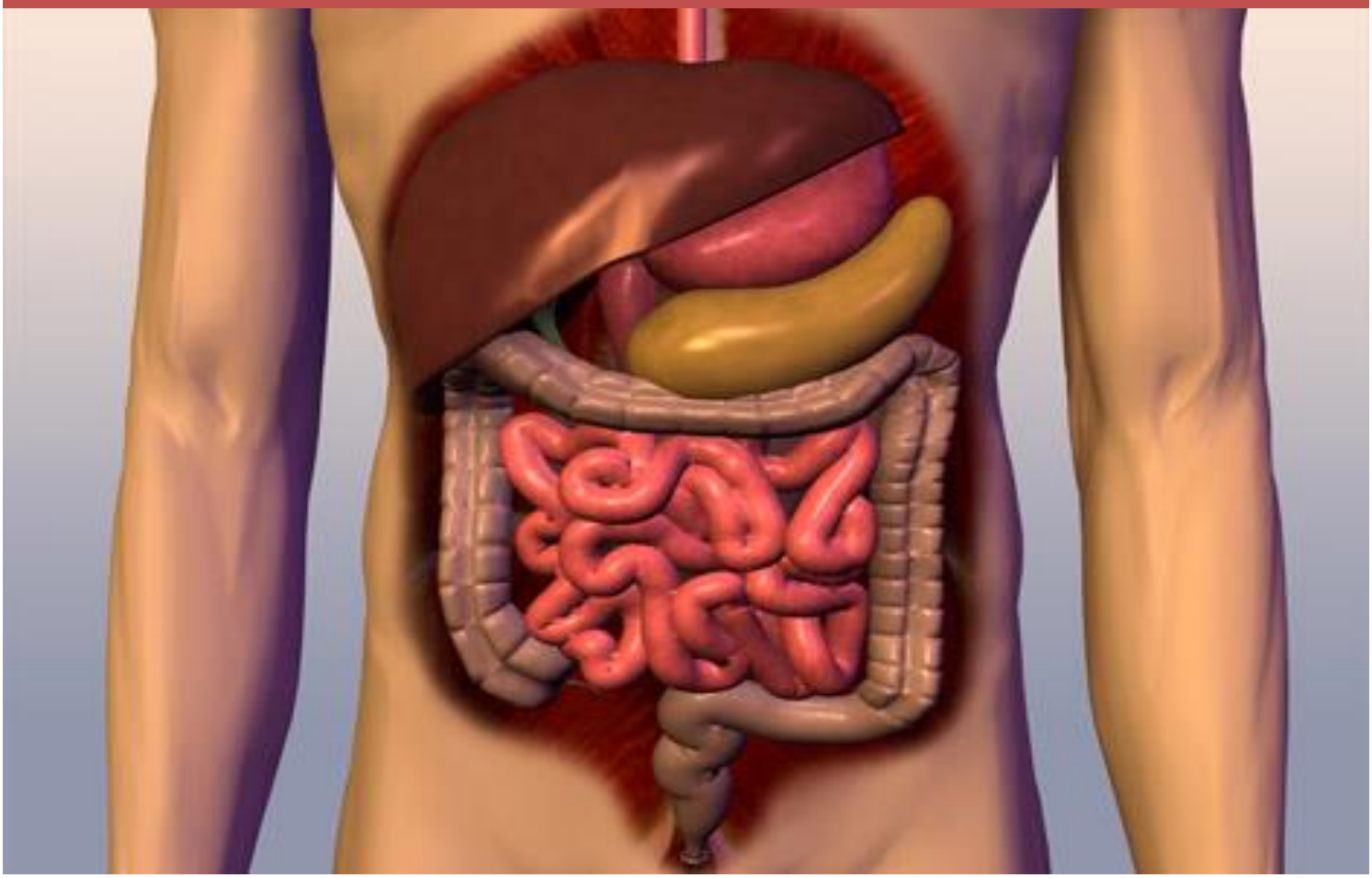


Lecture Two

Peptic ulcer disease

432 ***Pathology*** *Team*

Done By: Zaina *Alsawah*

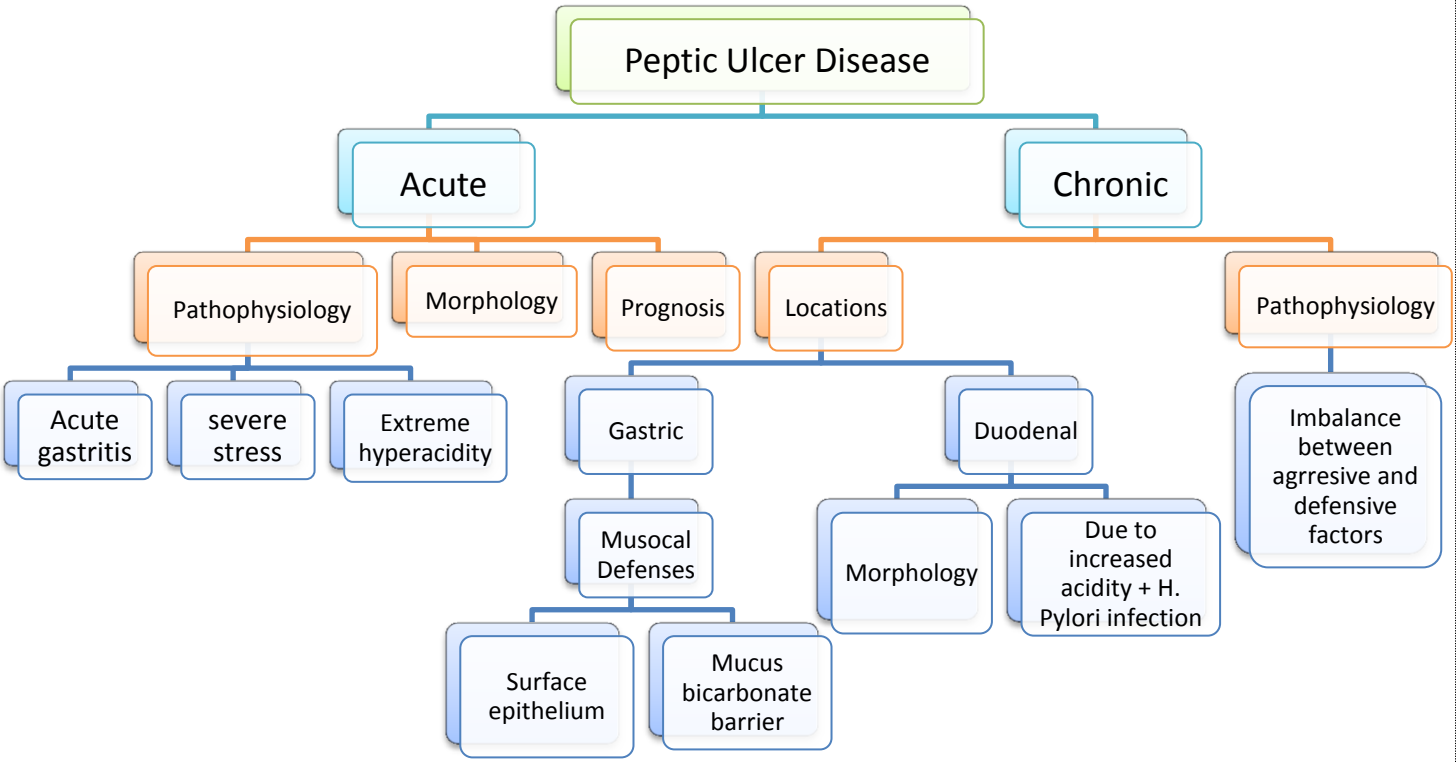
Reviewed By: Mohammed *Adel*

GIT Block

Color Index: female notes are in purple. Male notes are in Blue. Red is important. Orange is explanation.

Peptic Ulcer Disease

Mind Map:



Peptic Ulcer

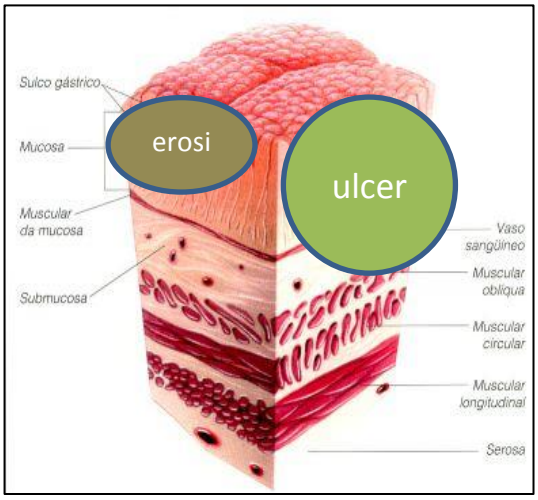
Definitions:

Ulcer is breach in the mucosa of the alimentary tract extending through muscularis mucosa into submucosa or deeper.

Chronic ulcers heal by Fibrosis.

Erosion is a breach in the epithelium of the mucosa only.

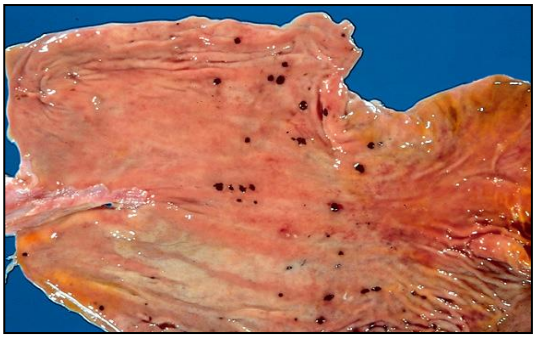
They heal by regeneration of mucosal epithelium unless erosion was very deep then it will heal by fibrosis.



Types of Ulcer:

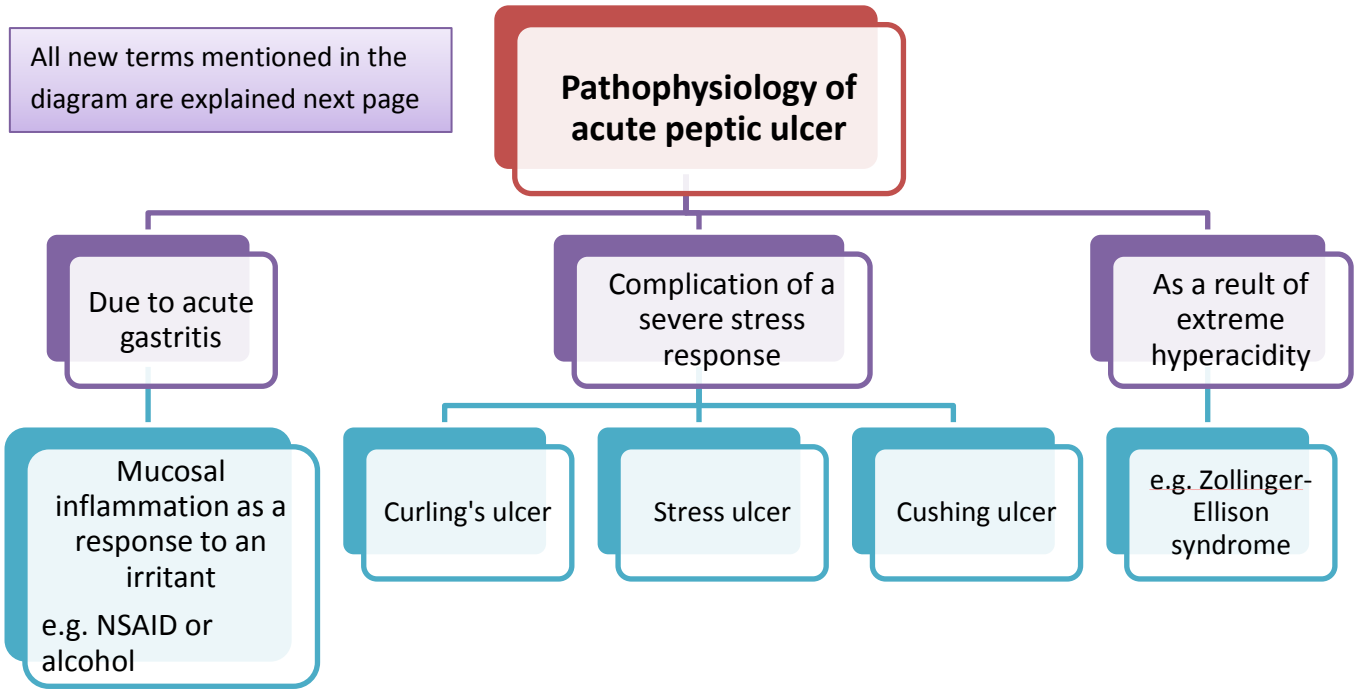
1-Acute Peptic Ulcers (Stress ulcers):

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



Pathophysiology:

All new terms mentioned in the diagram are explained next page

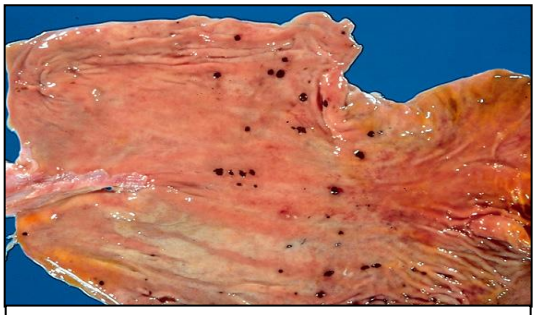


- **Stress Ulcers: most commonly affecting critically ill patients with shock, sepsis, or severe trauma.**
- **Cushing Ulcer: with patients with intracranial diseases (cerebrovascular accidents) and that's because it causes direct stimulation of vagal nuclei which causes gastric acid hypersecretion**
- **Curling's sulcer: associated with severe burns and trauma**
- **Zollinger-Ellison syndrome: rare gastrin-secreting tumors that cause uncontrolled release of gastrin and the result is massive acid production leading to ulcer formation.**

Morphology:

Acute stress ulcers **(not necessary stress in stomach, it could be stress in the overall body e.g. trauma, hemorrhage…)** 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).



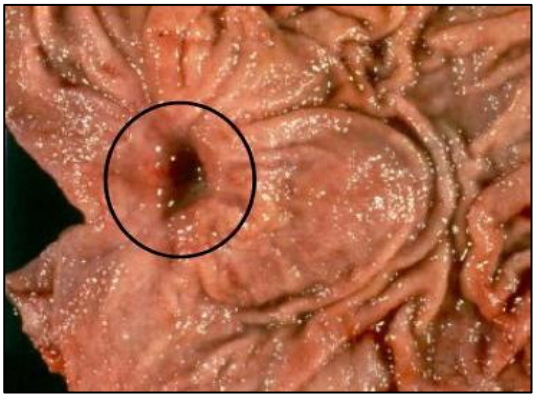
Small, multiple and mostly superficial but could be deep also.

Prognosis:

The gastric mucosa can recover completely if the person does not die from the primary disease. **So patient recovers if the underlying cause (burn, trauma…) is treated.** (About 1% to 4% of patients admitted to hospital intensive care units acutely develop superficial gastric erosion or ulcers, which may be associated with lethal bleeding).

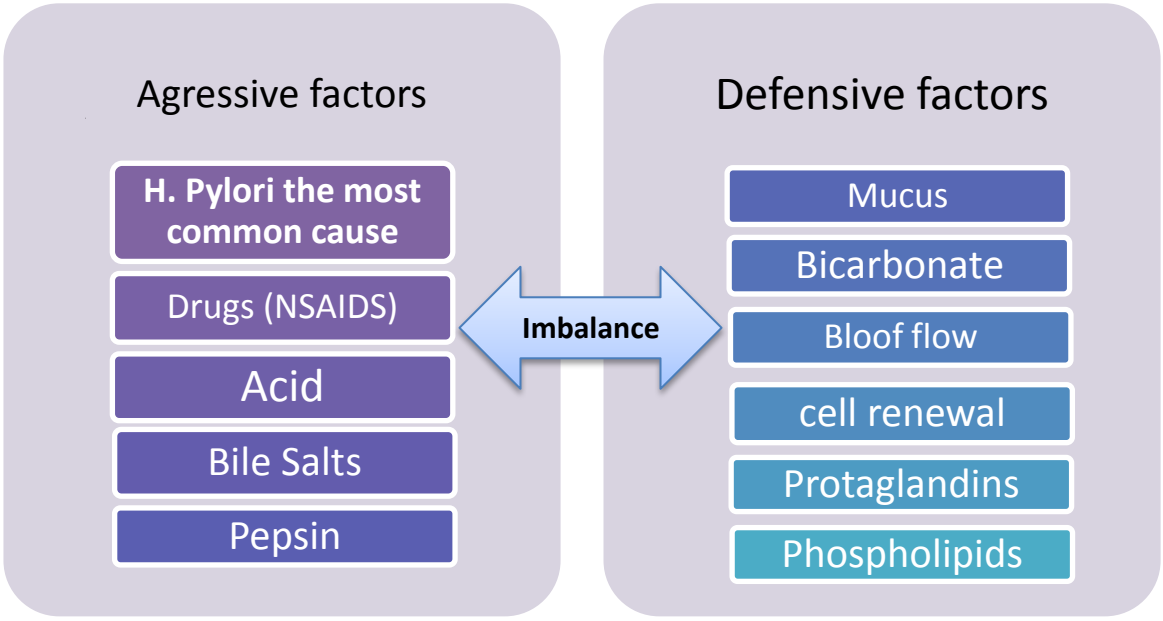
2-Chronic Peptic Ulcer:

Peptic ulcers are chronic, recurring lesions that occur most often in middle-aged to older adults without obvious precipitating conditions, other than chronic gastritis. **(Chronic Gastritis is the main predisposing factor for chronic peptic ulcer.Most common cause of chronic gastritis is infection with H. Pylori which will cause increase gastric acid secretion leading to ulcers).**



Pathophysiology of chronic peptic ulcer:

Due to **imbalance** between the aggressive factors and defensive factors



Other causes of chronic peptic ulcers:

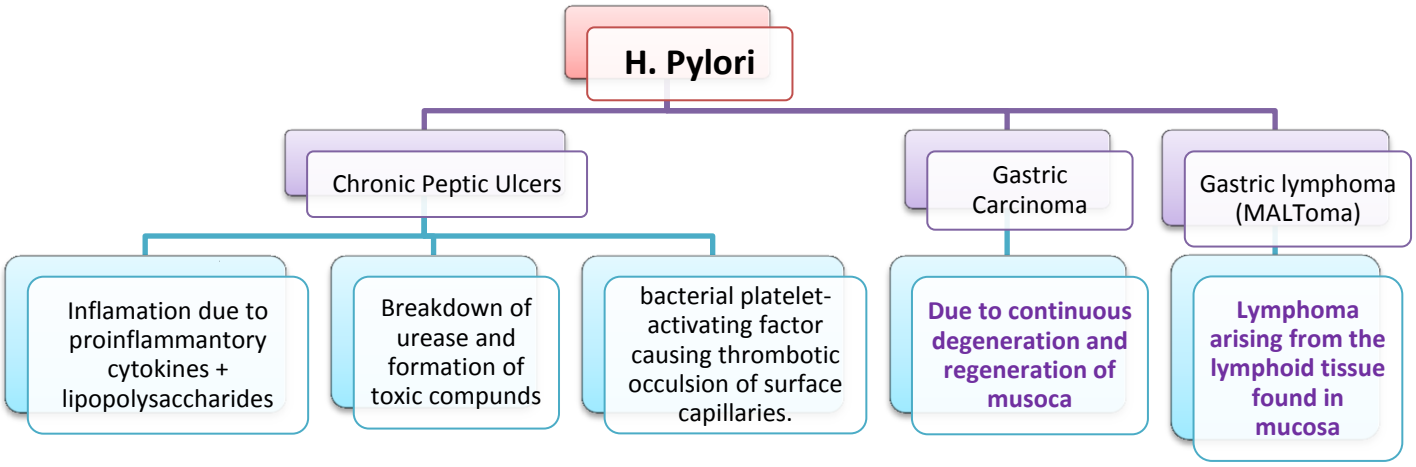
1- **NSAIDs and Aspirin:**
   - Block the Cyclooxygenase, thus no more Prostaglandin production.
   - Prostaglandins protective effects: 1- Enhance Bicarbonate secretion to neutralize HCl2- Increase vascular perfusion which is important for epithelial regeneration.

2- **High dose of corticosteroids:**
   - Suppress prostaglandin synthesis.
   - Impairs healing.

3- **Cigarette smoking**
   - Impairs mucosal blood flow.
   - Impairs healing.

4- **Chronic renal failure, and hyperparathyroidism**
   - They're associated with hypercalcemia: stimulates gastrin production and therefore increases acid secretion

5- **Helicobacter pylori infection** (Next page)

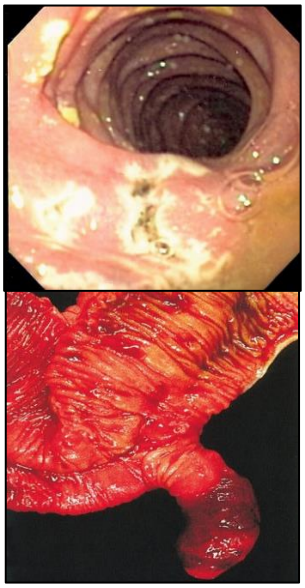


Locations of Chronic Peptic Ulcer:

May occur in any portion of the GI tract exposed to acidic gastric juices.
98% located in first portion of duodenum **(most common site)** or stomach, ratio in duodenum:Stomach = 4:1 **(it develops in duodenum 4 times more than in stomach).**

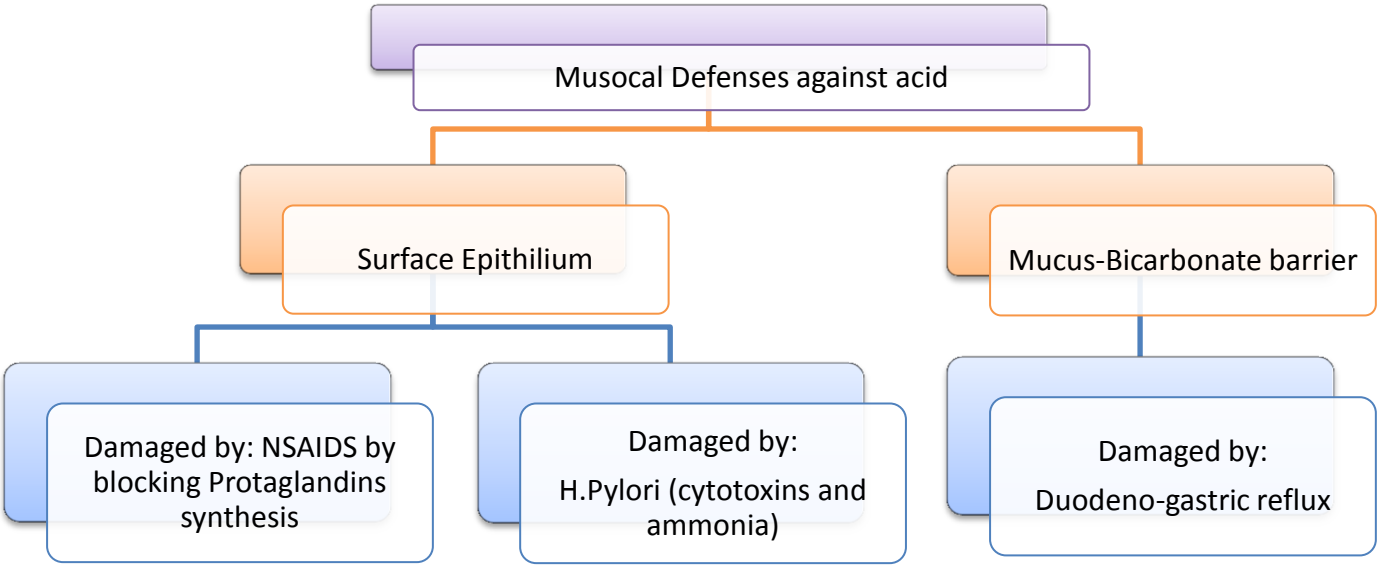
Other Locations:

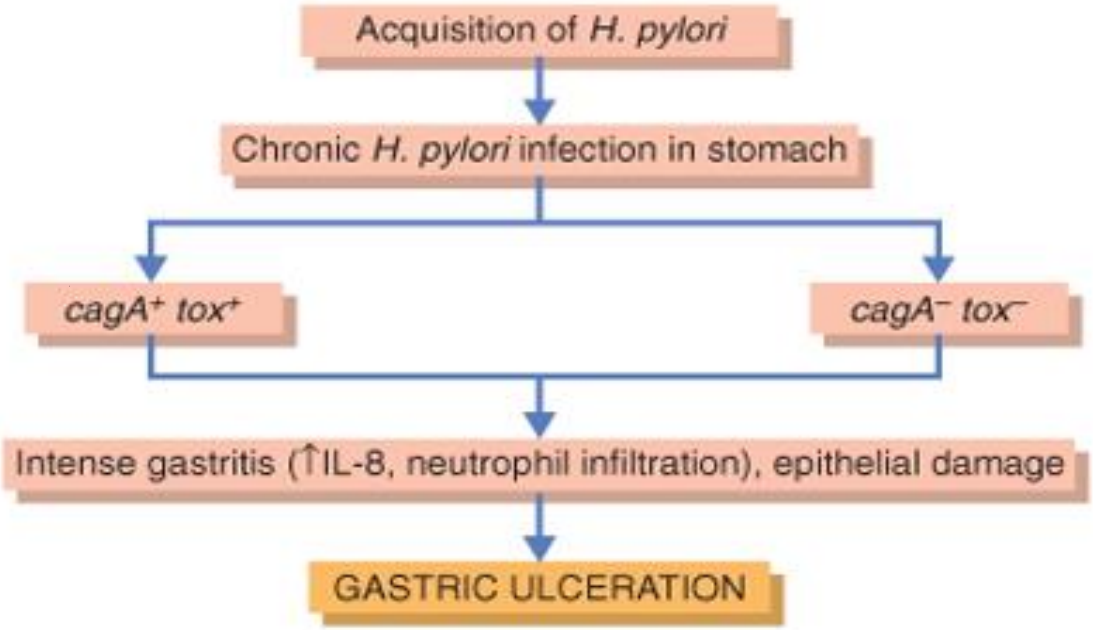
- Esophagus: as a result of GERD or acid secretion by ectopic gastric mucosa.
- Gastric mucosa within a Meckel diverticulum can result in peptic ulceration of adjacent mucosa.
- In Zollinger-Ellison syndrome: multiple peptic ulcerations in the stomach, duodenum, and even the jejunum. **Ulcers characteristics in this case: they are multiple + occur in areas that are not usual for ulcers such as jejunum.**



Meckel's diverticulum is a congenital malformation in which there's remnant of omphalocoele of the embryo. It is lined by gastric epithelium containing parietal cells and chief cells. So this area will develop peptic ulcer due to increased acid secretion. Most common site: in ilium.

Gastric ulcers

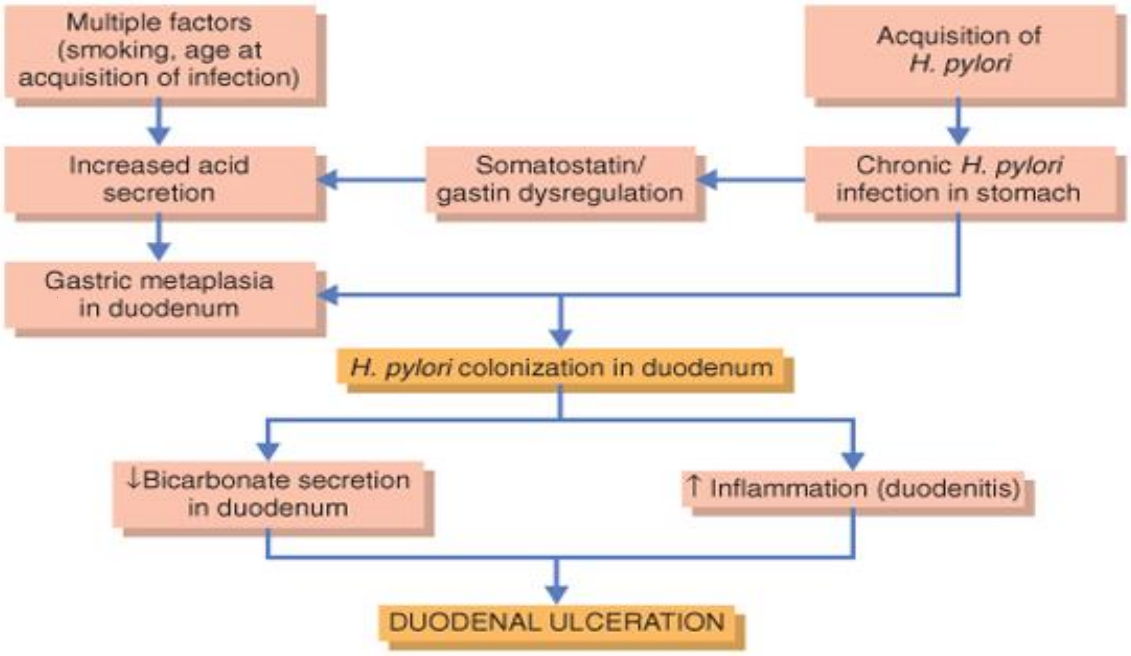




CagA is the virulence factor of Helicobacter pylori

Duodenal ulcers (No H. Pylori in Duodenum because it prefers the acidic medium not the alkaline so it's only present in stomach but we see its effect in the duodenum because of increase acidity)

- 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 controls.
- Helicobacter Pylori does not colonize normal duodenal epithelium
- Helicobacter is involved in duodenal ulceration because there is gastric metaplasia in response to excess acid. **Gastric metaplasia** paves the way for colonization by Helicobacter. **Sometimes duodenal mucosa will undergo gastric metaplasia and becomes just like gastric mucosa and they begin to secrete acid and only then H. Pylori can colonize in the duodenum.**
- 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.
- Although more than 70% of individuals with PUD are infected by H. pylori, fewer than 20% of H. pylori–infected individuals develop peptic ulcer.



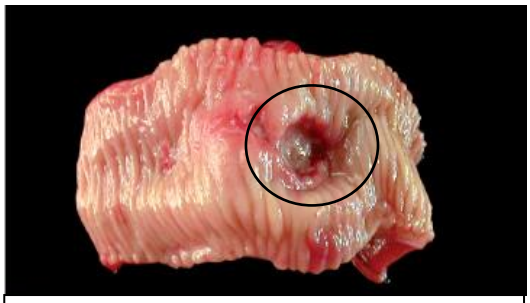
REMEMBER:
In Peptic ulcers of the stomach: breakdown of mucosal defense is much more important than excessive acid production.
In Duodenal ulcers: increased production of acid + H. Pylori.

Morphology:

Gross

Benign peptic ulcer:

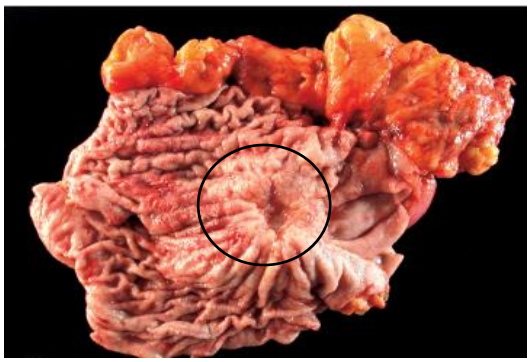
- Usually less than 20 mm in diameter but they may > 100 mm in diameter.
- The classic peptic ulcer is a round oval, sharply punched- out defect

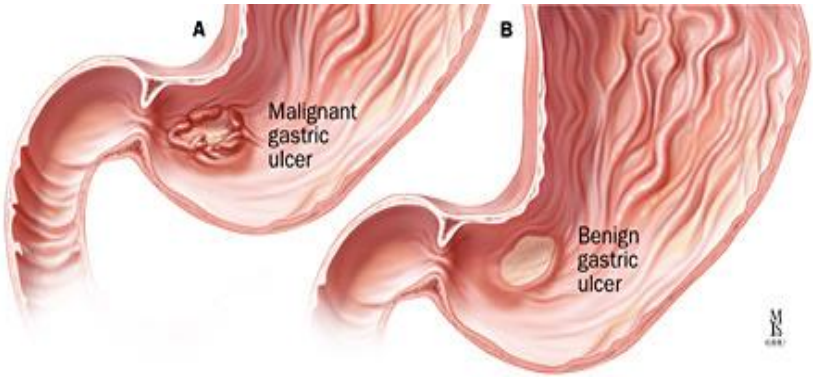


Usually solitary, deep, involving the mucosa and submucosa

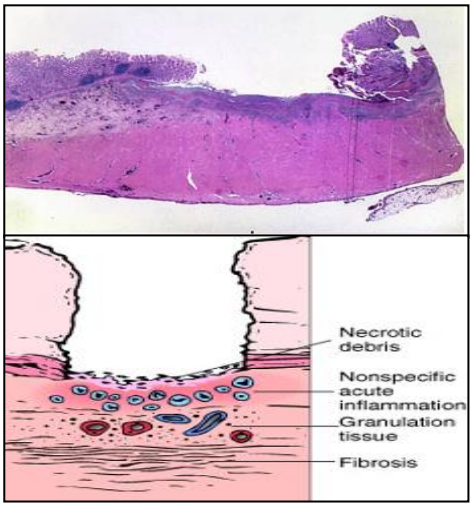
Malignant peptic ulcer:

- In contrast, heaped-up margins are more characteristic of cancers

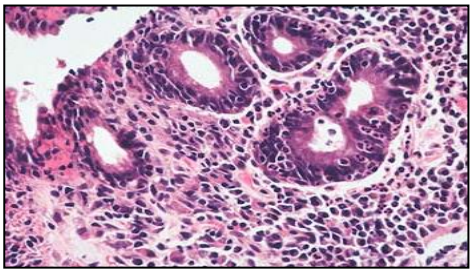




Microscopy:



1- The base consists of necrotic tissue and polymorph exudate overlying inflamed granulation tissue which merges with mature fibrous (scar) tissue. (Fibrosis is characteristic for chronic peptic ulcer).



2- The presence of neutrophils within the gastric glands signifies active inflammation and, most of the time, the presence of H. Pylori.

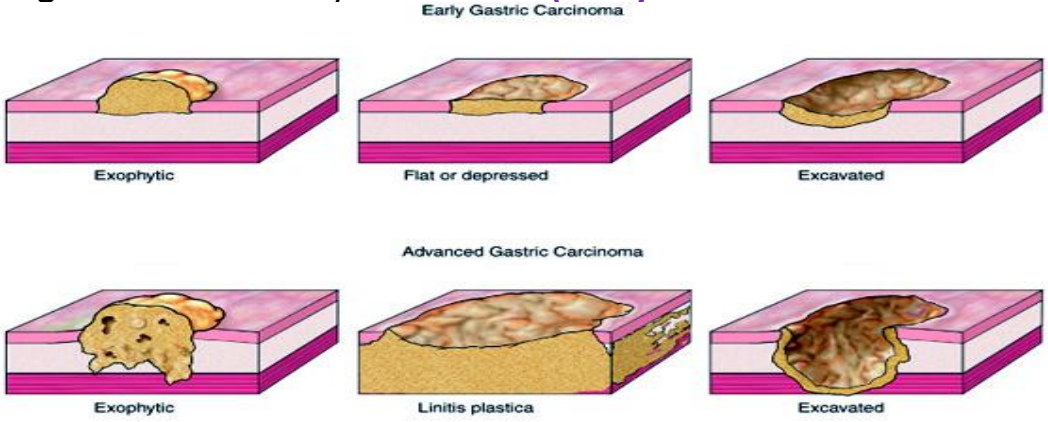
Clinical Features:

- Epigastric Pain (the most common symptom).
- Gnawing (burning sensation).
- Occurs 2-3 hours after meals.
- Relieved by food or antacids.
- Patient awakens with pain at night.

Some present with complications such as iron deficiency anemia, frank hemorrhage, or perforation.

Complications of Chronic Peptic Ulcers:

- **Hemorrhage**. **(3 main manifestations of hemorrhage: 1- Melena (black feces), 2- Hematemesis (vomiting of blood), 3- Coffee-ground vomitus (due to iron exposition to gastric acid, so iron becomes oxidized. This reaction causes the vomitus to look like ground coffee)).**
- **Penetration**. The ulcer penetrates the full thickness of the stomach or duodenal wall, progressing into adherent underlying tissue, e.g. the pancreas or liver.
- **Perforation**. This leads to peritonitis.
- **Fibrous stricture.** In the stomach, ulcers may cause pyloric stenosis.
- **Malignant change**. This is extremely uncommon. **(rarely in stomach and never in Duodenum).**



Therapy:

Current therapies for PUD are aimed at:

- *H. pylori* eradication by: Antibiotics.
- Acid suppression by:
  - Proton pump inhibitors.
  - H2 blockers.

Summary (from Robbins Basic Pathology)

Acute and Chronic Gastritis:

- **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 penetration. Acute gastritis can progress to acute 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.**
- **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.**

Questions from Female doctor's slides

Case Scenario

A 49-year-old secretary presents to medical outpatients with a 7-month history of epigastric pain. She had been widowed in the last year, her husband having died of cancer. The patient had been left to support two children. She had recently become a vegetarian to cut down on meat costs. She smokes five cigarettes per day but does not drink alcohol. She has been treated with antacids by her GP, but this has not controlled the symptoms. In the clinic, she complains of epigastric pains which are sharp and burning and radiate her subcostal margin to the right. The pain is worse at night and is relieved by food. On examination, there is epigastric tenderness and clinical signs of anemia.

1. What are the possible causes of this clinical presentation?

Stress-related duodenal ulcer that is not responding to existing treatment. Ulcer repair is compromised by the high levels of stress, poor diet and cigarette smoking. The differential diagnosis includes gastric ulceration with or without reflux esophagitis and, although atypical, biliary disease should be considered.

2. What are the predisposing causes?

Duodenal ulceration is thought to be a consequence of an imbalance between damaging effects of acid and pepsin attack on the mucosal defenses of the duodenum.

1- The pH of the duodenal lumen is decreased.
2- Patients also empty food from their stomachs at a greater rate, so that after a meal there is less food available to buffer the secreted acid as it passes into the lumen of the duodenum.
3- NSAIDs.
4- Stress.
5- Smoking and Alcohol intake.
6- There are four major factors that account for the tendency of duodenal ulcer patients to hypersecrete acid and pepsin:
    1. Increased parietal cell mass.
    2. Increased stimulation of acid secretion.
    3. Increased parietal cell sensitivity to stimulants.
    4. Loss of inhibitory control of acid secretion.

3-What investigations should be performed?

- Fiberoptic endoscopy is the investigation of choice (as it allows any ulcer observed to be biopsied to exclude neoplastic disease and to confirm or refute the presence of Helicobacter pylori).
- Blood counts (to exclude anemia from previous bleeding).

4- Are acute gastric ulcers associated with Helicobacter pylori?

- No

5-Do chronic peptic ulcers of duodenum undergo malignant transformation?

- No

6-What are the complications of chronic peptic ulcers?

(1) Bleeding; (2) Perforation; (3) Penetration into an adjacent viscus; (4) Obstruction from edema or from scarring of the pylorus or duodenum; (5) Intractable pain. Malignant transformation does not occur in duodenal ulcers and is extremely rare in gastric ulcers.

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us: 432PathologyTeam@gmail.com

432 Pathology Team

*Good Luck ^_^*