Gastrointestinal Drugs

The digestive system consists of two basic anatomical divisions:

- The Alimentary canal (GI) tract extends from the mouth to the anus.
- The accessory organs. Accessory organs of digestion include the salivary glands, liver, gallbladder, and pancreas.

** **The overall function of the digestive system**
is to extract nutrients from food so that they may be used to fuel the metabolic processes in the body. Because food is a complex substance, multiple steps are necessary before cells can use its components.
These steps are **ingestion, propulsion, digestion, absorption, and defecation.**

Physiology of the stomach:
The stomach secretes substances that promote the processes of chemical digestion. Gastric glands extending deep into the mucosa of the stomach contain several cell types that are critical to digestion and that are important to the pharmacotherapy of digestive disorders:

• **Chief cells** secrete **pepsinogen,** an inactive form of the enzyme pepsin that chemically breaks down proteins.

• **Parietal cells** secrete 1 to 3 liters of **hydrochloric acid (HCL)**each day. This strong acid helps to

- break down food.
- activates pepsinogen.
- kills microbes that may have been ingested.

Parietal cells also secrete **intrinsic factor**, which is essential for the absorption of vitamin B12.

• **Entero-endocrine cells** secrete **hormones** that modify the digestive processes.

In the stomach, the most important secretion is gastrin, which stimulates acid production by the parietal cells.

*** Because of these combination of secretions the gastric juice or fluid is the most acidic fluid in the body, having a pH of 1.5 to 3.5.

*** **A number of natural defenses protect the stomach mucosa against this extremely acidic fluid:**

A. **Certain cells** that line the surface of the stomach secrete a thick, **mucous layer and bicarbonate ion to neutralize the acid.**

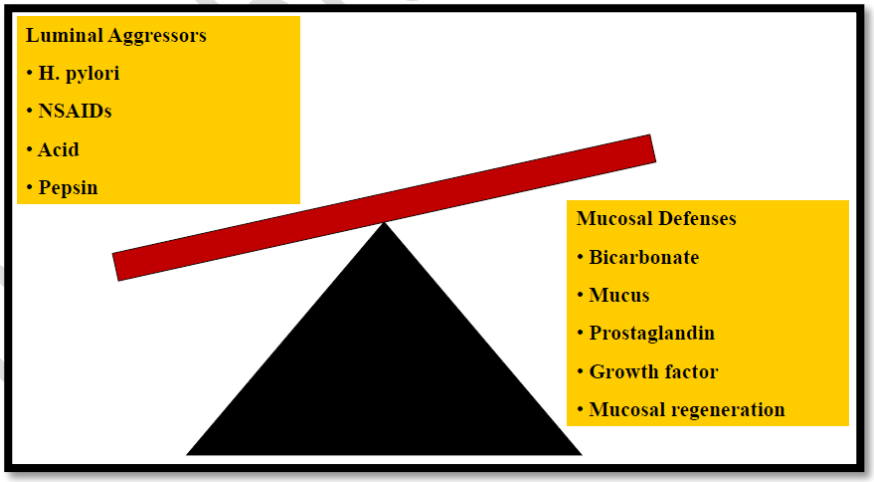
B. **On reaching the duodenum,** the stomach contents are further **neutralized by bicarbonate from pancreatic and biliary secretions.**

Peptic ulcer (PUD)

Peptic ulcer disease (PUD) is caused by an erosion of the mucosal layer of the stomach or duodenum. Peptic ulcer is a lesion located in either the stomach (**gastric ulcer**) or the small intestine (**duodenal ulcer**).

Common causes or aggressive factors of PUD

- Infection with *Helicobacter pylori*.
- nonsteroidal anti-inflammatory drugs (NSAIDs).
- Gastric Acid.
- Pepsin.
- Smoking.
- Other factors (Genetics, Foods, Stress).



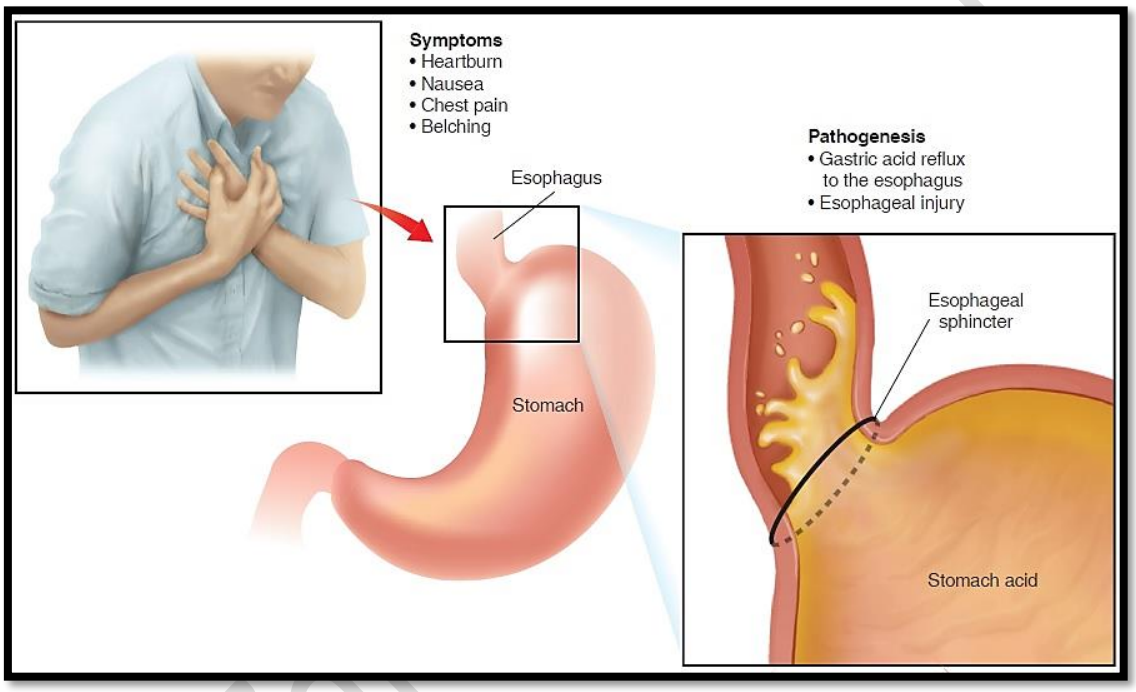
(Pathophysiology of PUD)

Gastroesophageal reflux disease (GERD)

GERD is caused by acidic stomach contents entering the esophagus. Although most often considered a disease of people older than age 40, GERD can also occur in infants.

Causes: is inappropriate relaxation of the lower esophageal sphincter (LES), a ring of smooth muscle that normally prevents reflux of gastric acid. In people with GERD, the LES undergoes frequent, transient relaxation, thereby allowing pressure in the stomach to force gastric contents up into the esophagus.

Other factors that can contribute to GERD include obesity, hiatal hernia, delayed gastric emptying, and impaired clearance of acid from the esophagus



(Pathophysiology of GERD)

Pharmacotherapy of Peptic Ulcer Disease (PUD) & GERD

four primary classes, plus one miscellaneous group:

- H2-receptor antagonists
- Proton pump inhibitors
- Antacids
- Antibiotics
- Miscellaneous drugs

1. H2-receptor antagonists

a. Examples: cimetidine (Tagamet), famotidine (Pepcid), ranitidine (Zantac)

b. Mechanism of action: Suppress acid secretion by blocking H2 receptors on parietal cells.

c. Therapeutic Uses:

1. Gastric and Duodenal Ulcers
2. Gastroesophageal Reflux Disease (GERD).
3. Heartburn, Acid Indigestion, and Sour Stomach

d. Side effects: few side effects, occur mostly in elderly patient include confusion, hallucinations, CNS depression.

2. Proton pump inhibitors

a. Example: Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole.

b. Mechanism of action: act by blocking the enzyme responsible for the secretion of HCL in the stomach. by binding irreversibly to the enzyme H+, K+-ATPase. More effective in reduce acid secretion than H2-receptor antagonist. and have a longer duration of action.

c. Indication: Indications include peptic ulcer and GERD.

d. Adverse effects: Adverse effects are generally minor and include headache, nausea, diarrhea, rash, and abdominal pain.

3. Antacids

a. Example: Aluminum hydroxide, Calcium carbonate, Magnesium hydroxide.

b. Mechanism of action: Antacids are alkaline substances that have been used to neutralize stomach acid by react with gastric acid to form neutral salts.

c. Indication: They are most effectively used in combination with other antiulcer agents for the symptomatic relief of heartburn due to PUD or GERD.

d. Adverse effects: When given in high doses, aluminum compounds may interfere with phosphate metabolism and cause constipation.

4. Antibiotics

a. Example: Amoxicillin, Bismuth, Clarithromycin, Metronidazole, Tetracycline.

b. Mechanism of action: Eradicate *H. pylori* (gram-negative bacterium is associated with 90% of all duodenal ulcers and 75% of all gastric ulcers).

*** antibiotics used as a single therapy or combination with other antibiotics or with a proton pump inhibitor or an H2-receptor antagonist

c. **Indication:** should be given to all patients with gastric or duodenal ulcers and confirmed infection with *H. pylori*.

5. **Miscellaneous Drugs**

a. **Example**: Sucralfate, Misoprostol

b. **Mechanism of action:**

1. Sucralfate: Forms a barrier over the ulcer crater that protects against acid and pepsin.
2. Misoprostol: Protects against NSAID-induced ulcers by stimulating secretion of mucus and bicarbonate, maintaining submucosal blood flow, and suppressing secretion of gastric acid.

Laxatives:

Constipation is identified by a decrease in the frequency and number of bowel movements. Stools may become dry, hard, and difficult to evacuate from the rectum.

Laxatives: Laxatives are drugs that promote evacuation of the large bowel, or defecation.
Cathartic implies a stronger and more complete bowel emptying.

Important indications:

• Relieve simple, chronic constipation
• Accelerate the removal of ingested toxic substances after overdose or poisoning
• Accelerate the removal of dead parasites after anti-helminthic drug therapy
• Cleanse the bowel prior to diagnostic or surgical procedures of the colon or genitourinary tract, including colonoscopy or barium enema

Classifications:

• Bulk-forming agents (Methylcellulose): absorb water, thus adding size to the fecal mass. They are often taken prophylactically to prevent constipation.
• Stool softeners (surfactants) (Docusate sodium): reduce surface tension by causing more water and fat to be absorbed into the stool. They are often used in clients who have undergone recent surgery.
• Stimulants irritate (Bisacodyl): the bowel to increase peristalsis; they may cause cramping in clients.
• Osmotic laxatives (Lactulose): such as saline are not absorbed in the intestine; they pull water into the fecal mass to create a waterier stool.
• Miscellaneous agents include mineral oil (Glycerin suppository): which acts within the intestine by lubricating the stool and the colon mucosa.

Antidiarrheal Drugs

Diarrhea is an increase in the frequency and fluidity of bowel movements. Diarrhea is not a disease; it is a symptom of an underlying disorder.

Causes

include infection, maldigestion, inflammation, and functional disorders of the bowel (e.g., irritable bowel syndrome).

serious complications of diarrhea

- Dehydration.
- electrolyte depletion.

Management of diarrhea

(1) diagnosis and treatment of the underlying disease.
(2) replacement of lost water and salts.
(3) relief of cramping.
(4) reducing passage of unformed stools.

Antidiarrheal medications:

(1) specific antidiarrheal drugs. (drugs that treat the underlying cause of diarrhea. Included opioids)
(2) nonspecific antidiarrheal drugs. (to provide symptomatic relief; these drugs do not influence the underlying cause) (e.g.: **Bismuth Subsalicylate**, **Anticholinergic Antispasmodics.** Muscarinic antagonists (e.g., atropine)

Opioids:

1. **Examples:** Diphenoxylate+atropine, Difenoxin+atropine, Loperamide.
2. **Mechanism of action:**

By activating opioid receptors in the GI tract, these drugs:

a. decrease intestinal motility and thereby slow intestinal transit, which allows more time for absorption of fluid and electrolytes.
b. decreases secretion of fluid into the small intestine and increases absorption of fluid and salt.
c. As a result, the fluidity and volume of stools are reduced, as is the frequency of defecation.