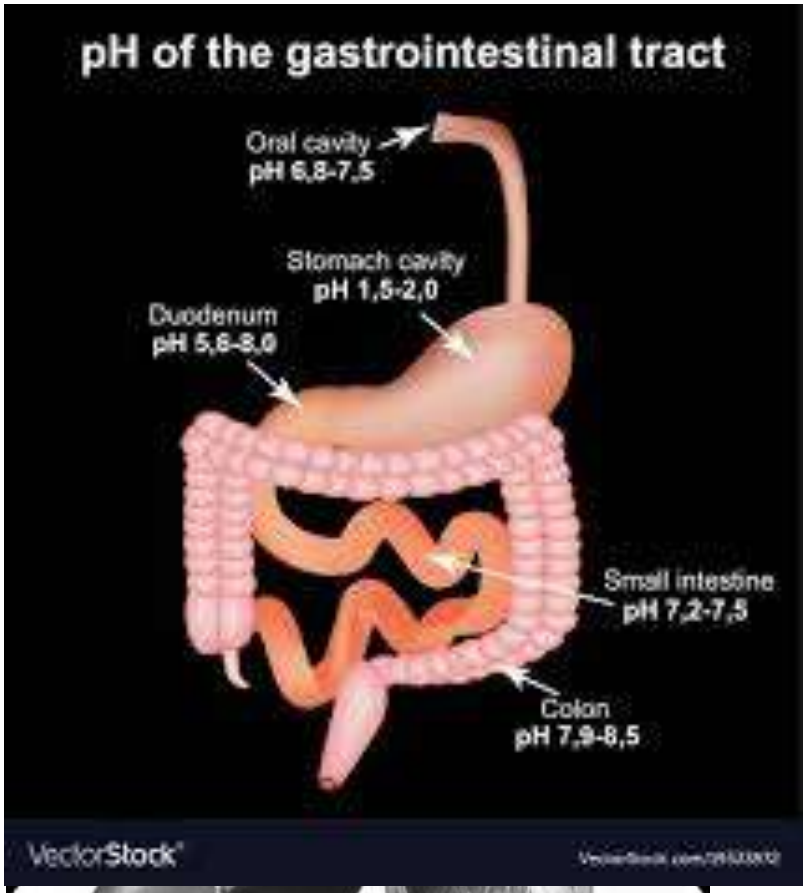
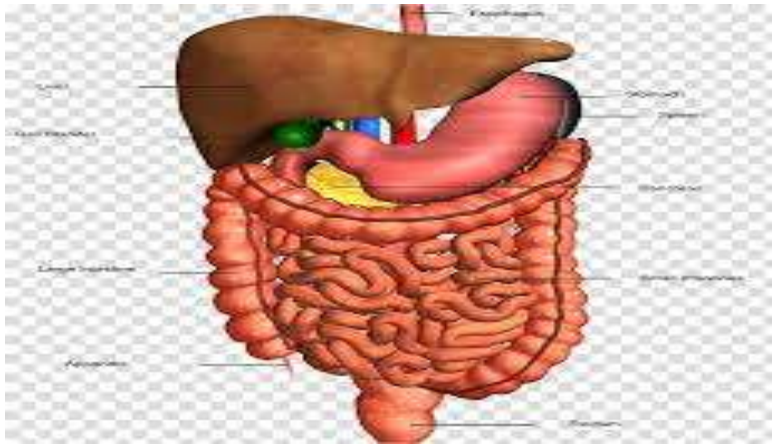
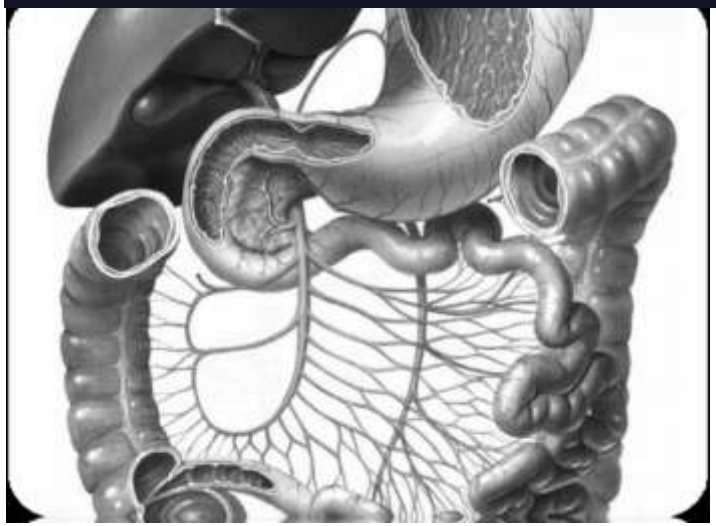

pH of the gastrointestinal tract
Oral cavity
pH 6,8-7,5
Stomach cavity
pH 1,5-2,0
Duodenum
pH 5,6-8,0
Small intestine
pH 7,2-7,5
Colon
pH 7,9-8,5
VectorStock





Upper GIT Disorders

1- Peptic Ulcer Disease (NSAID-RELATED ULCER) (H. Pylori Caused Ulcer)

2- GERD(Gastro Esophageal Reflux Disease)

3- Upper GIT Bleeding

4- Dyspepsia

Lower GIT DISORDERS

1- Inflammatory Bowel Disease

Ulcerative Colitis (UC) And Crohn's Disease (CD)

2- Irritable Bowel Syndrome IBS

3- Diarrhea

4- Constipation

5- Flatulence and Gases

Acid-Related Diseases

1- Hyperacidity

characterized by symptoms of overproduction of HCl by the parietal cells as indigestion, sour stomach, heartburn, acid stomach

2- Peptic ulcer diseases

3- Gastroesophageal Reflux Disease (GERD)

4- Helicobacter pylori (H. pylori)

➢ **Glands of the Stomach are Cardiac, Pyloric and Gastric. Cells of the Gastric Gland are :**

1- **Parietal cells** that produce and secrete HCl, Maintains stomach at pH of 1 to 4. HCl is secreted when cells are stimulated by food, Large fatty meals, Excessive amounts of alcohol, Emotional stress. Primary site of action for many acid-controller drugs.

2- **Chief cells** that secrete pepsinogen (proenzyme) which becomes pepsin when activated by exposure to acid. Pepsin breaks down proteins (proteolytic).

3-**Mucoid cells** which is Mucus-secreting cells that provide a protective mucous coat and protect against self-digestion by HCl.

➢**Imbalance of Imbalance of the three cells of the gastric gland and their secretions cause ACID RELATED DISORDERS.**

Acid - Controlling Agents

1- Antacids

More quickly and efficiently neutralize stomach acid, but their action is only temporary

2- H2 receptor antagonist

Stop acid secretion and may not relieve symptoms for at least 45 minutes

3- Proton pump inhibitors

Typically longer duration of action than H2Ras

❑*Antacids*

- **Antacids are weak bases that react with gastric acid to form water and a salt to diminish gastric acidity.**
- **Neutralizing acid and raising intragastric pH give rapid onset of action but short duration (about 30 minutes on an empty stomach).**
- **The duration of action can be extended to 3 hours when given with or within 1 hour after a meal.**

Used as first-line therapy for intermittent (less than twice week)

- **food delays stomach emptying allowing more time for the antacid to react).**

Commonly used Antacids

1-Aluminum hydroxide and magnesium hydroxide or combinations of salts of aluminum and magnesium (e.g. Gaviscon and Maalox).

Some products (Gaviscon) contain the antirefluxant alginic acid, which forms a viscous layer on top of gastric contents to act as a barrier to reflux.

2- Calcium carbonate

3- Sodium bicarbonate [NaHCO3] but this antacid is not recommended for long-term use as its systemic absorption can produce transient metabolic alkalosis.

4- Antacids and Antiflatulents combination

Antiflatulents used to relieve the painful symptoms associated with gas.

Adverse effects

1-Aluminum hydroxide tends to cause constipation, hypophosphatemia and osteomalacia.

2- Magnesium hydroxide tends to produce diarrhea.

(Preparations that combine both, help in normalizing bowel Function).

3- Magnesium hydroxide accumulation may occur in patients with renal impairment (the failing kidney cannot excrete extra magnesium, resulting in hypermagnesemia).

4- Sodium bicarbonate [$NaHCO_3$] (not recommended for long-term use) as its systemic absorption can produce transient metabolic alkalosis.

Sodium content may cause problems in patients with heart failure (HF), hypertension or renal insufficiency (fluid retention).

5- Calcium carbonate; ingestion of an inappropriately high amount cause of milk-alkali syndrome

Drug interactions

1-Chelation (fluoroquinolones, tetracyclines)

2- Reduced absorption of some drugs due to increase in pH. (ketoconazole, itraconazole, iron, atazanavir, delavirdine,indinavir, nelfinavir).

3- Increase absorption of some drugs, leading to potential toxicity. (raltegravir, saquinavir)

4-The bioavailability of ciprofloxacin is reduced when administered with an antacid, because aluminum and magnesium ions chelate with the antibiotic to form an insoluble and inactive complex.

Solution: The administration of ciprofloxacin 2 hours before an antacid increases ciprofloxacin bioavailability more than when administered 2 hours after the antacid.
The majority of these drug interactions can be avoided by separating the antacid from the interacting drug by a minimum of 2 hours.

Histamine receptor 2 antagonists (H2RA)

- **MECHANISM**
- **Reversibly inhibit histamine-2 receptors on the parietal cell thus reduce the secretion of gastric acid.**

(suppress gastric acid and pepsin secretion by competitively and reversibly occupying H2 receptors so block the binding of histamine to H2 receptors).

Cimetidine, famotidine, nizatidine, ranitidine

H2RA indication

1)Peptic ulcers, Promote the healing of duodenal and gastric ulcers.

Recurrence is common if H. pylori is present and the patient is treated with these agents alone.

Patients with NSAID-induced ulcers should be treated with PPIs, because these agents heal and prevent future ulcers more effectively than H2 antagonists do.

2) Acute stress ulcers

3) Gastroesophageal reflux disease (GERD)

4) Erosive esophagitis Therapy with H2RAs is less efficacious than therapy with PPIs

5) Upper gastrointestinal bleeding

Adverse effects

Overall, less than 3% incidence of side effects

1-Central nervous system (CNS) effects such as headache, dizziness, fatigue, somnolence, and confusion are the most common.

2- Cimetidine in high doses may induce impotence gynecomastia and galactorrhea (continuous release/discharge of milk).

SMOKING has been shown to decrease the effectiveness of H2 blockers (increases gastric acid production)

Drug interactions

1) Affect the absorption of drugs dependent on lower gastric pH (e.g., ketoconazole, itraconazole, iron, atazanavir, delavirdine, indinavir, nelfinavir).

2) Increases in absorption leading to potential toxicity (raltegravir, saquinavir).

3) Cimetidine also inhibits cytochrome P450 (CYP) enzymes, therefore interfere with the metabolism of Warfarin and theophylline

4) Cimetidine and ranitidine may also compete with medications and creatinine for tubular secretion in the kidney. (famotidine do not have this effect)

Tachyphylaxis or tolerance has been described with all H2RAs because of up-regulation of the H2 receptor site.

Tolerance to the antisecretory effect may develop after several days of continuous use but can be avoided by taking the H2RA only when needed.

Proton pump inhibitors (PPI)

- “proton pump” when the parietal cells release positive hydrogen ions (protons) during HCl production.
- PPI irreversibly bind to H+/K+ ATPase enzyme (proton pump).
- It takes about 18 hrs for the enzyme to be resynthesized, and acid secretion is inhibited during this time resulting achlorhydria (all gastric acid secretion is blocked).

Advantages

- Irreversibly inhibit the final step in gastric acid secretion; greater degree of acid suppression achieved and typically longer duration of action than H2Ras.
- Examples: Lansoprazole, Omeprazole, Rabeprazole, Pantoprazole, Esomeprazole

PPI INDICATIONS

- Treatment and prophylaxis stress ulcer
- ▪ Treatment of GERD
- ▪ Erosive esophagitis
- ▪ Active duodenal ulcer
- ▪ Pathologic hypersecretory conditions (Zollinger-Ellison syndrome, in which a gastrin-producing tumor causes hypersecretion of HCl)
- ▪ Prevent or treat NSAID-induced ulcers.
- ▪ Used with antimicrobial regimens to eradicate H. pylori.

Adverse reactions

- *Safe for short term therapy*
- Prolonged acid suppression with PPIs (and H2 antagonists) may result in low vitamin B12 because acid is required for its absorption in a complex with intrinsic factor.
- Elevated gastric pH may also impair the absorption of calcium carbonate.

Sucralfate

- Cytoprotective agent
- Consists of complex of octasulfate of sucrose and aluminum hydroxide.
- In acidic environment, it undergoes cross linking and produce viscous, sticky polymer that adhere to the epithelial cells and ulcer forming a protective barrier over these areas
- Protects these areas from pepsin, which normally breaks down proteins (making ulcers worse). Little absorption from the gut

Adverse effects

- May cause constipation
- May impair absorption of other drugs
- Should not be administered with PPIs, H2 antagonists, or antacids because it requires an acidic pH for activation.

Misoprostol

- Synthetic prostaglandin analog which has cytoprotective activity.
- Protect gastric mucosa from injury by enhancing local production of mucus or bicarbonate.
- Used for prevention of NSAID-induced gastric ulcers.
- Misoprostol is contraindicated in pregnancy, since it can stimulate uterine contractions and cause miscarriage.
- Dose-related diarrhea and nausea are the most common adverse effects and limit the use of this agent.