Drags that affect the function of the digestive system

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Acid-Controlling Agents

Acid-Related Pathophysiology

The stomach secretes:

- Hydrochloric acid (HCl)
- Bicarbonate
- Pepsinogen
- Intrinsic factor
- Mucus
- Prostaglandins

Glands of the Stomach

- Cardiac
- Pyloric
- Gastric*

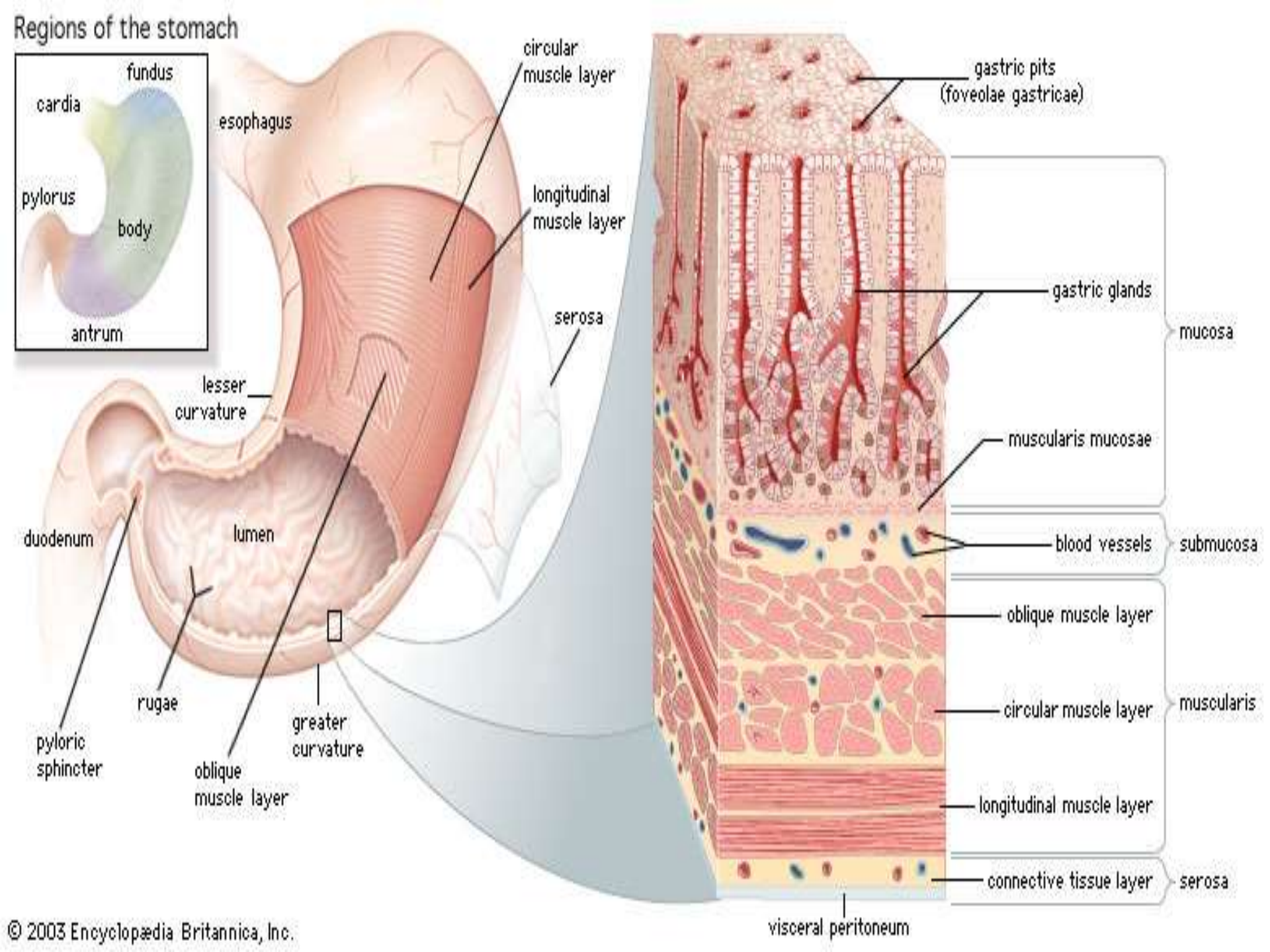
* **The cells of the gastric gland are the largest in number and of primary importance when discussing acid control**

Cells of the Gastric Gland

- Parietal cells
  - Produce and secrete HCl
  - Primary site of action for many acid-controller drugs
- Mucoid cells
  - Mucus-secreting cells (surface epithelial cells)
  - Provide a protective mucous coat
  - Protect against self-digestion by HCl
- Chief cells
  - Secrete pepsinogen, a proenzyme
  - Pepsinogen becomes *pepsin* when activated by exposure to acid
  - Pepsin breaks down proteins (proteolytic)

Hydrochloric Acid

- Secreted by the parietal cells when stimulated by food
- Maintains stomach at pH of 1 to 4
- Secretion also stimulated by:
  - Large fatty meals
  - Excessive amounts of alcohol
  - Emotional stress



Acid-Related Diseases

- Caused by imbalance of the three cells of the gastric gland and their secretions
- Most common: hyperacidity
- Clients report symptoms of overproduction of HCl by the parietal cells as *indigestion*, *sour stomach*, *heartburn*, *acid stomach*

Acid-Related Diseases (cont'd)

- PUD: peptic ulcer disease
- GERD: gastroesophageal reflux disease
- *Helicobacter pylori (H. pylori)*
  - Bacterium found in GI tract of 90% of patients with duodenal ulcers, and 70% of those with gastric ulcers
  - Combination therapy is used most often to eradicate *H. pylori*

Types of Acid-Controlling Agents

- Antacids
- H_2 antagonists
- Proton pump inhibitors

Antacids: Mechanism of Action

- Promote gastric mucosal defense mechanisms
- Secretion of:
  - Mucus: protective barrier against HCl
  - Bicarbonate: helps buffer acidic properties of HCl
  - Prostaglandins: prevent activation of proton pump which results in ⇓ HCl production

Antacids: Mechanism of Action (cont'd)

- Antacids DO NOT prevent the over-production of acid
- Antacids DO neutralizing the acid once it’s in the stomach

Antacids: Drug Effects

- Reduction of pain associated with acid-related disorders
  - Raising gastric pH from 1.3 to 1.6 neutralizes 50% of the gastric acid
  - Raising gastric pH 1 point (1.3 to 2.3) neutralizes 90% of the gastric acid
  - Reducing acidity reduces pain

Antacids: Aluminum Salts

- Forms: carbonate, hydroxide
- Have constipating effects
- Often used with magnesium to counteract constipation
- Examples
  - Aluminum carbonate: Basaljel
  - Hydroxide salt: AlternaGEL
  - Combination products (aluminum and magnesium): Gaviscon, Maalox, Mylanta, Di-Gel

Antacids: Magnesium Salts

- Forms: carbonate, hydroxide, oxide, trisilicate
- Commonly cause diarrhea; usually used with other agents to counteract this effect
- Dangerous when used with renal failure — the failing kidney cannot excrete extra magnesium, resulting in hypermagnesemia
- Examples
  - Hydroxide salt: magnesium hydroxide (MOM)
  - Carbonate salt: Gaviscon (also a combination product)
  - Combination products such as Maalox, Mylanta

Antacids: Calcium Salts

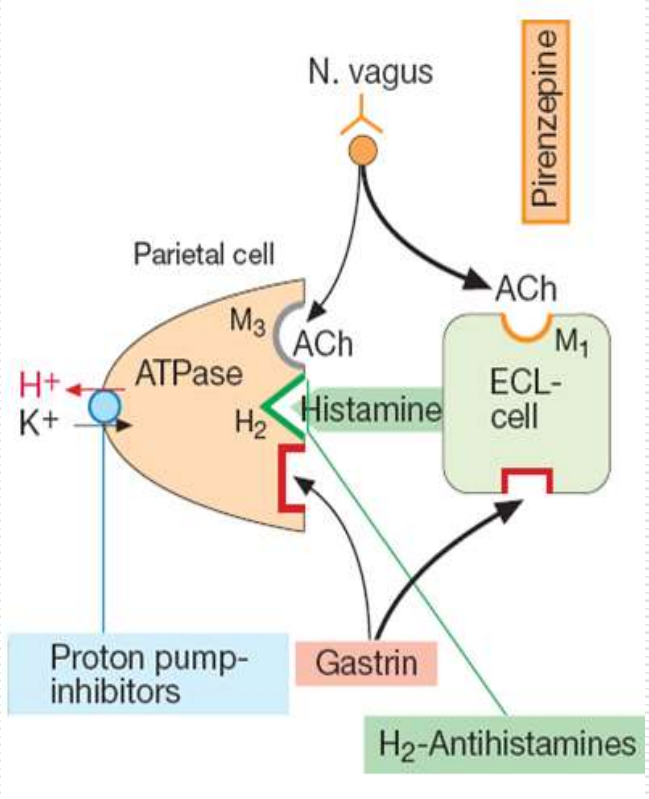
Forms: many, but carbonate is most common

- May cause constipation
- Their use may result in kidney stones
- Long duration of acid action may cause increased gastric acid secretion (hyperacidity rebound)
- Often advertised as an extra source of dietary calcium
  - Example: Tums (calcium carbonate)

Antacids: Sodium Bicarbonate

- Highly soluble
- Buffers the acidic properties of HCl
- Quick onset, but short duration
- May cause metabolic alkalosis
- Sodium content may cause problems in patients with CHF, hypertension, or renal insufficiency (fluid retention)

Histamine Type 2 (H_2) Antagonists



H_2 Antagonists

- Reduce acid secretion
- All available OTC in lower dosage forms
- Most popular drugs for treatment of acid-related disorders
  - cimetidine (Tagamet)
  - famotidine (Pepcid)
  - ranitidine (Zantac)

H_2 Antagonists: Mechanism of Action

- Block histamine (H_2) at the receptors of acid-producing parietal cells
- Production of hydrogen ions is reduced, resulting in decreased production of HCl

H_2 Antagonists: Indications

- GERD
- PUD
- Erosive esophagitis
- Adjunct therapy in control of upper GI bleeding
- Pathologic gastric hypersecretory conditions (Zollinger-Ellison syndrome)

H_2 Antagonists: Side Effects

- Overall, less than 3% incidence of side effects
- Cimetidine may induce impotence and gynecomastia
- May see:
  - Headaches, lethargy, confusion, diarrhea, urticaria, sweating, flushing, other effects

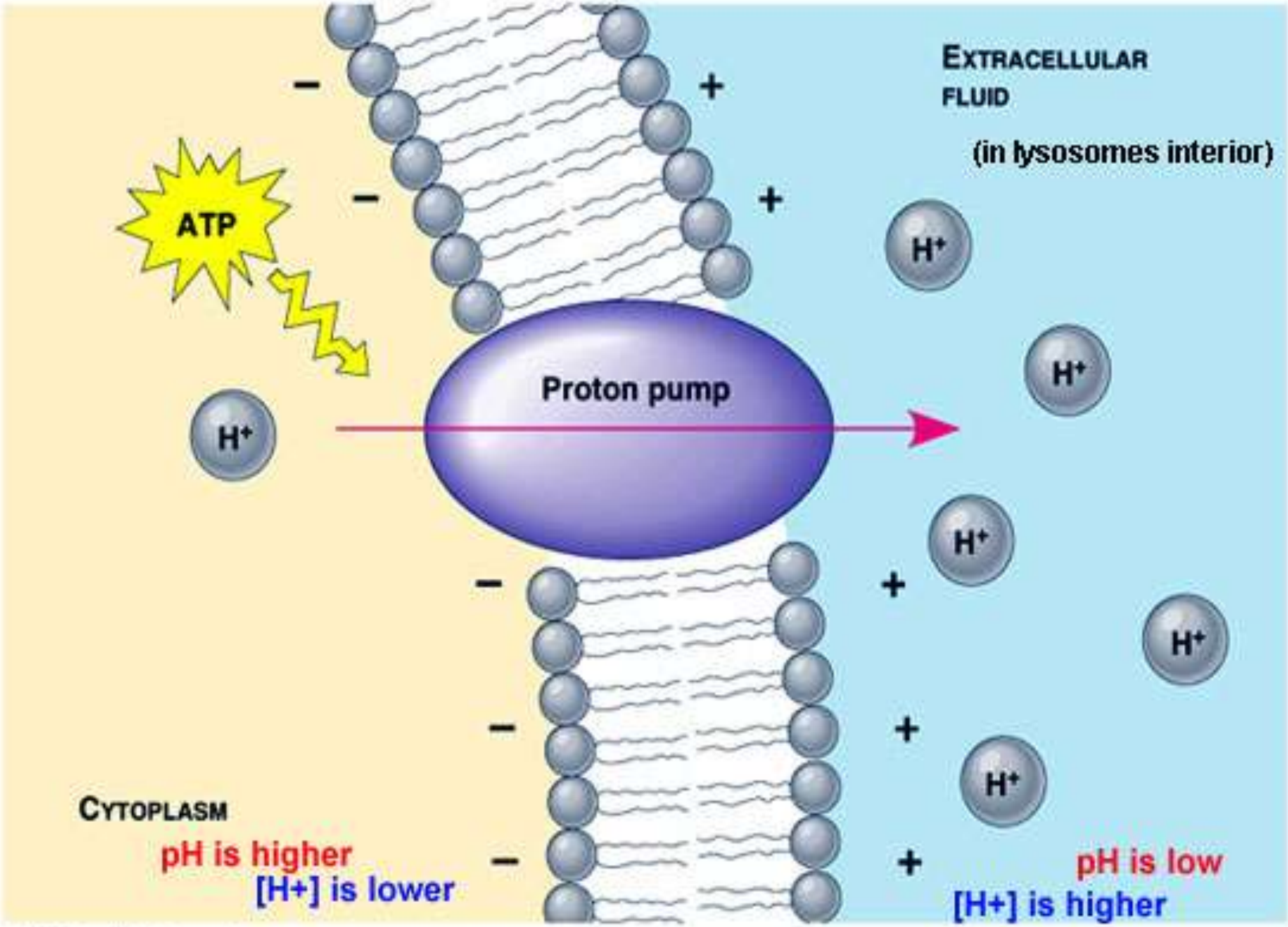
Proton Pump Inhibitors

Proton Pump

- The parietal cells release positive hydrogen ions (protons) during HCl production
- This process is called the "proton pump"
- H_2 blockers and antihistamines do not stop the action of this pump

Proton Pump Inhibitors: Mechanism of Action

- Irreversibly bind to H^+/K^+ ATPase enzyme
- Result: *achlorhydria*—ALL gastric acid secretion is blocked



Proton Pump Inhibitors: Drug Effect

- Total inhibition of gastric acid secretion
  - lansoprazole (Prevacid)
  - omeprazole (Prilosec)*
  - rabeprazole (AcipHex)
  - pantoprazole (Protonix)
  - esomeprazole (Nexium)

*The first in this new class of drugs

Proton Pump Inhibitors: Indications

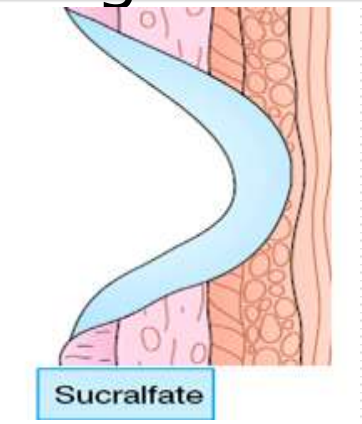
- GERD maintenance therapy
- Erosive esophagitis
- Short-term treatment of active duodenal and benign gastric ulcers
- Zollinger-Ellison syndrome
- Treatment of *H. pylori*–induced ulcers

Proton Pump Inhibitors: Side Effects

- Safe for short-term therapy
- Incidence low and uncommon

Other Drugs: sucralfate (Carafate)

- Cytoprotective agent
- Used for stress ulcers, erosions, PUD
- Attracted to and binds to the base of ulcers and erosions, forming a protective barrier over these areas
- Protects these areas from pepsin, which normally breaks down proteins (making ulcers worse)



sucralfate (Carafate) (cont'd)

- Little absorption from the gut
- May cause constipation, nausea, and dry mouth
- May impair absorption of other drugs, especially tetracycline
- Binds with phosphate; may be used in chronic renal failure to reduce phosphate levels
- Do not administer with other medications

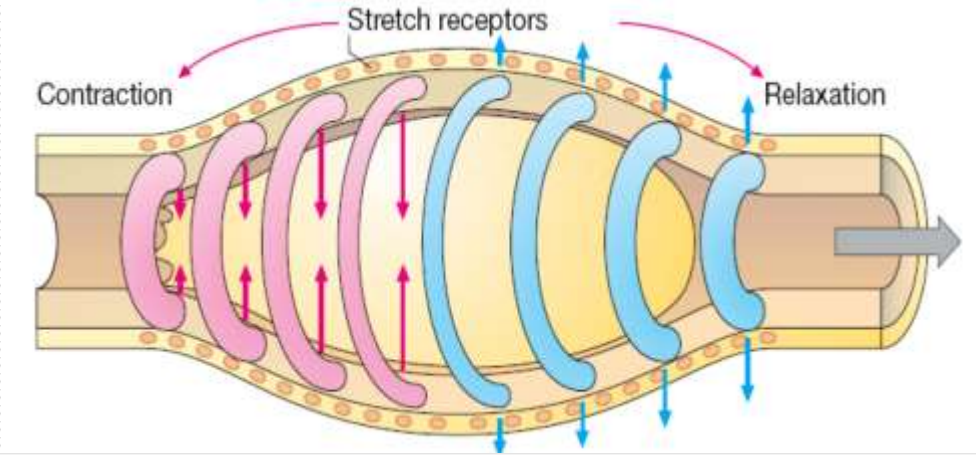
misoprostol (Cytotec)

- Synthetic prostaglandin analog
- Prostaglandins have cytoprotective activity
  - Protect gastric mucosa from injury by enhancing local production of mucus or bicarbonate
  - Promote local cell regeneration
  - Help to maintain mucosal blood flow

misoprostol (Cytotec) (cont'd)

- Used for prevention of NSAID-induced gastric ulcers
- Doses that are therapeutic enough to treat duodenal ulcers often produce abdominal cramps, diarrhea

Antidiarrheals and Laxatives



Diarrhea

- Abnormal frequent passage of loose stool *or*
- Abnormal passage of stools with increased frequency, fluidity, and weight, or with increased stool water excretion

Diarrhea (cont'd)

Acute diarrhea

- Sudden onset in a previously healthy person
- Lasts from 3 days to 2 weeks
- Self-limiting
- Resolves without sequelae
- Bacterial, viral, protozoal, nutritional

Diarrhea (cont'd)

Chronic diarrhea

- Lasts for more than 3 weeks
- Associated with recurring passage of diarrheal stools, fever, loss of appetite, nausea, vomiting, weight loss, and chronic weakness
- Tumors, diabetes, irritable bowel syndrome

Antidiarrheals: Mechanism of Action

Adsorbents

- Coat the walls of the GI tract
- Bind to the causative bacteria or toxin, which is then eliminated through the stool
- Examples: bismuth subsalicylate (Pepto-Bismol), kaolin-pectin, activated charcoal

Antidiarrheals: Mechanism of Action (cont'd)

Anticholinergics

- Decrease intestinal muscle tone and peristalsis of GI tract
- Result: slowing the movement of fecal matter through the GI tract
- Examples: belladonna alkaloids, atropine

Antidiarrheals: Mechanism of Action (cont'd)

Intestinal flora modifiers

- Bacterial cultures of *Lactobacillus* organisms work by:
  - Supplying missing bacteria to the GI tract
  - Suppressing the growth of diarrhea-causing bacteria
- Example: *L. acidophilus* (Lactinex)

Antidiarrheals: Mechanism of Action (cont'd)

Opiates

- Decrease bowel motility and relieve rectal spasms
- Decrease transit time through the bowel, allowing more time for water and electrolytes to be absorbed
- Examples: loperamide (Imodium), diphenoxylate (Lomotil)

Antidiarrheal Agents: Side Effects

Adsorbents

- Increased bleeding time
- Constipation, dark stools
- Confusion, twitching
- Hearing loss, tinnitus, metallic taste, blue gums

Antidiarrheal Agents: Side Effects (cont'd)

Anticholinergics

- Urinary retention, hesitancy, impotence
- Headache, dizziness, confusion, anxiety, drowsiness
- Dry skin, rash, flushing
- Blurred vision, photophobia, increased intraocular pressure
- Hypotension, hypertension, bradycardia, tachycardia

Antidiarrheal Agents: Side Effects (cont'd)

Opiates

- Drowsiness, sedation, dizziness, lethargy
- Nausea, vomiting, anorexia, constipation
- Respiratory depression
- Bradycardia, palpitations, hypotension
- Urinary retention
- Flushing, rash, urticaria

Laxatives

Constipation

- Abnormally infrequent and difficult passage of feces through the lower GI tract
- Symptom, not a disease
- Disorder of movement through the colon and/or rectum
- Can be caused by a variety of diseases or drugs

Laxatives: Mechanism of Action

Bulk forming

- High fiber
- Absorbs water to increase bulk
- Distends bowel to initiate reflex bowel activity
- Examples:
  - methylcellulose (Citrucel)
  - Polycarbophil (FiberCon)

Laxatives: Mechanism of Action (cont'd)

Emollient

- Stool softeners and lubricants
- Promote more water and fat in the stools
- Lubricate the fecal material and intestinal walls
- Examples:
  - Stool softeners: docusate salts (Colace, Surfak)
  - Lubricants: mineral oil

Laxatives: Mechanism of Action (cont'd)

Hyperosmotic

- Increase fecal water content
- Result: bowel distention, increased peristalsis, and evacuation
- Examples:
  - sorbitol (increases fluid movement into intestine)
  - lactulose (Chronulac)

Laxatives: Mechanism of Action (cont'd)

Saline

- Increase osmotic pressure within the intestinal tract, causing more water to enter the intestines
- Result: bowel distention, increased peristalsis, and evacuation

Laxatives: Mechanism of Action (cont'd)

- Saline laxative examples:
  - magnesium sulfate (Epsom salts)
  - magnesium hydroxide (MOM)
  - magnesium citrate
  - sodium phosphate (Fleet Phospho-Soda, Fleet enema)

Laxatives: Mechanism of Action (cont'd)

Stimulant

- Increases peristalsis via intestinal nerve stimulation
- Examples:
  - castor oil (Granulex)
  - senna (Senokot)

Laxatives: Indications

Laxative Group	Use
Bulk forming	Acute and chronic constipation Irritable bowel syndrome Diverticulosis
Emollient	Acute and chronic constipation Softening of fecal impaction; facilitation of BMs in anorectal conditions

Laxatives: Indications (cont'd)

Laxative Group	Use
Hyperosmotic	Chronic constipation
	Diagnostic and surgical preps
Saline	Acute constipation
	Diagnostic and surgical preps
	Removal of helminths

Laxatives: Indications (cont'd)

Laxative Group	Use
Stimulant	Acute and chronic constipation Diagnostic and surgical bowel preps

Laxatives: Side Effects

- Bulk forming
  - Impaction
  - Fluid overload
- Emollient
  - Skin rashes
  - Decreased absorption of vitamins
- Hyperosmotic
  - Abdominal bloating
  - Rectal irritation

Laxatives: Side Effects (cont'd)

- Saline
  - Magnesium toxicity (with renal insufficiency)
  - Cramping
  - Diarrhea
  - Increased thirst
- Stimulant
  - Nutrient malabsorption
  - Skin rashes
  - Gastric irritation
  - Rectal irritation

Antiemetic and Antinausea Agents

Definitions

- Nausea
  - Unpleasant feeling that often precedes vomiting
- Emesis (vomiting)
  - Forcible emptying of gastric, and occasionally, intestinal contents
- Antiemetic agents
  - Used to relieve nausea and vomiting

VC and CTZ

- Vomiting center (VC)
- Chemoreceptor trigger zone (CTZ)
  - Both located in the brain
  - Once stimulated, cause the vomiting reflex

Indications

- Specific indications vary per class of antiemetics
- General use: prevention and reduction of nausea and vomiting

Mechanism of Action and Indications

- Anticholinergic agents (ACh blockers)
  - Bind to and block acetylcholine (ACh) receptors in the inner ear labyrinth
  - Block transmission of nauseating stimuli to CTZ
  - Also block transmission of nauseating stimuli from the reticular formation to the VC
  - Scopolamine
  - Also used for motion sickness

Mechanism of Action

- Antihistamine agents (H_1 receptor blockers)
  - Acts by binding to H_1 and M-cholinergic receptors
  - Prevent cholinergic stimulation in vestibular and reticular areas, thus preventing emesis
  - Diphenhydramine (Benadryl, Dimedrol), promethazine (Phenergan)
  - Also used for nonproductive cough, allergy symptoms, sedation

Mechanism of Action (cont'd)

- Neuroleptic agents
  - Block dopamine receptors on the CTZ
  - chlorpromazine (Thorazine), prochlorperazine (Compazine)
  - Also used for psychotic disorders, intractable hiccups

Mechanism of Action (cont'd)

- Prokinetic agents
  - Block dopamine in the CTZ
  - Cause CTZ to be desensitized to impulses it receives from the GI tract
  - Also stimulate peristalsis in GI tract, enhancing emptying of stomach contents
  - Metoclopramide (Reglan)
  - Also used for GERD, delayed gastric emptying

Thank you for attention!