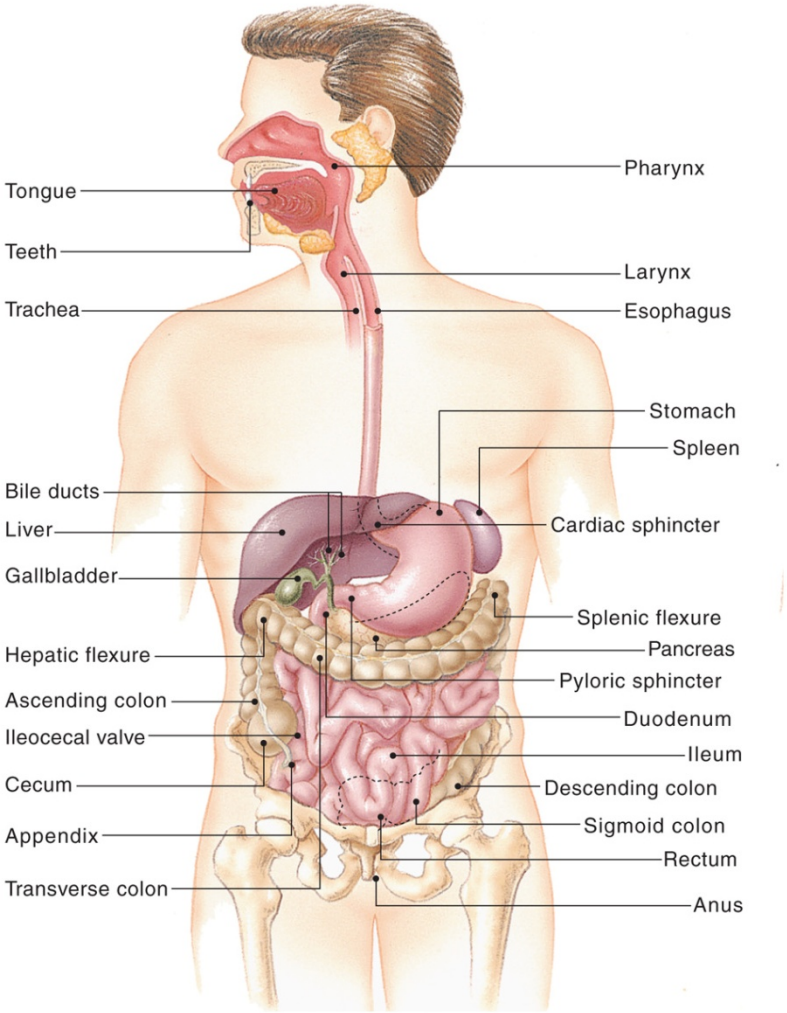
Gastrointestinal and Antiemetic Drugs


Tongue
Teeth
Trachea
Pharynx
Larynx
Esophagus
Stomach
Spleen
Bile ducts
Liver
Gallbladder
Cardiac sphincter
Splenic flexure
Pancreas
Hepatic flexure
Pyloric sphincter
Ascending colon
Duodenum
Ileocecal valve
Ileum
Cecum
Descending colon
Sigmoid colon
Appendix
Rectum
Transverse colon
Anus

GI drugs

Drugs used for:

1) Peptic ulcers and gastroesophageal reflux disease (GERD)

2) Chemotherapy-induced emesis

3) Diarrhea

4) Constipation

Peptic ulcer

Causes of peptic ulcer:

- Infection with gram-negative Helicobacter pylori
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs)
- Increased hydrochloric acid secretion
- Inadequate mucosal defense against gastric acid
- Tumors (rare)

Drugs for Peptic ulcer

Treatment of peptic ulcer

1) Eradicating the H. pylori infection

2) Reducing secretion of gastric acid with the use of proton pump inhibitors or H_2-receptor antagonists

3) Providing agents that protect the gastric mucosa from damage such as **misoprostol** and **sucralfate**

4) Neutralizing gastric acid with nonabsorbable antacids

Drugs for Peptic ulcers and GERD

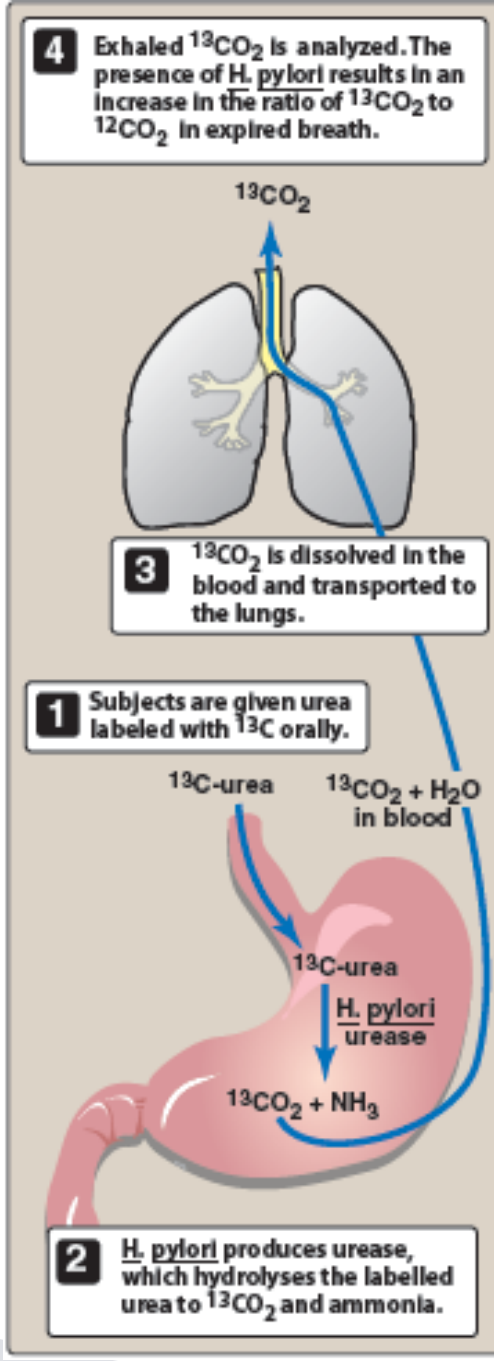
- Antimicrobials
- H_2-receptor antagonists
- Proton pump inhibitors
- Prostaglandins
- Antacids

Drugs for Peptic ulcers

- Antimicrobial agents (For H. pylori)
  - Metronidazole
  - Amoxicillin
  - Clarithromycin
  - Tetracyclines
  - Bismuth compounds

Antimicrobial agents

- Optimal therapy for patients with peptic ulcer disease infected with H. pylori requires antimicrobial treatment
- Endoscopic biopsy of the gastric mucosa or various noninvasive methods are used, including serologic tests and urea breath tests to document infection with H. pylori
- Eradication of H. pylori results in rapid healing of active peptic ulcers and low recurrence rates


4 Exhaled $^{13}CO_2$ is analyzed. The presence of H. pylori results in an increase in the ratio of $^{13}CO_2$ to $^{12}CO_2$ in expired breath.
$^{13}CO_2$
3 $^{13}CO_2$ is dissolved in the blood and transported to the lungs.
1 Subjects are given urea labeled with ^{13}C orally.
^{13}C-urea
$^{13}CO_2 + H_2O$ in blood
^{13}C-urea
H. pylori urease
$^{13}CO_2 + NH_3$
2 H. pylori produces urease, which hydrolyses the labelled urea to $^{13}CO_2$ and ammonia.

Antimicrobial agents for PU

- GERD is not associated with H. pylori infection and does not respond to treatment with antibiotics
- Triple therapy consisting of a PPI combined with either metronidazole or amoxicillin plus clarithromycin for 2 weeks
  - (Amoxicillin, omeprazole, clarithromycin)
    - Peptipac®, Triopac®
- Quadruple therapy of bismuth subsalicylate and metronidazole plus tetracycline plus a PPI, administered for a 2-week course
- Treatment with a single antimicrobial drug is less effective, results in antimicrobial resistance, and is absolutely not recommended
- Switching antibiotics is not recommended
- Bismuth salts inhibit pepsin and increase the secretion of mucus

H_2-receptor antagonists

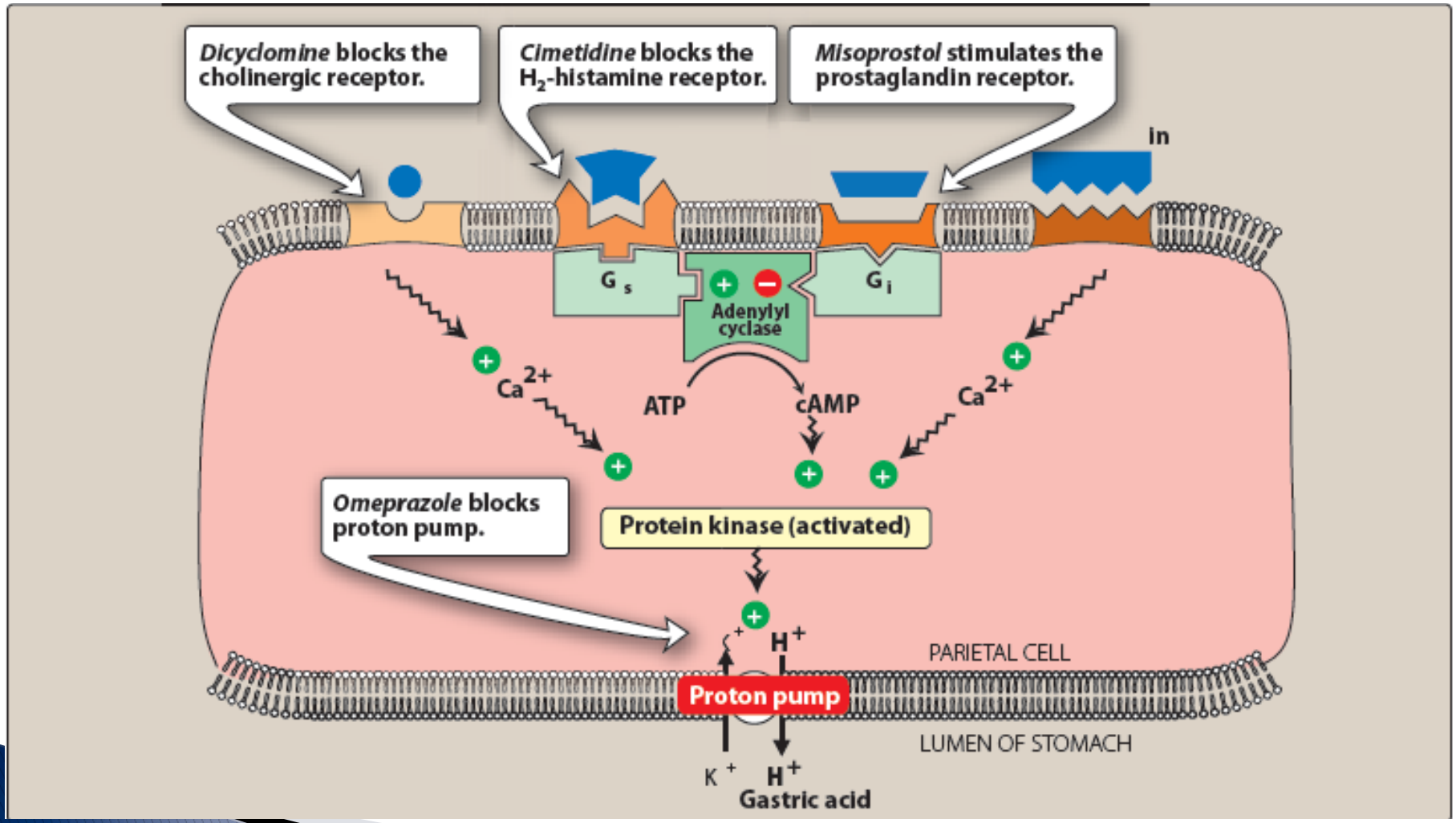
- Ranitidine (Zantac®, Randin®, Ratidine®, GI-care®)
- Famotidine (Famodin®, Famo®, Gastrex®)
- Cimetidine (Cemidin®, Cimetag®, Tagamet®)
- Nizatidine

H_2-receptor antagonists

- Gastric acid secretion by parietal cells of the gastric mucosa is stimulated by acetylcholine, histamine, and gastrin
- The receptor-mediated binding of acetylcholine, histamine, or gastrin results in the activation of protein kinases, which stimulates the H+/K+-adenosine triphosphatase (ATPase) proton pump to secrete hydrogen ions in exchange for K+ into the lumen of the stomach
- Receptor binding of prostaglandin E2 and somatostatin diminish gastric acid production
- Histamine binding causes activation of adenylyl cyclase, whereas binding of prostaglandin E2 inhibits it
- Gastrin and acetylcholine act by inducing an increase in intracellular calcium levels

H_2-receptor antagonists

- Antagonists of the histamine H_2 receptor are used to inhibit gastric acid secretion
- By competitively blocking the binding of histamine to H_2 receptors, these agents reduce the intracellular concentrations of cAMP and, secretion of gastric acid
- Inhibit basal, food-stimulated, and nocturnal secretion of gastric acid after a single dose
- Cimetidine use is limited by its adverse effects and drug-drug interactions


Dicyclomine blocks the cholinergic receptor.
Cimetidine blocks the H_2-histamine receptor.
Misoprostol stimulates the prostaglandin receptor.
in
G_s
G_i
Adenylyl cyclase
Ca^{2+}
ATP
cAMP
Ca^{2+}
Omeprazole blocks proton pump.
Protein kinase (activated)
H^+
PARIETAL CELL
Proton pump
LUMEN OF STOMACH
K^+
H^+
Gastric acid

H_2-receptor antagonists therapeutic uses

- Peptic ulcer
- Acute stress ulcers
- Gastroesophageal reflux disease (GERD)

H_2-receptor antagonists

Peptic ulcers:

- Effective in promoting the healing of duodenal and gastric ulcers
- Recurrence is common after treatment with H_2 antagonists is stopped
- Patients with NSAID-induced ulcers should be treated with PPIs, because these agents heal and prevent future ulcers better than H_2 antagonists

H_2-receptor antagonists

Acute stress ulcers

- H_2 blockers are given as intravenous infusion to prevent and manage acute stress ulcers associated with high-risk patients in intensive care units

- PPIs have gained favor for this indication because tolerance may occur with these agents in this setting

H_2-receptor antagonists

Gastroesophageal reflux disease (GERD):

- Low doses of H_2 antagonists is used for the prevention and treatment of heartburn (GERD)
- H_2-receptor antagonists act by stopping acid secretion and may not relieve symptoms for at least 45 minutes
- Antacids more quickly and efficiently neutralize secreted acid already in the stomach, but their action is only temporary
- PPIs are now used preferentially in the treatment of GERD

H_2-receptor antagonists

- The dosage of all these drugs must be decreased in patients with hepatic or renal failure
- Cimetidine can interfere in the metabolism of many drugs
- Cimetidine inhibits CYP450 and can slow metabolism and potentiate the action of several drugs resulting in serious adverse effects

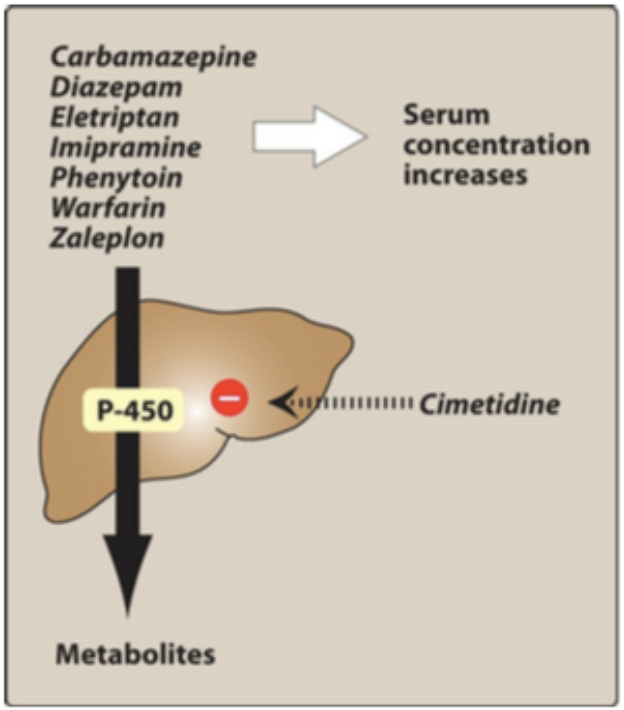


Figure 40.5 Drug interactions with *cimetidine*.

H_2-receptor antagonists

- Adverse effects:
  - Headache
  - Dizziness
  - Diarrhea
  - Muscular pain
  - Cimetidine can also have endocrine effects because it acts as a nonsteroidal antiandrogen
    - These effects include gynecomastia, and galactorrhea
- Drugs such as ketoconazole, which depend on an acidic medium for gastric absorption, may not be efficiently absorbed if taken with H_2 receptor antagonists

Proton pump inhibitors

- Omeprazole (Locid®, Losec®, Marial®, Mepral®, Pepticum®)
- Esomeprazole (Nexium®, Ezomax®)
- Lansoprazole (Lanso®, Lanton®, Zoton®)
- Dexlansoprazole
- Pantoprazole (Pantover®, Controloc®)
- Rabeprazole

Proton pump inhibitors

- Bind to the H+/K+-ATPase enzyme system (proton pump) of the parietal cell and suppress the secretion of hydrogen ions into the gastric lumen, inhibiting gastric acid secretion
- The membrane-bound proton pump is the final step in the secretion of gastric acid
- More effective than H_2 antagonists in suppressing gastric acid production and healing peptic ulcers

PPIs

- PPIs are prodrugs with an acid-resistant enteric coating to protect them from premature degradation by gastric acid
- The coating is removed in the alkaline duodenum, and the prodrug is absorbed and transported to parietal cells
- There, it is converted to the active form, which forms a stable covalent bond with H+/K+-ATPase
- It takes about 18 hours for the enzyme to be resynthesized
- At standard doses, all PPIs inhibit both basal and stimulated gastric acid secretion by ~90%

PPIs Therapeutic uses

- The superiority of the PPIs over the H_2 antagonists for suppressing acid production and healing peptic ulcers has made them the preferred drugs for
  - Stress ulcer treatment and prophylaxis
  - Treating erosive esophagitis and active duodenal ulcer
  - Long-term treatment of pathologic hypersecretory conditions (e.g. Zollinger-Ellison syndrome, in which a gastrin-producing tumor causes hypersecretion of HCl)

PPIs Therapeutic uses

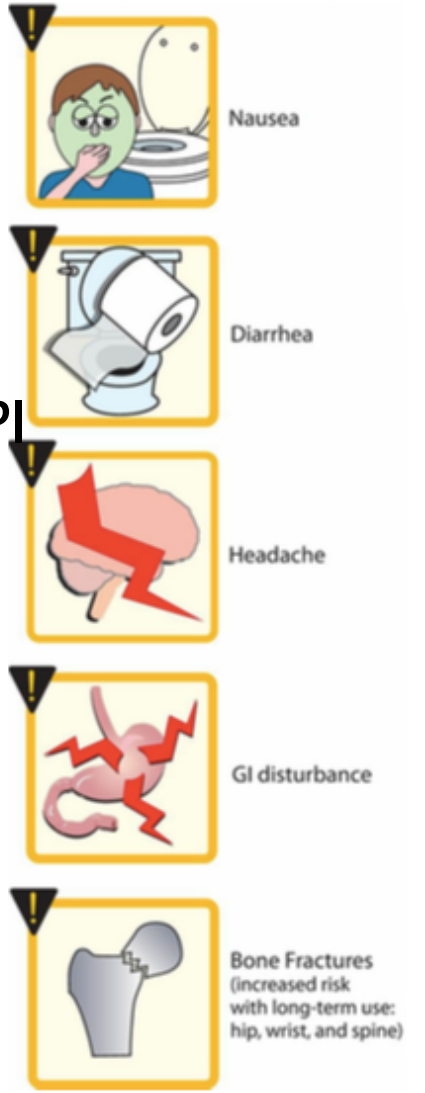
- Approved for the treatment of GERD and have gained favor over H_2 antagonists
- PPIs reduce the risk of bleeding from an ulcer caused by aspirin and other NSAIDs
- Used with antimicrobial regimens to eradicate H. pylori

PPIs Therapeutic uses

- PPIs should be taken 30 to 60 minutes before breakfast or the largest meal of the day
- If an H_2-receptor antagonist is also needed, it should be taken well after the PPI for best effect because the H_2 antagonists will reduce the activity of the proton pump
- In patients with GERD in whom a once-daily PPI is only partially effective, increasing to a twice-daily regimen or keeping the PPI in the morning and adding an H_2 antagonist in the evening may improve symptom control

PPIs Adverse Effects

- Diarrhea
- Clostridium difficile colitis
  - Patients must be counseled to discontinue PPI therapy if they have diarrhea for several days and to contact their physicians
- Possible increased risk of fractures of the hip, wrist, and spine
  - The greatest risk is associated with patients taking the PPIs for one year or greater



igure 40.6 Some adverse effects of proton pump therapy.
l = gastrointestinal.

PPIs Drug Interactions

Drug interactions

- Decrease the effectiveness of clopidogrel due to inhibition of CYP2C19
  - Increase risk of cardiovascular events
- Omeprazole inhibits the metabolism of warfarin, phenytoin, diazepam, and cyclosporine through competitive inhibition of CYP450 enzymes
- Prolonged therapy may result in low vitamin B12, because acid is required for its absorption
- Prolonged elevation of gastric pH can cause incomplete absorption of calcium carbonate products
  - Use calcium citrate as a source of calcium for patients taking prolonged acid-suppressing medications

Prostaglandins

- Prostaglandin E, produced by the gastric mucosa, inhibits secretion of HCl and stimulates secretion of mucus and bicarbonate (cytoprotective effect)

- A deficiency of prostaglandins is involved in the pathogenesis of peptic ulcers

Prostaglandins

- Misoprostol (Cytotec®)
  - A stable analog of prostaglandin approved for the prevention of gastric ulcers induced by NSAIDs
  - Less effective than H_2 antagonists and the PPIs for acute treatment of peptic ulcers
  - Has cytoprotective actions, but is clinically effective only at higher doses that diminish gastric acid secretion
  - Routine prophylactic use of misoprostol may not be justified except in patients who are taking NSAIDs and are at high risk of NSAID-induced ulcers such as elderly patients and those with ulcer complications

Prostaglandins

- Misoprostol
  - Like other prostaglandins, misoprostol produces uterine contractions, dislodging of the fetus, and is contraindicated during pregnancy
  - Adverse effects: diarrhea and nausea

Antacids

- Weak bases that react with gastric acid to form water and a salt to diminish gastric acidity
- Antacids also reduce pepsin activity because pepsin is inactive at a pH greater than 4

Antacids

- Aluminum hydroxide
- Magnesium hydroxide
- Calcium carbonate
- Systemic absorption of sodium bicarbonate can produce transient metabolic alkalosis and is not recommended for long-term use
- Food delays stomach emptying allowing more time for the antacid to react

Antacids

- Aluminum hydroxide + Magnesium hydroxide (Maalox®)
- Calcium carbonate + Magnesium carbonate (Rennie®)
- Calcium carbonate (Tums®)

Antacids Therapeutic uses

- Aluminum- and magnesium-containing antacids are used to:
  - Provide symptomatic relief of peptic ulcer disease and GERD
  - Promote healing of duodenal ulcers
  - Used as last-line therapy for acute gastric ulcers
- Calcium carbonate preparations are also used as calcium supplements for the treatment of osteoporosis

Antacids Adverse effects

- Aluminum hydroxide causes constipation
- Magnesium hydroxide causes diarrhea
- The binding of phosphate by aluminum-containing antacids can lead to hypophosphatemia
- Sodium bicarbonate
  - Can cause systemic alkalosis
  - Liberates CO_2, causing belching and flatulence
  - The sodium content of antacids can be an important consideration in patients with hypertension or congestive heart failure

Mucosal protective agents

- Cytoprotective compounds
- Enhance mucosal protection mechanisms, preventing mucosal injury, reducing inflammation, and healing existing ulcers.
  - Sucralfate (Ulsanic®)
  - Bismuth subsalicylate (Pink Bismuth®, Kalbeten®)

Mucosal protective agents

Sucralfate

- A complex of aluminum hydroxide and sulfated sucrose
- Binds to positively charged groups in proteins of both normal and necrotic mucosa
- Forms complex gels with epithelial cells creating a physical barrier that impairs diffusion of HCl and prevents degradation of mucus by pepsin and acid
- Stimulates prostaglandin release, mucus and bicarbonate output
- Inhibits peptic digestion
- By these mechanisms, sucralfate effectively heals duodenal ulcers and is used in long-term maintenance therapy to prevent their recurrence
- Does not prevent NSAID-induced ulcers, and does not heal gastric ulcers

Mucosal protective agents

Sucralfate

- Requires an acidic pH for activation and should not be administered with PPIs, H_2 antagonists, or antacids
- Little of the drug is absorbed systemically
- Very well tolerated, but it can interfere with the absorption of other drugs by binding to them

Mucosal protective agents

Bismuth subsalicylate

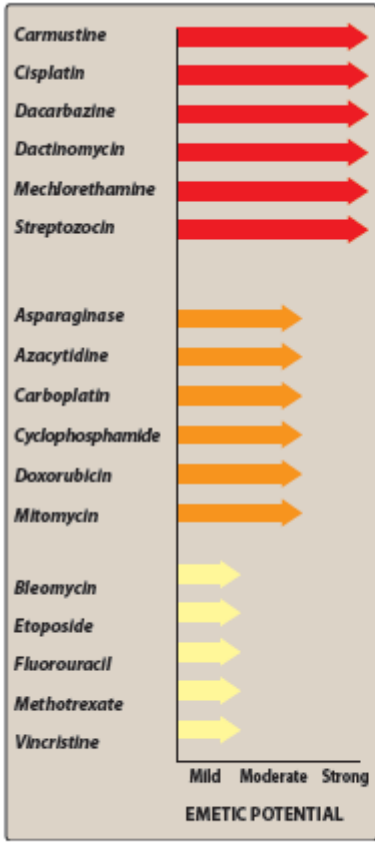
- Effectively heals peptic ulcers
- Has antimicrobial actions
- Inhibits the activity of pepsin
- Increases secretion of mucus, and interact with glycoproteins in necrotic mucosal tissue to coat and protect the ulcer crater

Drugs used to control chemotherapy induced emesis

- Nausea and vomiting may occur in a variety of conditions (motion sickness, pregnancy, and hepatitis) and are always unpleasant for the patient
- The nausea and vomiting produced by many chemotherapeutic agents demands especially effective management
- 70% -80% percent of all patients who undergo chemotherapy experience nausea or vomiting

Drugs used to control chemotherapy induced emesis

- Several factors influence the incidence and severity of chemotherapy-induced emesis including
  - The specific chemotherapeutic drug
  - The dose
  - Route and schedule of administration
  - Patient variables
    - Young patients and women are more susceptible than older patients and men



Drugs used to control chemotherapy induced emesis

- 10% – 40% of patients experience nausea or vomiting in anticipation of their chemotherapy (anticipatory vomiting)
- Emesis not only affects the quality of life but can also lead to rejection of potentially curative antineoplastic treatment
- Uncontrolled vomiting can produce dehydration, profound metabolic imbalances, and nutrient depletion

Drugs used to control chemotherapy induced emesis

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Mechanisms that trigger vomiting

- Two brainstem sites have key roles in the vomiting reflex pathway
  - Chemoreceptor trigger zone
    - Found outside the blood–brain barrier, thus can respond directly to chemical stimuli in the blood or CSF
  - The vomiting center
    - Located in the lateral reticular formation of the medulla
    - Coordinates the motor mechanisms of vomiting
    - Responds to afferent input from the vestibular system, the periphery (pharynx and gastrointestinal tract), and higher brainstem and cortical structures
      - The vestibular system functions mainly in motion sickness

Emetic actions of chemotherapeutic agents

- Chemotherapeutic agents can activate the medullary chemoreceptor trigger zone, or vomiting center
- Several neuroreceptors, including dopamine receptor Type 2 (D_2) and serotonin Type 3 ($5\text{-}HT_3$), play critical roles
- The color or smell of chemotherapeutic drugs and even stimuli associated with chemotherapy can activate higher brain centers and trigger emesis
- Chemotherapeutic drugs can also act peripherally by causing cell damage in the GI tract and releasing serotonin from the enterochromaffin cells of the small intestinal mucosa
- The released serotonin activates $5\text{-}HT_3$ receptors on vagal and splanchnic afferent fibers, which then carry sensory signals to the medulla, leading to the emetic response

Antiemetic drugs

- Antiemetics represent a variety of classes with various efficacies

- Anticholinergic drugs like the muscarinic receptor antagonist scopolamine and H1-receptor antagonists, such as dimenhydrinate, meclizine, and cyclizine are very useful in motion sickness but are ineffective against substances that act directly on the chemoreceptor trigger zone

Antiemetic drugs

- Scopolamine
- Dimenhydrinate (Dramine®)
- Cyclizine
- Meclizine (Meclozine)
  - Meclozine + pyridoxine (Ancozine®, Paravomine®)

Antiemetic drugs

- Phenothiazines
- 5-HT_3 receptor blockers
- Substituted benzamides
- Butyrophenones
- Benzodiazepines
- Corticosteroids
- Substance P/neurokinin-1 receptor blocker

Antiemetic drugs

Phenothiazines

- Prochlorperazine
- Act by blocking dopamine receptors
- Effective against low or moderately emetogenic chemotherapeutic agents (e.g. fluorouracil and doxorubicin)
- Side effects:
  - Hypotension and restlessnes (Dose limiting)
  - Extrapyramidal symptoms
  - Sedation

Antiemetic drugs

5-HT3 receptor blockers

- Ondansetron
- Granisetron
- Palonosetron
- Dolasetron

Antiemetic drugs

5-HT_3 receptor blockers

- Important in treating emesis linked with chemotherapy, because of their longer duration of action
- Selectively block 5-HT_3 receptors in the periphery (visceral vagal afferent fibers) and in the brain (chemoreceptor trigger zone)
- Can be administered as a single dose prior to chemotherapy (intravenously or orally)
- Efficacious against all grades of emetogenic therapy
- Extensively metabolized by the liver, doses should be adjusted in patients with hepatic insufficiency
- Side Effects:
  - Headache
  - Electrocardiographic changes, such as a prolonged QT interval, can occur with dolasetron

Antiemetic drugs

Substituted benzamides

- Metoclopramide (Emistop®, Pramin®)
- Effective at high doses against the emetogenic cisplatin, preventing emesis in 30%–40% percent of patients and reducing emesis in the majority
- Antidopaminergic side effects like sedation, diarrhea, and extrapyramidal symptoms, limit its high-dose use

Antiemetic drugs

Butyrophenones

Droperidol

Haloperidol

- Act by blocking dopamine receptors
- Moderately effective antiemetics
- Droperodol may prolong the QT interval, and is reserved for patients with inadequate response to other agents
- High-dose haloperidol was found to be nearly as effective as high-dose metoclopramide in preventing cisplatin-induced emesis

Antiemetic drugs

Benzodiazepines

- Lorazepam (Lorocare®, Lorivan®)
- Alprazolam (Xanax®, Xanagis®, Prazolex®)
- The antiemetic potency of lorazepam and alprazolam is low
- Their beneficial effects may be due to their sedative, anxiolytic, and amnesic properties
- These same properties make benzodiazepines useful in treating anticipatory vomiting

Antiemetic drugs

Corticosteroids

- Dexamethasone
- Methylprednisolone
- Effective against mildly to moderately emetogenic chemotherapy
- Most frequently used in combination with other agents
- Their antiemetic mechanism is not known
- Can cause insomnia and hyperglycemia in patients with diabetes mellitus

Antiemetic drugs

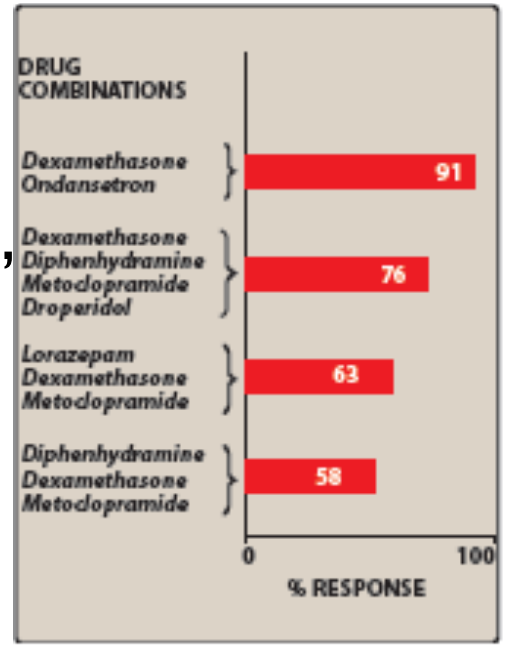
Substance P/neurokinin-1 receptor blocker

- Aprepitant
- Targets the neurokinin receptor in the brain and blocks the actions of the natural substance
- Aprepitant administered orally with dexamethasone and palonosetron
- Undergoes extensive metabolism, primarily by CYP3A4
- Affect the metabolism of other drugs
- Induce CYP3A4
  - Concomitant use with warfarin can shorten the its halflife
- Side effects: constipation and fatigue
- Only indicated for highly or moderately emetogenic chemotherapy regimens

Antiemetic drugs

Combination regimens:

- Antiemetic drugs are often combined to increase antiemetic activity or decrease toxicity
- Corticosteroids, most commonly dexamethasone, increase antiemetic activity when given with high-dose metoclopramide, a 5-HT3 antagonist, phenothiazine, butyrophenone, or a benzodiazepine
- Antihistamines, such as diphenhydramine, are often administered in combination with high-dose metoclopramide to reduce extrapyramidal reactions or with corticosteroids to counter metoclopramide induced diarrhea



Antidiarrheals

- Increased motility of the gastrointestinal tract and decreased absorption of fluid are major factors in diarrhea

- Antidiarrheal drugs used to treat acute diarrhea include
  - **Antimotility agents**
  - **Adsorbents**
  - **Agents that modify fluid and electrolyte transport**

Antidiarrheals

Antimotility agents

- Diphenoxylate
- Loperamide (Diacare®, Imodium®)
- Both are analogs of meperidine and have opioid-like actions on the gut
- Activate presynaptic opioid receptors in the enteric nervous system to inhibit acetylcholine release and decrease peristalsis
- At the usual doses, they lack analgesic effects
- Side effects: drowsiness, abdominal cramps, and dizziness
- Contribute to toxic megacolon and should not be used in young children or in patients with severe colitis

Antidiarrheals

Adsorbents

- Aluminum hydroxide
- Methylcellulose
- Used to control diarrhea
- Act by adsorbing intestinal toxins or microorganisms and/or by coating or protecting the intestinal mucosa
- Much less effective than antimotility agents and
- Can interfere with the absorption of other drugs

Antidiarrheals

Agents that modify fluid and electrolyte transport

- Bismuth subsalicylate
- Used for traveler's diarrhea
- Decreases fluid secretion in the bowel
- Its action may be due to its salicylate component as well as its coating action
- Adverse effects may include black tongue and black stools

Constipation

- Common condition caused by
  - Diminished fluid intake
  - Slow motility of waste material through large intestine
  - Certain foods, medications, diseases

Laxatives

- Laxatives are commonly used for constipation to accelerate the movement of food through GIT
- Increase the potential for loss of pharmacologic effect of poorly absorbed, delayed acting, and extended-release oral preparations by accelerating their transit through the intestines
- May cause electrolyte imbalances when used chronically
- All of these drugs, except for the chloride channel activator lubiprostone, have a risk of dependency for the user

Laxatives

- Irritants and stimulants
- Bulk laxatives
- Saline and osmotic laxatives
- Stool softeners (emollient laxatives or surfactants)
- Lubricant laxatives
- Chloride channel activators

Laxatives

Irritants and stimulants

- Senna
- Bisacodyl
- Castor oil

Laxatives

- **Senna (Laxikal Forte®, Agiolax®)**
  - Its active ingredient is a group of sennosides, a natural complex of anthraquinone glycosides
  - Taken orally, senna causes evacuation of the bowels within 8 to 10 hours
  - Also causes water and electrolyte secretion into the bowel
  - In combination products with a docusate-containing stool softener, it is useful in treating opioid-induced constipation

Laxatives

- **Bisacodyl (Dilax®, Laxadin®)**
  - Potent stimulant of the colon
  - Acts directly on nerve fibers in the mucosa of the colon
  - Adverse effects include abdominal cramps and the potential for atonic colon with prolonged use
  - Milk and drugs that may increase the gastric pH, such as antacids, PPIs, and H_2-receptor antagonists, should not be taken at the same time as the enteric-coated tablets
    - These agents may cause the enteric coating to dissolve prematurely in the stomach, resulting in stomach irritation and pain

Laxatives

- **Castor oil**
  - Broken down in the small intestine to ricinoleic acid, which is very irritating to the stomach and increases peristalsis
  - Pregnant patients should avoid castor oil because it may stimulate uterine contractions

Laxatives

Bulk laxatives

- The bulk laxatives include hydrophilic colloids (from indigestible parts of fruits and vegetables)
- Form gels in the large intestine, causing water retention and intestinal distension, thereby increasing peristaltic activity
- Similar actions are produced by methylcellulose, psyllium seeds, and bran
- Should be used cautiously in patients who are immobile because of their potential for causing intestinal obstruction

Laxatives

Saline and osmotic laxatives

- Magnesium citrate
- Magnesium hydroxide
- Sodium phosphate
  - Nonabsorbable salts that hold water in the intestine by osmosis
  - This distends the bowel, increasing intestinal activity and producing defecation in a few hours
- Electrolyte solutions containing PEG are used as colonic lavage solutions to prepare the gut for radiologic or endoscopic procedures
  - PEG powder for solution is available as a laxative
- Lactulose is a semisynthetic disaccharide sugar that also acts as an osmotic laxative
  - It cannot be hydrolyzed by intestinal enzymes
  - Oral doses are degraded in the colon by colonic bacteria into lactic, formic, and acetic acids
  - This increases osmotic pressure, causing fluid accumulation, colon distension, soft stools, and defecation

Laxatives

Stool softeners (emollient laxatives or surfactants)

- Docusate sodium
- Docusate calcium
- Docusate potassium
- Surface-active agents that become emulsified with the stool produce softer feces and ease passage
- May take days to become effective and are often used for prophylaxis rather than acute treatment

Laxatives

Lubricant laxatives

- Include mineral oil and glycerin suppositories
- Act by facilitating the passage of hard stools
- Mineral oil should be taken orally in an upright position to avoid its aspiration and potential for lipid or lipoid pneumonia

Laxatives

Chloride channel activators

- Lubiprostone
- Activate chloride channels to increase fluid secretion in the intestinal lumen
  - This eases the passage of stools and causes little change in electrolyte balances
- Used in the treatment of chronic constipation
- Minimal drug–drug interactions because metabolism occurs quickly in the stomach and jejunum
- Side effect: Nausea, Diarrhea