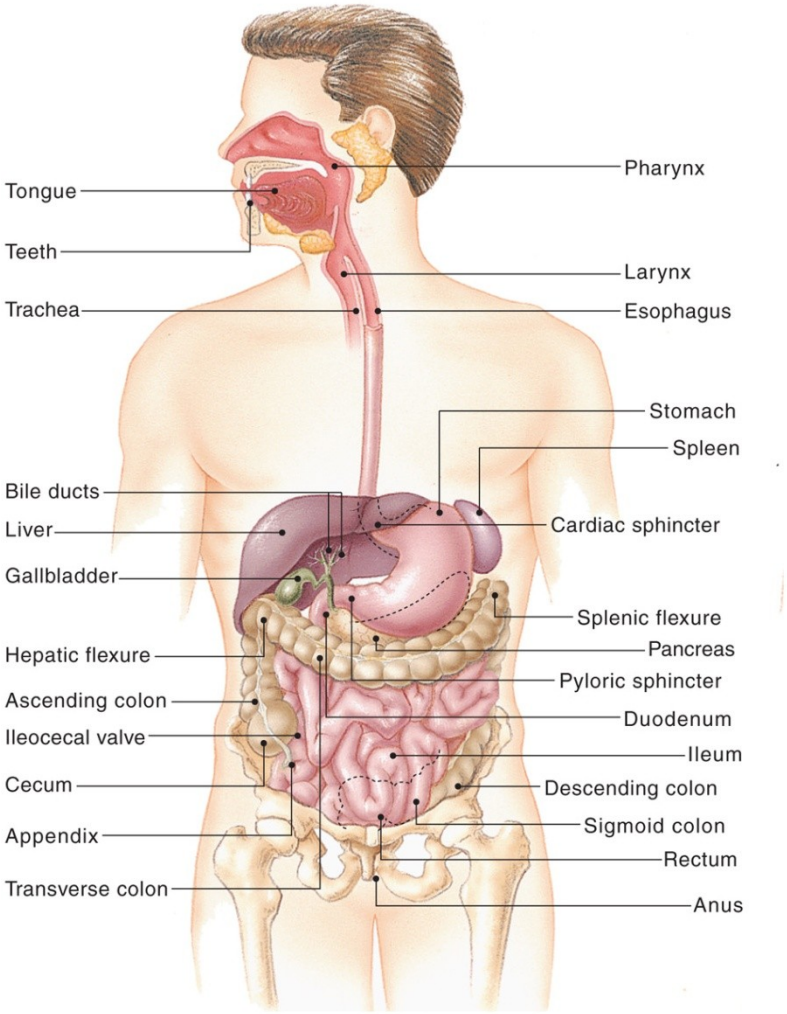
Gastrointestinal Drugs

Figure 40.1 The digestive system. *Source: Mulvihill, Mary Lou; Zelman, Mark; Holdaway, Paul; Tompary, Elaine; Raymond, Jill; Human Disease: A Systemic Approach, 6th edition, ©2006, p.276. Reprinted by permission of Pearson Education, Inc., Upper Saddle River, NJ.*



GI drugs

- Drugs used for:
  - Peptic ulcers and gastroesophageal reflux disease (GERD)
  - Chemotherapy-induced emesis
  - Diarrhea
  - Constipation

Drugs for Peptic ulcers and GERD

- 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 ulcers and GERD

- Treatment of peptic ulcer

  1) Eradicating the H. pylori infection

  2)Reducing secretion of gastric acid with the use of proton pump inhibitors or H2-receptor antagonists

  3)providing agents that protect the gastric mucosa from damage such as **misoprostol**

  4) Neutralizing gastric acid with nonabsorbable antacids

Drugs for Peptic ulcers and GERD

- Antimicrobials (For H. pylori)
- H_2-receptor antagonists
- Proton pump inhibitors
- Prostaglandins
- Antacids

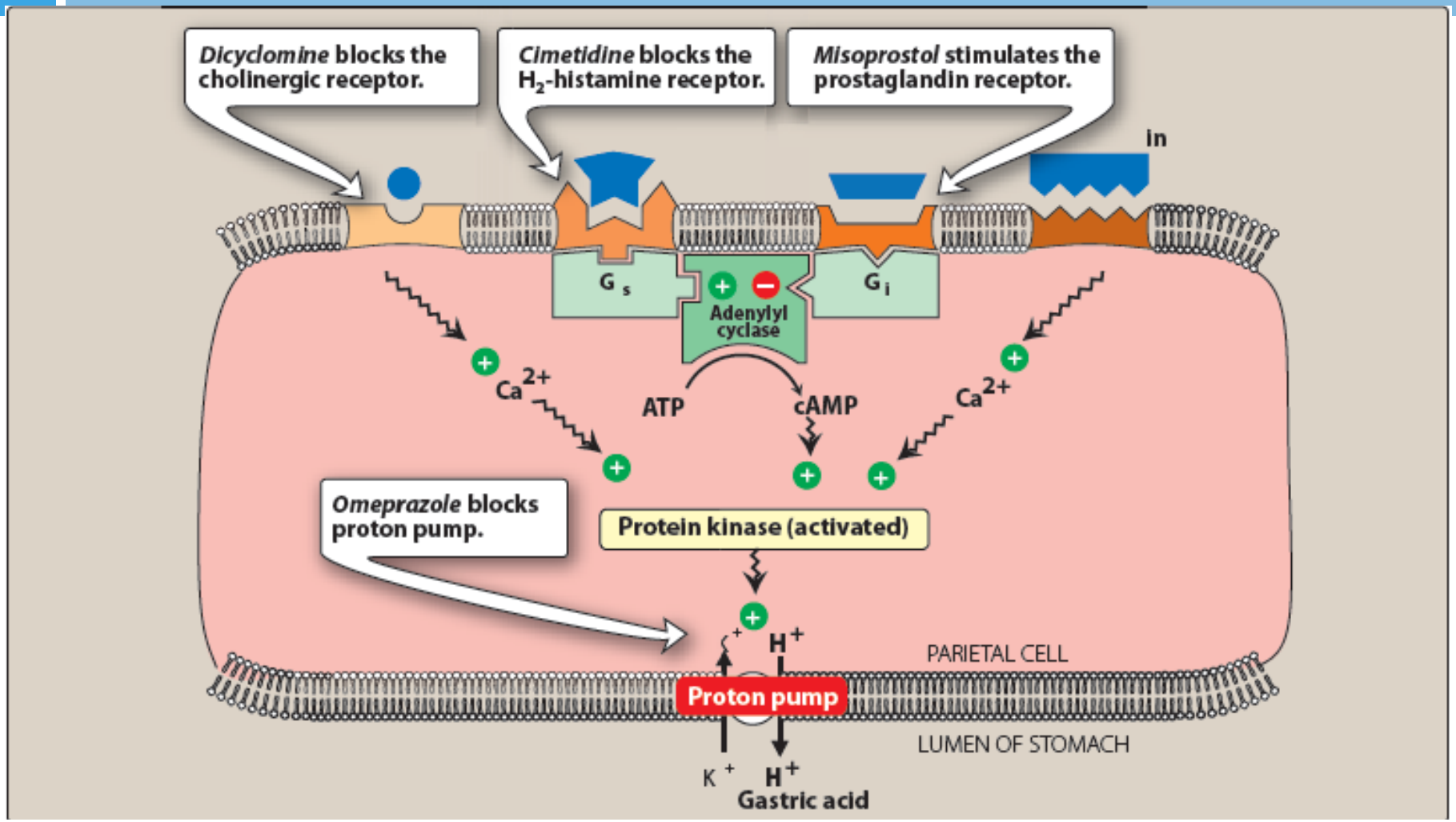
Drugs for Peptic ulcers

- Antimicrobial agents (For H. pylori)
  - Metronidazole
  - Amoxicillin
  - Clarithromycin
  - Tetracyclines
  - Bismuth compounds
- Proton pump inhibitors are also used in this condition

H_2-receptor antagonists

- Ranitidine
- Famotidine

- Block the binding of histamine to H_2 receptors inhibiting gastric acid secretion
- Therapeutic uses:
  - Peptic ulcer
  - GERD
- Their use is being replaced by proton pump inhibitors
- Adverse effects: Dizziness, diarrhea.


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

Proton pump inhibitors

- Omeprazole
- Esomeprazole
- Pantoprazole
- 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
- More effective than H2 antagonists in suppressing gastric acid production and healing peptic ulcers
- Therapeutic uses
  - Stress ulcer
  - Peptic ulcer
  - GERD
  - Erosive egophagitis
- Adverse effects: diarrhea, Nausea, GI disturbance

Prostaglandins

- Prostaglandin E inhibits secretion of HCl and stimulates secretion of mucus and bicarbonate (cytoprotective effect)
- **Misoprostol** is an analog of prostaglandin E1
- Adverse effects: Diarrhea, nausea
- Contraindicated during pregnancy

Antacids

- Aluminum hydroxide
- Magnesium hydroxide
- Calcium carbonate
- Weak bases that react with gastric acid and diminish gatric acidity
- Used for symptomatic relief of peptic ulcer and GERD

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

Antiemetic drugs

- Antiemetics represent a variety of classes with various efficacies

- Anticholinergic drugs like the muscarinic receptor antagonist scopolamine and H_1-receptor antagonists, such as dimenhydrinate, meclizine, and cyclizine are very useful in motion sickness

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 (serotonin) receptor blockers

- Ondansetron
- Important in treating emesis linked with chemotherapy, because of their longer duration of action
- Can be administered as a single dose prior to chemotherapy (intravenously or orally)
- Efficacious against all grades of emetogenic therapy
- Side Effects:
  - Headache
  - Electrocardiographic changes, such as a prolonged QT interval, can occur with dolasetron

Antiemetic drugs

- Haloperidol
- Act by blocking dopamine receptors
- Moderately effective antiemetics

Antiemetic drugs

Benzodiazepines

- Lorazepam
- Alprazolam
- 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

- 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

Constipation

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

Laxatives and Cathartics

- Treat or prevent constipation
- Prepare bowel for surgery or diagnostic procedures
- Promote emptying of large intestine
- Stimulants and herbal agents
  - Stimulate peristalsis
- Mineral oil
  - Lubricates fecal mass

Types of Laxatives

- Bulk-forming agents absorb water, adding size to fecal mass
- Stool softeners or surfactants cause more water and fat to be absorbed into stools
- Stimulants irritate bowel to increase peristalsis

Laxatives

- Psyllium mucilloid
- Mechanism of action: swells and increases size of fecal mass
- Used to promote passage of stool

Laxatives

- Saline or osmotic laxatives are not absorbed in intestine
  - Example Magnesium hydroxide
  - Pull water into fecal mass to create more watery stool
- Herbal agents are natural products available OTC
  - Most commonly used herbal laxative is senna
- Miscellaneous agents include mineral oil
  - Acts by lubricating stool and colon mucosa

Diarrhea

- Treatment depends on severity and etiology
- Opioids for severe diarrhea
  - Most effective
  - Slow peristalsis

Antidiarrheals, Opioids

- Diphenoxylate with atropine
- Mechanism of action: slows peristalsis
- Used for moderate to severe diarrhea
- Adverse effects: dizziness and drowsiness

Medications for Simple Diarrhea

- Loperamide
- Bismuth compounds
- Psyllium preparations
- Probiotic supplements