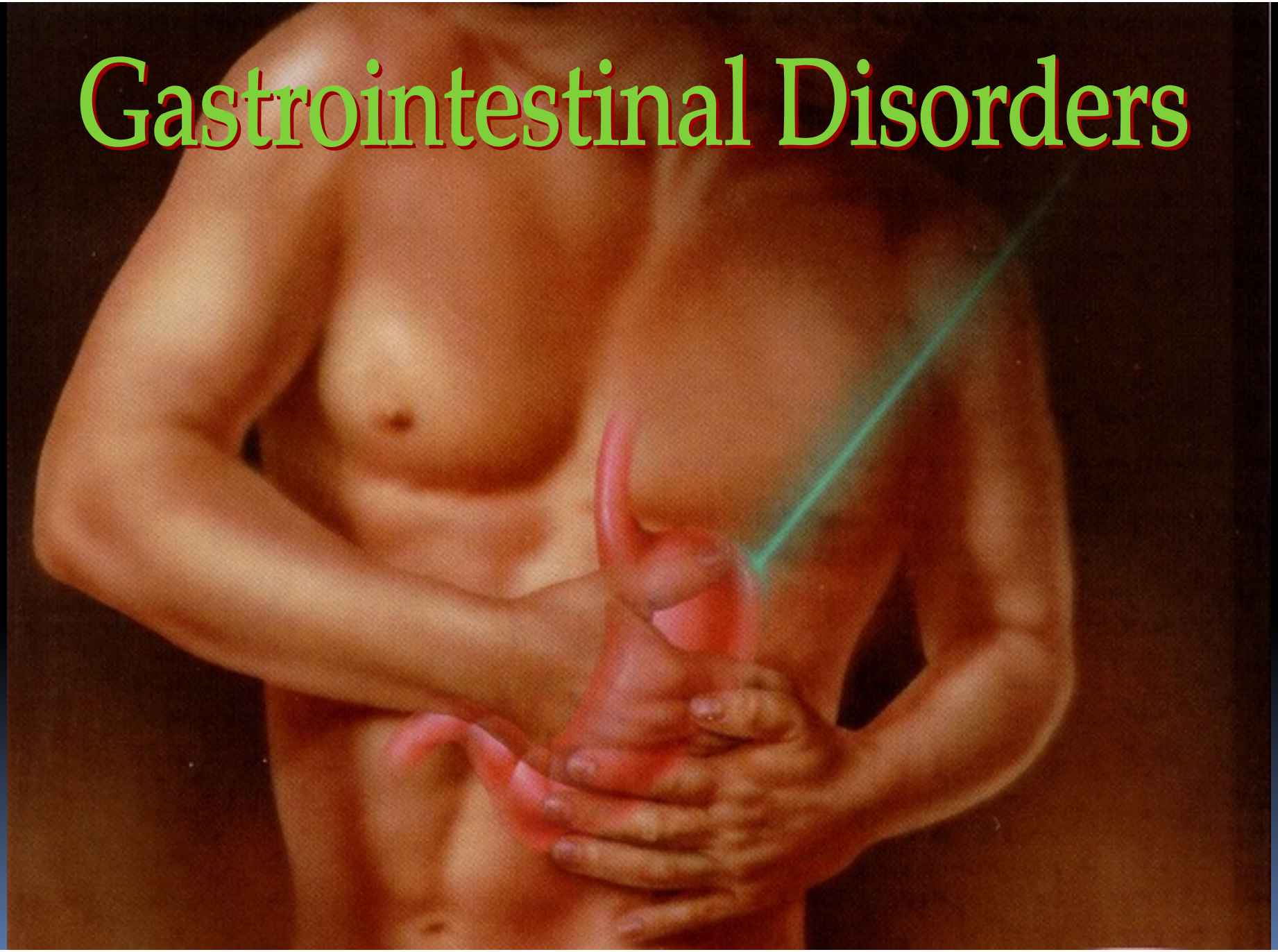
Gastrointestinal Disorders



Antacids: Maalox / Mylanta

MOA: Neutralize Gastric Acidity

Active Ingredients
(neutralizing agents)

(1) magnesium
(SE: osmotic diarrhea)

(2) aluminum
(SE: constipation)

* SE = Side Effect(s)

Antacids (cont.)

Milk of Magnesia (magnesium)

- magnesium → neutralizes hyperacidity
- magnesium → treats constipation

Amphojel (aluminum hydroxide)

- aluminum → neutralizes hyperacidity
- neutralizing agent → treats diarrhea

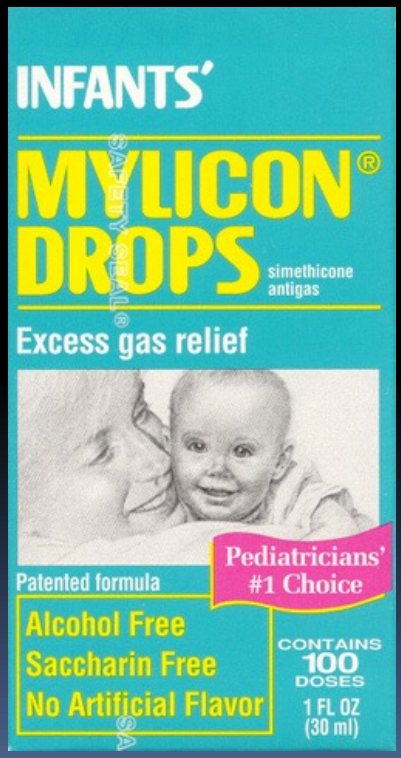
Antacids (Maalox, Mylanta)

- Onset: immediate (minutes)
- Duration: 30 minutes on an empty stomach, but 3 hours when taken within 1 hour of meals
- Alginic acid may be added to antacids → forms a viscous solution that floats on top of gastric contents → protects the esophageal mucosa from acid reflux
- Simethicone (surfactant) may be added to antacids → ”breaks up” gas bubbles → relieves gas
- Caution: small amounts of aluminum and magnesium are absorbed and can accumulate in renal insufficiency → toxicity
  - Magnesium: avoid in patients with CrCl < 30 ml/min
  - Aluminum: avoid in patients with renal failure (CrCl < 15 ml/min)

Antacids (cont.)

Simethicone (Mylicon)

Simethicone (surfactant) → decreases surface tension of gas bubbles → breaks up gas bubbles → relieves gas



Antacids (cont.)

Calicum Carbonate (TUMS)

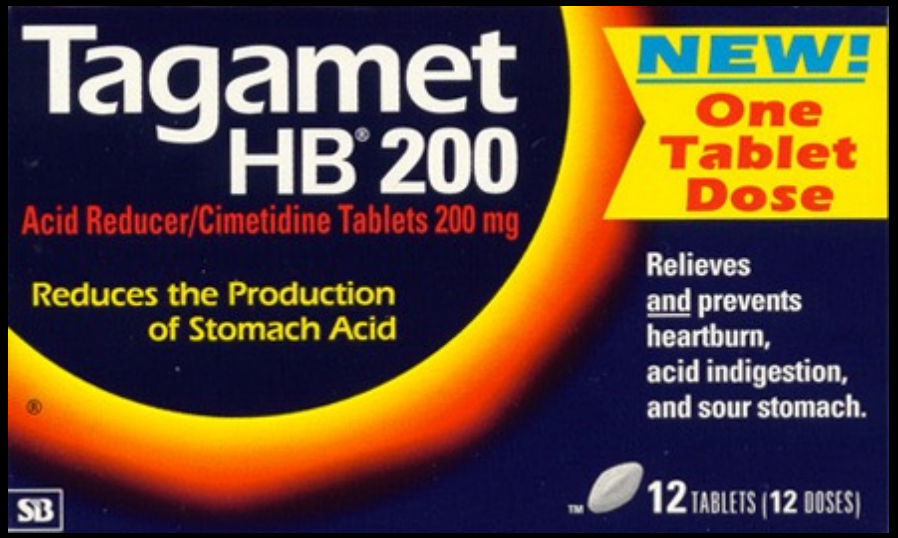
- moderate neutralizing capacity, compared to Maalox/Mylanta
- $CaCO_3$ → gas formation
  → burping / flatulence
- high-doses (4-8 grams/day)
  → hypercalcemia / metabolic alkalosis
  "milk-alkali syndrome" → kidney failure

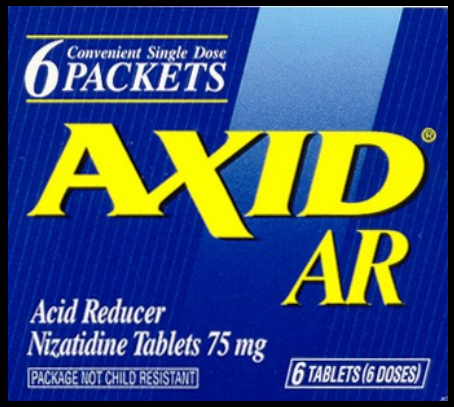
Antacids (cont.)

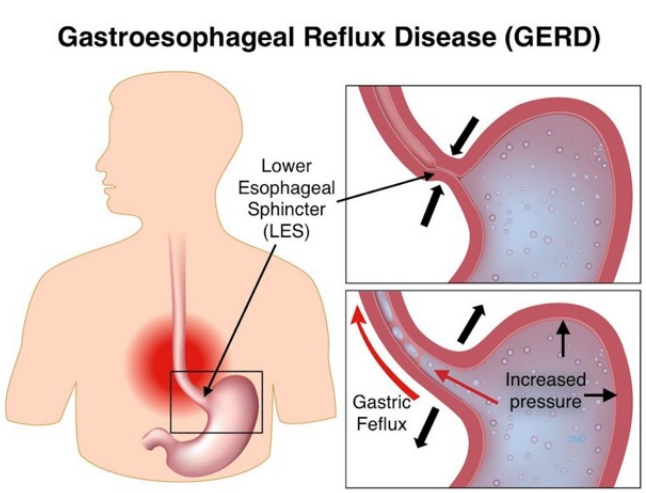
Sodium Bicarbonate
(Alka-Seltzer)

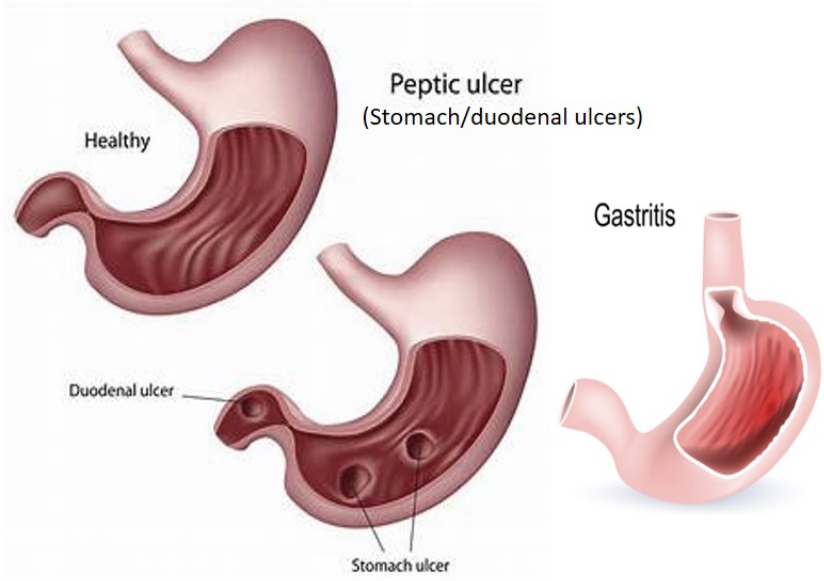
High sodium content (567 mg per tablet) → Na^+/H_2O retention → exacerbates hypertension, heart failure, chronic kidney disease

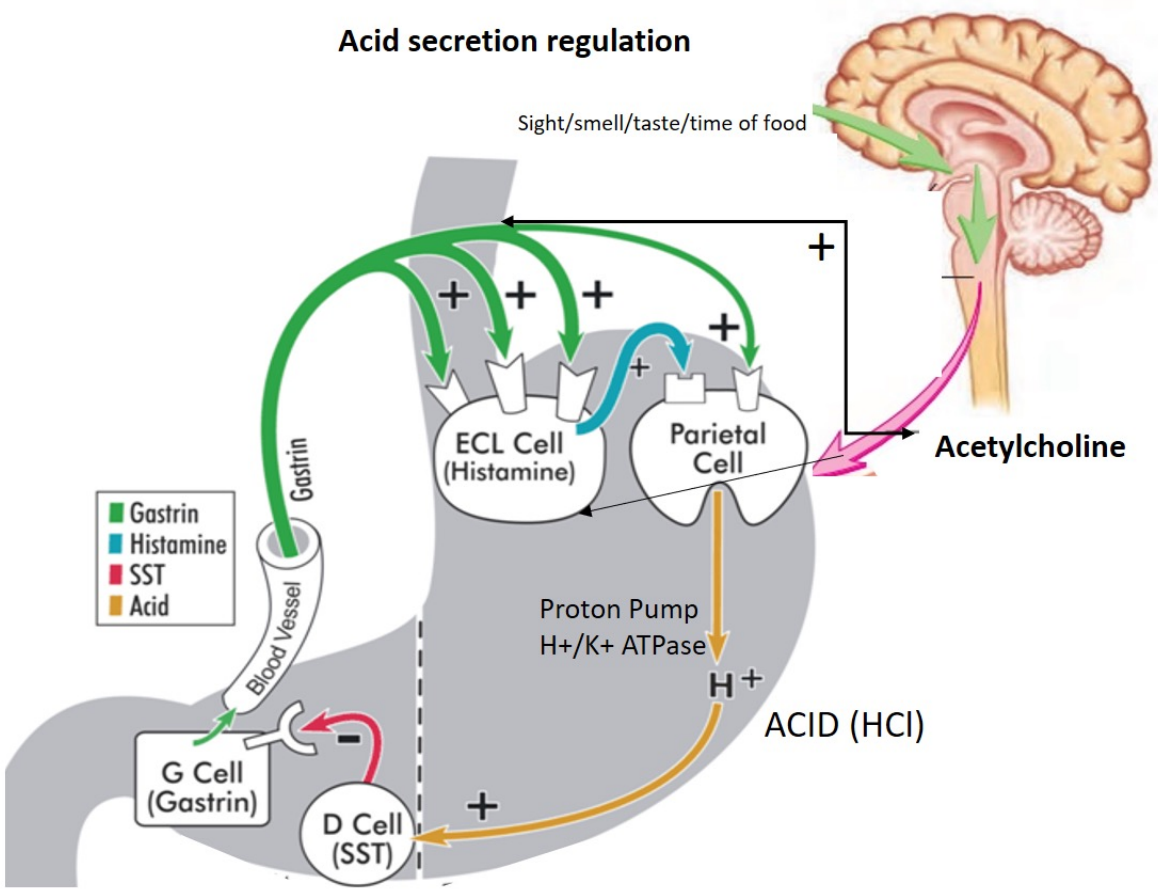
H_2 Receptor Antagonists (H_2RAs)





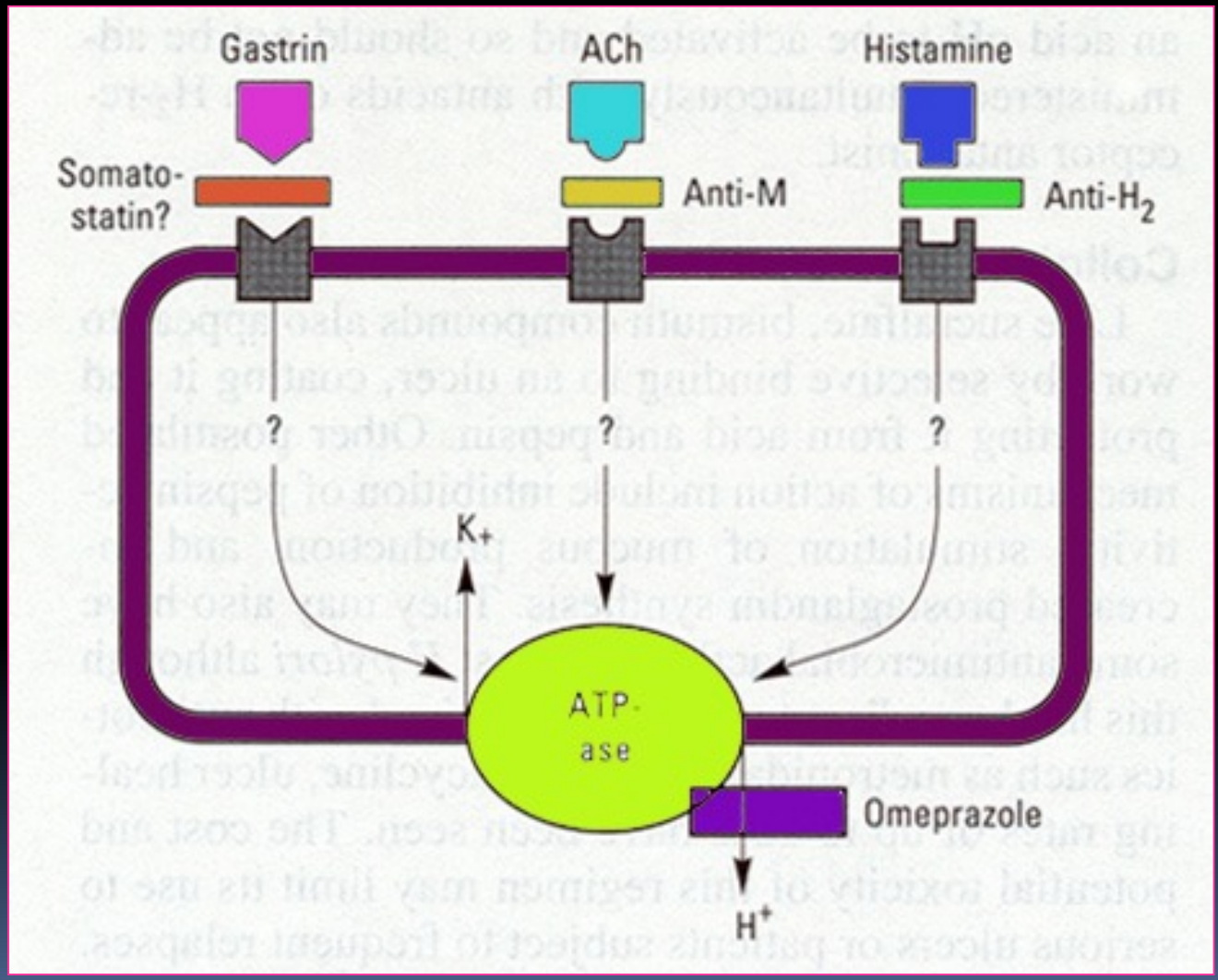






G-cells (antrum) → produce gastrin. D-cells protect stomach from overproduction of gastric acid by releasing somatostatin (SST) → inhibits production of gastrin. ACh and gastrin → increase release of histamine-2 from enterochromaffin-like (ECL) cells. Gastrin, Histamine-2, ACh (acetylcholine) → bind to receptors on parietal cells → gastric acid secretion

H_2 Receptor Antagonists (H_2RAs)



Histamine-2 Receptor Antagonists (H_2RA)

- H_2RAs are remarkably safe
- Oral absorption is rapid → peak serum drug concentration: 1-3 hours
- Side Effects (SEs)
  - GI Discomfort: diarrhea, constipation
  - CNS Effects: headache, dizziness, drowsiness, lethargy
  - Dermatologic Effects: rash
  - Hematologic Effect: thrombocytopenia (1%) is reversible upon discontinuation of H_2RA
- Cimetidine (Tagamet) has the greatest potential for drug-drug interactions → inhibits hepatic cytochrome P-450 isoenzymes → inhibits metabolism of theophylline, phenytoin, warfarin → drug toxicities

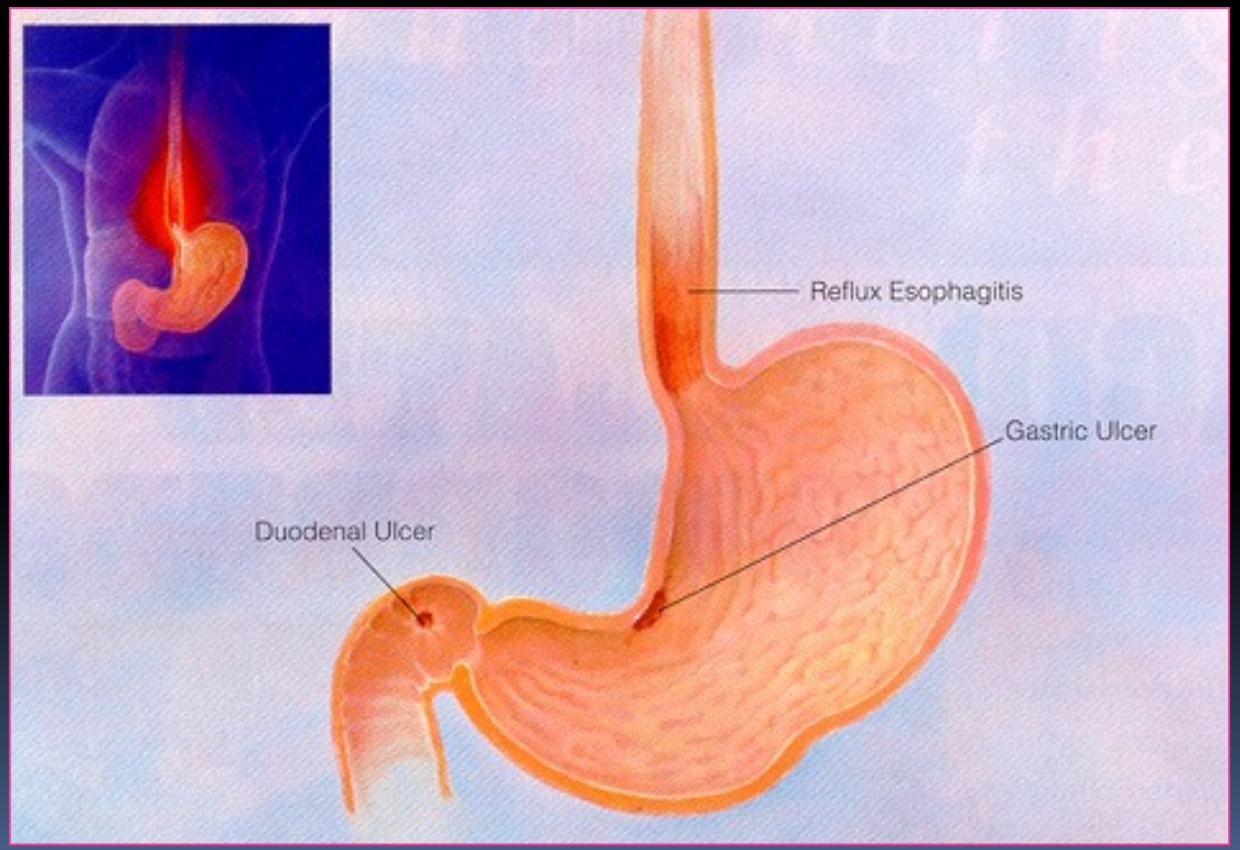
Histamine-2 Receptor Antagonists (H_2RA)

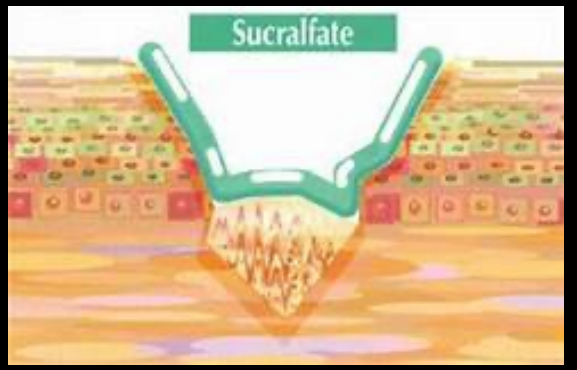
- Tachyphylaxis or tolerance may develop after 2-6 weeks of H_2RA therapy due to upregulation of H_2 receptor sites.
- Development of tachyphylaxis limits the use of H_2RAs in management of GERD and other conditions requiring long-term therapy.

Sucralfate (Carafate)

(cytoprotective agent)

MOA: binds to gastric ulcer forming a protective barrier





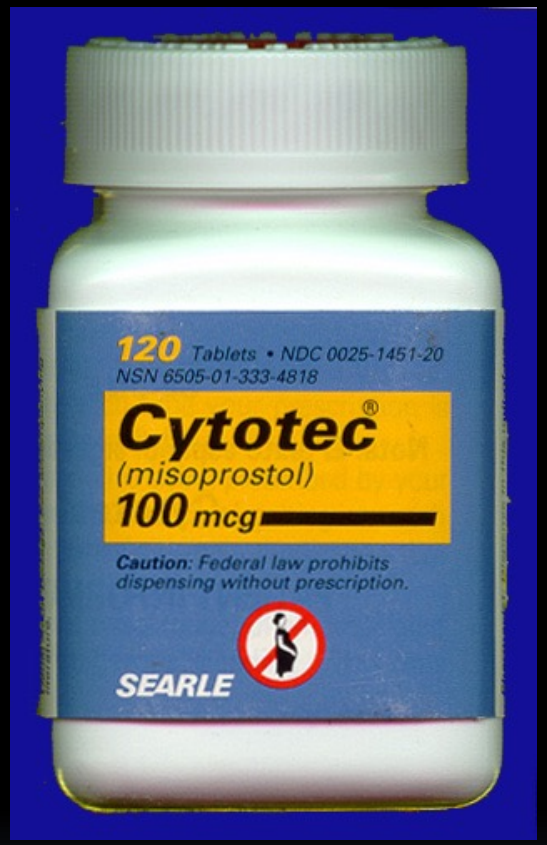
Sucralfate (Carafate)

- Sucralfate may also have protective affect by stimulating release of mucosal prostaglandins (PGE)

- SE: constipation (1-3%) due to aluminum content
- Caution: aluminum content may accumulate in patients with renal insufficiency → "aluminum encephalopathy" (i.e., dementia), and anemia

- Aluminum binds dietary phosphate (GI tract) → hypophosphatemia
- Sucralfate tablets are large and may be difficult for geriatrics to swallow → use liquid formulation

Misoprostol (Cytotec)



MOA: synthetic prostaglandin (PG) analog

- stimulates the production of mucus and bicarbonate ("mucoprotective shield")
- improves mucosal blood flow
- reduces mucosal cell turnover
- mildly inhibits gastric acid secretion (less than H_2RAs)

SE: diarrhea (up to 30%), abdominal cramping

- take with food and reduce daily dose to minimize incidence of diarrhea

Caution: misoprostol is contraindicated in pregnancy.

- use in women in childbearing years requires negative serum pregnancy test and adequate contraception

Proton Pump Inhibitors (PPIs)

MOA:

- PPIs irreversibly bind to the proton pump and inhibit gastric acid secretion
- PPIs are the most potent inhibitors of gastric acid secretion (superior to H_2RAs)
- PPIs are indicated for patients who experienced tx failure with maximum doses of H_2RA
- Dosage reduction of PPIs is not required in renal insufficiency

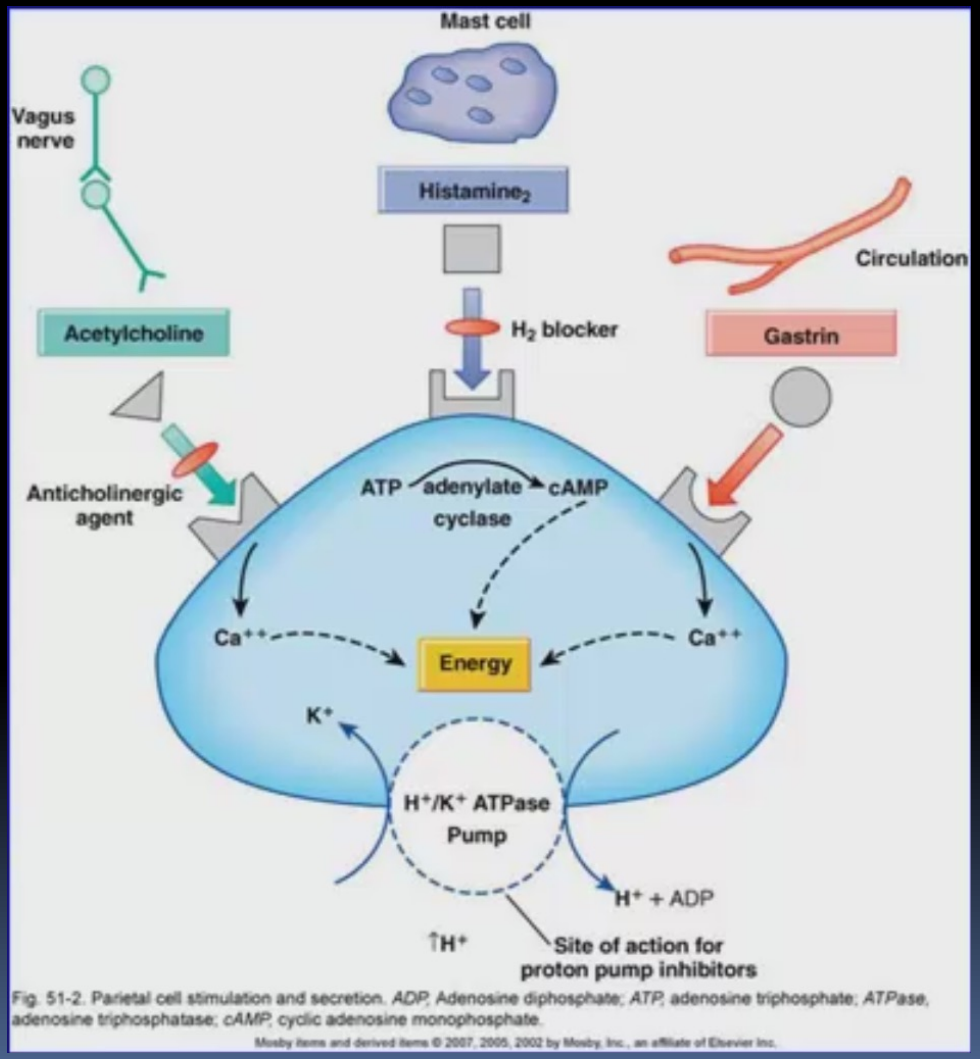


Fig. 51-2. Parietal cell stimulation and secretion. *ADP*, Adenosine diphosphate; *ATP*, adenosine triphosphate; *ATPase*, adenosine triphosphatase; *cAMP*, cyclic adenosine monophosphate.

Proton Pump Inhibitors (PPIs)

Table 1. Availability, Formulations, and Dosages for Proton Pump Inhibitors in Adults

Drug	*Availability*	*Route of administration*	*Starting dosage**	*Cost of generic (brand)†*
Dexlansoprazole (Dexilant)	Prescription	Oral	30 mg per day	NA ($153)
Esomeprazole (Nexium)	Prescription	Oral or IV	Oral: 20 mg per day IV: 20 mg per day for 10 days	Oral: NA ($201) IV: NA ($381)‡
Lansoprazole (Prevacid)	Prescription	Oral	15 mg per day	$106 ($196)
Lansoprazole (Prevacid 24H)	Over-the-counter	Oral	15 mg per day for 14 days§	NA ($13)
Omeprazole (Prilosec, Zegerid)	Prescription	Oral	20 mg per day	$33 ($196)
Omeprazole (Prilosec OTC, Zegerid OTC)	Over-the-counter	Oral	20.6 mg (Prilosec OTC) or 20 mg (Zegerid OTC) per day for 14 days§	$7 ($13)
Pantoprazole (Protonix)	Prescription	Oral or IV	Oral: 40 mg per day IV: 40 mg per day for 7 to 10 days	Oral: $16 ($186) IV: $42 ($42)‡
Rabeprazole (Aciphex)	Prescription	Oral	20 mg per day	NA ($250)

IV = intravenous; NA = not available.

**—Number of weeks of recommended treatment varies.*

†—*Estimated retail price of one month's treatment (unless otherwise specified) based on information obtained at http://www.drugstore.com (accessed January 31, 2012) or at a national retail chain.*

‡—*Estimated wholesale price based on information obtained at Red Book online. Micromedex 2.0. Micromedex Healthcare Series [Internet database]. Greenwood Village, Colo.: Thomson Reuters (accessed January 31, 2012).*

§—*Patients should not take more often than 14 days per month every four months.*

Proton Pump Inhibitors (PPIs)

Short-Term SEs of PPIs (infrequent and comparable to H_2RAs)

- GI discomfort: nausea, diarrhea, abdominal pain
- CNS: headache, dizziness

Long-Term SEs of PPIs (usually with high doses)

- Atrophic gastritis has been "rarely" associated with patients on long-term therapy PPIs for *Helicobacter pylori*.
- Risk of *C. difficile* and other enteric infections has been observed due to ability of pathogens to survive in a less acidic GI environment; however the overall risk is low.
- Vit B_{12} deficiency, since gastric acid is required to extract Vit B_{12} from dietary sources. Monitor Vit B12 levels in PPI patients.

Long-Term SEs of PPIs

- Hypomagnesemia may occur with long-term use of PPIs due to reduced intestinal absorption. Monitoring serum magnesium levels is recommended in patients on long-term PPI therapy.

- Hypocalcemia and increase risk of fractures is associated with reduced calcium absorption due to hypochlorhydria. Since calcium citrate does not require acid for absorption, it is the recommended calcium supplement in patients on long-term PPI therapy.

- Iron malabsorption secondary to long-term gastric acid suppression with PPIs, however this does not appear to be of clinical significance unless a patient requires oral iron supplementation. Higher doses and longer duration of iron supplementation are recommended in these patients.


PHARMACY
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