Drugs For Peptic Ulcer

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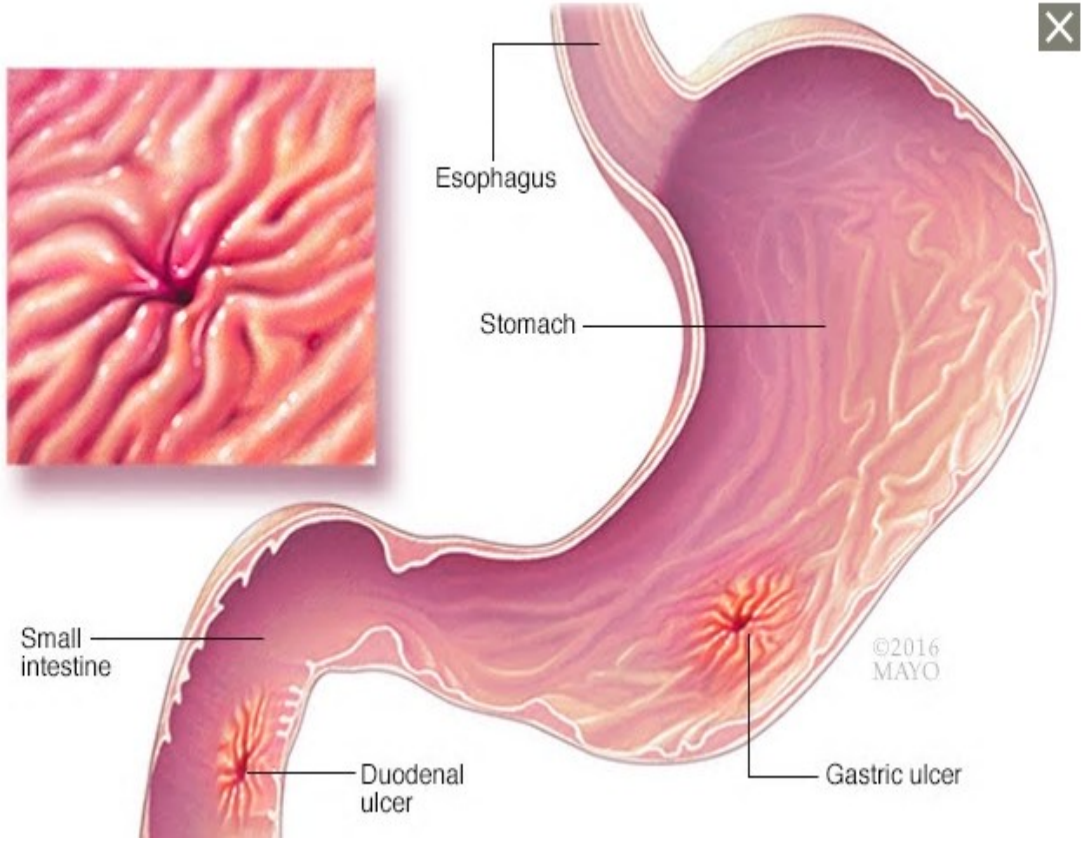
Peptic Ulcer Disease (PUD)

- **Peptic ulcers** commonly involve stomach (**gastric) ulcer or duodenum (duodenal) ulcer**
- The most common symptom is **burning stomach pain**
- Complications is **bleeding**
- **Relapse is common when treatment is stopped**



Major Causative Factors

- Long-term use of aspirin & NSAIDs (elderly)
- Infection with gram negative Helicobacter pylori
- Increased hydrochloric acid (HCL) secretion
- Steroids, smoking, alcohol, stress

Treatment Approach

- Eradicate H. pylori infection
- **Reduce gastric acid secretion**
  - H2-receptor antagonists
  - Proton pump inhibitors (PPIs)
- Agents that protect gastric mucosa from damage such as **misoprostol and sucralfate**
- Patients unable to tolerate above therapies, neutralized gastric acid with **antacids**

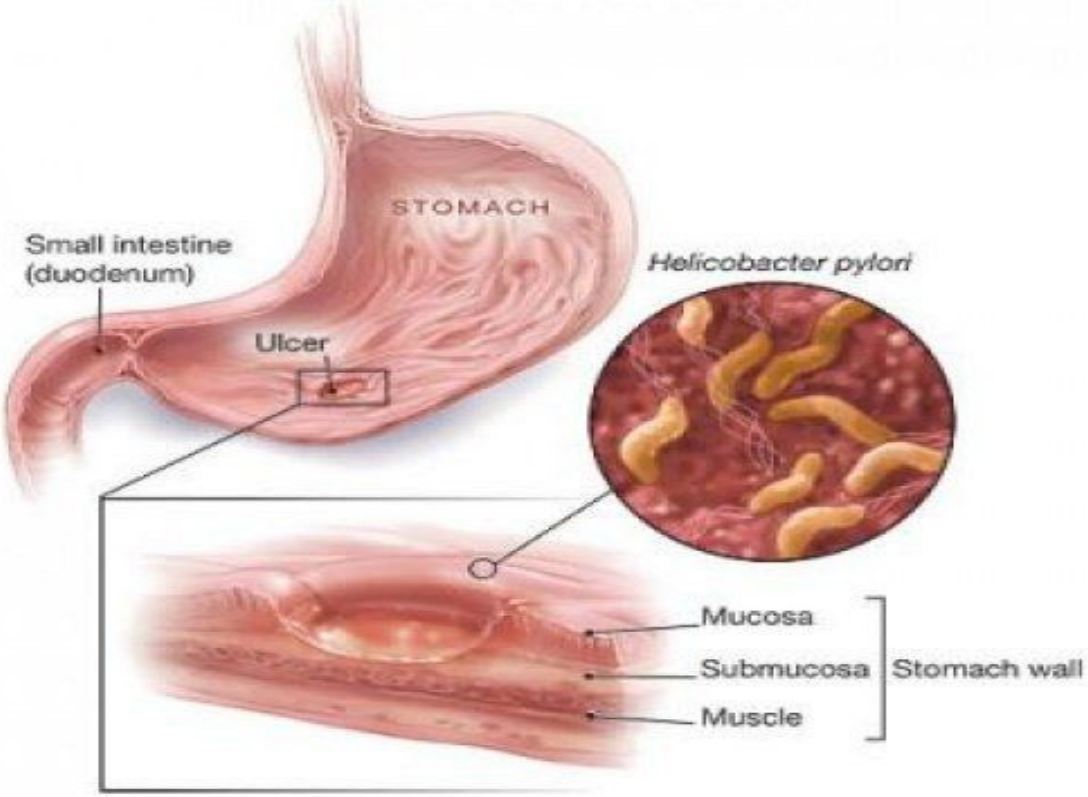
- **The goals of treatment for peptic ulcer:**
  - Relieve pain
  - Heal ulcer
  - Prevent recurrence and complications

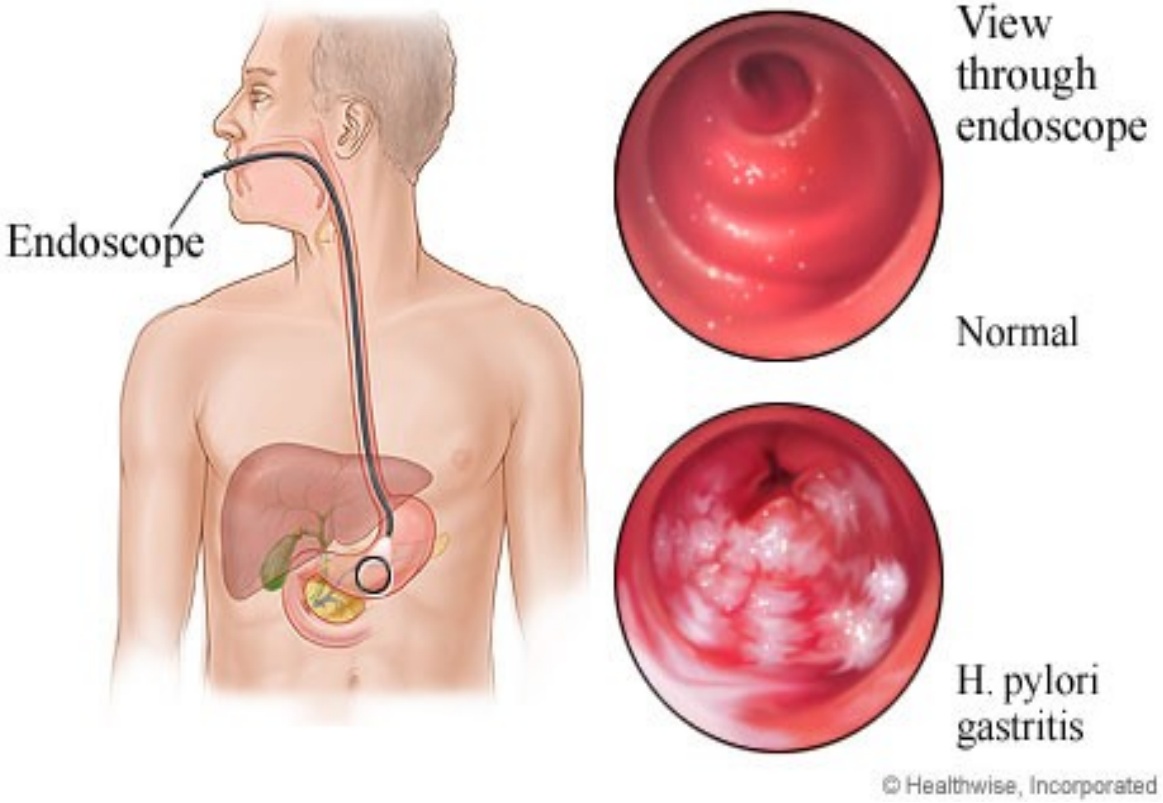
Classes of Drugs to Treat PUD

- **Antimicrobial agents:** Amoxicillin, clarithromycin, metronidazole, tetracycline
- **H2 receptor blockers:** cimetidine, famotidine, ranitidine
- **Proton pump inhibitors (PPIs):** esomeprazole, lansoprazole, omeprazole, pantoprazole
- **Prostaglandins:** misoprostol
- **Antacids:** Aluminum hydroxide, magnesium hydroxide, calcium carbonate
- **Mucosal protective agents:** Bismuth subsalicylate, sucralfate

Antimicrobial Agents

- Useful for patients with **PU infected with H. pylori**
- **Diagnosis of H.pylori:** Endscopic biopsy of gastric mucosa, serological tests, urea breath tests
- **Eradication of H.pylori** results in **rapid healing of active peptic ulcer, low recurrence rate and reduce risk of bleeding**
- Successful eradication **80-90%**


STOMACH
Small intestine
(duodenum)
Ulcer
Helicobacter pylori
Mucosa
Submucosa
Muscle
Stomach wall


Endoscope
View through endoscope
Normal
H. pylori gastritis
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- **Combination therapy:**
- **Triple therapy:** PPI, clarithromycin, plus either amoxicillin or metronidazole
- **Quadrable therapy:** PPI, metronidazole, tetracycline, bismuth subsalicylate
- Duration: for **2-week course**
- **GERD (Gastroesophageal reflux disease) (heartburn sensation) is not associated with H.pylori infection** and does not response to treatment with antibiotics

H2-Recptor Antagonists

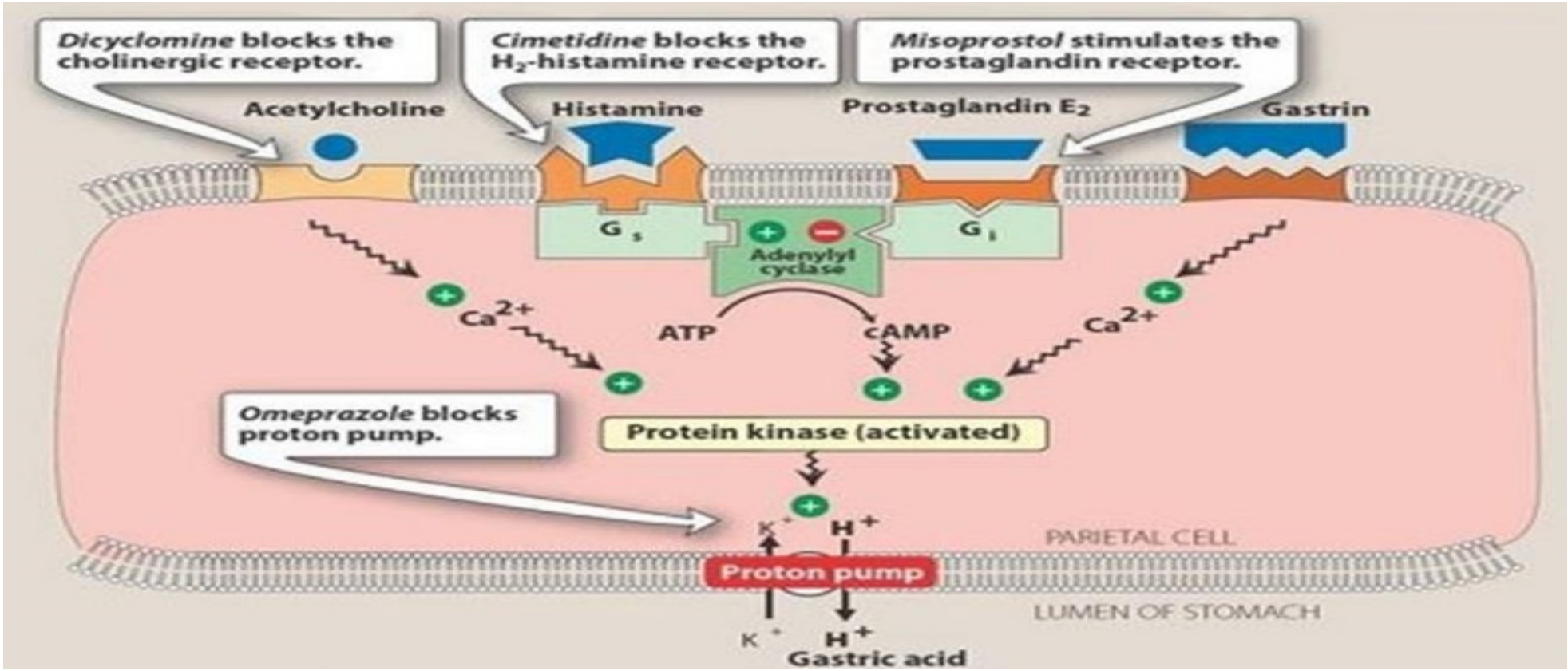
- **Cimetidine, famotidine (famodar), ranitidine (zantac)**
- **Block actions of histamine** at all **H2 receptors**
- **Completely inhibit gastric acid secretion** induced by histamine or gastrin
- Uses of these agents has **decreased with the use of PPIs**
- **Therapeutic uses:**
- Healing of Peptic ulcers
- Prevention & treatment of GERD (50% no benefit, use PPIs)

- All H2 antagonists can be given **orally or IV**
- **Cimetidine: short half-life**, **inhibits CYP P450** (slow metabolism of warfarin, diazepam, phenytoin, carbamazepine)
- **Ranitidine**: **longer half-life**, **more potent than cimetidine**
- **Famotidine:** similar to ranitidine, 20-50 more potent than cimetidine
- They need **45 mins to relieve symptoms**
- Dose should be reduced in **hepatic and renal failure**

- **Side effects:**
- Headache, dizziness, diarrhea, muscular pain
- **CNS:** confusion, hallucinations (elderly, after IV administration)
- **Cimetidine: Endocrine (antiandrogen)** effects (gynecomastia, galactorrhea, reduced sperm count, impotence) **(limited use)**

Proton pump inhibitors (PPIs)

- **Omeprazole, esomeprazole (Nexium), lansoprazole, pantoprazole**
- Bind to **H/K ATPase (proton mump)** of parietal cell, suppressing secretion of hydrogen ions into gastric lumen
- **PPIs superior than H2 antagonists** in **suppression of acid production and peptic ulcer healing**


Dicyclomine blocks the cholinergic receptor.
Cimetidine blocks the H_2-histamine receptor.
Misoprostol stimulates the prostaglandin receptor.
Acetylcholine
Histamine
Prostaglandin E_2
Gastrin
G_s
G_i
Adenylyl cyclase
Ca^{2+}
ATP
cAMP
Ca^{2+}
Omeprazole blocks proton pump.
Protein kinase (activated)
K^+
H^+
PARIETAL CELL
Proton pump
LUMEN OF STOMACH
K^+
H^+
Gastric acid

Therapeutic Uses

- Eradication of H. pylori
- GERD
- Prevention & treatment of NSAIDs-induced ulcer
- Reduce risk of bleeding from NSAIDs-induced ulcer
- Erosive esophagitis
- Active duodenal ulcer
- Hypersecretion conditions (Zollinger-Ellison syndrome: gastrin – producing tumor causes hypersecretion of HCL)

- Should be taken **30 mins before meal**
- Acid suppression takes **1-2 hrs**
- **Given orally** (sustained release formulation)
- **Intravenous injections**
- **Omeprazole** inhibits metabolism of warfarin, phenytoin, diazepam, cyclosporine

- **Adverse effects:**
- Flatulence, diarrhea, Clostridium difficile colitis
- Dry mouth, sleep disturbances, taste disturbances
- Prolonged therapy: low B12

Prostaglandins

- **Prostaglandins E2**, produced by gastric mucosa, **inhibits secretion of HCL**, **stimulates secretion of mucus and bicarbonate** (cytoprotective effect)
- **Misoprostol (Cytotec)** is analog of prostaglandin E1
- **Uses:** prevention of NSAID-induced ulcers (elderly, patients with ulcer complications)
- **Less effective than H2 antagonists and PPIs** for **acute treatment of peptic ulcer**

- **Adverse effects:** Diarrhea, nausea, abdominal pain
- **Misoprostol** produces uterine contractions, **contraindicated during pregnancy**

Antacids

- **Aluminum hydroxide (Maalox) , magnesium hydroxide, calcium carbonate**
- **React with gastric acid to form water and salt**, **diminish gastric acidity**
- **Uses:** They are used as **last-line therapy for GERD, duodenal ulcer**
- **Adverse effects:**
- Aluminum hydroxide: constipation
- Magnesium hydroxide: diarrhea

Mucosal Protective Agents

- **Bismuth subsalicylate, sucralfate**
- **Cytoprotective compounds**, **enhances mucosal protection**, prevent mucosal injury, reduce inflammation, healing ulcers
- **Sucralfate:**
- Complex of **aluminum hydroxide and sulfate sucrose**
- Form gel with epithelia cells, creates physical barrier that impairs diffusion of HCL
- Stimulate prostaglandin release

- **Heals duodenal ulcers**, long-term therapy to prevent recurrence
- **Should not be administered with H2 antagonists or antacids** (requires acidic PH for activation)