PUD | Peptic Ulcer Disease

Causes

- **Typical:** *Helicobacter pylori*, NSAIDs, critical illness (SRMD)
- **Atypical:** hypersecretion, viral infections, vascular insufficiency, radiation/chemo, genetic, idiopathic
- **Etiology:** disruption of normal mucosal defense mechanisms, hypersecretion of acid
- **Risk factors:** smoking, psychological stress, diet, chronic diseases

Complications

Upper GI bleed, perforation, obstruction (scarring, edema) Mortality: gastric ulcers > duodenal ulcers

Clinical presentation

- **Pain:** epigastric abdominal pain, nocturnal pain, severity in clusters → food helps with pain
- **GI complaints:** heartburn, belching, bloating, nausea, vomiting, anorexia

Treatment

- **Proton Pump Inhibitors**
  - Omeprazole, esomeprazole, lansoprazole, rabeprazole, pantoprazle, dexlansoprazole
  - MOA: bind to H+/K+ ATPase pumps → inhibit active secretion of gastric acid
  - Admin: take 30-60 mins before meals; need to take continuously because effects ↑ over 3-4 days; enteric coated or buffered for pH sensitivity
  - Dosage forms
  - SE: fairly well tolerated overall, headache, nausea, abdominal pain
  - Contraindications: sodium bicarb formulatios
  - Interactions: pH dependent drugs (e.g. calcium, ketoconazole), clopidogrel
- **Histamine$_2$ Receptor Antagonists**
  - Cimetidine, famotidine, nizatidine, ranitidine
  - MOA: blocks histamine at H2 receptors on gastric parietal cells → inhibits gastric acid secretion
  - May develop tolerance over time, not recommended for maintenance
  - SE: thrombocytopenia (reversible)
  - Contraindications: moderate to severe renal failure may require dose reductions
  - Interactions: cigarette smokers may require higher doses, CYP450 (cimetidine), pH dependent drugs
- **Sucralfate** (Carafate)
  - MOA: forms protective coating on gastric lining
  - Admin: take on empty stomach, many doses per day needed (↓compliance), taken before meals
  - SE: constipation, seizures (especially with Al antacids)
  - Interactions: oral fluoroquinolones
- **Misoprostol** (Cytotec)
  - Prostaglandin E1 analog
  - MOA: replaces protective prostaglandins
  - Efficacy: comparable to H2RA or sucralfate
  - SE: diarrhea
  - Contraindications: pregnancy (also avoid in women who could potentially get pregnant)
- **Bismuth subsalicylate**
  - MOA: antibacterial effect, local gastroprotective effect, stimulates prostaglandins
  - SE: black stool, black hairy tongue
  - Contraindications: elderly, renal failure, salicylate sensitivity
  - Interactions: salicylates
- **Antacids**
  - MOA: neturalize gastric acid, inactivate pepsin, bind bile salts
  - Interactions: interferes with absorption of pH dependent drugs (e.g. enteric coating), need to separate by 2 hours
  - Aluminum antacids: interferes with phos absorption (e.g. sucralfate), may cause constipation
  - Magnesium antacids: avoid use in CrCl <30mL/min, may cause diarrhea
  - Calcium antacids: may cause hypercalcemia and milk-alkali syndrome

H. pylori induced ulcers

- **H. pylori:** pH sensitive, gram negative, microaerophilic, spiral shaped, lives between mucus layer & surface epithelial cells
- **Consequences** of H. pylori infection: chronic gastritis, PUD, gastric cancer, MALT lymphoma
  - H. pylori causes mucosal injury through direct mucosal damage, inflammatory response, hypergastrinemia
  - H. pylori enhances carcinogenic conversion of gastric epithelial cells
- **Transmission:** fecal-oral, oral-oral, or gastro-oral
- **Testing:** stool antigen, serologic tests, urea breath test, mucosal biopsy, empiric treatment
- **Treatment regimens**

3 drug regimen	PPI + clarithromycin 500mg bid + amoxicillin 1g bid
	PPI + clarithromycin 500mg bid + metronidazole 500mg bid
4 drug regimen	PPI + bismuth subsalicylate 525mg qid + metronidazole 250-500mg qid + tetracycline 500mg qid
	PPI + bismuth subsalicylate 525mg qid + metronidazole 250-500mg qid + clarithromycin 250-500mg qid
Sequential therapy	PPI days 1-10, amoxicillin 1g bid days 1-5, metronidazole 250-500mg bid days 6-10, clarithromycin 250-500mg bid days 6-10

PPIs can be qd or bid

  - **1st line:** PPI-based 3 drug regimen for 10-14 days (PrevPac easy to use)
    - Do not substitute antibiotics
  - **2nd line:** PPI-based 3 drug regimen with different antibiotic –or– 4 drug regimen
  - **SE:** taste disturbances, N/V/D, abdominal pain, colitis, candidiasis

NSAID-induced ulcers

- **Risk factors**
  - **Established:** >60 y/o, previous ulcers or complications, corticosteroid, NSAID, ASA, anticoagulant or coagulopathy, antiplatelet drug, bisphosphonates, SSRIs, chronic illness
  - **Possible:** NSAID dyspepsia, *H. pylori*, rheumatoid arthritis, alcohol
  - **Questionable:** smoking
- **Nonselective NSAIDs:** indomethacin, prioxicam, ibuprofen, naproxen, sulindac, ketoprofen, ketorolac, flurbiprofen
- **Partially selective NSAIDs:** etodolac, nabumetone, meloxicam, celecoxib, diclofenac
- **Selective COX-2 inhibitors:** rofecoxib, valdecoxib
- **Salicylates:** aspirin, salsalate, trisalicylate
- **Treatment:** R/O H. pylori infection, stop NSAID, start PPI, H_2RA, or sucralfate
  - If cannot stop NSAID: start PPI, misoprostol, switch to selective COX2 inhibitor

Zollinger-Ellison's Syndrome

- **Acid hypersecretion** with recurrent peptic ulcers due to gastrin-producing tumor
  - 65% of gastrin-producing tumors are malignant
- **Clinical presentation:** multiple ulcers, recurrent/refractory PUD, esophagitis & ulcer complications, diarrhea, steatorrhea, Vit B_{12} malabsorption →PPIs can mask clinical presentation
- **Diagnosis:** serum gastrin >1000 pg/mL, BAO > 15 mEq/hr if intact stomach (>5 mEq/hr if previous gastric surgery), pH<2
- **Treatment**
  - Need to identify and remove tumor
  - Goal: BAO 1-10mEq/hr an hour before PPI dose
  - **PPIs** = DOC
  - **Octreotide:** (–)gastric acid secretion, (–)gastrin release, long-acting repeatable octreotide stabilizes tumor growth
  - Metastatic gastrinoma: surgical resection, chemo