NR 565 Exam Final Study Guide

- **Antacids**: weak bases that react with hydrochloric acid to form salt & water.
  - Used in the treatment of Hyperacidity, GERD, PUD, hyperphosphatemia, and calcium deficiency
  - Contain combinations of
    - metallic cation (aluminum, calcium, magnesium, and sodium)
    - and basic anion (hydroxide, bicarbonate, carbonate, citrate, and trisilicate)
- **Pharmacodynamics, Pharmacokinetics, Pharmacotherapeutics**
  - Neutralize Gastric Acidity (causes ^pH of the stomach and duodenal bulb)
  - Inhibit proteolytic activity of pepsin
  - Increase lower esophageal sphincter tone
  - Acid-neutralizing capacity ANC varies between products expressed in mEqs
  - If ingested in a fasting state, antacids reduce acidity for approximately 20 to 40 minutes
  - If taken 1 hr after a meal, acidity is reduced for 2 to 3 hrs
  - A second dose taken after a meal maintains reduced acidity for more than 4 hrs after the meal
  - The action of antacids occurs locally in the GI tract with minimal absorption, minimal metabolism
  - ALL antacids are contraindicated in the presence of severe abdominal pain of unknown cause, especially if accompanied by fever

-HIGH SODIUM content: pts w/ HTN, CHF, marked renal failure, or on low-sodium diets need to use low sodium preparation

-Concurrent administration with enteric-coated drugs, destroys the coating= alters absorption, ^ the risk for adverse effects

-Administrations should be separated by at least 2 hours to decrease drug/drug interactions

1. **Calcium based antacids**: TUMS, Caltrate, Calcarb
   - Prescribed to treat calcium deficient states, i.e. chronic renal failure, post-menopause, and osteoporosis
   - Used to bind phosphates in CRF
   - Require Vitamin D for absorption from the GI tract
   - Excreted mainly in feces, 20% in urine
   - **ADR:** Contraindicated in the presence of hypercalcemia and renal calculi
   - Can cause constipation- increase bulk, fluids and mobility, stool softener
   - Administered 30min- 1hr on empty stomach or 3hr after meals
   - Should not be administered with food containing large amounts of oxalic acid (spinach, rhubarb), or phytic acid (bran, cereals), they decrease the absorption of calcium
   - Taking w/ foods containing phosphorus (milk, dairy) can lead to milk-alkali syndrome (N/V, confusion, headache).
   - Taking with acidic fruit juice improve absorption
2. **Aluminum based:** AlternaGEL, Amphojel, Mylanta
   - Inhibit smooth muscle contraction and slow gastric emptying
   - Used to bind phosphates in CRF
   - Not absorbable with routine use
   - Aluminum concentrated in the CNS
   - Bind with phosphate and excreted in feces
   - Prolonged use in patients with renal failure may result in dialysis osteomalacia
     - Aluminum deposits in bone and osteomalacia occurs
   - Elevated aluminum tissue levels contribute to the development of dialysis encephalopathy
   - Used to treat hyperphosphatemia in pts w/ renal failure & phosphate renal stone prevention
   - Can cause constipation- increase bulk, fluids and mobility, stool softener

Aluminum is not easily removed by dialysis b/c it is bound to albumin & transferrin = do not cross dialysis membrane

3. **Magnesium based:** Milk of mag, Maalox, Mylanta
    - Can be used to treat magnesium deficiencies from malnutrition, alcoholism, or mag-depleting drugs
    - Contraindicated in patients with renal failure & used with caution in pts with renal insufficiency
    - Not absorbable with routine use
    - Excreted in the urine
    - Contraindicated in patients with renal failure, use with caution for patients with any degree of renal insufficiency
        - Malfunctioning kidney is unable to excrete magnesium and hypermagnesemia may result
    - Can cause diarrhea- increase fiber intake (Alkalosis may occur in renal impairment)

The malfunctioning kidney cannot excrete magnesium= hypermagnesemia

Clinical Use and Dosing

Drug	Indication	Dosage Form	Dosage Schedule
Aluminum hydroxide	Hyperphosphatemia		*Adolescents or adults:* 300–600 mg 3 or 4 times a day, max 3,000 mg/day *Children:* 30 mg/kg/day
AlternaGEL Amphojel Alu-Tab Alu-Cap Generic	Hyperacidity	Liquid: 600 mg/5 mL Tablets: 300 mg, 600 mg Tablets: 500 mg Capsules: 500 mg (sodium content <1.2 mg) Suspension: 320 mg/5 mL Concentrated suspension: 450 mg/5 mL Concentrated suspension: 675 mg/5 mL Concentrated liquid: 600 mg/5 mL	*Adults:* Tablets or capsules: 500–1,500 mg 3–6 times daily between meals and at bedtime Suspension: 5–30 mL prn between meals and at bedtime *Children:* 300–900 mg per dose between meals and at bedtime
Calcium carbonate	Calcium deficiency in chronic renal failure		*Adults:* 1–2 g/day in divided doses *Children:* 45–65 mg/kg/day in 4 divided doses Adjust dose based on serum calcium concentration
Alka-Mints Tums Maalox Chewables Generic	Postmenopause or osteoporosis Hyperacidity	Tablets, chewable: 850 mg (sodium content <5 mg) Tablets, chewable: 500 mg (sodium content <2 mg) Extra-strength, chewable: 750 mg (sodium content <4 mg) Ultra, chewable: 1,000 mg (sodium content <4 mg) Tablets: 600 mg Tablets: 500, 600, 650, 1,250 mg	*Adults:* 1,000–1,500 mg elemental calcium/d *Children >11 yr and adults:* TUMS (500 mg calcium carbonate) chew 2–4 tablets for symptoms, not to exceed 15 tablets/d; TUMS E-X (750 mg calcium carbonate) chew 2–4 tablets for symptoms, not to exceed 10 tablets/d *Children 5 yr to 11 yr:* 800 mg calcium carbonate for symptoms; do not exceed 4,800 mg/d *Children 2–5 yr:* 400 mg as needed; do not exceed 1,200 mg/d
Magnesium hydroxide Phillips' Chewables Phillips' Milk of Magnesia Generic	Hyperacidity	Tablets: 311 mg Liquid: 400 mg/5 mL Concentrated liquid: 800 mg/5 mL Liquid: 400 mg/5 mL	*Children >12 yr and adults:* Tablets: 622–1,244 mg up to qid Liquid: 5–15 mL up to qid with water Liquid concentrate: 2.5–7.5 mL up to qid with water
Phillips' Caplets Phillips' Milk of Magnesia	Laxative	Caplets: 500 mg Liquid: 400 mg/5 mL	*Adults:* 30–60 mL at bedtime with water *Adults and children ≥ 12 yrs:* 2 to 4 caplets daily

Generic		Liquid: 400 mg/5 mL	*Children:* 2–5 yr: 5–15 mL/d at bedtime 6–11 yr: 15–30 mL/d at bedtime
Aluminum hydroxide-magnesium hydroxide combinations Maalox Maalox Advanced Extra Strength Mylanta Regular Strength Mylanta Ultimate Strength Generic	Hyperacidity	Aluminum hydroxide 200 mg and magnesium hydroxide 200 mg and simethicone 20 mg per 5 mL Aluminum hydroxide 400 mg and magnesium hydroxide 400 mg and simethicone 40 mg per 5 mL Aluminum hydroxide 200 mg and magnesium hydroxide 200 mg and simethicone 20 mg per 5 mL Aluminum hydroxide 500 mg and magnesium hydroxide 500 mg per 5 mL	Tablets: 1 or 2 prn *Adults and children >12 yr:* 2–4 tsp bid, max *Adults and children >12 yr:* 2–4 tsp bid, max 8 tsp /24 h *Adults and children >12 yr:* 2–4 tsp between meals and at bedtime, max 24 tsp/24 h *Adults and children >12 yr:* 2–4 tsp between meals and at bedtime, max 9 tsp/24 h
Maalox Mylanta Regular Strength	Peptic ulcer disease	Aluminum hydroxide 200 mg and magnesium hydroxide 200 mg and simethicone 20 mg per 5 mL	Suspension: 15–30 mL prn Suspension: 15–30 mL 1 h and 3 h after meals and at bedtime
	Gastroesophageal reflux disease		*Children >12 yr and adults*: Suspension: 5–30 mL every 30–60 min for acute management; 5–30 mL 1 h and 3 h after meals and at bedtime for maintenance *Infants and children <12 yr*: Suspension: 0.5 mL/kg (average dose 2–15 mL) 1–2 h after meals or feedings; max 15 mL/dose

- **Rational drug selection**
  - ANC, sodium content, and cost
  - Combination products with aluminum hydroxide and magnesium hydroxide have the highest ANC (use is moderate to severe disease
- **Monitoring**
  - Serum phosphate, potassium, and calcium during chronic use
  - These drugs may cause increased serum calcium and decreased serum phosphate
  - Chronic magnesium hydroxide use may cause elevated Mg levels in patients with renal failure or the elderly with decreased renal function
- **Patient education**
  - Take as prescribed, especially related to mealtimes
  - Take 1-3 hrs after meals and at bedtime
  - Chewable tablets chew thoroughly and drink half a glass of water
  - Shake suspensions before administration
  - Many drug interactions, separate doses by 2 hours apart
  - Calcium based antacids should not be administer with food containing large amounts of oxalic acid (spinach, rhubarb) or phytic acid (brans, cereals) decrease absorption
  - Avoid taking with food containing phosphorus (milk, dairy products) can cause milk-alkali syndrome (NV, confusion, HA)
  - Consult provider: before taking antacids for more than 2 weeks if a problem recurs, if relief is not obtained, or if symptoms of GI bleeding (black, tarry stools, coffee ground emesis
  - Aluminum and calcium antacids may cause constipation: increase bulk, increase fluid intake, and more mobility, stool softened
  - Magnesium antacids may cause diarrhea, increase fiber
  - Avoid smoking, avoid flat lying body position while sleeping, foods that irritate the gastric mucosa (spicy foods), or stimulate acid production (alcohol) and foods that decrease lower esophageal sphincter tone (caffeine, chocolate, fatty foods)

➢ Antidiarrheals:

- Diarrhea that lasts for less than 2 weeks is considered acute; if it lasts more than 2 weeks, it is considered chronic.
- **Pharmacodynamics, Pharmacokinetics**
- Three main classes **absorbent preparations** (kaolin and pectin (Kapectolin) and bismuth subsalicylate (Pepto-Bismol, Kaopectate Liquid), **opiates** (diphenoxylate with atropine (Lomotil), diphenoxin with atropine (Motofen), and loperamide (Imodium)) and anticholinergics (IBD)
- Contraindications: Drugs that decrease gastric motility or delay intestinal transit time have induced toxic megacolon, especially in those with inflammatory bowel disease
- All antidiarrheals (except Crofelemer) require cautious use in older adults and when there is r/f impaction
- Older adults are especially sensitive to diphenoxylate or difenoxin r/t atropine and anticholinergic properties
- Not recommended for children under 12, none of the antidiarrheals are safe for children under 2 years old
- Antidiarrheals are contraindicated in the Tx of diarrhea in most children
- Standard of care: oral rehydration therapy
- **ADRS** Rebound constipation is the main adverse effect

-Kaolin-pectin (kapectolin): Acute diarrhea

- Kaolin is a clay-like powder that attracts and holds onto bacteria
- Pectin thickens the stool by absorbing moisture
- Used to treat simple diarrhea
- Act locally in the bowel, not systemically absorbed
- Pregnancy Category B

-Bismuth subsalicylate (Pepto bismol): Acute diarrhea, travelers' diarrhea

- Antisecretory and antimicrobial effects
- Also used as part of a multidrug regimen for H. pylori
- Undergoes chemical dissociation in GI, salicylate moiety is absorbed
- Salicylate is metabolized in the liver and more than 90% is excreted in urine
- Contraindicated in children or teenagers during or after recovery from chickenpox or flu-like illness
- Contraindicated for patients with ASA hypersensitivity
- For bismuth subsalicylate, additional reactions that all patients should be warned about are gray/black stools and black tongue, the results of the bismuth. Patients should be told to expect this reaction and that it does not indicate GI bleeding.
- Bismuth subsalicylate may potentiate the risk for toxicity if taken w/ aspirin
- R/f hypoglycemia in large doses with insulin or oral hypoglycemics

-Crofelemer (fulyzaq): Symptomatic relief of noninfectious diarrhea in adult pts w/ HIV/AIDS on antiretroviral therapy

- Botanical blocking chloride secretion from the epithelial cells in the intestinal lumen, decreasing water loss and normalizing the flow of chloride and water in the intestinal tract
  - Minimal absorption after PO administration
  - Metabolism and excretion are not known
  - In clinical trials more likely to have URI, bronchitis, and cough than placebo group
  - Adverse GI effects flatulence, increased bilirubin, and nausea

-diphenoxylate w/atropine (Lomotil): Acute diarrhea

- Constipating meperidine congener, lacks analgesic activity
- At high doses can produce euphoria and physical dependence
- Anticholinergics are useful only with inflammatory bowel disease
- Well absorbed from GI tract

- The atropine crosses the BBB (produces mild to moderate anticholinergic effects)
- Rapidly and extensively metabolized to diphenoxylic acid (it's metabolite)
- Excreted in urine and feces
- The atropine component of diphenoxylate and difenoxin contraindicates their use in narrow-angle glaucoma and requires cautious use in prostatic hyperplasia.
- Children, especially those with Down syndrome have increased sensitivity to atropine
- Use with extreme caution in children, not recommended for use in children younger than 12 y/o
- Do not use with E. Coli, Salmonella, Shigella, or in pseudomembranous colitis
- **ADRs:** r/t atropine: anticholinergic effects (dry mouth, flushing, tachycardia, urinary retention)
    - Crosses BBB=dizziness, drowsiness, sedation, HA, euphoria, or depression
- Additive or potentiating CNS effects with other CNS depressants and additive anticholinergic effects with other drugs that share these effects

-Difenoxin w/atropine (Motofen): Acute diarrhea9*****

- Anticholinergics are useful only with inflammatory bowel disease
- Rapidly metabolized to an inactive hydroxylated metabolite
- Excreted mainly as conjugates in urine and feces
- The atropine component of diphenoxylate and difenoxin contraindicates their use in narrow-angle glaucoma and requires cautious use in prostatic hyperplasia.
- Children, especially those with Down syndrome have increased sensitivity to atropine
- Use with extreme caution in children, not recommended for use in children younger than 12 y/o
- Do not use with E. Coli, Salmonella, Shigella, or in pseudomembranous colitis
- **ADRs:** r/t atropine: anticholinergic effects (dry mouth, flushing, tachycardia, urinary retention)
    - Crosses BBB=dizziness, drowsiness, sedation, HA, euphoria, or depression
- Additive or potentiating CNS effects with other CNS depressants and additive anticholinergic effects with other drugs that share these effects

-Loperamide (Imodium): Acute diarrhea, travelers' diarrhea, chronic diarrhea associated w/inflammatory bowel disease

- Binds to opiate receptors of the intestinal wall, slows gastric motility
- Reduces fecal volume, increases viscosity and bulk, diminishes loss of fluid and electrolytes
- Does not cross BBB, limited CNS ADRs
- Partially metabolized by the liver and undergoes enterohepatic recirculation to be completely metabolized
- Eliminated in feces
- **ADRs:** r/t atropine: anticholinergic effects (dry mouth, flushing, tachycardia, urinary retention)
    - To a lesser degree than diphenoxylate and difenoxin
    - Dizziness and drowsiness (less CNS effects than difenoxin or diphenoxylate
- Additive or potentiating CNS effects with other CNS depressants and additive anticholinergic effects with other drugs that share these effects

Pharmacotherapeutics

- Precaution and contraindications
- Drugs that reduce intestinal motility or delay intestinal transit time may cause toxic megacolon, especially in IBD
- Diphenoxylate with atropine difenoxin with atropine, and loperamide should be used cautiously in IBD
    - D/C if ABD distension occurs
- Use Diphenoxylate with atropine difenoxin with atropine, and loperamide use with caution in advanced hepatorenal disease and in all patients with abnormal LFTs (hepatic coma may occur)
- Atropine: contraindicated in narrow-angle glaucoma and requires cautious use in prostatic hyperplasia
- Children (especially those with Downs syndrome) have increased sensitivity to atropine
- Clinical Use and Dosing

Simple, Acute Diarrhea

- Absorbent preparations for adults: Kaolin-pectin or bismuth subsalicylate taken after each loose stool may be effective
- Majority of acute diarrhea are self-limiting, hydration important
- Maintain hydration
    - Commercial hydrating fluids (Pedialyte) or powdered salts
    - A pinch of table salt and a half-teaspoon of honey in 8 oz of fruit juice (older children and adults)
    - Non-diet colas without carbonations (older children and adults)
    - Alternate these solutions with 8 oz of water with one-quarter teaspoon baking soda to replenish electrolytes (NA, K, bicarbonate, and Cl)
- If the absorbents do not resolve the problem, diphenoxylate or difenoxin or loperamide may be added

Chronic Diarrhea Associated with IBD

- Steroids and sulfasalazine are needed
- Loperamide may be used as adjunct therapy
    - May significantly improve symptoms especially with added fiber and anticholinergics
    - If clinical improvement does not occur with doses of 16 mg/day for 10 days, symptoms are unlikely to be controlled by further use

Chronic Diarrhea Associated with Pancreatic Insufficiency

- Malabsorption r/t pancreatic insufficiency requires enzyme supplements, antidiarrheals not indicated

Chronic Infantile Diarrhea

- Bismuth subsalicylate: 2.5 mL every 4 hrs for children 2 to 24 months, 5 mL for 24-48 month children, and 10 mL for children 48 to 70 months

Diarrhea in HIV/AIDS Patients Taking Antiretroviral Drugs

- Crofelemer (Fulyzaq) symptomatic relief of noninfectious diarrhea in adults with HIV/AIDS on ARV therapy
- 125 mg tablet twice a day without regard for food

Traveler's Diarrhea

- Bismuth subsalicylate: two tablets or 2 Fl oz before each meal and at bedtime (QID) for up to 3 weeks
- Prevention and treatment
- High-risk areas: Central and South American, Africa, Middle East, Mexico, and Asia
- E. Coli is the most common causative agent followed by Campylobacter, Shigella, and Salmonella

Rational Drug Selection

- Indication: Acute diarrhea, any of the antidiarrheals are appropriate
- Subsalicylate and loperamide are the only drugs indicated for traveler's diarrhea
- Loperamide is the only drug with an indication for IBD
- Generic and brand name formulations available

Monitoring: No specific monitoring

Patient Education

- Take as directed, do not double doses, do not exceed max number of doses in 24 hrs
- Notify provider if diarrhea continues beyond 48 hrs or if ABD pain, fever, or distention occurs
- Use calibrated measuring devices for liquids, shake suspensions before measured

- Drug interactions may occur, especially with diphenoxylate and loperamide
- Do not take any OTC antidiarrheal before contacting your provider if taking digoxin, cephalosporin antimicrobials, warfarin or heparin, or CNS depressants (including ETOH)
- R/f salicylate poisoning if taking ASA and bismuth subsalicylate
- R/f rebound constipation
- Stop drug when s/s of diarrhea are reduced
- Bismuth subsalicylate can turn the tongue and stools gray/black
- Drugs with atropine: dry mouth, flushing, tachycardia, and urinary retention
- Loperamide also exhibits these reactions but to a lesser degree, add fiber and use oral rehydrating solutions
- GHWT
- Bland food diet, remove milk, could it be lactose intolerance?

Drug	Indication	Dosage Form	Initial Dose	Additional Doses
Bismuth subsalicylate*†	Acute diarrhea	Tablets/chewable: 262 mg	*Adults:* 524 mg every 30 min or 1,048–1,200 mg every 60 min as needed	Not to exceed 4.2 g/24 h
Pepto-Bismol		Liquid: 262 mg/15 mL		Not to exceed 2.4 g/24 h
Kaopectate		Liquid: 524 mg/15 mL		Not to exceed 1.4 g/24 h
				Not to exceed 704 mg/24 h
			Children 9–12 yr: 262–300 mg every 30–60 min as needed	May repeat q4h; not to exceed 6 doses/24 h
			Children 6–9 yr: 176 mg every 30–60 min as needed	
			Children 3–6 yr: 88 mg every 30–60 min as needed	
			Children <3 yr weighing >13 kg: 88 mg	
			Children <3 yr weighing 6.4–8 kg: 44 mg	
			May repeat q4h; not to exceed 6 doses/24 h	
	Traveler's diarrhea		524 mg (2 tablets or 30 mL of 262 mg/15 mL liquid) every 30 min for up to 8 doses	Not to be used for more than 48 h
Crofelemer (Fulyzaq)	Symptomatic relief of noninfectious diarrhea in adult patients with HIV/AIDS on anti-retroviral therapy	125 mg delayed-release tablet	1 tablet bid, with or without food	
Difenoxin with atropine Motofen	Acute diarrhea	Tablets: 1 mg difenoxin and 0.025 mg atropine sulfate	*Adults:* 2 mg	1 mg after each loose stool or 1 mg every 3–4 h as needed. Total 24 h dose not to exceed 8 mg
Diphenoxylate with atropine Lomotil	Acute diarrhea	Tablets: 2.5 mg diphenoxylate, 0.025 mg atropine sulfate	*Adults:* 5 mg tid to qid initially	5 mg daily as needed; not to exceed 20 mg/d

		Liquid: 2.5 mg diphenoxylate, 0.025 mg atropine sulfate/5 mL	*Children 2–12 yr:* all doses qid and in liquid form *2 yr/11–14 kg:* 1.5–3 mL *3 yr/12–16 kg:* 2–3 mL *4 yr/14–20 kg:* 2–4 mL *5 yr/16–23 kg:* 2.5–4.5 mL *6–8 yr/17–32 kg:* 2.5–5.5 mL *9–12 yr/23–55 kg:* 3.5–5 mL	Not recommended for children <2 yr Reduce dosage as soon as control of symptoms is achieved; maintenance dosage may be as low as one-fourth of initial daily dose; maximum daily dose 20 mg Overdosage may result in respiratory depression
Kaolin-pectin Kapectolin Kao-Spen	Acute diarrhea	Suspension: 5.2 g kaolin plus 260 mg pectin/30 mL; 5.85 mg kaolin plus 130 mg pectin/30 mL Also comes in combinations with paregoric, bismuth, carboxy-methylcellulose, and others	*Adults:* 60–120 mL after each loose stool *Children >12 yr:* 40–60 mL after each loose stool *Children 6–12 yr:* 30–60 mL after each loose stool *Children 3–6 yr:* 15–30 mL after each loose stool	
Loperamide Imodium A-D Imodium Generic	Acute diarrhea, traveler's diarrhea	Tablets/capsule: 2 mg Liquid: 1 mg/5 mL	*Adults:* 4 mg initially *Children 9–11 yr or 30–47 kg:* 2 mg initially *Children 6–8 yr or 24–30 kg:* 1 mg initially	2 mg after each loose stool; not to exceed 8 mg/d for OTC use or 16 mg/d for prescription use 1 mg after each loose stool; not to exceed 6 mg/24 h; OTC use not to exceed 48 h 1 mg after each loose stool; not to exceed 4 mg/24 h; OTC use not to exceed 48 h
	Chronic diarrhea associated with inflammatory bowel disease		*Adults only:* 4 mg initially	2 mg after each loose stool until symptoms resolved; maintenance dose is usually 4–8 mg/d in divided doses; not to exceed 16 mg/d

➢ Cytoprotective Agents:

- Agents used to treat or prevent ulcer formation
- Two drugs sucralfate (Carafate) and misoprostol (Cytotec)
  - ❖ **Pt should report onset of black tarry stools or severe abdominal pain, which may indicate treatment failure and GI bleeding**

Sucralfate (Carafate):

- **Pharmacodynamics-**Basic aluminum salt that binds to necrotic ulcer tissue where it acts as a barrier to acid, pepsin, and bile salts.
  - Action is largely topical, no acid-neutralizing activity, little is absorbed
  - May directly absorb bile salts and stimulate endogenous prostaglandin synthesis (formation of protective mucosa)
- **Pharmacokinetics**
- Minimal absorption, action is largely topical
- Essentially not absorbed, 90% excreted in feces
- **Pharmacotherapeutics**
- No specific precautions or contraindications
- Pregnancy Category B
- Safety in children not established
- **ADRs** Minor and rare: constipation, dizziness, gastric discomfort
- **Drug/Drug interactions**: Decrease absorption of other drugs

    - Separate administration of interacting drugs by 2 hours, give other drug first
- Take on an empty stomach
- Causes constipation- increased fluids, dietary bulk, and exercise
- Do not use with digoxin or warfarin= decreases effectiveness
- Indication for active duodenal ulcer x8wks and maintenance after healing x2wks

Misoprostol (Cytotec):

- **Pharmacodynamics:** A methyl analogue of prostaglandin E1
- Inhibits gastric secretion through inhibition of histamine-stimulated cyclic adenosis monophosphate (AMP) production
- Inhibits basal and nocturnal gastric acid secretion and acid secretion in response to stimuli
    - meals, histamine, and coffee by binding to prostaglandin E receptors, mucosal protective qualities.
- Mucosal protective qualities as well
    - Binds to prostaglandin E receptors which facilitate mucus and bicarbonate production
- Can be taken with food and still be effective
- **Pharmacokinetics**
- Rapidly and extensively absorbed after PO administration (distribution unknown)
- Rapidly converted into a free acid
- Does not affect CYP450 system
- Half-life is 20-40 mins however renal impairment doubles its half-life
- Metabolite excreted in urine
- **Pharmacotherapeutics**
- Use with caution with caution in renal impairment (no routine adjustments)
- Use with caution in the elderly r/t decreased renal function
- **Pregnancy X:** Can produce uterine contractions endangering pregnancy causing spontaneous abortion, premature birth, or birth defects. Women of childbearing age should have a negative pregnancy test before prescribed and start misoprostol on day 2 or 3 of menstrual period. If pregnancy is suspected, drug should be stopped immediately.
- **ADRs** GI or gynecological
    - Most common: diarrhea, ABD pain, nausea, and flatulence
    - Postmenopausal bleeding, spotting, cramps, hypermenorrhea, menstrual disorder, and dysmenorrhea
- **Drug/Drug interactions:** R/f increased diarrhea when given with magnesium based antacid
- Indicated for prophylaxis and treatment of duodenal ulcers associated with NSAID use

Clinical Use and Dosing

Prophylaxis and Treatment of Duodenal Ulcers Associated with NSAID Use

- NSAIDs inhibit prostaglandin synthesis and damage the mucosal lining of the stomach
- R/f ulcer formation
- Misoprostol is FDA approved for this use (prophylaxis or treatment)
- Dosage 200 mcg QID with food ACHS
- If unable to tolerate 100 mcg QID with food ACHS

Treatment of Duodenal Ulcers from Other Causes

- Sucralfate used short term (up to 8 wks) for Tx of an active ulcer
- Dosage 1 gram QID on an empty stomach, 1 hr before meals, and HS
- Healing usually occurs in 2 weeks
- Maintenance therapy after ulcer has healed is 1 g BID
- Off label use for treating gastric and esophageal ulcers-same dosing schedule
- May have some advantages over antacids and H2Ras in stress ulcer prophylaxis

- Misoprostol: less effective for Tx of duodenal ulcers from other causes
    - Off-label: in doses >400mcg/day, Tx for duodenal ulcers not responsive to H2Ras

Rational Drug Selection

- Sucralfate: drug of choice for women of childbearing age
- Sucralfate preferred over misoprostol for treatment of active duodenal ulcers not caused by NSAIDs

Monitoring

- No specific monitoring parameters
- Negative pregnancy test for misoprostol

Patient Education

- Take exactly as prescribed
- Sucralfate on an empty stomach, Sucralfate is given for 4 to 8 weeks, increase fluid intake, dietary bulk, and exercise to reduce incidence of constipation
- Misoprostol with food, Misoprostol given for the duration of NSAID therapy, can cause diarrhea, if persists x1WK notify provider
- Continue therapy even if you feel better

Table 20-9 Dosage Schedule: Cytoprotective Agents

Drug	Indication	Dosage Forms	Dosage Schedule
Misoprostol Cytotec	Prophylaxis and treatment of duodenal ulcers due to NSAID use	Tablets: 100, 200 mcg	200 mcg qid with food. Last dose usually at bedtime. Taken for duration of NSAID therapy. If this dose is not tolerated, 100 mcg qid may be used.
Sucralfate Carafate	Active duodenal ulcer Maintenance after healing of duodenal ulcer	Tablets: 1 g Suspension: 1 g/10 mL	1 g qid taken 1 h before meals and at bedtime 1 g bid taken on empty stomach

➢ Antiemetics:

Drug classes with antiemetic properties: antihistamines, phenothiazines, sedative hypnotics, cannabinoids, 5-HT3 receptor antagonist, anticholinergics, and a substance P/neurokinin 1 receptor antagonist

Antihistamines: dimenhydrinate (Dramamine), diphenhydramine (Benadryl), hydroxyzine (Vistaril), meclizine (Antivert)

- **Pharmacodynamics:** Antihistamines with significant antiemetic activity have strong anticholinergic effects as well as histamine 1 blocking effects
- **MOA:** Bind to central cholinergic receptors to produce antiemetic effects

- especially with motion sickness due to the depression of conduction in the vestibulocerebellar pathway

- **Pharmacokinetics:** All the antiemetic drugs (except for TD scopolamine) are well absorbed after PO administration
- **Pharmacotherapeutics:** Cautious use in narrow-angle glaucoma, seizure disorders, pyloric obstruction, hyperthyroidism, CVD, and prostatic hypertrophy
    - **Contraindicated in severe liver disease r/t extensive liver metabolism**
    - Cautious use in the elderly, dose reductions may be needed
    - Dimenhydrinate and diphenhydramine are Pregnancy Category B and safe for use in children
    - Meclizine is pregnancy Category B (safety and efficacy in children less than 12 not established)
    - Hydroxyzine Pregnancy Category C, has been used safely during labor (safety in children or lactation not established)

ADRs: Common adverse reactions: drowsiness, dry mouth, blurred vision & urinary retention

- Paradoxical excitation may occur in children
- Drug/Drug: additive CNS depression with other drugs that produce CNS depression and additive anticholinergic effects with other drugs that have anticholinergic effects or adverse reactions

Phenothiazines: prochlorperazine (Compazine), perphenazine, promethazine (Phenergan)

- **Pharmacodynamics:** block dopamine receptors in the chemoreceptor trigger zone (CTZ)
    - Also bind to and block cholinergic, alpha 1 adrenergic, and histamine 1 receptors
    - Use as antiemetics is limited due to sedating and EPM effects
- **Pharmacotherapeutics:** Produce extrapyramidal reaction **Contraindicated in Parkinson's Disease**
    - **Contraindicated in narrow-angle glaucoma, bone marrow depression, and sever CVD or hepatic disease**
    - Cautious use in respiratory impairment cause by acute pulmonary infection or chronic respiratory disorders (asthma or emphysema)
    - May lead to the development of "silent pneumonia"
    - Suppress cough reflex, aspiration of vomitus is possible
    - Use with caution in those with r/f aspiration
    - Pregnancy Category C
    - Children of all ages are more prone to developing extrapyramidal reactions
    - Prochlorperazine: avoided in children younger than 5 r/t extrapyramidal reactions
    - R/f respiratory depression and sudden death in children 2 years of age or older
- **Adverse reactions:** drowsiness, (extrapyramidal reactions) dystonia, akathisia, tardive dyskinesia
    - Dry mouth, dry eyes, blurred vision, constipation, and urinary retention
    - ability to mask post-surgical and neurological conditions
    - potential for agranulocytosis and blood dyscrasias 4-10 weeks after initiation
    - can cause urine to turn pink to reddish brown (does not indicate hematuria)
- **Promethazine Black Box Warning: Fatal respiratory depression in children younger than 2 years old**
    - Drug/Drug: additive CNS depression with other drugs that produce CNS depression and additive anticholinergic effects with other drugs that have anticholinergic effects or adverse reactions
    - Additive hypotensive effects with antihypertensive agents or acute ingestion of ETOH
    - Concurrent administration of lithium increases r/f extrapyramidal reactions
    - May mask s/s of lithium toxicity
    - Antithyroid agents increase r/f agranulocytosis

Cabbabinoid: dronabinol (Marinol)

- **Pharmacodynamics:** Work in the CNS like cannabis to prevent NV associated w. chemotherapy & as an appetite stimulant, especially in HIV pts
- **Pharmacotherapeutics:** Use with caution in patient with Hx of seizure disorder r/t lowering of seizure threshold
    - Cardiac disorders**:** monitor for hypotension, possible hypertension, syncope, or tachycardia
    - High potential for abuse
    - Pregnancy Category C
- **Adverse reactions:** euphoria (should not drive), depression, dizziness, paranoid thoughts, somnolence, and abnormal thoughts
    - Cardiac effects include palpitations, tachycardia, and hypotension
    - Seizures and seizure-like activity
    - Drug/Drug interactions: Interacts with other CNS depressants, additive CNS depression with benzos, barbiturates, ETOH, opioids, antihistamines, muscle relaxants, and other CNS depressants

5-HT3 receptor agonists: palonosetron (Aloxi), dolasetron mesylate (Anzemet), granisetron (Kytril, Sancuso) and ondansetron (Zofran)

- **Pharmacodynamics:** Block serotonin both peripherally and on vagus nerve terminals & the chemoreceptor trigger zone (CTZ) to decrease emesis
- **Pharmacotherapeutics:** Potential to mask progressive ileus
    - Zofran contains aspartame, use with caution in phenylketonuria
    - Dolasetron, granisetron, and palonosetron are Pregnancy Category B
- **Adverse reactions:** constipation, headache, fatigue, dizziness, diarrhea.
    - **Less** common but **concerning** rare cases of tachycardia, bradycardia, hypotension, and QT prolongation

Anticholinergic: Scopolamine (Transderm Scop)

- **Pharmacodynamics:** Belladonna alkaloid anticholinergic acts as a competitive inhibitor of muscarinic in the parasympathetic nervous system
    - Blocks cholinergic transmission from the reticular center to the vomiting center in the brain
    - Anticholinergic effect: decreases secretion of saliva and decreases GI motility
- **Pharmacotherapeutics: Contraindicated:** pts w/ narrow angle glaucoma
    - Caution: pts with open-angle glaucoma or gastrointestinal or bladder neck obstruction
    - Use cautiously in the elderly due to CNS effects
        - Pregnancy Category C, no approved for use in children
- **Adverse reactions:** dry mouth, drowsiness, blurred vision, dilated pupils
    - Withdraw syndrome: dizziness, NV, HA
- Applied in the hairless area behind the ear 4 hours prior to needed effect and can be left in place up to 3 days. Wash hands after handling patch to avoid getting medication in the eyes (can cause blurry vision & pupil dilation)
- Decrease secretion of saliva and decrease gastric motility

NKI receptor antagonist: Aprepitant (Emend)

- **Pharmacodynamics:** crosses the blood brain barrier and occupies the NK1 receptors to prevent n/v in pts receiving chemotherapy
- **Pharmacotherapeutics:** Contraindicated in patients who are hypersensitive to any component of the product
    - Inhibits CYP3A4=increase serum concentrations of other drugs that are metabolized by CYP3A4
    - Pregnancy Category C and not approved for use in children
- **Adverse reactions:** fatigue, dizziness, hiccups, possible elevated ALT/AST, BUN
    - Drug/drug interactions: Inducer of CYP3A4 and can increase plasma concentrations of drugs metabolized via CYP3A4 system
        - Including: hormonal contraceptives and some chemotherapy agents

- **Concurrent use of Aprepitant and pimozide, terfenadine, astemizole, or cisapride is contraindicated due to potentially life-threatening reactions**

Misc.: trimethobenzamide (Tigan)

- **Pharmacodynamics:** Inhibits emetic stimulation of the CTZ

Rational Drug Selection:

Treatment of Nausea and Vomiting Due to Drugs or Gastroenteritis

- Often improves with Tx using an antiemetic
- 5-HT3 receptor antagonists: low side-effect profile and tolerance
- Phenothiazines: also, a good initial and short-term treatment choice, not for children
- Trimethobenzamide: also, effective
- Antihistamines: can be used, less serious ADRs, better for longer term applications
- Dronabinol: only approved for use in chemotherapy associated NV and appetite stimulation
- Aprepitant: Approved for post-operative NV and in conjunction with other antiemetic agents for prevention of acute and delayed NV associated with initial and repeated doses of emetogenic CA chemo

Motion sickness:

- Antihistamines are useful r/t action on vestibular system and CTZ, rapid onset of action and prolonged effect
- Dimenhydrinate and meclizine: the most used
- Meclizine is also used to treat vertigo
- TD scopolamine: indicated for prevention of NV associated with motion sickness in adults and is commonly used in patients on ships

Monitoring:

- When used as a single dose or very short-term, no specific monitoring required
- If Tx for longer than a few days: following monitoring parameters are suggested
- Promethazine has been associated with bone marrow depression (CBC prior to initiating therapy)
- Phenothiazines associated with blood dyscrasias that occur between week 4-10 of therapy
    - CBC prior to initiating therapy and after 4 weeks

Patient Education

- Motion sickness: take 1 to 2 hrs prior to departure (except for ER-12 hrs prior)
- ADRs: drowsiness, dry mouth, dry eyes, constipation, and urinary retention
- Phenothiazines: turns urine pink to reddish brown: this is not hematuria

Drug	Indications	Dosage Form	Dosage Schedule	Notes
Aprepitant Emend	Prevention of chemotherapy-induced nausea and vomiting Prevention of post-operative nausea and vomiting	Capsules: 40, 80, 125 mg	Prevention of chemotherapy-induced nausea and vomiting: Day 1: 125 mg PO Day 2: 80 mg PO Day 3: 80 mg PO Post-operative nausea and vomiting: 40 mg PO within 3 h of anesthesia	For chemotherapy-induced nausea and vomiting, patients are coadministered dexamethasone 12 mg day 1 and 8 mg days 2–4
Dimenhydrinate Dramamine Generic	Antiemetic	Tablets: 50 mg Chewable tablets: 50 mg Liquid: 12.5 mg/5 mL	*Children >12 yr and adults:* 50 mg PO/IM or 25 mg ER capsules q4h; not to exceed 400 mg/d; PR = 50–100 mg q6–8h	For motion sickness, give dose 1–2 h prior to departure or ER dose 12 h prior to departure
Dramamine Gravol		Chewable tablets: 50 mg Liquid: 12.5 mg/5 mL Quick-dissolve tablets: 15 mg Liquid: 15 mg/5 mL	*Children 6–12 yr:* 25–50 mg (PO/IM) q6–8h; not to exceed 150 mg/d *Children 2 to 5 yrs:* 12.5–25 mg (PO/IM) q 6–8 h, maximum dose 75 mg/day	Use calibrated measuring device when giving liquid doses
Gravol Generic		Rectal suppositories: 25, 50, 100 mg	*Children 8–12 yr:* PR = 25–50 mg q8–12 h *Children 6–8 yr:* 12.5–25 PR q8–12 h *Children 2–6 yr:* Up to 12.5–25 mg q6–8 h; not to exceed 75 mg/d	
Diphenhydramine Benadryl Generic	Antiemetic	Soft gels: 25 mg Tablets: 25 mg	*Adults:* 25–50 mg q6h PO; 10–50 mg q2–3h IM; not to exceed 300 mg/d	For motion sickness, give dose 1–2 h prior to departure or ER dose 12 h prior to departure
		Chewable tablets: 12.5 mg	*Children >20 lb (9.1 kg):* 12.5–25 mg 3–4 times daily (5 mg/kg) not to exceed 300 mg/d	
		Liquid: 6.25 mg/ 5mL	*Children:* 1–1.5 mg/kg q4–6h PO; not to exceed 300 mg/d	Use calibrated measuring device when giving liquid doses.
		Injection: 50 mg/mL	IM = 1.25 mg/kg qid; not to exceed 300 mg/d	Give IM into deep, well-developed muscle; avoid SC administration
Hydroxyzine Atarax Vistaril	Antiemetic	Tablets: 10, 25, 50 mg Tablets: 100 mg Capsules: 25, 50, 100 mg Injection: 25 mg/mL, 50 mg/mL	*Children >12 yr and adults:* 25–100 mg PO/IM tid or qid	Tablets may be crushed and capsules opened and administered with food or fluid for patients with difficulty in swallowing
		Syrup: 10 mg/5 mL	*Children 6–12 yr:* 12.5–25 mg PO/IM q6h *Children <6 yr:* 12.5 mg q6h (General calculation for children: 0.5 mg/kg q6h)	Give IM into deep, well-developed muscle using Z track. Do not use deltoid. Injection is painful. Rotate sites frequently. Avoid SC or IV administration.
Meclizine Dramamine Less Drowsy Antivert Generic	Motion sickness	Tablets: 12.5, 25, 50 mg Chewable tablets: 25 mg Capsules: 25 mg	*Children >12 yr and adults:* 25–50 mg	Take 1 h prior to travel. May repeat dose every 24 h for duration of journey

	Vertigo		Adults: 25–100 mg daily in divided doses	
	Nausea and vomiting in pregnancy		Lowest dose that relieves nausea	Pregnancy Category B
Prochlorperazine Compazine Generic	Antiemetic	Tablets: 5, 10, 25 mg Spansules (SR): 10, 15, 30 mg Syrup: 5 mg/5 mL Injection: 5 mg/mL Suppositories: 2.5, 5, 25 mg	*Children >12 yr and adults:* 5–10 mg PO/IM tid or qid; not to exceed 40 mg/d *Children 19–39 kg:* 2.5 mg PO/PR tid or 5 mg bid; not to exceed 15 mg/d *Children 15-18 kg:* 2.5 mg PO/PR bid or tid; not to exceed 10 mg/d *Children >2 yr or 10-14 kg:* 2.5 mg PO/PR qd or bid; not to exceed 7.5 mg/d	Do not crush or chew ER capsules. Administer with food or milk or a full glass of water to minimize GI distress. Dilute syrup in citrus or chocolate-flavored drinks. Give IM into deep, well-developed muscle. Keep patient recumbent for at least 30 min following injection to avoid hypotensive effects. Do not use in pediatric patients under 2 yr of age or under 20 lb.
Promethazine Phenergan Generic	Antiemetic	Tablets: 12.5, 25, 50 mg Syrup: 6.25 mg/5 mL Suppositories: 12.5, 25, 50 mg Injection: 25 mg/mL, 50 mg/mL	*Adults:* 25 mg PO/IM/PR q4h *Children >2 yr:* 0.25–0.5 mg/kg q4–6h PO/IM/PR. Do not exceed 25 mg/dose.	For motion sickness, give dose 1–2 h prior to departure. Administer with food, water, or milk to minimize GI distress. Tablets may be crushed and mixed with food or fluids for patients with difficulty in swallowing. Use calibrated measuring device when giving liquid doses. Give IM into deep, well-developed muscle; SC administration may cause tissue necrosis. Do not administer to children <2 yr. Use with extreme caution in children using the lowest, most-effective dose.
Trimethobenzamide Tigan Generic	Antiemetic	Capsules: 100, 250, 300 mg Injection: 100 mg/mL	*Adults:* 300 mg PO tid/qid; IM = 200 mg tid/qid *Children:* 15–20 mg/kg/day PO divided tid/qid OR *Children > 40 kg*: 300 mg tid/qid *Children 15–40 kg:* 100–200 mg PO tid/qid or 15 mg/kg/d in 3–4 divided doses *Children <15 kg*: 100 mg PR tid/qid	Capsules can be opened and contents mixed with food or fluid for patients with difficulty in swallowing. Inject deep into well-developed muscle to minimize tissue irritation.
Dronabinol Marinol	Refractory nausea and vomiting associated with cancer chemotherapy	Capsules: 2.5 mg, 5 mg, 10 mg	*Adults and children:* 5 mg/m^2 1–3 h before chemotherapy. Then every 2–4 h after chemo. May increase as needed by increments of 2.5 mg/m^2 to a max of 15 mg/m^2	Individualize the dosing

	Anorexia associated with weight loss in patients with AIDS		*Adults:* 2.5 mg bid before lunch and supper; dosage can be reduced to 2.5 qhs	
Dolasetron Anzemet	Prevention of nausea and vomiting after chemotherapy or surgery	Tablets: 50, 100 mg Injection solution: 20 mg/mL	*Children ≥16 yr and adults:* 100 mg within 1 h before chemotherapy or 2 h before surgery *Children 2 yr–16 yr:* 1.8 mg within 1 h of chemotherapy or 1.2 mg within 2 h before surgery	Dolasetron injection solution may be diluted in apple juice and taken orally. This solution is stable for 2 h.
Ondansetron Zofran Generic	Prevention of nausea and vomiting associated with chemotherapy Post-operative nausea and vomiting Gastroenteritis	Tablets: 4, 8 mg ODT (disintegrating tab): 4, 8 mg Solution: 4 mg/5 mL	*Adults:* 24 mg administered 30 min before the start of chemotherapy or 8 mg tid *Children 4–11 yr:* 4 mg tid *Infants and children < 40 kg:* 0.1 mg/kg/dose before induction of anesthesia *Children > 12 yr:* 4 mg *Adults:* 16 mg PO 1 h before induction of anesthesia, OR 4 mg IV *Infants and children 6 mo to 10 yr:* 8–15 kg: 2 mg/dose × 1 15–30 kg: 4 mg/dose × 1 > 30 kg: 8 mg/dose × 1	Routine use of ondasetron is not recommended in most cases of acute gastroenteritis.
Scopolamine Transderm Scop	Prevention of nausea and vomiting associated with motion sickness	Transdermal patch: 1.5 mg	*Adults:* Apply patch to hairless area behind one ear and leave in place for 3 days	Transdermal patch is programmed to deliver 1 mg over 3 days.

➢ Histamine-2 receptor antagonists: H2Ras

- Histamine 2 blockers aka histamine 2 antagonists (H2Ras)

Do not inhibit acetylcholine, so they reduce gastric acid secretion by only 35%-50%

Cimetidine (Tagamet), Famotidine (Pepcid), Nizatidine (Axid), Ranitidine (Zantac)

- Used to reduce gastric acid in NPO pts for prophylaxis and management of duodenal and gastric ulcers and GERD (not first-line treatment of GERD), if no esophageal erosive disease is present H2RA's can be used for maintenance therapy for relief of GERD symptoms
- Also used for heart burn, acid indigestion and "sour stomach"

- **Pharmacodynamics: MOA:** Inhibit acid secretion by gastric parietal cells through a reversible blockade of histamine at H2 receptors
  - potent inhibitors of all phases of gastric acid secretion, including muscarinic agonists and gastrin
  - Effect volume and H ion concentration of gastric juice, gastric emptying, and lower esophageal sphincter pressure (each drug to varying degrees)
    - Cimetidine, ranitidine, and famotidine have no effect on gastric emptying
    - Cimetidine and famotidine have no effect on lower esophageal sphincter pressure
    - Ranitidine, nizatidine, and famotidine have little or no effect on fasting or postprandial serum gastrin
    - Ranitidine does not affect pepsin secretion or pentagastrin-stimulated IF secretion
  - **Pharmacokinetics**
    - All drugs are well absorbed with PO administration

    - All are metabolized to differing degrees by the CYP450 system and excreted in differing percentages unchanged in urine
- **Pharmacotherapeutics**
- Caution: Renal impairment (dosage adjustments, r/f CNS ADRs), Elderly (due to decrease in renal function)
- Contraindicated: Nizatidine and Ranitidine DO NOT rx for patients w. hx of liver disease (causes hepatocellular injury, hepatitis) elevated ALT AST
- Pregnancy Category B, excreted in breast milk, use caution in breastfeeding mothers
- Famotidine is labeled safe for infants & neonates (has caused agitation, stopped when drug d/ced)
- Cimetidine can cause gynecomastia & impotence
    - CNS reversible reactions (mental confusion, agitation, psychosis, depression, and disorientation)
- Hematological adverse reactions include agranulocytosis, granulocytopenia, thrombocytopenia, and aplastic anemia (rare)
- **Less Common** side effects: drowsiness, dizziness, constipation (increase fiber and fluid intake), or diarrhea & nausea
- **Drug/Drug Interactions**: Related to CYP450 system
    - Cimetidine is most problematic (metabolized by CYP1A2, CYP2C9, and CYP2D6)
    - Other drugs metabolism inhibited by cimetidine (r/f increased serum levels and toxicity
- **Clinical Use and Dosing**

  GERD-most effective if used as on demand therapy for symptoms relief

    - Tachyphylaxis: Not first line therapy to treat GERD
    - If not erosive disease, may be used as maintenance therapy after PPI treatment
    - Infants and children have been successfully treated however no longer recommends H2Ras as empiric treatment in infants
- **Rational Drug Selection**
    - No specific drug is preferred over another for effectiveness
    - Consider costs
- **Monitoring**
    - LFTs r/t potential for hepatocellular damage
    - Renal impairment: renal function assessment prior to initiation of therapy
- **Patient Education**
- Should be taken w/ meals or immediately after & at bedtime, daily doses are best @ bedtime,
- take 1 hour away from other drugs,
- & two hours away from sucralfate
- OTC preparations should not be taken for more than 2 wks without consulting healthcare provider
- Report black tarry stools- may indicate GI bleeding.
- Sore throat, diarrhea, rash, confusion, or hallucinations should be reported promptly (might need dosage adjustment or discontinuation),
- advise pt to stop smoking (interferes with absorption of H2RA & increases gastric secretion)

Drug	Indication	Dosage Form	Initial Dose	Maintenance Dose
Cimetidine Tagamet Tagamet HB 200	Short-term treatment of active duodenal ulcer	Tablets: 200, 300, 400, 800 mg Liquid: 300 mg/5 mL Injection: 300 mg/2 mL	*Adults:* 800 mg at bedtime or 300 mg qid with meals and at bedtime or 400 mg bid *Infants:* 10–20 mg/kg/d divided q 6 to 12 h *Children:* 20–40 mg/kg/d in 4 divided doses	*Adults:* 400 mg at bedtime; dosage not to exceed 2.4 g/d. In severe renal impairment, use 300 mg every 8–12 h. *Children:* 20 mg/kg/d; 10–15 mg/kg/d in renal impairment
	Duodenal ulcer prophylaxis		*Adults:* 800 mg at bedtime	Same
	Treatment of active benign gastric ulcer		*Adults:* 800 mg at bedtime or 300 mg qid with meals and at bedtime	800 mg at bedtime. In severe renal impairment, use 300 mg every 8–12 h. No information concerning usefulness of treatment periods >8 wk.
	GERD		*Adults:* 800 mg bid in morning and at bedtime or 400 mg qid with meals and at bedtime *Children:* 20–40 mg/kg/d in 4 divided doses	*Adults:* Same dose for up to 12 wk. Use >12 wk has not been established. May go as high as 600 mg qid if needed. In severe renal impairment, use 300 mg every 8–12 h.
	Pathological hypersecretory conditions		*Adults:* 300 mg to 600 mg qid with meals and at bedtime	*Children:* 20 mg/kg/d; 10–15 mg/kg/d if renal impairment Individualize dose. Do not exceed 2,400 mg/d. Continue as long as clinically indicated.
	Heartburn, indigestion, sour stomach		*Adults:* 200 mg (OTC) 30 min before a meal. Max 2 tablets/24 h.	Take up to 400 mg bid. Do not take maximum dose for more than 2 wk without consulting health-care provider.
Famotidine Pepcid Generic	Short-term treatment of active duodenal ulcer	Tablets: 10, 20, 40 mg Powder for oral suspension: 40 mg/5 mL when reconstituted Injection: 10 mg/mL	*Adults:* 40 mg/d at bedtime or ≤20 mg bid (in morning and at bedtime) *Children:* 1–2 mg/kg/d in 1 or 2 divided doses	*Adults:* 20 mg at bedtime for up to 8 wk. Most heal in 4 wk. If CCr <10 mL/min, give 20 mg at bedtime or increase dosing interval to 36–48 h. *Children:* Same dose for up to 8 wk. Most heal in 4 wk.
	Duodenal ulcer prophylaxis		*Adults:* 20 mg at bedtime	Same

	Treatment of benign active gastric ulcer		*Adults:* 40 mg at bedtime	Same dose. If CCr <10 mL/min, give 20 mg at bedtime or increase dosing interval to 36–48 h. No data to support treatment beyond 8 wk.
	GERD		*Adults:* 20 mg bid (in morning and at bedtime) *Children:* 1–2 mg/kg/d in 1 or 2 divided doses	*Adults:* 20 mg for up to 6 wk. If erosive disease, 20–40 mg bid for up to 12 wk. *Children:* Same dose. Treatment trial for 2–4 wk.
Pepcid Complete	Heartburn, acid indigestion, and sour stomach	Chewable tablet: Famotidine 10 mg, calcium carbonate 800 mg, magnesium hydroxide 165 mg	*Adults:* Relief: 10 mg (1 tablet) with water Prophylaxis: 10 mg 1 h prior to meal that is expected to cause symptoms *Adults and children >12 yr:* Chew and swallow 1 tablet prn; do not exceed 2 tablets in 24 h.	Can be used up to bid for <2 wk
Nizatidine Axid	Short-term treatment of active duodenal ulcer	Capsule: 150, 300 mg Solution: 15 mg/ mL	*Adults:* 300 mg at bedtime or 150 mg bid (in morning and at bedtime) *Infants 6 mo to Children 11 yr:* 5–10 mg/kg/d divided bid	300 mg at bedtime. If CCr 20–50 mL/min, give 150 mg at bedtime. If CCr <20 mL/min, give 150 mg every 2 or 3 d.
	Maintenance of healed duodenal ulcer		*Adults:* 150 mg at bedtime	150 mg at bedtime
	GERD		*Adults and children >12 yr:* 150 mg bid (in morning and at bedtime)	150 mg bid
Ranitidine Zantac Generic	Short-term treatment of active duodenal ulcer	Tablets: 75, 150, 300 mg Effervescent tablets: 150 mg Geldose: capsules: 150 mg Syrup: 15 mg/mL Efferdose: granules: 150 mg	*Adults:* 100–150 mg bid (in morning and at bedtime) or 300 mg at bedtime *Infants and children <16 yr:* 4–8 mg/kg/day, max 300 mg/day	150 mg at bedtime. If CCr <50 mL/min, give 150 mg at bedtime.
	Duodenal ulcer prophylaxis		*Adults:* 150 mg at bedtime	150 mg at bedtime
	Treatment of benign active gastric ulcer		*Adults:* 150 mg bid (in morning and at bedtime)	150 mg at bedtime
	GERD		*Adults:* 150 mg bid (in morning and at bedtime); if erosive disease, give 150 mg qid *Infants and children < 6 yr:* 4–10 mg/kg/d, max 300 mg/d	*Adults:* 150 mg bid. If CCr <50 mL/min, give 150 mg at bedtime. If erosive disease, give 150 mg bid.
	Pathologic hypersecretory conditions Heartburn, acid indigestion, and sour stomach		*Children:* 2–4 mg/kg/d in 2 divided doses *Adults:* 150 mg bid (in morning and at bedtime) *Adults:* Relief: 75 mg up to bid	*Children:* 2 mg/kg/d in 2 divided doses Individualize dose; doses up to 6 g/d have been used Can be used up to bid for <2 wk

- **Prokinetics:** metoclopramide (Reglan)
  - AKA gastrointestinal stimulants
  - Do not stimulate gastric, biliary, or pancreatic secretions
  - Used to treat gastroparesis associated with DM, GERD, and emesis with chemotherapy

Pharmacodynamics: MOA: Stimulates motility in the upper GI tract,

- increases tone and amplitude of gastric contractions,
- relaxes the pyloric sphincter and duodenal bulb,
- and increases peristalsis of the duodenum and jejunum,
- resulting in accelerated gastric emptying and increased speed of gastric transit
- Improves gastroesophageal reflux disease symptoms by increasing lower esophageal tone
- Also is a dopamine receptor agonist in the CNS, including the chemotherapy trigger zone leading to prevention of emesis
- Actions similar to phenothiazines: Produces sedation and may cause tardive dyskinesia or EPS
- Induces release of prolactin and transient increases of aldosterone

Pharmacokinetics

- Well absorbed after PO administration
- Injectable formulation is available
- High bioavailability, low protein binding
- Widely distributed, crosses BBB and placenta, enters breast milk (greater than plasma)
- Minimally Metabolized by the liver, liver function is not an issue
- Excreted in urine (clearance is affected by renal function)
- Renal impairment requires dose adjustment: dose cut in half CCr <40

Pharmacotherapeutics

- **BLACK BOX WARNING**: risk for developing tardive dyskinesia and parkinsonian-like symptoms, the risk increases the longer it's in use, treatment should not exceed 12 weeks and be discontinued immediately if signs of movement disorder, **Report involuntary movement of the eyes, face, or limbs immediately**
- **Contrindicated**: in the presence of disorders in which stimulation of GI motility is dangerous (GI hemorrhage, mechanical obstruction, new surgery on the GI tract, or perforation),
- dopamine- associated activity affects the CNS & can cause depression (mild- severe w. suicidal ideation), use with caution
- **Contraindicated** in pt.s w. pheochromocytoma b/c the drug can cause hypertensive crisis
- **Safe to administer to pt**.s with hx of impaired hepatic function if renal function is normal
- Safety and effectiveness not established in infants and children
  - EPS is more common in children, use with caution

ADRs

- Most serious reaction is EPS (dystonic reaction and tardive dyskinesia and parkinsonian-like symptoms d/c in pt. exhibiting movement d/o
- Neuroleptic malignant syndrome
- More common: Depression, dizziness, diarrhea, and hypoglycemia in DM
- Less common: galactorrhea, amenorrhea, gynecomastia, impotence secondary to hyperprolactinemia, and fluid retention r/t elevations in aldosterone
- Incidence of ADRs correlated with the dose and duration of therapy

Drug interactions: Largely related to its cholinergic and dopaminergic activity

- Additive CNS depression
- Increased r/f EPS when taking other drugs with a r/f EPS
- Drugs with anticholinergic effects reverse the action of metoclopramide
- Hypertensive crisis if administered with MAOIs

Clinical Use and Dosing:

GERD: principal effect is on symptoms of postprandial and daytime heartburn

- For adults, for symptoms throughout the day 10 mg taken 30 minutes prior to each meal and at bedtime is recommended
- If symptoms are confined to specific situation (after evening meal): 10 to 20 mg dose prior to that meal or at bedtime
- Patient who are more sensitive to the therapeutic dose (older adults) 5mg/dose
- Neonatal 0.1 to 0.15 mg/kg/dose Q 6 hrs
- GERD in infants and children 0.4 to 0.8 mg/kg/day divided in 4 doses (30 minutes prior to teach meal)

Nausea and Vomiting

- Action on the chemoreceptor trigger zone to prevent NV
- Post-op NV in children 14 years old or younger, older children, and adults
- For high doses (as with chemo), pretreat with diphenhydramine to prevent EPS

Diabetic Gastroparesis

- Dose 10 mg 30 minutes AC and HS for 2 to 8 weeks
- Route of administration dependent of severity of symptoms
- If early: PO is adequate
- If more severe: Parenteral therapy 10 mg IV over 1 to 2 minutes for up to 10 days may be needed before PO therapy can be initiated
- Rectal formulations available
- Be cognizant that renal impairment is common in DM, dose adjustments for CCr <40

Rational Drug Selection

- Efficacy: higher cost and increased ADRs, difficult to justify its use in place of H2Ras or PPIs
- Length of therapy: Not used for management of GERD is Tx must be long-term (8 weeks)
- Concomitant Diseases: Cautious use for those at r/f EPS, renal disease

Monitoring

- Renal function assessed before therapy
- Educate about EPS

Patient Education

- Drowsiness, avoid driving until response is known
- CNS depression with ETOH and additive CNS depression
- Notify immediately if involuntary movement of the eyes, face, or limbs occurs
- Change in mood should be reported (depression/suicidal ideation)
- Avoid ETOH, NSAIDs, large meals, fatty foods, chocolate, caffeine, citrus, ad good or fluid intake within 3 hours of HS

Drug	Indication	Available Dosage	Dosage Schedule	Notes
Metoclopramide Reglan Generic	GERD	Tablets: 5 mg Tablets: 10 mg Syrup: 5 mg/5 mL Injection: 5 mg/mL	*Adults:* Treatment: 10–15 mg qid (30 min before meals and at bedtime) Prophylaxis: 20 mg at bedtime *Children:* 0.4–0.8 mg/kg/d in 4 divided doses (30 min before meals and at bedtime)	Some patients respond to doses as low as 5 mg. Dose not to exceed 0.5 mg/kg/d. Therapy not to exceed 8 wk. Patients with CCr <40 mL/min, initiate therapy with half the recommended dose.
	Diabetic gastroparesis		*Adults:* 10 mg qid (30 min before meals and at bedtime)	

➢ Proton pump inhibitors (PPI's):

Esomeprazole (Nexium), Lansoprazole (Prevacid), Omeprazole (Prilosec), Pantoprazole (Protonix), Rabeprazole (Aciphex), Dexlansoprazole (Dexilant, Kapidex)

- Antisecretory drugs used to treat conditions characterized by hyperacidity
- Used to treat: erosive gastritis, GERD, and Zollinger-Ellison syndrome, part of the multidrug regiment for short-term treatment of active PUD (especially duodenal ulcers caused by H. pylori)

Pharmacodynamics: MOA:

- Do not exhibit anticholinergic or H2 blockade but suppress gastric acid secretion
- Inhibition of basal and stimulated acid secretion (regardless of stimulus) by suppressing gastric acid secretion via reduction of H+ secretion and inhibition of the H +/K+/ATPase enzyme system at the secretory surface of the parietal cell itself to block the final step of H+ secretion.

Pharmacokinetics

- PPI's are ironically acid labile & so most are formulated as EC tablets or granules
- All should be taken on an empty stomach before a meal, in the AM if possible
  - Food decreases absorption
- All drugs are distributed to the parietal cells of the stomach
- Extensively metabolized by CYP450 system (CYP2C19 and CYP3A4)
- Little unchanged drug is excreted in urine, 90% of metabolites excreted in urine
- Significant biliary excretion
- Older adults have decreased elimination rates of all drugs (decreased renal function, associated with age)

Pharmacotherapeutics

- Caution: only true contraindication is hypersensitivity to ingredients
- Extensively metabolized in the liver (CYP450), use caution hx of hepatic dysfunction & the elderly
  - No dose adjustments required
- Omeprazole is Pregnancy Category C
- Lansoprazole, esomeprazole, pantoprazole, and rabeprazole are Pregnancy Category B
- Safety and efficacy of pantoprazole and rabeprazole have not been established in children younger than 12

ADRs

- Typically, well tolerated when used for short-term treatment
  - Dizziness, drowsiness, ABD pain, constipation, diarrhea, and flatulence

- PPI's **long term** can cause nutrient deficiencies such as Iron (iron deficiency anemia), vitamin B12, and calcium (all need an acidic environment for absorption)
- places increased risk for megaloblastic anemia and
- hip-fractures (osteoporosis) in at risk persons (age & female gender),
- concern for cellular level changes increased risk for gastric cancers
    - Atrophic gastritis with long term omeprazole use is a risk factor for gastric carcinoid tumors
        - PPI long-term may also increase risk of C.Diff, salmonella, and campylobacter infections
        - Short-term use ^ risk of pneumonia

Stomach acid provides a natural defense against microbial pathogens

Drug Interactions

- Related to CYP450 system
- PPIs may decrease the effects of atazanavir, indinavir, and nelfinavir (coadministration not recommended)
- All PPI's may interfere w/ drugs that need gastric acid for absorption such as ketoconazole, ampicillin, digoxin, and iron salts,
- Increased monitoring of INR is required if warfarin is administered w/ PPI's
- Plavix and omeprazole **Black Box Warning** Regarding poor metabolizers of CYP2C19 and concurrent administration of medications that interfere with CYP2C19.
- Co-administration of Plavix and Omeprazole decreases effectiveness of **Plavix by 46%**
- **may lead to clot formation-**
- **FDA issued warning DO NOT USE CONCURRENTLY** with **omeprazole** & **esomeprazole**…
- use PPI w/ less CYP2C19 function such as **dexlansoprazole, lansoprazole, and pantoprazole**

Clinical Use and Dosing

Duodenal and Gastric Ulcers

- Uncomplicated gastric ulcers include testing and treating for H. pylori and acid-suppressive therapy with PPIs
- Lansoprazole, omeprazole, esomeprazole, and rabeprazole used for treatment of active duodenal ulcer and active benign gastric ulcer
- Once-daily dosing taken before a meal, preferably in the morning
- Triple regimens combine a PPI with two antibiotics for 14 days
- Quadruple regiment combines a PPI with two antibiotics and bismuth subsalicylate

GERD

- All should be taken on an empty stomach before a meal, in the AM if possible
    - Food decreases absorption
- Stepwise therapy, Step-up or step-down approach may be used
- Steps based on symptom relief and degree of esophageal damage
- Treatment begins with lifestyle modifications and OTC antacids or H2Ras (most have tried before seeking care)
- ACG recommends, 8 weeks of PPIs for symptoms relief and healing of erosive esophagitis associated with GERD
- Standard one a day therapy started and tailored to symptoms relief.
- If nighttime symptoms are an issue dosing can be adjusted or twice a day dosing can be used
- Another option would be to add an H2RA before bed
- Failure to achieve symptom relief after 3 months or s/s of complications refer to GASTRO
- PPIs may mask symptoms of gastric CAs
- Alarm symptoms (dysphagia, painful swallowing, noncardiac chest pain, weight loss, hematemesis, and choking) suggest endoscopy as part of the initial evaluation
- All PPIs are approved to treat GERD
- Once daily dosing is taken 30 to 60 minutes before breakfast, Length of therapy is 8 weeks, An addition 4 weeks may be needed

- Nonresponsive patients require referral
- Patients may need long-term intermittent therapy for GERD

Hypersecretory Conditions (Zollinger-Ellison Syndrome)

- All PPIs can be used for treatment
- Usually requires higher dosing than GERD or PUD

Rational Drug Selection

- Drug interactions: Lansoprazole is be choice for patients taking drugs metabolized by CYP450 system
- All PPIs interaction with atazanavir
- Other drugs interfere with Warfarin
- Difficulty swallowing: omeprazole, esomeprazole, and lansoprazole capsules can be opened, and intact granules added to applesauce
- Do not crush or chew granules
- Lansoprazole comes in a quick-dissolve tablet (Prevacid SoluTab) or as granules for suspension
- For tube feeding: omeprazole capsules or granules mix with an acidic juice or water

Monitoring

- Monitor disease being treated
- Test for H. pylori
- Stop therapy for 2 weeks before undergoing urea breath testing to diagnose H. pylori (false-negative)

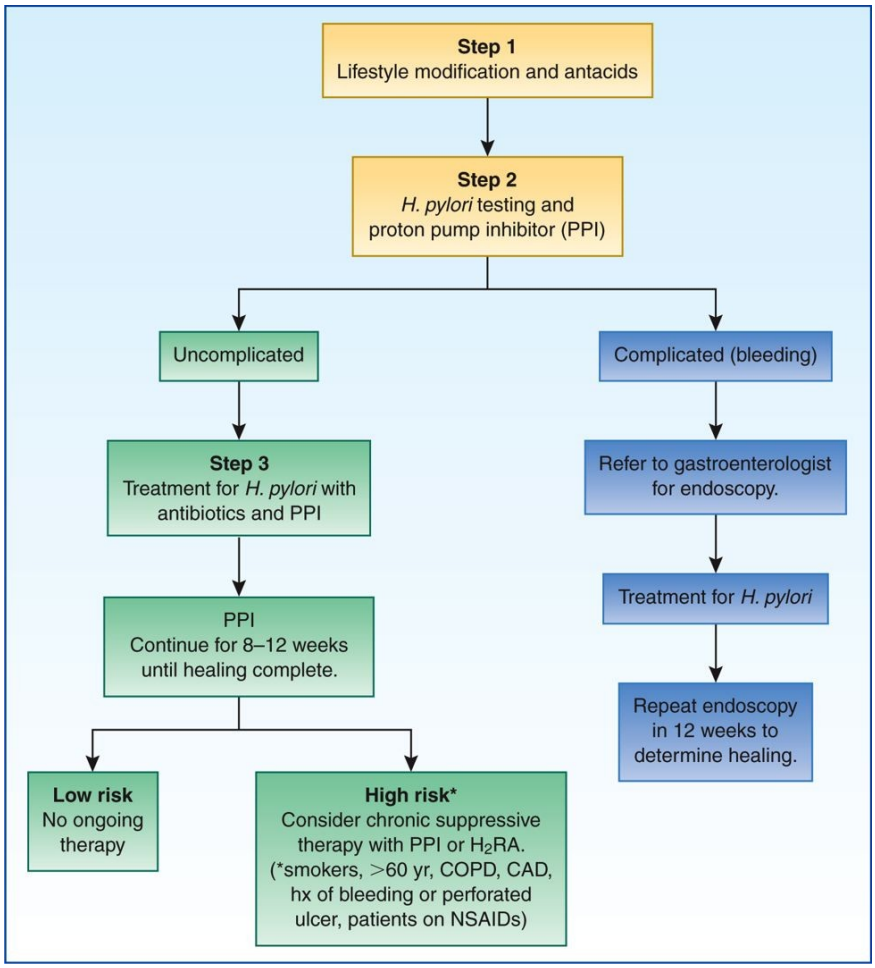
Patient Education

- Take exactly as prescribed
- Take before a meal
- Drugs taken daily; AM administration preferred
- May be taken with antacids
- Drowsiness or dizziness
- Report onset of black, tarry stools (GI bleed), diarrhea, ABD pain, or persistent HA, may indicate progression of disease or ADRs
- Lifestyle modifications

Drug	Indication	Dosage Form	Initial Dose	Maintenance Dose
Esomeprazole Nexium	GERD with erosive esophagitis	Capsules: delayed-release: 20, 40 mg Granules for suspension: 10, 20, 40 mg/packet	*Adolescents and adults:* 20 or 40 mg daily for 4–8 wk. Maintenance: 20 mg daily for 4 wk. *Children:* <20 kg: 10 mg daily for 8 wk; >20 kg: 10–20 mg daily for 8 wk	20 mg/d
	Symptomatic GERD *H. pylori* eradication/ prevent duodenal ulcer		*Adults:* 20 mg daily for 8 wk *Children 1–11 yr:* 10 mg daily for 8 wk Triple therapy: Esomperazole 40 mg daily + amoxicillin 1 g bid + clarithromycin 500 mg bid for 7–10 d	
Lansoprazole Prevacid	Duodenal ulcer *H.pylori* eradication/ prevent duodenal ulcer	Capsules, delayed-release: 15, 30 mg Tablet: 15, 30 mg Suspension: 3 mg/mL	*Children 12 yr and adults:* 15 mg qd for 4 wk *H. pylori:* Triple therapy: Lansoprazole 30 mg bid + amoxicillin 1 g bid + clarithromycin 500 mg tid for 10 d Double therapy: Lansoprazole 30 mg tid + amoxicillin 1 g tid for 14 d	15 mg qd
	Benign gastric ulcer		30 mg daily for <8 wk	
	Erosive esophagitis		30 mg daily for <8 wk	15 mg qd
	Hypersecretory disorders		60 mg daily	Up to 90 mg bid; doses >120 mg/d must be divided
	Erosive esophagitis		*Adults:* 30 mg once daily for up to 8 wk *Children 12–17 yr and adults:* 30 mg once daily for up to 8 wk *Children 1–11 yr:* ≤30 kg: 15 mg daily for up to 12 wk >30 kg: 30 mg daily for up to 12 wk	If not healed, repeat dose for additional 8 wk Increase to 30 mg bid in patients who remain symptomatic after 2 wk of therapy

	Gastric ulcer associated with NSAID therapy		*Adults:* 30 mg daily for up to 8 wk	15 mg/d for up to 12 wk
	GERD	Prevacid OTC: Capsules, delayed-release: 15 mg	*Children 12–17 yr and adults:* 15 mg daily for up to 8 wk *Children 1–11 yr:* ≤30 kg: 15 mg daily for up to 12 wk >30 kg: 30 mg daily for up to 12 wk	
Omeprazole Prilosec Generic	Duodenal ulcer	Capsules, delayed-release: 10, 20, 40 mg Granules for suspension: 2.5, 10 mg/packet	*Adults:* 20 mg daily for 4–8 wk *Infants and children*: 15–30 kg: 10 mg bid, >30 kg: 20 mg bid *H. pylori:* Triple therapy: Omeprazole 20 mg bid + clarithromycin 500 mg bid + amoxicillin 1 g bid for 10 d Double therapy: Omeprazole 40 daily + clarithromycin 500 mg tid for 14 d; then omeprazole 20 mg daily for 14 additional d	
	Benign gastric ulcer		40 mg daily for 4–8 wk	
	Erosive esophagitis		20 mg daily for 4–8 wk	20 mg qid
	GERD		*Children 2–18 yr:* ≤20 kg: 10 mg daily for 4–8 wk >20 kg: 20 mg daily for 4–8 wk	Note: On a per kg basis doses are higher for children than adults.
	Hypersecretory disorders		*Adolescents > 16 yr and adults:* 60 mg daily	Up to 120 mg tid; doses >80 mg/d must be divided
Pantoprazole Protonix	Symptomatic GERD	Tablets: delayed-release: 20 40 mg Granules for suspension: 40 mg/packet	20–40 mg daily for 7–10 d	20 mg/d
	GERD with erosive esophagitis		40 mg daily for up to 8 wk	40 mg/d If not healed, repeat same dose for additional 8 wk
	Hypersecretory disorders		Individualized. 40 mg bid; may treat for up to 2 yr	Doses up to 240 mg/d have been used
Rabeprazole Aciphex	Duodenal ulcers	Tablets, delayed-release: 20 mg	*Adults and adolescents >12 yr:* 20 mg daily after the morning meal for up to 4 wk	If not healed, repeat dose for 4 wk
	GERD		*Adults and adolescents >12 yr:* 20 mg daily for 4 wk	If symptoms, repeat dose for 4 wk
	Erosive esophagitis		20 mg daily for 4–8 wk	If not healed, repeat dose for 4 wk
	H. pylori eradication/ prevent duodenal ulcer		Triple therapy: Rabeprazole 20 mg bid + amoxicillin 1 g bid + clarithromycin 500 mg bid for 7 d	
	Hypersecretory disorders		Individualized: 60 mg daily; may treat for up to 1 yr	Dose up to 100 mg/d or 60 mg bid have been used
Dexlansoprazole Dexilant Kapidex	Erosive esophagitis	Delayed-release capsules: 30, 60 mg 60 mg capsule	Treatment: 60 mg daily for 8 wk Maintenance for healed EE: 30 mg daily for up to 6 mo	Moderate hepatic dysfunction: 30 mg/d Not recommended for children <18 yr
	GERD		30 mg daily for 4 wk	

Stepped-approach algorithm for peptic ulcer disease.



➢ Laxatives

- Six classes of drugs: stimulants, osmotics, bulk-producing laxatives, lubricants, surfactant, and hyperosmolar laxatives (methylnaltrexone (Relistor) mu-opioid receptor antagonist, used for opioid induced constipation)

  All share contraindication of use in the presence of nausea, vomiting, or undiagnosed abdominal pain, or if bowel obstruction is suspected or diagnosed

- All share precautions for dependency, chronic use of laxatives may result in electrolyte imbalances, steatorrhea, osteocalcin, and vitamin and mineral deficiencies

"Laxative abuse syndrome" most common in women w/ depression, personality disorders, or anorexia nervosa.

- Tartrazine sensitivity- may cause allergic reactions including asthma, seen in pts who also have aspirin sensitivity.
- Common adverse reactions: excessive bowel activity, cramping, flatulence, and bloating
- **Few drug interactions**

❖ **Stimulants:** cascara, senna, Bisacodyl, and castor oil

- **Pharmacodynamics: MOA:** Direct action on intestinal mucosa by stimulating the myenteric plexus, releasing prostaglandins and increase cyclic adenosine monophosphate (cAMP), increasing secretion of electrolytes and peristalsis
- **Pharmacotherapeutics:**
  - Bisacodyl Caution: patients with cardiovascular disease

        - bisacodyl is safe during pregnancy
        - Cascara sagrada: Avoid in patients with alcohol intolerance
            - Can cause diarrhea in breastfed infant, enters breast milk
- **Contraindications:** Caster oil is contraindicated in pregnancy- can cause uterine contractions
- **Drug of choice when rapid response is needed**
- **Used most commonly** for constipation associated w/ reduced mobility, constipating drugs, reduce motility, neurogenic bowel r/t to spinal cord injury, & IBS. Also used to bowel prep for radiological or surgical procedures

- **Osmotics:**

magnesium hydroxide, magnesium citrate, sodium phosphate, polyethylene glycol electrolyte solution, and polyethylene glycol (PEG) 3350

- **Pharmacodynamics: MOA:** exerts it effects mainly by drawing water into the intestinal lumen to increase intraluminal pressure, hypertonic salt-based solutions that cause the diffusion of fluid from the plasma into the intestine to dilute the solution to an isotonic state.
    - Magnesium salts also increase cholecystokinin by the duodenum
        - Pharmacokinetics: 30% may be absorbed
        - Widely distributed, cross the placenta, and enter breast milk
        - Metabolized by the liver
    - Sulfate salts are most powerful
    - Polyethylene glycol electrolyte solution is used to cleanse the entire GI tract for diagnostic purposes, to flush poisons, and remove parasites
- **Pharmacotherapeutics:**
    - **Contraindications: Magnesium hydroxide is contraindicated in any degree of renal insufficiency** (kidney might not be able to excrete the Magnesium)
    - **Contraindications: Hypermagnesemia, hypocalcemia, and heart block**
    - Magnesium hydroxide is Pregnancy Category B
    - PEG 3350 should not be used in children under the age of 4
    - **Polyethylene glycol electrolyte solution to treat constipation in children is contraindicated** r/t electrolyte disturbance
- **Second drug of choice when rapid response is needed**

Bulk- Producing laxatives: psyllium, methylcellulose, polycarbophil

- **Pharmacodynamics:** Safest and most physiological, action is similar to adding fiber into diet
- **MOA:** consist of natural and semisynthetic polysaccharides and cellulose when combined with water in the intestine produces mechanical distension resulting in increased peristalsis
- May be used for long term management of simple chronic constipation, situations when straining should be avoided, and management of chronic, watery diarrhea
- **Pharmacokinetics:** No absorption
- **Pharmacotherapeutics:** Caution: pts. w/ narrowed esophageal or intestinal lumen,
    - avoid in patients who are impacted
-
- **Drug of choice when rapid response is not needed, and long-term management is needed (suited for older adults and pregnancy)**

Lubricants: Mineral oil

- **MOA:** lubricates the intestine to facilitate passage of stool by retarding colonic absorption of fecal water and soften the stool
- **Pharmacodynamics:** Major concerns of decrease absorption of fat-soluble vitamins
- **Pharmacokinetics:** No distribution, local action
- **Pharmacotherapeutics:** Caution: very young, older adults and those with dysphasia are at high risk for lipid aspiration pneumonia,
    - avoid use during pregnancy due to decrease in absorption in fat-soluble vitamins = hypothrombinemia in newborn

Surfactants: docusate sodium, docusate calcium, docusate potassium

- Referred to as stool softeners
- **Pharmacodynamics: MOA:** reduce surface tension of the oil- water interface on the stool and facilitate admixture of fat and water into the stool, producing an emollient action
- Most beneficial when feces are hard or dry, situations when passing stool is painful, when straining should be avoided
- Can be administered safely to ALL ages and during pregnancy- no precautions or contraindications
    - **Pharmacokinetics:** No distribution, local action
    - **Pharmacotherapeutics:** No specific contraindications or precautions

Hyperosmolar laxatives 'misc.': Glycerin, Lactulose

- **Pharmacodynamics: MOA:** hyperosmotic compound that draws water from extravascular spaces into the lumen of the intestine, resulting in more liquid stool
- **Glycerin** is used to treat fecal impactions caused by neurogenic bowel, in which the bowel is filled with feces but cannot be evacuated
    - **Pharmacokinetics:** 80% metabolized by the liver
- **Lactulose** is used to treat chronic constipation in the elderly
    - only laxative used to treat hepatic encephalopathy: lowers the pH of the colon, which in turn inhibits the diffusion of ammonia across colonic membranes
- **Pharmacokinetics:** No distribution, local action
- **Pharmacotherapeutics: Caution:** in volume depletion
    - Older adults are arf dehydration
    - lactulose can cause hyperglycemia- caution with DM

❖ **Chloride Channel Activators:** Lubiprostone (Amitiza)

- **Pharmacodynamics: MOA:** is a bicyclic fatty acid derived from prostaglandin E1 that acts by specifically activating CIC-2-chloride channels on the apical aspect of gastrointestinal epithelial cells, producing a chloride-rich fluid secretion.
- These secretions soften the stool, increase motility, and promote spontaneous bowel movements.
- Used for chronic idiopathic constipation, IBS with constipation in women aged 18 and older, and chronic opioid-induced constipation in adults with chronic noncancer pain
- **Pharmacotherapeutics:** Most common ADR for Lubiprostone is nausea, may be relieved by administration with food
    - **Adverse effects:** nausea (may be relived w. food), diarrhea, dyspnea can occur in patients taking 24mcg BID

❖ **Opioid- Receptor Antagonists: Methylnaltrexone**

- **Pharmacodynamics: MOA:** Antagonist to the mu-receptor in the GI track and treats the constipation patients experience when taking opioids without affecting the analgesic effect of opioids
    - Does not cross the BBB therefore does not affect kappa receptor analgesic effect of opioids
- **Pharmacokinetics:** Metabolized in the liver into 5 metabolites
- **Pharmacotherapeutics: Caution:** can cause opioid withdrawal, monitor closely
- **Adverse reactions:** abdominal pain, nausea, diarrhea, hyperhidrosis
- Do not take with other opioid antagonists, additive effects

Rapid Response and Short Term

- Stimulants are the drug of choice when rapid response is needed
    - All are equally effective, short term
- Osmotic laxative work quickly as well
    - Magnesium hydroxide produces evacuation in 6 to 8 hours and is generally administered before HS
    - PEG 3350produces a BM in 1 to 3 days
- Docusate sodium is the preferred surfactant

Slower Response and Long Term

- Bulk-forming laxatives are the drug of choice when rapid response is not needed and long term management with the least ADRs
    - Well suited for older adults
    - Product choices depends upon patient's acceptance of texture and taste
- Lactulose can be used if the bulk forming laxatives do not work or not well tolerated
    - Works well in older adults and children

Special Indications

- Polyethylene glycol electrolyte solutions is the best drug for cleansing the bowel for radiological or surgical procedures
    - Highly effective and no electrolyte disturbances
- Lactulose: effective in reducing ammonia levels in the blood and brain with patient who have hepatic encephalopathy
- Lubiprostone is indicated for the treatment of constipation associated with IBS in women aged 18 and older or chronic idiopathic constipation, opioid induced constipation with chronic noncancer pain
- Methylnaltrexone is indicated for constipation associated with chronic opioid use

Pregnancy

- Bulk forming laxatives and surfactant are safe and effective for regular use throughout pregnancy and for lactating women
- Magnesium hydroxide is Preg Cat B and can be used intermittently

Monitoring

- For patients taking laxatives for more than 6 months, laboratory assessment of fluid and electrolytes, K, and Mg l
- Careful monitoring r/t hepatic encephalopathy
- For older adults taking lactulose for more than 6 months: lab assessment of K, Cl, and CO2

Patient Education

- Do not take laxatives with NV or ABD pain, may indicate serious d/o

- Rapid acting laxatives are best taken in the morning
- Slower acting ones are best taken at bedtime
- Taking on an empty stomach with a full glass of water produces more rapid results
- Do not crush or chew EC tablets
- Liquids can be given with fruit juice
- Be careful when pouring bulk forming powder: hypersensitivity reactions have occurred when powder inhaled
- Lifestyle management

Drug	Indication	Dosage Form	Dose	Notes
Bisacodyl Dulcolax	Constipation	Tablets: 5 mg Suppositories: 10 mg	*Children >12 yr and adults:* Tablets: 10–15 mg once daily PR: 10 mg once daily *Children 2–11 yr:* Tablets: 5 mg (0.3 mg/kg) once daily PR: 5 mg once daily *Children <2 yr:* PR: 5 mg single dose	Up to 30 mg have been used as preparation for bowel procedure
Cascara sagrada	Constipation	Tablets: 325 mg	*Children >12 yr and adults:* Tablets: 300 mg–1 g once daily Extract tablet: 200–400 mg daily	Tablets and liquids come in combinations with docusate and milk of magnesia
Castor oil Generic	Constipation	Oil	*Children >12 yr and adults:* 15–60 mL in a single dose *Children 2–11 yr:* 5–15 mL in a single dose	
Docusate calcium Surfak	Constipation	Capsules: 50, 240 mg	*Calcium* *Adults:* 240 mg once daily *Children >6 yr:* 50–150 mg once daily	
Docusate potassium (Diocto-K, Dialose, Kasof)		Capsules: 100, 240 mg	*Potassium* *Adults:* 100–300 mg once daily *Children >6 yr:* 100 mg once daily at bedtime	
Docusate sodium (Colace)		Capsules: 50, 100 mg Syrup: 60 mg/15 mL Liquid: 150 mg/15 mL	*Sodium* *Children >12 yr and adults:* 50–500 mg once daily *Children 6–11 yr:* 40–120 mg once daily *Children 3–6 yr:* 20–60 mg once daily *Children <3 yr:* 10–40 mg Suppository: *Adults:* 50–100 mg or 1 suppository	
Glycerin PR	Constipation	Suppositories: Adult, Pediatric	*Children >6 yr and adults:* 2–3 g as suppository or 5–15 mg as enema *Children <6 yr:* 1–1.7 g as a suppository or 2–5 mL as enema	

Lactulose (Cephulac, Chronulac, Enulose) Generic	Constipation	Syrup: 10 g lactulose/ 15 mL	*Adults:* 15–30 mL once daily *Children:* 7.5 mL once daily	May use up to 60 mg/d; unlabeled use
	Hepatic encephalopathy		*Adults:* 30–45 mL tid–qid *Children and adolescents:* 40–90 mL daily in divided doses *Infants:* 2.5–10 mL daily in divided doses	May be given q1–2 h initially; goal is 2–3 soft stools/d; discontinue if diarrhea develops
Magnesium salts Epsom salts Magnesium hydroxide Milk of magnesia Magnesium citrate	Constipation	Granules: 40 mEq Mg^{2+} per 5g Chewable tablets: 300 and 600 mg Liquid: 80 mEq Mg^{2+} per 30 mL Liquid: 77 mEq Mg^{2+} per 100 mL	*Hydroxide (milk of magnesia)* *Children >12 yr and adults:* 30–60 mL once daily (in concentrate: 10–20 mL once daily) *Children 6–11 yr:* 15–30 mL in single or divided doses *Children 2–5 yr:* 5–15 mg in divided doses	
	Bowel prep or bowel cleanout if impacted		*Citrate* *Children >12 yr and adults:* 240 mL *Children 6–11 yr:* 100 mL	
Polyethylene glycol/ electrolyte solution (Colyte, GoLYTELy)	Bowel prep	In oral solution or powder for oral solution	*Adults:* 240 mL every 10 min (up to 4 L) until fecal discharge is clear with no solid material *Children:* 25–40 mg/kg/h until fecal discharge is clear with no solid material	Tastes salty, making it difficult to take. Ice it. May suck on hard candy or breath mints to make more palatable.
PEG 3350 (Miralax)	Constipation	Powder for solution: 17 g/dose	*Adults:* oral 17 g daily *Children >4 yr:* 0.7–1.5 g/kg daily, do not exceed 17 g	Mix with 4 to 8 oz of beverage
Psyllium (Fiberall, Konsyl, Metamucil)	Constipation	Powder: 3.4 g psyllium/5 mL, 6 g psyllium/5 mL Wafers: 1.7 g psyllium, 3.4 g psyllium Effervescent powder: 3.4 g/5 mL	*Adults:* 1–2 tsp/packet/wafer (3–6 g psyllium) in or with a full glass of liquid bid–tid *Children >6 yr:* 1 tsp/packet/wafer (1.5–3 g psyllium) in or with ½–1 glass of liquid bid–tid	Up to 30 g/d in divided doses Up to 15 g/d in divided doses
Senna (Senokot, Fletcher's Castoria)	Constipation	Tablets: 187 mg Granules: 326 mg Syrup: 218 mg/5 mL Liquid: 33.3 mg/mL	*Children >12 yr and adults:* 360 mg–2 g at bedtime *Children 6–11 yr:* 50% of adult dose *Children 1–5 yr:* 33% of adult dose Rectal: *Children >12 yr and adults:* 30 mg qid–bid	Fletcher's Castoria lists a children's dose of 10–15 mL (6–15 yr) and 5–10 mL (2–5 yr)

➢ GERD (Treatment, dosing, and patient education)

o Treatment

- Goals of treatment: reduce or eliminate symptoms, heal any esophageal lesions, manage, or prevent complications such as stricture, Barret's esophagus, or esophageal carcinoma, and prevent relapse
- Meeting these goals requires both lifestyle modification and drug therapy
- Each of the contributing factors (decreased LES tone, acid, peristalsis, and mucosal exposure) are targets for pharmacological management
- Drugs to Improve LES tone:
  - metoclopramide and bethanechol: Not considered for monotherapy
    - Most useful in combination with aid suppression with gastroparesis

        - Do not heal esophageal lesions
    - Antacids: dual purpose: improve LES tone and increase gastric pH
- Drugs to Reduce the Amount of Acid
    - Two main classes: H2RAs and PPIs
    - H2RA: act on parietal cells to decrease the amount of acid
        - May be used as maintenance acid suppression or heartburn therapy without erosive GERD
        - ACG guidelines recommend a trial of nighttime H2Ras for patient taking daytime PPIs to treat nighttime reflux
    - PPI: First-line therapy for GERD
        - Improve esophageal healing
- Drugs to Improve Peristalsis
    - A few patients continue to report symptoms despite reduced acid secretion
    - Prokinetics: improve LES tone and peristalsis
    - Metoclopramide may provide some benefit but has ADRs
- Drugs to Decrease Mucosal Exposure
    - Cytoprotective agents: sucralfate (Carafate) and misoprostol (Cytotec)

o Dosing

- PPI therapy: First line therapy for moderate or severe GERD or erosive disease
    - Length of therapy 8 weeks
    - No major differences in response between the PPIs
    - Maintenance PPI should be prescribed for patients who have symptoms that recur after PPI therapy is d/c or complications such as erosive esophagitis or Barrett's esophagitis
    - Reassess in 6 to 12 months to determine if weaning can occur
    - Patients who do not respond to PPIs need referred to GASTRO
- H2RA Dosing:
    - Cimetidine 800 mg BID or 400 mg QID with meals and before bed x 12 weeks
    - Famotidine 20 mg BID up to 6 to 12 weeks
    - Nizatidine 150 mg BID
    - Ranitidine 150 mg BID (no longer available in the US)

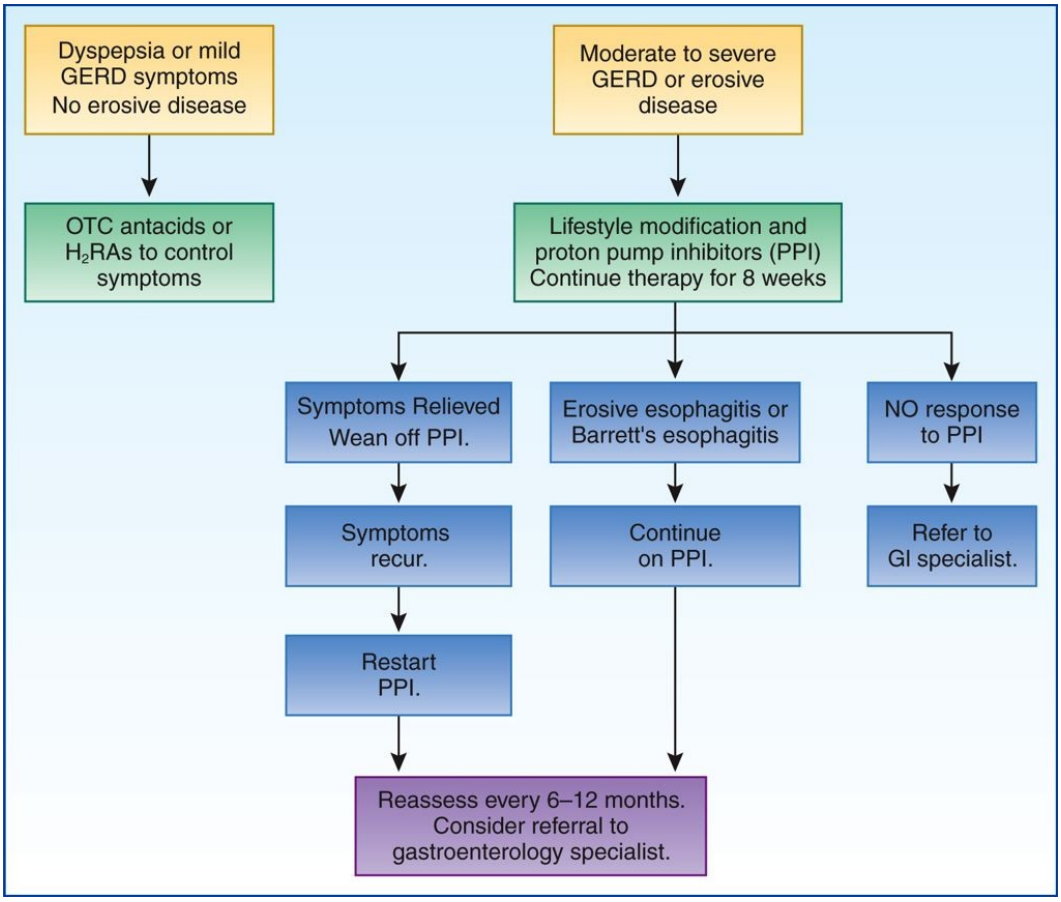
o Patient Education

- **PPI Patient Education**:
    - All should be taken on an empty stomach before a meal, in the AM if possible
        - Food decreases absorption
    - Stepwise therapy, Step-up or step-down approach may be used
    - Steps based on symptom relief and degree of esophageal damage
    - Treatment begins with lifestyle modifications and OTC antacids or H2Ras (most have tried before seeking care)
    - ACG recommends, 8 weeks of PPIs for symptoms relief and healing of erosive esophagitis associated with GERD
    - Standard one a day therapy started and tailored to symptoms relief.
    - If nighttime symptoms are an issue dosing can be adjusted or twice a day dosing can be used
    - Another option would be to add an H2RA before bed
    - Failure to achieve symptom relief after 3 months or s/s of complications refer to GASTRO
    - PPIs may mask symptoms of gastric CAs
    - Alarm symptoms (dysphagia, painful swallowing, noncardiac chest pain, weight loss, hematemesis, and choking) suggest endoscopy as part of the initial evaluation
    - All PPIs are approved to treat GERD

- Once daily dosing is taken 30 to 60 minutes before breakfast, Length of therapy is 8 weeks, An addition 4 weeks may be needed
- Nonresponsive patients require referral
- Patients may need long-term intermittent therapy for GERD

- **H2RA Patient Education:**
  - Should be taken w/ meals or immediately after & at bedtime, daily doses are best @ bedtime,
  - take 1 hour away from other drugs,
  - & two hours away from sucralfate
  - OTC preparations should not be taken for more than 2 wks without consulting healthcare provider
  - Report black tarry stools- may indicate GI bleeding.
  - Sore throat, diarrhea, rash, confusion, or hallucinations should be reported promptly (might need dosage adjustment or discontinuation),
  - advise pt. to stop smoking (interferes with absorption of H2RA & increases gastric secretion)

Algorithm for gastroesophageal reflux disease (GERD)



PUD (Treatment, Dosing, and Patient Education)

- Largely treated in the primary care setting
- Risk factors: smoking, habitual NSAID or ETOH use, significantly caused by H. pylori infection which requires eradication
- Two categories duodenal ulcers and gastric ulcers
- All recommended treatment regimens include a combination of a PPI and antimicrobial therapy

- Antimicrobials: clarithromycin, tetracycline, amoxicillin, levofloxacin, and metronidazole
- Given in a tiple drug regimen (Two antimicrobials and a PPI x 14 days) or a quadruple drug regimen that includes bismuth subsalicylate
- Acid suppression by the PPI in conjunction with the antimicrobial help alleviate ulcer relate symptoms, heals gastric mucosal inflammation, and may enhance the efficacy of antimicrobial agent against H. pylori
- Goals of treatment: eradicate H. pylori, heal ulcers, manage, or prevent complications such as GI bleeding or gastric carcinoma, prevent relapse, and reduce or eliminate symptoms
- Meeting these goals requires both lifestyle modification and drug therapy
- Algorithm: outlines the steps in treating peptic ulcers, consists of healing the ulcer and preventing ulcer recurrence through eradication of H. pylori
    - Step 1: lifestyle modification, OTC antacids or H2RA
    - Step 2: h. pylori testing and PPI if uncomplicated Step 3
    - Step 3: Treatment for H. pylori with ABX and PPI
        - PPI continue for 8-12 weeks until healing complete
            - If low risk: No ongoing therapy
            - If high risk: Consider chronic suppressive therapy with PPI or H2RA (smokers, >60 y/o, COPD, CAD, Hx of bleeding or perforated ulcer, patients on NSAIDs)
    - If complicated (bleeding)-Refer to GASTRO for endo-Tx for H. Pylori-Repeat endo in 12 weeks to determine healing

- Antacids: Aluminum hydroxide/magnesium hydroxide combination
    - Maalox 15-30 mL PRN 1 hr and 3 hr after meals and before bed
- PPIs-multidrug regimen for ulcers, short-term therapy
    - Take on an empty stomach before meals
- Education:
    - Stop taking PPIs two weeks before H pylori testing ARF false negative
    - Take all medications are prescribed
    - ADRs
    - Reasons why the drugs are being taken

IBS (Treatment, Dosing and Patient Education)

- Laxatives: stimulants and chloride channel activators
- Stimulants: cascara, sena, bisacodyl, and castor oil
    - Caster oil: contraindicated in pregnancy
- Chloride channel activator: Lubiprostone (Amitiza)
    - IBS with constipation in women 18 and older
    - Nausea, take with food
    - Nausea diarrhea, and dyspnea in doses 24 mcg BID
- Do not take laxatives with NV or ABD pain, may indicate serious d/o
- Rapid acting laxatives are best taken in the morning
- Taking on an empty stomach with a full glass of water produces more rapid results
- Do not crush or chew EC tablets
- Liquids can be given with fruit juice
- Lifestyle management

Traveler's Diarrhea (Treatment, Dosing, and Patient Education)

- Bismuth subsalicylate and loperamide (Imodium)
- Bismuth subsalicylate: two tablets or 2 Fl oz before each meal and at bedtime (QID) for up to 3 weeks
    - 524 mg every 30 minutes for up to 8 doses
- Prevention and treatment
- High-risk areas: Central and South American, Africa, Middle East, Mexico, and Asia
- E. Coli is the most common causative agent followed by Campylobacter, Shigella, and Salmonella
- Decrease ASA intake while taking bismuth subsalicylate: salicylate toxicity
- Can turn the tongue and stool black/gray: not cause for concern, normal finding
- Loperamide (Imodium): Adults 4 mg initially, 2 mg after each loose stool, not to exceed 8 mg/day OTC or 16mg/day Rx

Black box warning for metoclopramide:

- **BLACK BOX WARNING**: risk for developing tardive dyskinesia and parkinsonian-like symptoms, the risk increases the longer it's in use, treatment should not exceed 12 weeks and be discontinued immediately if signs of movement disorder, **Report involuntary movement of the eyes, face, or limbs immediately**

Step wise progression of PPIs: antacids and lifestyle modifications followed by PPI trial

Effectiveness of different PPIs: No significant differences between effectiveness of PPIs

Triple therapy for H.Pylori Eradication:

- All include a BID dose of PPI
- Most popular ABX are clarithromycin (Biaxin) and amoxicillin
- Clarithromycin plus amoxicillin plus a PPI all BID for 10-14 days is most favorable
- Pregnant women should not take tetracycline ARF fetal harm
- Children younger than 8 should not take tetracycline ARF discoloration of teeth

	Drug 1	Drug 2	Drug 3	Drug 4	Comments
Triple therapy	Proton pump inhibitor bid	Clarithromycin 500 mg bid or metronidazole 500 mg bid	Amoxicillin 1 g bid	—	Treat for 10–14 d Usual first-line therapy
Triple therapy	Proton pump inhibitor bid	Clarithromycin 500 mg bid	Metronidazole 500 mg bid	—	Treat for 7–14 d Use as first-line therapy in penicillin-allergic patients
Quadruple therapy	Proton pump inhibitor bid *or* Ranitidine 150 mg bid	Metronidazole 250 mg qid	Tetracycline* 500 mg qid	Bismuth subsalicylate 525 mg qid	Treat for 10–14 d Usually used as second-line therapy in patients who fail first-line therapy
Levofloxacin-based triple therapy	Proton pump inhibitor bid	Levofloxacin 250–500 mg bid	Amoxicillin 1 gm bid		Treat for 10–14 d Second-line or rescue therapy

Chapter 34 GERD and PUD

Misoprostol use for duodenal ulcer prophylaxis and treatment

Misoprostol (Cytotec):

Prophylaxis and Treatment of Duodenal Ulcers Associated with NSAID Use: not as reliable for Tx of ulcers from other causes

- NSAIDs inhibit prostaglandin synthesis and damage the mucosal lining of the stomach
- R/f ulcer formation
- Misoprostol is FDA approved for this use (prophylaxis or treatment)
- Dosage 200 mcg QID with food ACHS
- If unable to tolerate 100 mcg QID with food ACHS
- Misoprostol with food, Misoprostol given for the duration of NSAID therapy, can cause diarrhea, if persists x1WK notify provider
- Continue therapy even if you feel better

- **Pharmacodynamics:** A methyl analogue of prostaglandin E1
- Inhibits gastric secretion through inhibition of histamine-stimulated cyclic adenosis monophosphate (AMP) production
- Inhibits basal and nocturnal gastric acid secretion and acid secretion in response to stimuli
    - meals, histamine, and coffee by binding to prostaglandin E receptors, mucosal protective qualities.
- Mucosal protective qualities as well
    - Binds to prostaglandin E receptors which facilitate mucus and bicarbonate production
- Can be taken with food and still be effective
- **Pharmacokinetics**
- Rapidly and extensively absorbed after PO administration (distribution unknown)
- Rapidly converted into a free acid
- Does not affect CYP450 system
- Half-life is 20-40 mins however renal impairment doubles its half-life
- Metabolite excreted in urine
- **Pharmacotherapeutics**
- Use with caution with caution in renal impairment (no routine adjustments)
- Use with caution in the elderly r/t decreased renal function
- **Pregnancy X:** Can produce uterine contractions endangering pregnancy causing spontaneous abortion, premature birth, or birth defects. Women of childbearing age should have a negative pregnancy test before prescribed and start misoprostol on day 2 or 3 of menstrual period. If pregnancy is suspected, drug should be stopped immediately.
- **ADRs** GI or gynecological
    - Most common: diarrhea, ABD pain, nausea, and flatulence
    - Postmenopausal bleeding, spotting, cramps, hypermenorrhea, menstrual disorder, and dysmenorrhea
- **Drug/Drug interactions:** R/f increased diarrhea when given with magnesium based antacid
- Indicated for prophylaxis and treatment of duodenal ulcers associated with NSAID use

Mechanism of action for Lubiprostone

- **Pharmacodynamics: MOA:** is a bicyclic fatty acid derived from prostaglandin E1 that acts by specifically activating CIC-2-chloride channels on the apical aspect of gastrointestinal epithelial cells, producing a chloride-rich fluid secretion.
- These secretions soften the stool, increase motility, and promote spontaneous bowel movements.
- Used for chronic idiopathic constipation, IBS with constipation in women aged 18 and older, and chronic opioid-induced constipation in adults with chronic noncancer pain