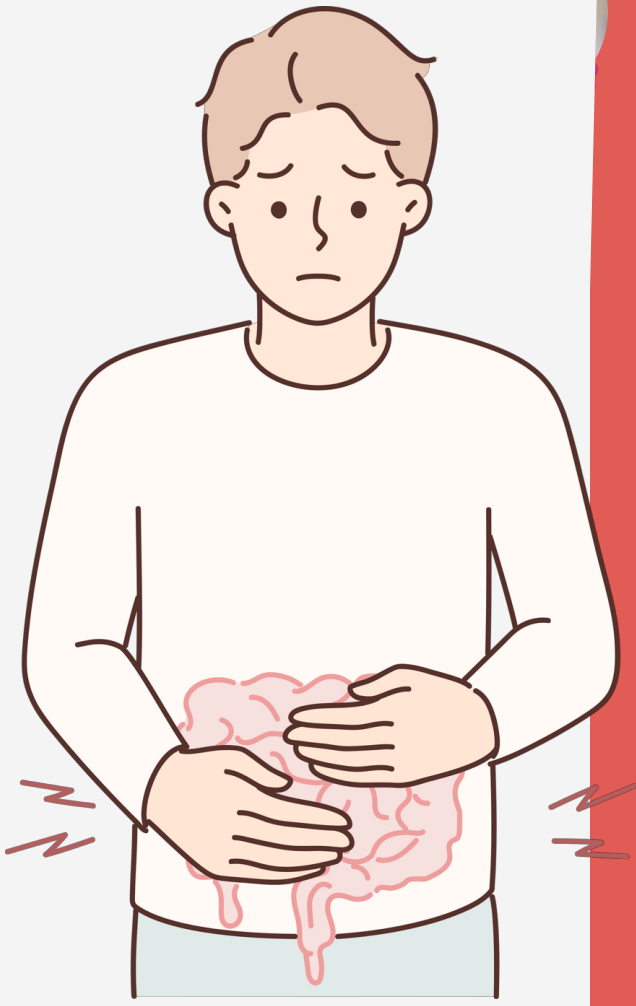
PHARMACOLOGY 201 | DR. MORA

Gastrointestinal System

Laxatives, Antidiarrheals, GI Supportive Medications



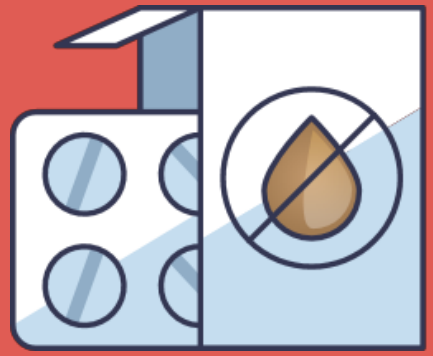
Learning Objectives

1. Define the major classes of laxatives and antidiarrheals based on their mechanisms of action
2. Identify the first-line pharmacologic treatments for common GI conditions, including constipation, diarrhea, and hepatic encephalopathy
3. Differentiate between osmotic, stimulant, bulk-forming, and stool softener laxatives in terms of clinical use
4. Recognize contraindications for antimotility agents, particularly in infectious diarrhea
5. Explain the role of lactulose and rifaximin in reducing ammor. hepatic encephalopathy

Learning Objectives

6. Describe the components and purpose of standard H. pylori eradication therapy
7. Compare adverse effect profiles of laxative classes to guide safe prescribing in vulnerable populations (e.g., renal impairment, pregnancy)
8. Apply pharmacologic principles to select appropriate agents for bowel preparation before procedures
9. Identify key drug interactions and safety concerns for commonly used GI medications, such as QT prolongation with loperamide and clarithromycin
10. Recognize the long-term management benefits of ursodeoxycholic cholestatic liver diseases

Bowel Regimen Drugs



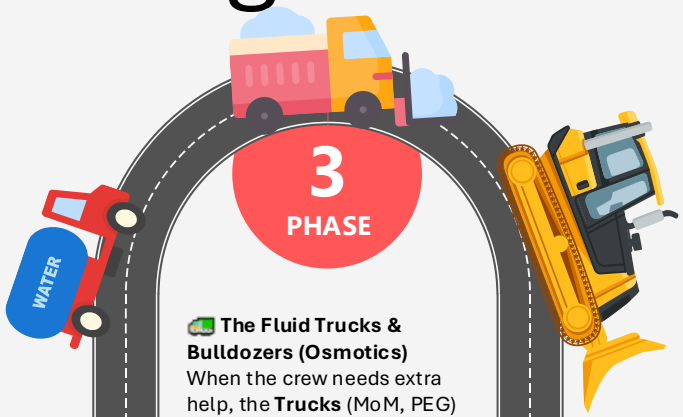
Bowel Regimen Drugs

1 PHASE

The Prep Crew (Psyllium & Docusate)
Before the big job starts, Psyllium shows up with bags of **fiber** to **bulk up** and keep things smooth.
Docusate follows, spraying everything down with **detergent** to **soften and liquefy** the worksite so the crew won't struggle.

The Traffic Controllers (Senna & Bisacodyl)
Sometimes traffic slows down. Senna and Bisacodyl jump in to **wave their flags**, signaling the colon to **move faster**. They're best on a **set schedule** to prevent total standstill.

PHASE 2



3 PHASE

The Fluid Trucks & Bulldozers (Osmotics)
When the crew needs extra help, the **Trucks** (MoM, PEG) roll in with **gentle water delivery**, filling the area to loosen things up.
If things are backed up bad, the **Plows** (Magnesium citrate) arrive to **push harder**. Still no progress? Call in the **Bulldozers** (High-volume PEG, Lactulose) to clear the way completely, though it might get messy!

Navy Seals
When stool is stuck at the exit, **Docusate and Bisacodyl team up** for a precision strike.
Docusate preps the scene, **softening the target** and reducing resistance.
Bisacodyl follows with the final push, **activating the muscles** to force a swift evacuation.

PHASE 4

The Fire Hose Crew (Enemas)
Low on volume? Fleets or mineral oil give a **quick blast**. Need full force? The big guns—**Tap water or soap suds enemas**—flush the whole worksite.

PHASE 5

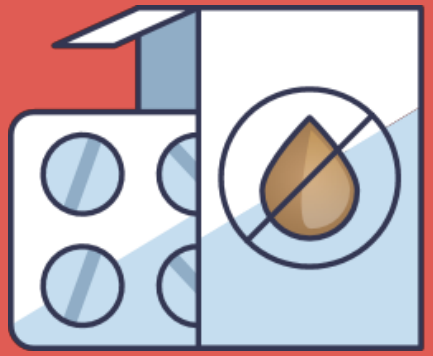
Bulk Forming Laxatives

Bulk-Forming Laxatives

- Psyllium (Metamucil), Methylcellulose (Citrucel), Calcium Polycarbophil (FiberCon)
  - MOA: bulk-forming laxatives absorb water and increase fecal mass
    → increase the softening and consistency of fecal mass
- 1st-line agents in the management of constipation → low cost, safe, effective, and easy to use
- Side Effects: may cause distention or flatulence (usually diminishes over several days)

Board Tip

First-line therapy for chronic constipation and safe in pregnancy.



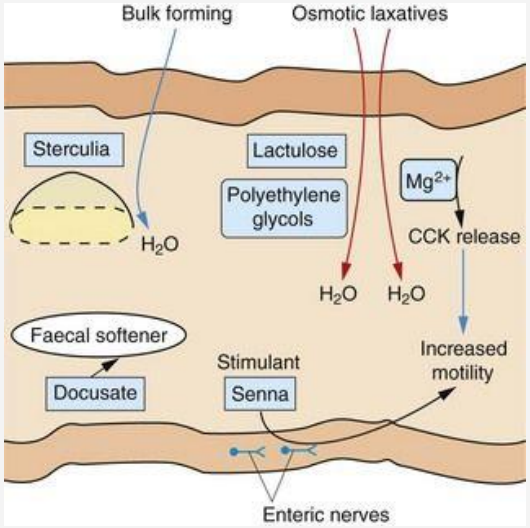

NOW
Digestive
Psyllium Husk Powder
Soluble Fiber
Excellent Source of Fiber
NON GMO Project VERIFIED
NET WT. 24 OZ. (680 g)
Vegetarian/Vegan
K


Easy Flip Top Cap
CITRUCEL
METHYLCELLULOSE FIBER THERAPY FOR IRREGULARITY
• Gentle and clinically proven effective*
• Gives you additional fiber to help relieve occasional constipation
• Fiber for irregularity that won't cause excess gas**
100 Fiber caplets

Bulk-Forming Laxatives

Mechanism of Action

Agent	Mechanism
Psyllium **Methylcellulose**	• Indigestible fibers absorb water → form bulky, soft stool → stimulate peristalsis



Bulk-Forming Laxatives

Indications

Agent	Indications
Psyllium **Methylcellulose**	• First-line for mild chronic constipation • IBS with constipation (IBS-C) • Preventative use in patients who should avoid straining

Bulk-Forming Laxatives

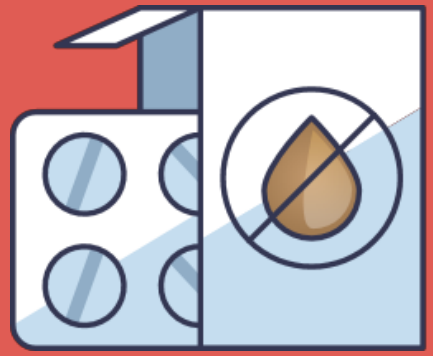
Adverse Effects & Contraindications

Agent	Adverse Effects	Contraindications
Psyllium **Methylcellulose**	• Bloating • Flatulence • Rare esophageal obstruction if taken without water	• Bowel obstruction • Dysphagia

Board Tip

First-line therapy for chronic constipation and safe in pregnancy.

Stool Softener




NDC 57896-401-01
GERI CARE®
STOOL SOFTENER
DOCUSATE SODIUM 100 mg
Compare to the active ingredient in COLACE® Regular Strength*
100 Softgels
Drug Facts
Active ingredient (in each softgel) Purpose
Docusate Sodium 100 mg ..... Stool Softener Laxative


Rugby®
NDC 0536-1304-85
Docusate Sodium Liquid
50 mg/5 mL
Stool Softener
Cherry Flavored
16 FL OZ (473 mL)

Stool Softener

Mechanism of Action

Agent	Mechanism
Docusate Sodium	• Surfactant that lowers stool surface tension → allows water and fat to soften stool

Surfactant Laxatives

- Docusate Sodium (Colace), Docusate Calcium (Surfak), Mineral Oil
  - MOA: lower surface tension of stool → allowing water to easily enter the stool
- generally, less effective than psyllium; therefore, usually combined with stimulant laxatives for greater efficacy → Senokot-S (docusate/senna)
- generally well-tolerated; however, mineral oil may cause lipoid pneumonia if aspirated

Stool Softener

Indications

Agent	Indications
Docusate Sodium	• Prevent straining in patients post-MI, post-surgery, or with hemorrhoids

Stool Softener

Adverse Effects & Contraindications

Agent	Adverse Effects	Contraindications
Docusate Sodium	• Mild diarrhea • Abdominal cramping	• Bowel obstruction

Board Tip

Ineffective if no water intake and does not treat active constipation well—used preventively.

Stimulant Laxatives

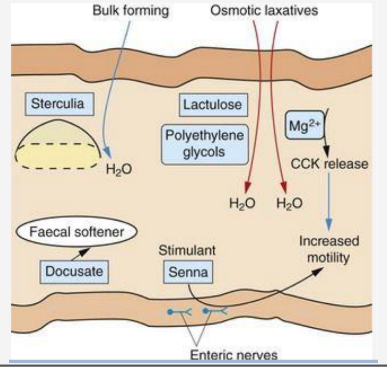
Stimulant Laxatives

- Bisacodyl tablet or suppository (Dulcolax), Senna (ExLax, Senokot), Cascara (Nature's Remedy)
    - MOA: stimulate fluid secretion and colonic contraction → bowel movement
        - onset (PO): 6-12 hours / onset (PR): 15-60 mins
- stimulant laxatives are generally recommended as "PRN" agents for patients with incomplete response to osmotic laxatives
- Side Effects: (1) cramping and (2) "laxative bowel" is a condition characterized by dependence on stimulant laxatives for bowel function


NDC 57896-555-10
HEALTH STAR
THE SENSIBLE CHOICE FOR PRICE AND HEALTH
SENNA-PLUS
STANDARDIZED SENNA CONCENTRATE
DOCUSATE SODIUM
NATURAL VEGETABLE LAXATIVE
WITH STOOL SOFTENER
Compare to active ingredients in SENOKOT-S®*
1000 Tablets
Directions
Age
Adults and children 12 years of age and older
Children under 12 years
Other information
Inactive ingredients
Dist. By: Geri-Care


MAJOR®
NDC 0904-6748-80
Compare to the active ingredient in Dulcolax® Laxative Tablets*
Bisacodyl USP
5 mg
Stimulant Laxative
Gentle, Dependable Constipation Relief
Actual Size
1000 Tablets
Comfort Coated Tablets
*This product is not manufactured or distributed by Sanofi-Aventis Deutschland GMBH, owner of the registered trademark Dulcolax® Laxative Tablets. 50844 REV01 9832716

Stimulant Laxatives



Mechanism of Action

Agent	Mechanism
Senna **Bisacodyl**	• Directly stimulates enteric neurons → increases acetylcholine-regulated peristalsis and fluid secretion

Stimulant Laxatives

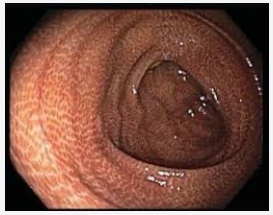
Indications

Agent	Indications
Senna **Bisacodyl**	• Short-term relief of constipation (avoid chronic use) ↳ avoid "laxative bowel" ↑ dependency

Stimulant Laxatives

Adverse Effects & Contraindications

Agent	Adverse Effects	Contraindications
Senna **Bisacodyl**	• Abdominal cramping • Electrolyte disturbances • Long-term use → Melanosis coli (benign pigmentation of colon)	• Bowel obstruction • Acute abdominal pain of unknown origin



Board Tip

Know that stimulant laxatives are inappropriate for chronic constipation due to dependence risk.

Osmotic Laxatives

Osmotic Laxatives

- PEG = Polyethylene Glycol (Miralax), Magnesium Hydroxide (MOM), Lactulose, Sorbitol (70%)
  - MOA: non-absorbable osmotic agents → increase secretion of water into the intestinal lumen → soften stools and promote defecation
- safe and effective for acute and chronic constipation → onset of action: 24 hours
  - Magnesium Citrate (11.6 GM of magnesium) → more rapid response in acute constipation (30 min - 3 hours)
  - Milk of Magnesia (MOM) contains 2.4 GM of magnesium / 30 ml
- magnesium containing laxatives should be avoided in patients with chronic renal insufficiency
  - Magnesium Citrate and MOM may cause hypermagnesemia in chronic renal insufficiency
- Lactulose, Sorbitol are non-digestible carbohydrates → may cause bloating, cramps, flatulence
- PEG (Miralax) is well-tolerated → does not cause flatulence


UNIT DOSE
Delivers 30 mL
NDC 0121-1154-30
LACTULOSE
SOLUTION USP 20 g/30 mL
Indication: For the treatment of constipation. See Insert.
(01) 0 03 01211 15430 9
Package Not Child-Resistant
Rx ONLY
PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605
UNIT DOSE
Delivers 15 mL
NDC 0121-4157-15
LACTULOSE
SOLUTION USP 10 g/15 mL
Indication: For the treatment of constipation. See Insert.
(01) 0 0301214 57715 0
Package Not Child-Resistant
Rx ONLY
PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605


Perrigo
Compare to MiraLAX® active ingredient*
NDC 45802-868-03
Polyethylene Glycol 3350
Powder for Solution
Osmotic Laxative
Relieves Occasional Constipation/Irregularity
Softens Stool
Unflavored Powder
Grit Free
NET WT 17.9 OZ (510 g)
30 Once-Daily Doses


Walgreens
Dye-Free
Magnesium Citrate
SALINE LAXATIVE
ORAL SOLUTION
SUGAR FREE
LOW SODIUM
10 FL OZ (296 mL)


GERI CARE
Original
Milk of Magnesia
SALINE LAXATIVE
• Original Flavor
• Effective Overnight Relief
12 FL OZ
355 mL

Osmotic Laxatives

Mechanism of Action

Agent	Mechanism
Lactulose	• Non-absorbable sugar (synthetic disaccharide) → pulls water into intestinal lumen • Metabolized by gut flora → acidifies colon → converts NH_3 to NH_4^+ → promotes ammonia excretion
Polyethylene Glycol (PEG)	• Large, inert osmotic polymer → increases water retention in stool → softens stool and increases motility
Magnesium Citrate **Milk of Magnesia**	• Magnesium draws water into intestines → increases peristalsis and stool volume

Osmotic Laxatives

Indications

Agent	Indications
Lactulose	• Chronic constipation • Hepatic encephalopathy (first-line for reducing ammonia)
Polyethylene Glycol (PEG)	• Occasional and chronic constipation • Colonoscopy preparation
Magnesium Citrate	• Acute constipation • Rapid bowel evacuation (colonoscopy prep)
Milk of Magnesia	• Occasional constipation • Often used for overnight relief

Osmotic Laxatives

Adverse Effects and Contraindications

Agent	Adverse Effects	Contraindications
Lactulose	• Flatulence • Bloating • Severe diarrhea → risk of dehydration and electrolyte abnormalities	• Galactosemia • Use caution in diabetics (contains sugars)
Polyethylene Glycol (PEG)	• Rare electrolyte imbalance in prolonged use	• Bowel obstruction • Toxic megacolon
Magnesium Citrate & Milk of Magnesia	• Hypermagnesemia (especially in CKD)	• Renal failure, • Bowel obstruction • Severe dehydration

• lactulose contains galactose
• galactosemia: inability to metabolize galactose

• lactulose contains fructose and lactulose sugars

• non-obstructive dilation of the colon → colonic inflam
• may be caused by ulcerative colitis, Crohn dz, C. diff

Board Tip

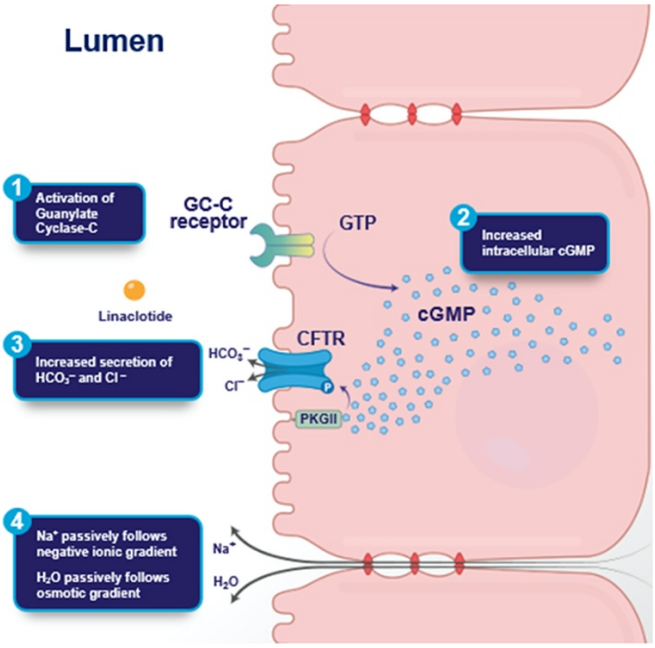
Osmotic laxatives are commonly tested with hepatic encephalopathy and pre-procedure bowel prep questions.

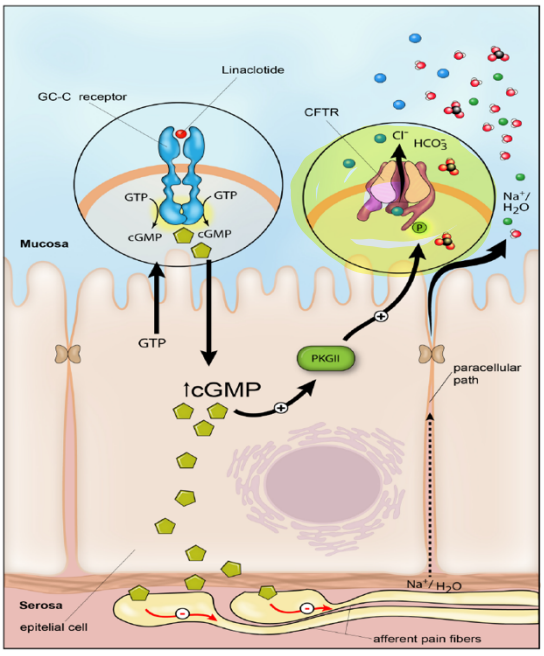
↳ lactulose

↳ magnesium citrate
↳ PEG

Chloride Secretory Agents

- Linaclotide (Linzess), Lubiprostone (Amitiza)
  - Linaclotide (guanylate cyclase agonist) → activates GC-C receptor → increases cGMP → cGMP stimulates secretion of chloride and bicarbonate into intestinal lumen → increases intestinal fluid by drawing Na^+ / H_2O and accelerates transit
  - Lubiprostone activates chloride channel → stimulates secretion of chloride and bicarbonate into intestinal lumen → increases intestinal fluid by drawing Na^+/H_2O and accelerates transit
- Dosage and Administration
  - Linaclotide (Linzess): 145 mcg PO daily (Onset: 12-24 hours)
  - Lubiprostone (Amitiza): 24 mcg PO BID (Onset: 24-48 hours)
- Side Effects
  - Linaclotide (Linzess) bloating, diarrhea / Lubiprostone (Amitiza): nausea, diarrhea
- Cost: Linzess (30 capsules) - $450 / Amitiza 24 mcg (30 capsules) - $200





Peripherally Acting Mu-Opioid Receptor Antagonists (PAMORA)

- Methylnaltrexone (Relistor) and Naloxegol (Movantik) → block peripheral opioid receptors (GI tract) without affecting central analgesia
- FDA-approved for treatment of opioid-induced constipation in patients taking opioids for chronic non-cancer pain, who have not responded to conventional laxatives
  - severe abdominal pain and bowel perforation may be associated with PAMORA use in cancer and bowel obstruction
- Methylnaltrexone: 8-12 mg SC daily / 450 mg PO daily (dosage adjustment in renal insuff)
- Naloxegol (Movantik): 12.5-25 mg PO daily (dosage adjustment in renal insuff)
- Efficacy: Methylnaltrexone SC formulation is more effective than oral Naloxegol and oral Methylnatrexone.
- Cost: Relistor 150 mg (30 tabs) $680 / Relistor Injectable: 12 mg (14 syringes): $2000
  Movantik 25 mg (30 tabs): $350
- Side Effects: abdominal pain, nausea, diarrhea, flatulence

Antidiarrheals

Antidiarrheals

Antimotility Agents

- Loperamide (Imodium), Diphenoxylate w/Atropine (Lomotil) → opioid analogs of meperidine (Demerol) that have opioid-like action on intestinal motility
    - MOA: activate opioid receptors → inhibit peristalsis, prolong transit time, reduce fecal volume, increase viscosity, and diminish fluid and electrolyte loss
- Loperamide (Imodium) - OTC
    - Dose: 4 mg PO initially, then 2 mg PO after each loose stool (max dose: 16 mg/day)
    - Side Effects: dizziness (1%), constipation (2-5%), abdominal cramps (<3%), nausea (3%)
- Diphenoxylate w/Atropine (Lomotil) – Rx
    - atropine is added to discourage abuse with diphenoxylate
    - Dose: 5 mg PO QID prn diarrhea
    - SE: (1-10%) anticholinergic effects (i.e., blurred vision), sedation, abdominal cramps, nausea

Bismuth Subsalicylate (Pepto Bismol) - OTC

- MOA: exerts antisecretory, antimicrobial, and some anti-inflammatory actions
    - Salicylate moiety → produces antisecretory effect
    - Bismuth → exerts antimicrobial effect against gastrointestinal bacteria and viral pathogens
- Side Effects: tongue and fecal discoloration (grayish black)
- Caution: Avoid use in patients allergic to salicylates (aspirin) and pediatrics (Reyes Syndrome)

Antidiarrheals

Mechanism of Action

Agent	Mechanism
Loperamide	• Peripheral mu-opioid agonist → inhibits peristalsis & ↑ anal sphincter tone
Bismuth Subsalicylate Pepto-Bismol Kaopectate	• Coats GI tract, binds toxins • Mild antimicrobial and anti-inflammatory effects
Diphenoxylate-Atropine	• Peripheral mu-opioid agonist → slows GI motility • Subtherapeutic atropine discourages abuse

Antidiarrheals

Indications

Agent	Indications
Loperamide	• Symptomatic treatment of acute diarrhea (non-infectious)
Bismuth Subsalicylate Pepto-Bismol Kaopectate	• Traveler's diarrhea • Dysentery (fevers and bloody diarrhea) • Dyspepsia • H. pylori adjunct
Diphenoxylate-Atropine	• Severe non-infectious diarrhea

Antidiarrheals

Adverse Effects & Contraindications

Agent	Adverse Effects	Contraindications
Loperamide	• Constipation • Rare cardiac arrhythmias with high doses	• Bloody diarrhea • C. difficile infection (colitis)
Bismuth Subsalicylate Pepto-Bismol Kaopectate	• Black stools/tongue • Salicylate toxicity	• Aspirin allergy • Children (Reye syndrome risk)
Diphenoxylate-Atropine	• CNS depression • Anticholinergic effects • Constipation	• Infectious diarrhea

Board Tip

Never use antimotility agents in infectious diarrhea (especially C. difficile).

Gallbladder/ Cholestasis Therapy


Rx
10 x 1 x 10 Tablets
Ursodeoxycholic
Acid Tablets IP
Ursokill-300
Ursodeoxycholic
Acid Tablets IP
Ursokill-300
Ursokill-300

Gallbladder/Cholestasis Therapy

Mechanism of Action

(1) protection of injured cholangiocytes against toxic effects of bile acids,
(2) stimulation of impaired biliary secretion,
(3) detoxification of hydrophobic bile acids, and
(4) inhibition of apoptosis of hepatocytes.

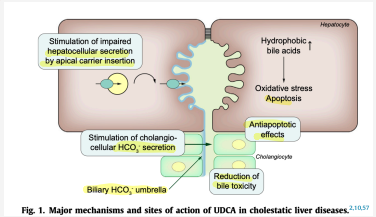
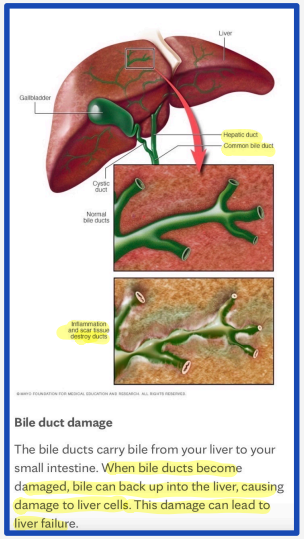


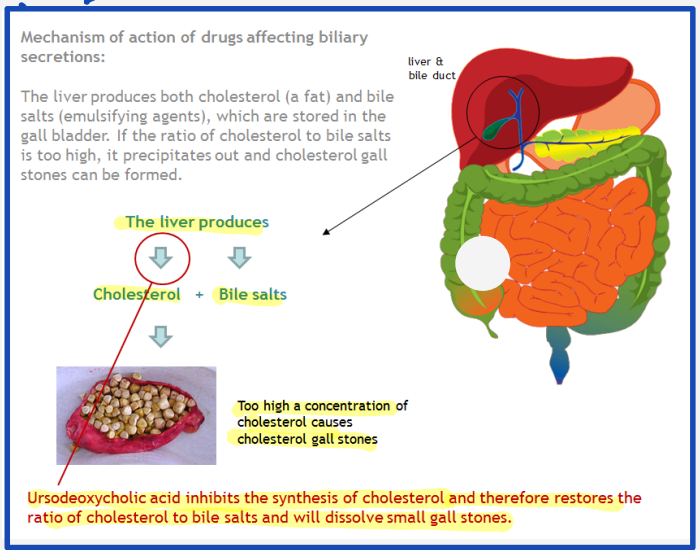
Fig. 1. Major mechanisms and sites of action of UDCA in cholestatic liver diseases.[7,10,57]

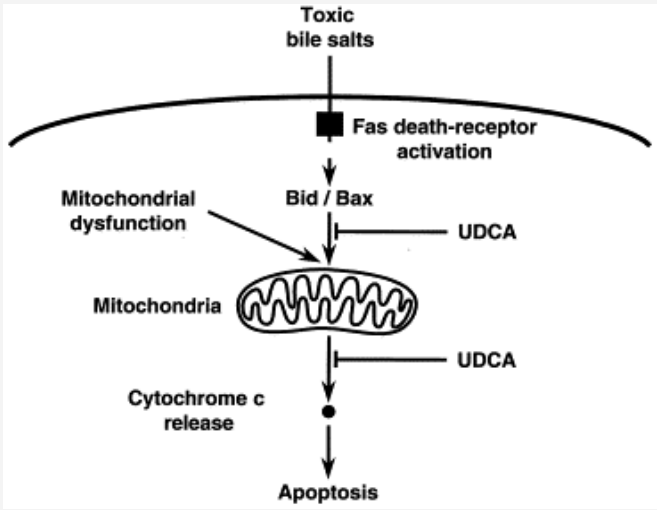
Agent	Mechanism
Ursodeoxycholic Acid (Actigall, Ursodiol)	• Hydrophilic bile salt that stabilizes hepatocyte membranes against toxic bile salts • Decreases cholesterol content in bile → tx in cholesterol gallstones



Bile duct damage

The bile ducts carry bile from your liver to your small intestine. When bile ducts become damaged, bile can back up into the liver, causing damage to liver cells. This damage can lead to liver failure.





Gallbladder/Cholestasis Therapy

Indications

- Currently, the use of UDCA has been approved for the treatment of PBC, cholesterol gallstones, and for prevention of gallstone formation in obese patients undergoing rapid weight reduction, e.g. after bariatric surgery.

Agent	Indications
Ursodeoxycholic Acid	• Primary biliary cholangitis (slows progression) • Cholesterol gallstones in patients unwilling/unable to have surgery

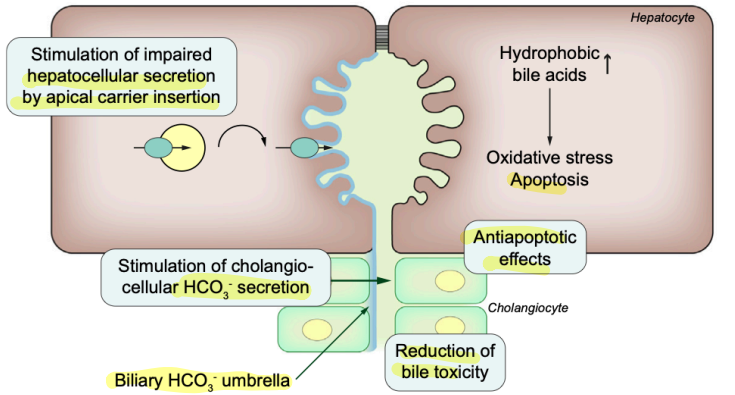
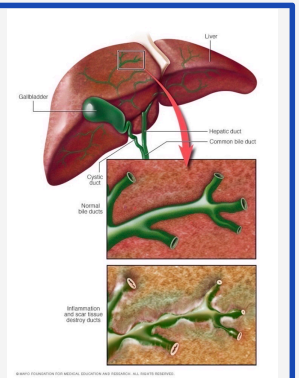


Fig. 1. Major mechanisms and sites of action of UDCA in cholestatic liver diseases.[2,10,57]

Primary biliary cholangitis is an autoimmune disease in which the bile ducts are inflamed and slowly destroyed. Ongoing inflammation in the liver can lead to bile duct inflammation and damage known as cholangitis. Inflammation in the smallest ducts spreads and eventually damages other cells in the liver. As the cells die, they're replaced by scar tissue, also known as fibrosis, that can lead to cirrhosis and liver failure.
Although it affects both sexes, primary biliary cholangitis mostly affects women. Researchers think a combination of genetic and environmental factors triggers the disease. It usually develops slowly. At this time, there's no cure for primary biliary cholangitis, but medicines may slow liver damage, especially if treatment begins early.



Bile duct damage

The bile ducts carry bile from your liver to your small intestine. When bile ducts become damaged, bile can back up into the liver, causing damage to liver cells. This damage can lead to liver failure.

Gallbladder/Cholestasis Therapy

Adverse Effects & Contraindications

Agent	Adverse Effects	Contraindications
Ursodeoxycholic Acid	• Diarrhea (2-9%) • Rare hepatotoxicity	• Calcified gallstones • Complete biliary obstruction

Board Tip Primary billiary cholestatis

First-line therapy for PBC (improves LFTs and survival).

Cirrhosis Medications

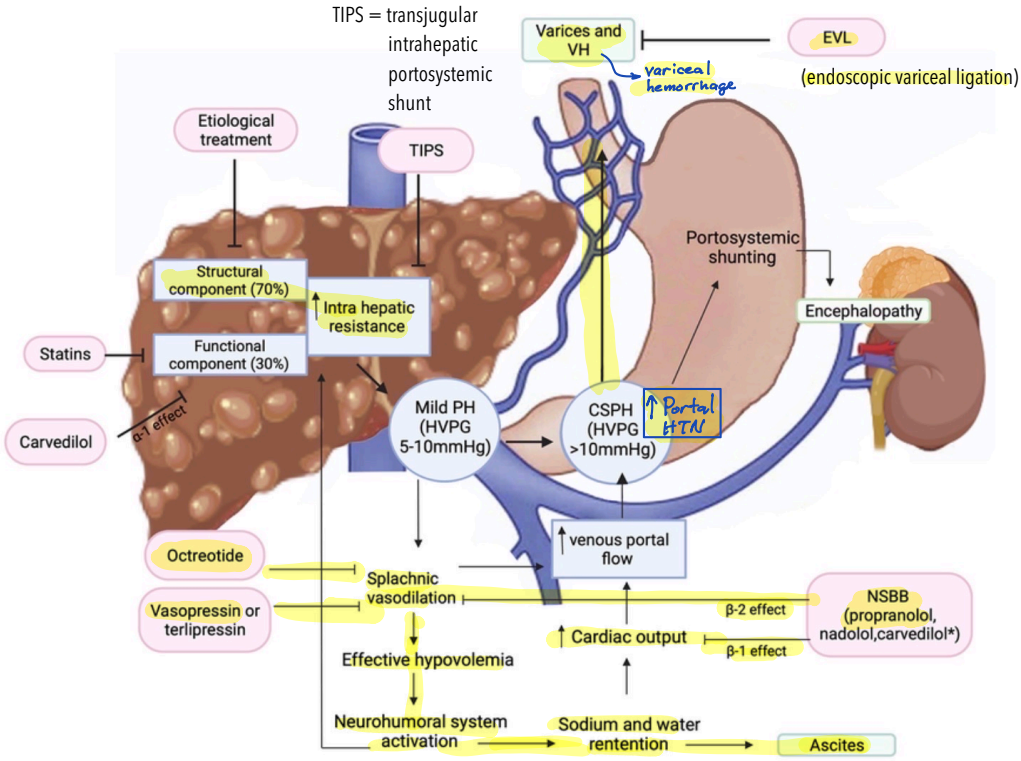

UNIT DOSE
Delivers 30 mL
NDC 0121-1154-30
LACTULOSE
SOLUTION USP 20 g/30 mL
Indication: For the treatment of constipation. See Insert.
(01) 0 03 01211 15430 9
Package Not Child-Resistant
Rx ONLY
PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605
UNIT DOSE
Delivers 15 mL
NDC 0121-4157-15
LACTULOSE
SOLUTION USP 10 g/15 mL
Indication: For the treatment of constipation. See Insert.
(01) 0 0301214 57715 0
Package Not Child-Resistant
Rx ONLY
PHARMACEUTICAL ASSOCIATES, INC.
GREENVILLE, SC 29605


Rifacan 400 Tablets
Rx Rifaximin Tablets 400 mg
10x10 TABLETS
Rifacan 400 Tablets

Major complications of cirrhosis include:

- Variceal hemorrhage
- Ascites
- Spontaneous bacterial peritonitis
- Hepatic encephalopathy
- Hepatocellular carcinoma
- Hepatorenal syndrome
- Hepatopulmonary syndrome

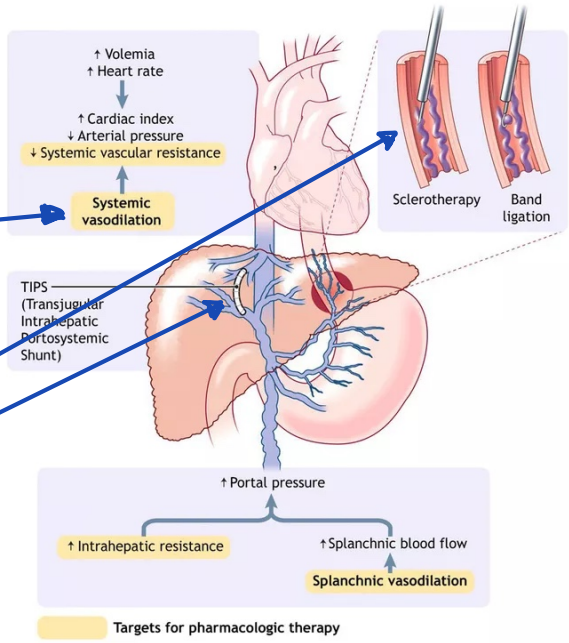
- Once these complications develop, patients are considered to have decompensated cirrhosis.
- Multiple factors can predispose to decompensation in a patient with cirrhosis. The most important risk factor is the development of portal hypertension and uncontrolled chronic liver disease, particularly alcohol use and viral hepatitis.
- Once decompensation has developed, patients should be considered for liver transplantation.

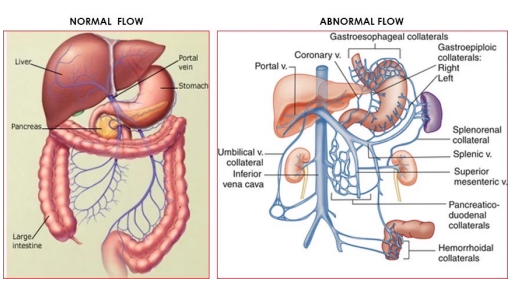


Pathophysiology of portal hypertension and mechanism of action of various therapies used in the management of portal hypertension and variceal hemorrhage. CSPH: clinical significant portal hypertension; EVL: endoscopic variceal ligation; HVPG: hepatic venous portal gradient; NSBB: nonselective beta-blockers; PH: portal hypertension; TIPS: transjugular intrahepatic portosystemic shunt; VH: variceal hemorrhage. *Carvedilol has additional α-1 blockade effect. Source: Created with BioRender.com.

Pathophysiology of portal hypertension in cirrhosis

- Portal hypertension results from increased intrahepatic vascular resistance and portal–splanchnic blood flow.
- In addition, cirrhosis is characterized by splanchnic and systemic arterial vasodilation.
- Splanchnic arterial vasodilation leads to increased portal blood flow and thus elevated portal hypertension.
- An increased hepatic venous pressure gradient leads to the formation of portosystemic venous collaterals.
- Esophagogastric varices represent the most clinically important collaterals given their associated high risk of bleeding.
- Treatment consists of pharmacologic therapy to decrease portal pressure, endoscopic treatment of varices (band ligation or sclerotherapy) to treat variceal bleeding, and creation of a transjugular intrahepatic portosystemic shunt (TIPS) to reduce portal pressure if drug therapy and endoscopic treatment fail

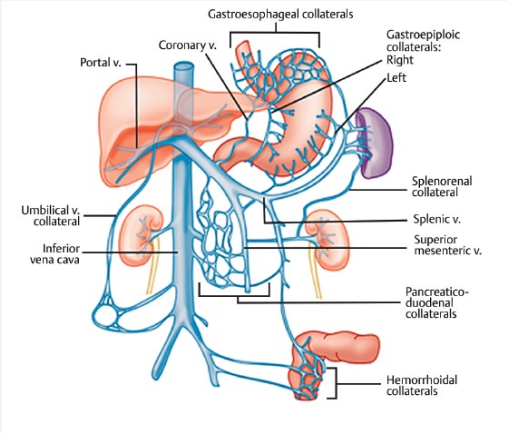


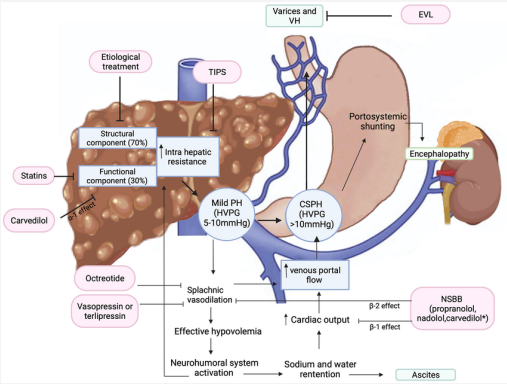


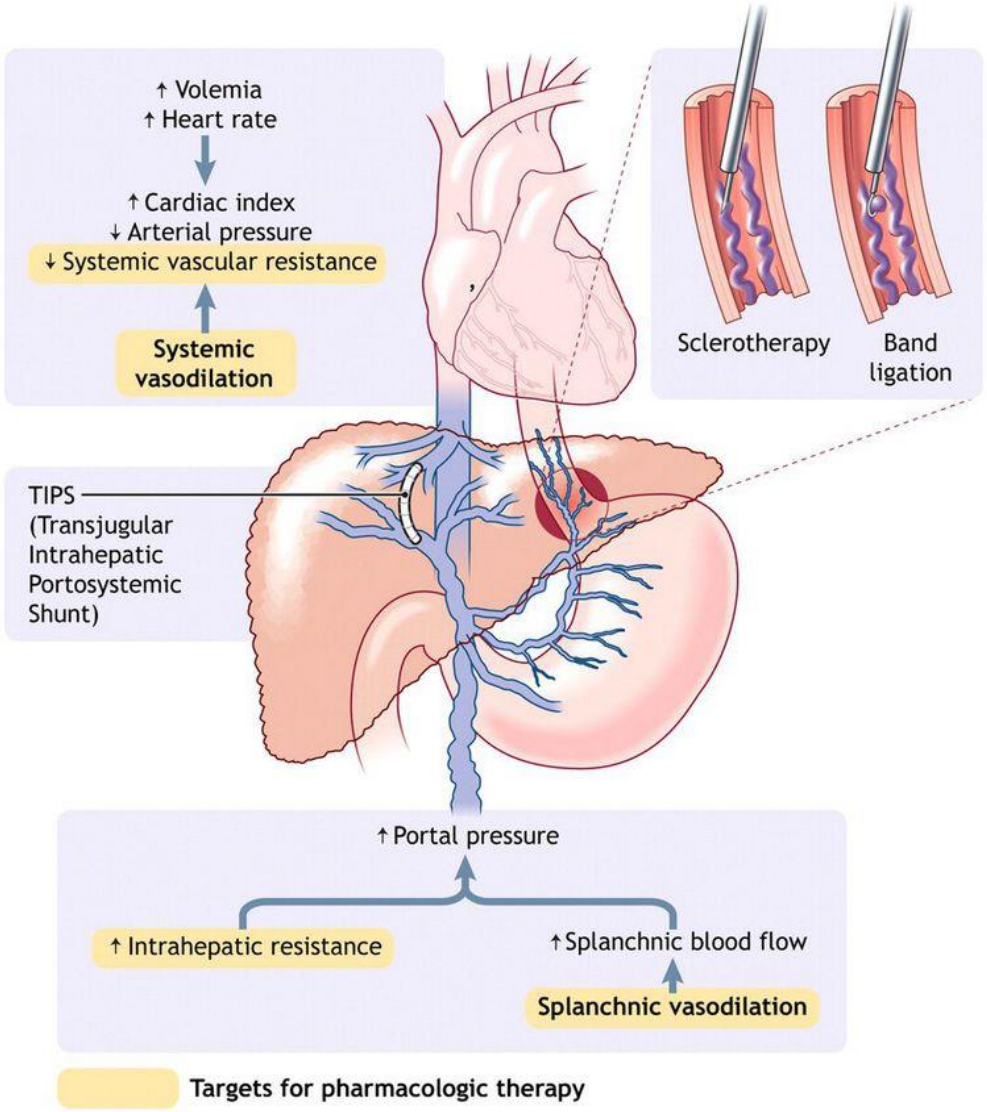
Cirrhosis Medications

Mechanism of Action

Agent	Mechanism
Lactulose	• Acidifies colon → traps NH_3 as NH_4^+ → reduces systemic absorption (NH_4^+ is not absorbable, whereas NH_3 is absorbable → neurotoxic)
Rifaximin	• Non-absorbable antibiotic → decreases ammonia-producing bacteria
Octreotide	• Synthetic somatostatin analog → inhibits splanchnic vasodilation • Decreases portal venous pressure and reduces variceal bleeding
Propranolol	• Non-selective beta-blocker → blocks β1 and β2 receptors • Reduces cardiac output and induces splanchnic vasoconstriction → lowers portal hypertension

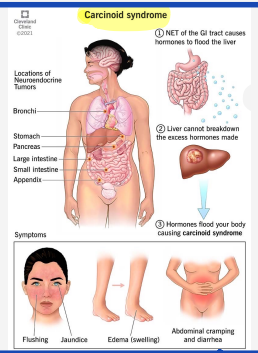

Gastroesophageal collaterals
Coronary v.
Gastroepiploic collaterals: Right
Left
Portal v.
Splenorenal collateral
Umbilical v. collateral
Splenic v.
Inferior vena cava
Superior mesenteric v.
Pancreatico-duodenal collaterals
Hemorrhoidal collaterals


Varices and VH
EVL
Etiological treatment
TIPS
Portosystemic shunting
Structural component (70%)
Intra hepatic resistance
Encephalopathy
Statins
Functional component (30%)
Carvedilol
Mild PH (HVPG 5-10mmHg)
CSPH (HVPG >10mmHg)
Octreotide
Splachnic vasodilation
NSBB (propranolol, nadolol,carvedilol*)
Vasopressin or terlipressin
Cardiac output
β-2 effect
β-1 effect
Effective hypovolemia
Neurohumoral system activation
Sodium and water rentention
Ascites


↑ Volemia
↑ Heart rate
↑ Cardiac index
↓ Arterial pressure
↓ Systemic vascular resistance
Systemic vasodilation
Sclerotherapy
Band ligation
TIPS (Transjugular Intrahepatic Portosystemic Shunt)
↑ Portal pressure
↑ Intrahepatic resistance
↑ Splanchnic blood flow
Splanchnic vasodilation
Targets for pharmacologic therapy

Cirrhosis Medications

A somatostatin analogue is a man made (synthetic) version of somatostatin. Octreotide slows down the production of hormones, especially the growth hormone and serotonin –> controls the symptoms such as diarrhoea and flushing of the skin.



Indications

Agent	Indications
Lactulose	• First-line for hepatic encephalopathy prevention and treatment
Rifaximin	• Add-on therapy for recurrent episodes
Octreotide	• Acute variceal bleeding (first-line) • Carcinoid syndrome (reduces flushing and diarrhea) • VIPoma (controls watery diarrhea)
Propranolol	• Primary and secondary prevention of variceal bleeding • Portal hypertension management • Adjunct in cirrhotic patients with large varices

A VIPoma ris a neuroendocrine neoplasm secreting vasoactive intestinal peptide (VIP), usually presenting with severe watery secretory diarrhea, which can result in hypokalemia and metabolic acidosis and with flushes. Administation of a somatostatin analog (SSA) can decrease the secretory diarrhea, further aiding in the restoration of fluid and electrolyte imbalances.

Cirrhosis Medications

Adverse Effects & Contraindications

Agent	Adverse Effects	Contraindications
Lactulose	• Severe diarrhea • Electrolyte disturbances	• Galactosemia • Use caution in diabetics
Rifaximin	• Nausea • Bloating	• Severe liver dysfunction (caution)
Octreotide	• Gallstones • Hyperglycemia or hypoglycemia	• Caution in diabetes, biliary disease
Propranolol	• Bradycardia • Hypotension • Bronchospasm	• Asthma • Severe bradycardia • Decompensated heart failure

Board Tip

First-line treatment is lactulose, with rifaximin added if symptoms recur.

Treatment Regimens for *Helicobacter Pylori*

General Considerations

- In the US, we generally assume clarithromycin resistance rates are greater than 15%, unless local data indicate otherwise.
- Data suggests that H. pylori resistance rates are high worldwide (>15%).

Bismuth Quadruple Therapy

- Preferred regimen in patients allergic to penicillin (PCN)
- Bismuth Subsalicylate (Pepto Bismol) + Metronidazole (Flagyl) + Tetracycline + PPI → 14 days
  - PPI (standard dose) PO BID → e.g., Lansoprazole (Prevacid) 30 mg PO BID
  - Bismuth Subsalicylate (300 or 524 mg) PO QID
  - Tetracycline (TCN) 500 mg PO QID
  - Metronidazole: 250 mg PO QID or 500 mg PO TID

- Pylera[R]: combination capsule which contains bismuth subcitrate, metronidazole, and tetracycline
  - Pylera: 3 capsules PO QID after meals and at bedtime (PC & HS)

Clarithromycin-Based Therapy

- Clarithromycin (Biaxin) + Amoxicillin (Amoxil) + Metronidazole (Flagyl) + PPI → 14 days
  - PPI (standard dose) PO BID → e.g., Lansoprazole (Prevacid) 30 mg PO BID
  - Clarithromycin 500 mg PO BID
  - Amoxicillin 1000 mg PO BID
  - Metronidazole 500 mg PO BID

H. pylori Therapy

Mechanism of Action

Agent	Mechanism
Proton Pump Inhibitors	• Irreversibly inhibits H^+/K^+ ATPase → reduces acid
Clarithromycin	• Inhibits 50S ribosomal subunit → stops protein synthesis
Amoxicillin	• Beta-lactam → inhibits bacterial cell wall synthesis

H. pylori Therapy

Indications

Agent	Indications
Tripel therapy (PPI + Clarithromycin + amoxicillin)	• H. pylori eradication

H. pylori Therapy

Adverse Effects & Contraindications

Agent	Adverse Effects	Contraindications
Proton Pump Inhibitor	• Increased risk of fractures • Hypomagnesemia • *C. difficile* infection • Rebound acid hypersecretion	• Long-term use in osteoporosis • Interstitial nephritis
Clarithromycin	• QT prolongation • GI upset • Cholestatic hepatitis	• QT prolongation • Hepatic dysfunction
Amoxicillin	• Hypersensitivity reactions • Jarisch–Herxheimer reaction	• Penicillin allergy

Board Tip

Substitute metronidazole for amoxicillin if penicillin-allergic; be aware of rising clarithromycin resistance.

12:25

Piperacillin-tazobactam

Table of Contents

- **Possible increased incidence of acute kidney injury.** Does combining vancomycin with piperacillin-tazobactam amplify the risk of vancomycin nephrotoxicity ?
  - Many observational retrospective studies have reported an increased risk of acute kidney injury in association with the combination of piperacillin-tazobactam and vancomycin as compared to either drug alone (Clin Infect Dis 2017;65:2137)
    - No reported increased risk of AKI if vancomycin is combined with cefepime or meropenem (Antimicrob Agents Chemother 2018;62:e00264-18).
    - The attributable nephrotoxicity due to vancomycin due in part to multiple confounders (J Antimicrob Chemother 75:1031, 2020)
  - In virtually all the pertinent studies the acute kidney injury endpoints utilized serum creatinine changes as a surrogate marker for changes in the glomerular filtration rate
    - In a rat model of vancomycin nephrotoxicity, there was a lack of augmentation of toxicity with concomitant piperacillin/tazobactam . Rather than changes in serum creatinine, a specific marker of tubular toxicity was utilized,
    - The authors speculate that the rise in serum creatinine with piperacillin/tazobactam is the consequence of piperacillin competing with creatinine for tubular secretion. In short, a functional and not toxic marker. See Clin Infect Dis 71:426, 2020.
    - Reference: J Antimicrob Chemother 75:1228, 2020.

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Table 17–10.

Treatment options for peptic ulcer disease.

Active *Helicobacter pylori*–associated ulcer

1. Treat with anti–*H pylori* regimen for 14 days. Best empiric treatment options:

Standard Bismuth Quadruple Therapy

- PPI orally twice daily[1,2]
- Bismuth subsalicylate 262 mg two tablets orally four times daily
- Tetracycline 500 mg orally four times daily
- Metronidazole 500 mg three times daily

OR

- PPI orally twice daily[1]
- Bismuth subcitrate potassium 140 mg/metronidazole 125 mg/tetracycline 125 mg (Pylera) three capsules orally four times daily[3]

Rifabutin-Based Triple Therapy (Talicia)[4]

- Omeprazole 40 mg orally every 8 hours
- Rifabutin 50 mg orally every 8 hours
- Amoxicillin 1000 mg orally every 8 hours

Vonoprazan Triple Therapy (Voquenza Triple Pak[5])

- Vonoprazan 20 mg orally, twice daily
- Amoxicillin 1 g orally, twice daily
- Clarithromycin 500 mg orally, twice daily

Vonoprazan Dual Therapy (Voquenza Dual Pak[5])

- Vonoprazan 20 mg orally, twice daily
- Amoxicillin 1 g orally, three times daily

Standard Triple Therapy (No longer recommended except in locales where clarithromycin resistance is < 15%)

- PPI orally twice daily
- Clarithromycin 500 mg orally twice daily
- Amoxicillin 1 g orally twice daily (or, if penicillin allergic, metronidazole 500 mg orally twice daily)

2. After completion of course of *H pylori* eradication therapy, continue treatment with PPI[1] once daily for 4–6 weeks if ulcer is large (> 1 cm) or complicated.
3. Confirm successful eradication of *H pylori* with fecal antigen or PCR test, or endoscopy with biopsy at least 4 weeks after completion of antibiotic treatment and 2 weeks after completion of PPI treatment.

UpToDate (2025)

In the United States, H. pylori rates of resistance to clarithromycin exceed 20 to 30 percent and are steadily increasing.

Question 1

A patient with hepatic encephalopathy is started on lactulose. What is the primary mechanism by which lactulose reduces serum ammonia?

A. Stimulates colonic motility

B. Traps ammonia as ammonium in the colon

C. Inhibits protein absorption

D. Increases bile acid secretion

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Question 2

A 65-year-old man with cirrhosis presents with acute variceal bleeding. What is the best initial pharmacologic therapy?

A. Propranolol

B. Octreotide

C. Rifaximin

D. Ursodeoxycholic acid

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A 65-year-old man with cirrhosis presents with acute variceal bleeding. What is the best initial pharmacologic therapy?

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D. Ursodeoxycholic acid

Question 3

A patient with hepatic encephalopathy is already on lactulose but continues to have recurrent episodes. What medication should be added?

A. Magnesium citrate

B. Rifaximin

C. Loperamide

D. Docusate

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Question 4

Which medication works by reducing cholesterol saturation in bile, making it ideal for treating primary biliary cholangitis?

A. Ursodeoxycholic acid

B. Polyethylene glycol

C. Diphenoxylate-atropine

D. Clarithromycin

Question 4

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