

Constipation

Constipation is the -

- infrequent bowel movements (typically <3 times per wk),
- difficulty during defecation, or
- the sensation of incomplete bowel evacuation.

Chandan Shrestha, PhD

Laxative

- Laxatives are commonly used to accelerate the movement of food through the gastrointestinal tract.
- These drugs can be classified on the basis of their mechanism of action-
 1. as irritants or stimulants of the gut,
 2. bulking agents, and
 3. stool softeners.

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Pharmacological Treatment

1. Bulking agent: Bran, Psyllium, Methyl Cellulose
2. Stool softener: Docussates (DOSS), Liquid Paraffin
3. Stimulant Purgatives:
 - a) Diphenylmethanes: Phenolphthalein, Bisacodyl
 - b) Anthraquinones: Senna, Cascara sagrada
 - c) 5-HT₄ agonist: Tegaserod
 - d) Fixed oil: Castor oil
4. Osmotic Purgatives:
 - a) Magnesium Salts: sulfate, hydroxide
 - b) Sodium salts: sulfate, phosphate
 - c) Sodium potassium tartrate
 - d) Lactulose

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Bulk forming: Bran, Psyllium, Methylcellulose

- They are indigestible, hydrophilic colloids that absorb water forming a bulky gel that distends the colon and promotes peristalsis.
- Side effects: Flatulence and abdominal distension
- Contraindication: faecal impaction or existing bowel obstruction
- Dose:
 - Bran: 3.5g bd or tid /d with food
 - Psyllium: 3-12 g mixed with water
 - Methyl Cellulose: 4-6 g/d

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Stool softener: Docussate, liquid paraffin

- Surface-active agents that become emulsified with the stool produce softer feces and ease passage.
- Adverse effect: Cramps and abdominal pain can occur. It is bitter; liquid preparations may cause nausea.
- Dose:
 - Docussate: 100-400 mg/d
 - Liquid paraffin: 15-30 mL/d

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Stimulant purgative: Bisacodyl

- are substances that act on the intestinal mucosa or nerve plexus, altering water and electrolyte secretion.
- They also Increase intestinal motility
- Adverse Effect: abdominal cramps, fluid and electrolyte depletion (potassium), atonic colon
- Contraindicated in intestinal obstruction, fecal impaction, ulcerative hemorrhoids.
- Dose:
 - Phenolphthalein: 60-130 mg
 - Bisacodyl: 5-15 mg
 - Castor oil: 15-25 mL

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Osmotic Purgative: Magnesium salt/ Sodium salt; Lactulose

- are nonabsorbable salts that hold water in the intestine by osmosis and distend the bowel, increasing intestinal activity and producing defecation in a few hours.
- Mag. salts are contraindicated in renal insufficient, while sod. salts in CHF and other sod retaining states.
- Preferred for preparation of bowel before surgery and colonoscopy; in food/drug poisoning.

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Lactulose

- It is a semisynthetic disaccharide of fructose and lactose which is neither digested nor absorbed in the small intestine → retains water.
- It is broken down in the colon by bacteria to osmotically more active products.
- In a dose of 10 g BO taken with plenty of water, it produces soft formed stools in 1-3 days.
- Flatulence and flatus is common, cramps occur in few. Some patients feel nauseated by its peculiar sweet taste.

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Diarrhea

- frequent passage of loose stool *or*
- Abnormal passage of stools with increased frequency, fluidity, and weight, or with increased stool water excretion

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Antidiarrheals

- Increased motility of the gastrointestinal tract and decreased absorption of fluid are major factors in diarrhea.
- Antidiarrheal drugs include
 1. Antimotility agents- codeine, Diphenoxylate, Loperamide)
 2. Adsorbents- bismuth subsalicylate, methylcellulose, and aluminum hydroxide, and
 3. Antisecretory: sulphasalazine, mesalazine, Racecadotril

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<i>Class</i>	<i>Drug</i>	<i>Use</i>
ABSORBANTS	Ispaghula Psyllium Methyl cellulose	Irritable bowel syndrome (IBS), Ileostomy/colostomy diarrhoea
ANTISECRETORY	Sulfasalazine Mesalazine Bismuth subsalicylate Atropine Octreotide Racecadotril	Ulcerative colitis, Other inflammatory bowel diseases (IBD) Travellers' diarrhoea Nervous, drug induced diarrhoea Carcinoid, VIP secreting tumour, diarrhoea in AIDS Acute secretory diarrhoeas
ANTIMOTILITY (Opioids) (also antisecretory)	Codeine Diphenoxylate-atropine Loperamide	Noninfective or mild travellers' diarrhoea; Idiopathic diarrhoea in AIDS, After anal surgery, colostomy.

ORS: ORAL REHYDRATION SOLUTION

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Antimotility drugs

- Opioid agonist
- Reduce bowel motility and diminish intestinal secretions while enhancing absorption.
- The utility of antimotility drugs in diarrhoea is limited to noninfective diarrhoea, mild traveller's diarrhoea.
- They are contraindicated in irritable bowel syndrome, ulcerative colitis and diverticulosis because they increase intraluminal pressure.
- Two drugs that are widely used to control diarrhea are diphenoxylate and loperamide.

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Diphenoxylate

- synthetic opioid, chemically related to pethidine; used exclusively as constipating agent; action is similar to codeine.
- Cross BBB, have CNS effects and potential for addiction → limit the use.
- contain small amount of atropine to discourage abuse.
- C/I: below 6 years of age

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Loperamide

- opiate analogue with major peripheral μ opioid and additional weak anticholinergic property.
 - As a constipating agent, it is much more potent than codeine.
 - Do not cross BBB; CNS effects are rare and occur only with high doses; no abuse liability
- A/E: abdominal cramps and rash (common)

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Antisecretory (Anticholinergics)

- Decrease intestinal muscle tone and peristalsis of GI tract → slowing the movement of fecal matter through the GI tract
- Examples: atropine

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Salfasalazine

- split by colonic bacteria to release 5-ASA and sulfapyridine.
- 5-ASA exerts a local antiinflammatory effect.
- Used ulcerative colitis and related inflammatory bowel diseases.
- Sulfapyridine- RA
- Nausea, vomiting, headache, malaise and anaemia are other frequent side effects.

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Mesalazine

- These are the official names given to 5-ASA.
- Realizing that 5-ASA is the active moiety in ulcerative colitis, but is not effective orally because of inability to reach the large bowel (it is absorbed in the small intestine), it has been formulated as delayed release preparations by coating with acrylic polymer.

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Racecadotril

- This recently introduced prodrug is rapidly converted to thiorphan, an enkephalinase inhibitor.
- It prevents degradation of endogenous enkephalins (ENKs) which are mainly δ opioid receptor agonists.
- Racecadotril decreases intestinal hypersecretion, without affecting motility, by lowering mucosal cAMP due to enhanced ENK action.
- It is indicated in the short-term treatment of acute secretory diarrhoeas.
- In contrast to loperamide/ diphenoxylate, it is not contraindicated in children.
- Side effects are nausea, vomiting, drowsiness, flatulence

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Specific microbial drug

- Cholera: tetracycline, cotrimaxazole, ciprofloxacin / norfloxacin, Ampicillin, erythromycin
- Clostridium difficile: metronidazole, vancomycin
- Bacterial growth: metronidazole
- Amoebiasis/ gardiasis : metronidazole, diloxanide furoate

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Rifaximin

- antibiotic used to treat traveler's diarrhea, irritable bowel syndrome, and hepatic encephalopathy.
- interferes with transcription by binding to the beta sub unit of bacterial RNA polymerase.

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