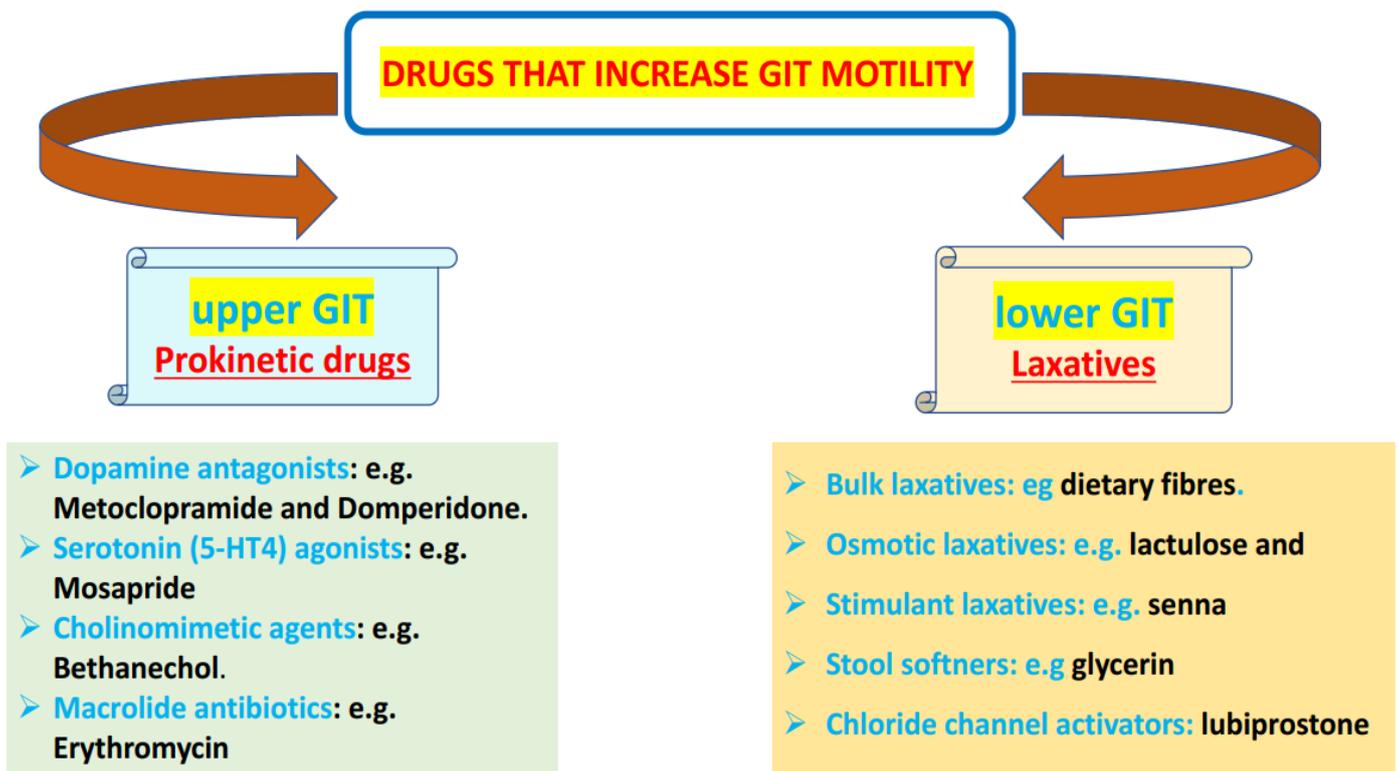
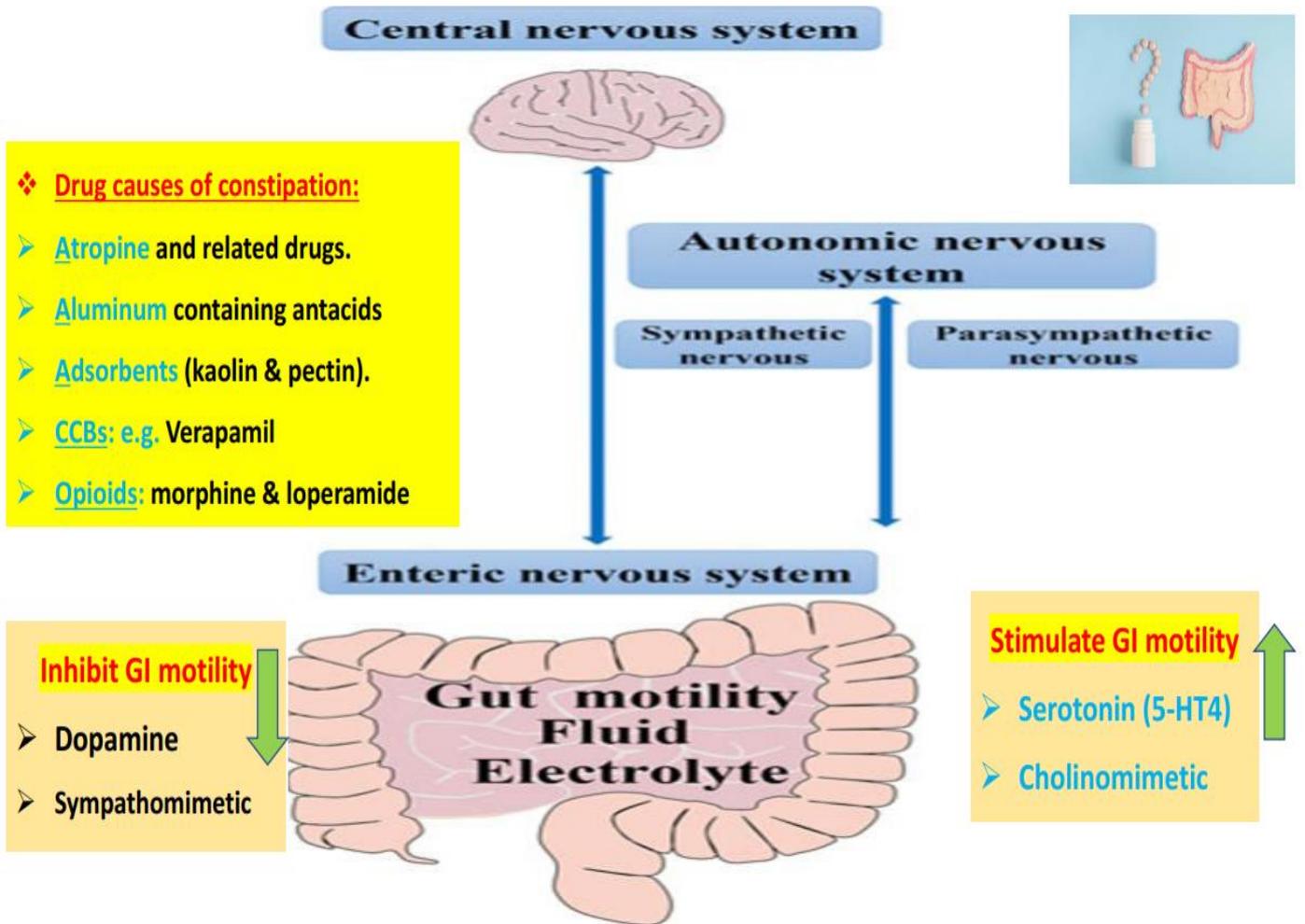
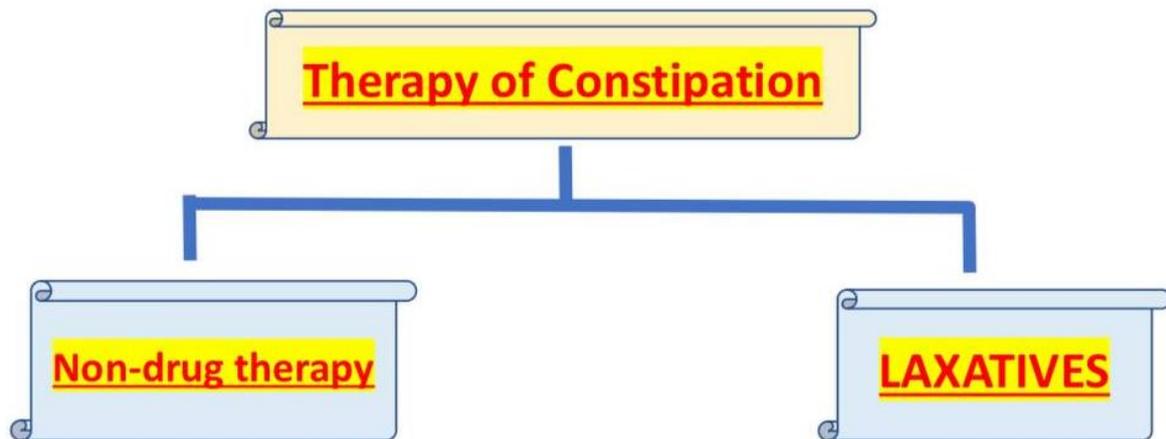


Treatment of Constipation and diarrhea



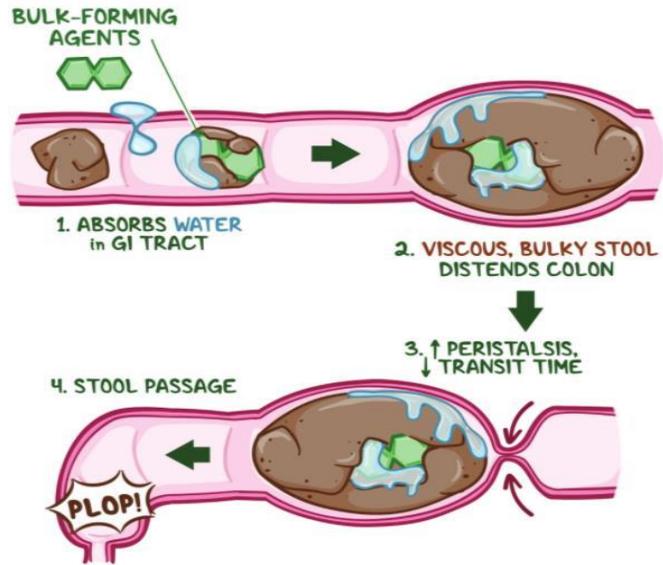


- It is the first line in all cases of constipation
- **Diet rich in fibers** e.g. fruits, vegetables.
- **Increase fluid intake**
- **Minimize tea and coffee.**
- **Physical exercise** to activate abdominal muscles and intestinal peristalsis.

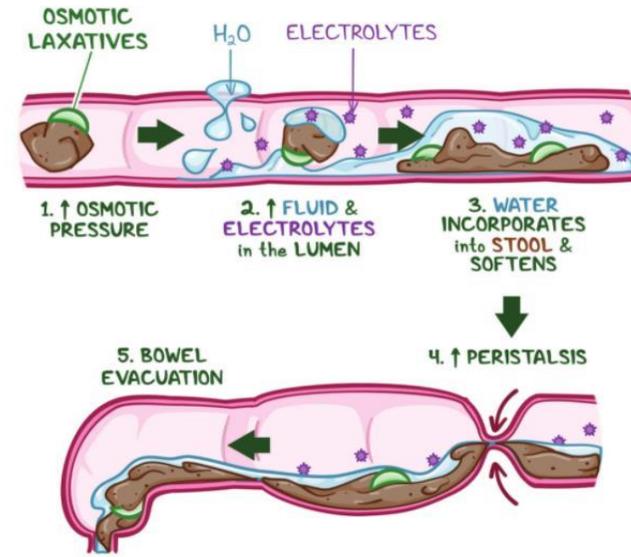
- **Bulk laxatives:** eg dietary fibres.
- **Osmotic laxatives:** e.g. lactulose
- **Stimulant laxatives:** e.g. senna
- **Lubricant laxatives:** e.g glycerin
- **Chloride channel activators:** e.g. lubiprostone

Treatment of Constipation

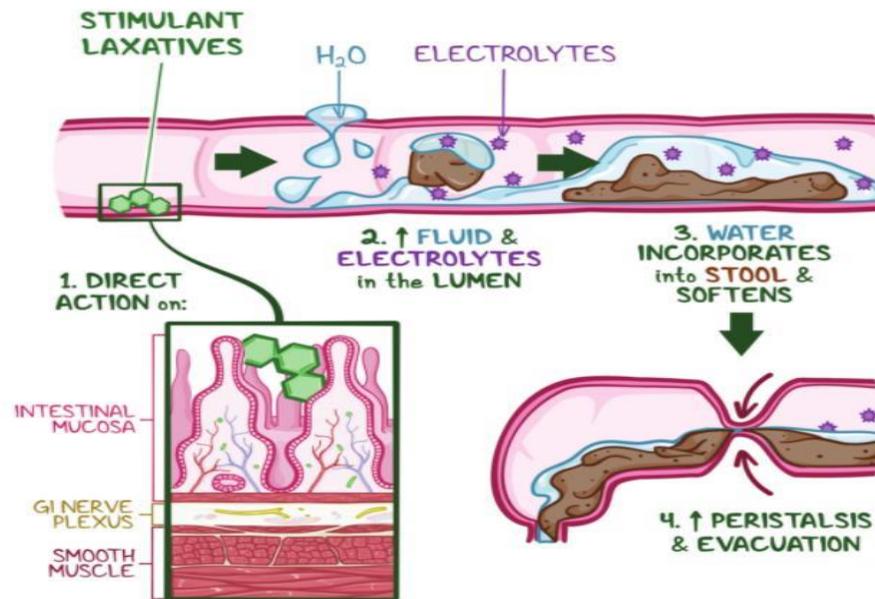
	1. Bulk-forming agents	2. Osmotic laxatives	3. Irritant (or stimulant) laxatives
Example	<ul style="list-style-type: none"> Dietary fibers. Methyl-cellulose. Bran. 	<ul style="list-style-type: none"> Mg sulfate & Na salts. Lactulose (Safe in pregnancy and hepatic encephalopathy) Polyethylene glycol. 	<ul style="list-style-type: none"> Castor oil. Senna. Bisacodyl.
MOA	<ul style="list-style-type: none"> Non-digestible fibers that retain water in the gut and distend the large intestine → activation of stretch receptors → stimulation of peristalsis. 	<ul style="list-style-type: none"> They are soluble but non-absorbable retained in gut lumen & retain water by their osmotic effect → activation of stretch receptors → stimulation of peristalsis. 	<ul style="list-style-type: none"> Direct stimulation of the enteric nervous system. Colonic electrolyte and fluid secretion.
Adverse effects	<ul style="list-style-type: none"> <u>Safe laxatives but may cause:</u> <ol style="list-style-type: none"> Bloating & abdominal distension. ↓ absorption of some drugs e.g. digoxin. 	<ul style="list-style-type: none"> <u>Mg & Na salts (saline laxatives):</u> <ul style="list-style-type: none"> may be absorbed systemically and produce hypermagnesemia and hypernatremia especially in patients with renal failure. <u>Lactulose</u> <ul style="list-style-type: none"> Produce abdominal discomfort. 	<ul style="list-style-type: none"> Passes in urine & cause urine discoloration It passes in breast milk and cause cathartic effect in the baby. Stimulate uterine contraction & abortion. Prolonged use → degeneration of gut nervous plexus → atonic (cathartic) colon. Laxative dependence



Bulk-forming agents



Osmotic laxatives



Irritant (or stimulant) laxatives

	4. Lubricant laxatives	5. Chloride channel activators	6. Opioid receptor antagonists:
Example	<ul style="list-style-type: none"> Liquid paraffin. Glycerin suppositories. Evacuant enema. 	<ul style="list-style-type: none"> Lubiprostone. 	<ul style="list-style-type: none"> Naloxegol. Methyl naltrexone bromide. Alvimopan.
MOA	<ul style="list-style-type: none"> Paraffin oil: <ul style="list-style-type: none"> ➤ it coats the fecal matter and retards water absorption by the colon. Glycerin: <ul style="list-style-type: none"> ➤ Has hygroscopic effect. MCQ ➤ Draws water from rectal mucosa and lubricates the anal canal. ➤ Stimulates reflex rectal contractions and promotes stool evacuation in 15-20 min. 	<ul style="list-style-type: none"> It acts by activating chloride channels to increase fluid secretion in the intestinal lumen. MCQ This eases the passage of stool and causes little change in electrolyte balance. 	<ul style="list-style-type: none"> Block intestinal μ opioid receptors but do not enter CNS, so analgesia is maintained. Therapy with opioids after surgery for treatment of pain as well as endogenous opioids may cause constipation by increasing non-propulsive colonic contractions, which result in prolonged transit time and increased absorption of fecal water. Use of opioids also may prolong the duration of post-operative ileus.
Adverse effects	<ul style="list-style-type: none"> Paraffin oil decreases absorption of fat-soluble vitamins (A, D, E, K). 		<ul style="list-style-type: none"> Nausea, abdominal pain, and diarrhea.

Treatment of Diarrhea

Diarrhea:

▪ Def:

- Passage of **three or more loose or liquid stools** per day or more frequent passage than is normal for the individual.

▪ Causes of diarrhea:

Infectious diarrhea:	<ul style="list-style-type: none">• Viral, bacterial, fungal, parasite (the most common).
Non-Infectious diarrhea:	<ul style="list-style-type: none">• Hormonal diarrhea: thyroxine in hyperthyroidism.• Malabsorption syndromes: bile acid malabsorption• Inflammatory diarrhea: inflammatory bowel diseases• Iatrogenic (drug induced) diarrhea:<ul style="list-style-type: none">➤ Overuse of laxatives.➤ Mg containing antacids.➤ Antibiotic-associated diarrhea (pseudomembranous colitis).

Treatment of diarrhea

- 1) Maintenance of **fluid and electrolyte balance** (first priority).
- 2) **Non-specific anti-diarrheal agents.**
- 3) **Specific anti-diarrheal agents** , treatment of the cause e.g.
 - a) **Antimicrobials** for infectious diarrhea.
 - b) **Anti-inflammatory drugs** for inflammatory bowel diseases.
- 4) **Probiotics:** introduce good bacteria into gut to combat diarrhea.
- 5) **Antispasmodic drugs:** if there is colic or abdominal cramps

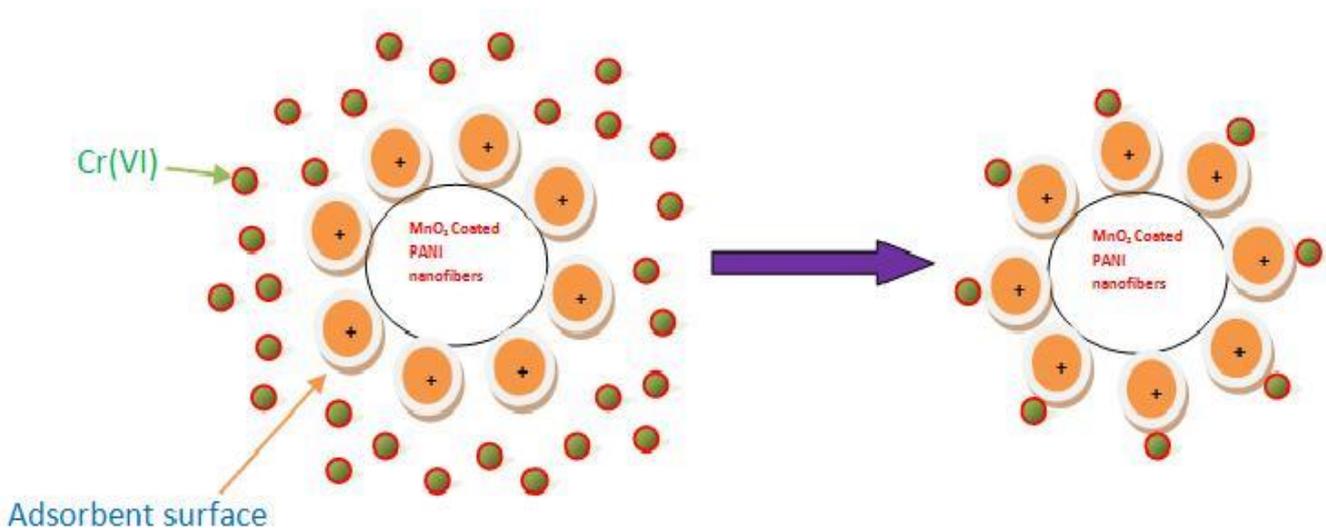
1. Maintenance of fluid and electrolyte balance

▪ Oral Rehydration Therapy (ORT):

- The **first line** in treatment. **MCQ**
- **Balanced salt solution** containing electrolytes and glucose (glucose is important for sodium and consequently water absorption).
- 90% of acute cases of childhood diarrhea can be corrected using **ORT only**.
- **Intravenous solutions:** if dehydration is severe.



2. Non-specific antidiarrheal therapy



	1) Adsorbents	2) Bismuth subsalicylate	3) Anti-cholinergic drugs	4) Synthetic opioid preparations
Example	<ul style="list-style-type: none"> Kaolin, pectin, activated charcoal, diosmectite. MCQ 		<ul style="list-style-type: none"> Atropine. Hyoscine. Propantheline. 	<ul style="list-style-type: none"> Diphenoxylate. Loperamide.
Mechanism	<ul style="list-style-type: none"> Adsorb water, microorganisms and toxins. They coat the mucosa and protect it. 	<ul style="list-style-type: none"> Bismuth: provides a protective coat for mucosa and binds toxins produced by pathogenic bacteria. Subsalicylate: hydrolyzed by intestinal bacteria into salicylic acid → ↓ intestinal inflammation, hypermotility & secretions 	<ul style="list-style-type: none"> Antidiarrheal action: ↓ colonic peristalsis by blocking M3 in GIT. Antispasmodic action: relieve cramps associated with diarrhea. 	<ul style="list-style-type: none"> They act on opioid μ (μ) and δ (δ) receptors in enteric nervous system leading to: <ul style="list-style-type: none"> ➤ ↑ segmenting (non-propulsive) contractions of small intestine. ➤ ↑ water absorption and ↓ water secretion by intestinal mucosal cells. ➤ ↓ Ach release by cholinergic neurons in ENS.
Adverse effects	<ul style="list-style-type: none"> They ↓ absorption of other drugs. 	<ul style="list-style-type: none"> Darkening of stool or tongue. MCQ Encephalopathy in presence of renal failure. 		<ul style="list-style-type: none"> Anti-cholinergic side effects : e.g. dry mouth. Addiction: if used for prolonged duration.

NB for Synthetic opioid preparations: مهم جدا

- **Loperamide** cannot cross BBB.
- **Diphenoxylate** can cross BBB in very small amount:
 - no CNS effects in **usual therapeutic doses** but it can cause addiction if used in **large doses** and for **prolonged duration**.
- **Commonly combined with atropine:**
 - **Lomotil** is a combination of diphenoxylate + atropine) to produce more ↓↓ in intestinal motility and decrease liability for abuse.

5) Zinc

Use:	<ul style="list-style-type: none">• Has a role in the normal functioning of the intestinal lining and immune system.• Zinc reduce the duration and number of diarrhea in children.
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6) Cholestyramine

Mechanism:	<ul style="list-style-type: none">• It binds bile acids in the intestine decreasing their irritation.
Use:	<ul style="list-style-type: none">• Used in diarrhea due to bile salt malabsorption. MCQ

7) Racecadotril

Nature:	<ul style="list-style-type: none">• An anti-secretory agent.
Mechanism:	<ul style="list-style-type: none">• It inhibits the enzyme enkephalinase so prevent degradation of endogenous enkephalines. MCQ

3. Specific anti-infective agents:

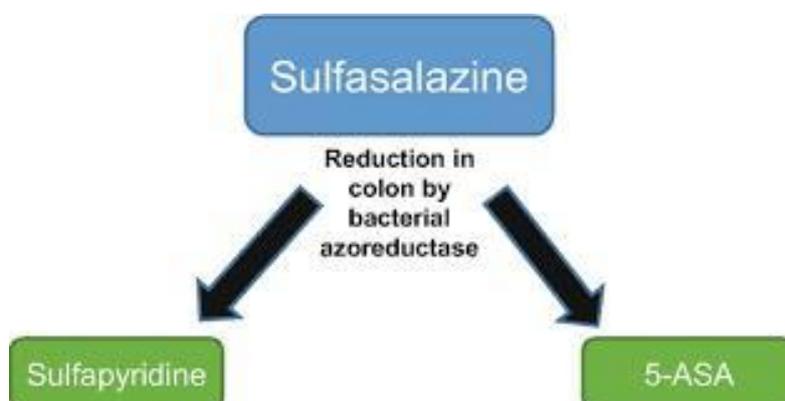
a) Anti-microbials for infectious diarrhea.

- It is **not necessary** in simple gastroenteritis as most cases are viral in origin.
- Chemotherapy is necessary in specific types of enteritis e.g. **MCQ**

<i>Clostridium difficile</i>	<ul style="list-style-type: none">• Vancomycin.• Metronidazole.
<i>Giardia lamblia</i>	<ul style="list-style-type: none">• Metronidazole.
<i>Campylobacter jejuni</i>	<ul style="list-style-type: none">• Azithromycin
<i>E. coli</i>	<ul style="list-style-type: none">• Ciprofloxacin
<i>Non-typhoid Salmonella</i>	<ul style="list-style-type: none">• Ciprofloxacin or ceftriaxone
<i>Shigella</i>	<ul style="list-style-type: none">• Azithromycin• Ciprofloxacin or co-trimoxazole.

b) Anti-inflammatory drugs

1. Sulfasalazine (5-aminosalicylic acid "5-ASA" + sulfapyridine).
2. Corticosteroids.
3. Immunosuppressive agents.



	1. Sulfasalazine	2. Corticosteroids	3. Immunosuppressive agents
Mechanism:	<ul style="list-style-type: none"> • <u>In the colon, metabolized by intestinal bacteria, to release 5-ASA and sulfapyridine:</u> MCQ ➤ Mesalamine (5-ASA) has anti-inflammatory & immunosuppressive. ➤ Sulfapyridine poorly absorbed sulfonamide with antibacterial action. 	<ul style="list-style-type: none"> • Stimulation of Na⁺ absorption from the intestine. • Anti-inflammatory action. • Given orally or as enema in severe cases. 	<ul style="list-style-type: none"> • <u>Cytotoxic drugs (azathioprine and 6-mercaptopurine):</u> <ul style="list-style-type: none"> ➤ used in ulcerative colitis and Crohn's disease in small dose. • <u>Infliximab (monoclonal antibodies):</u> <ul style="list-style-type: none"> ➤ works by inhibiting the activity of a pro-inflammatory cytokine as tumor necrosis factor-alpha (TNF-alpha). ➤ Used in Crohn's disease, ulcerative colitis and rheumatoid arthritis.
Therapeutic uses:	<ul style="list-style-type: none"> • Active ulcerative colitis. • Rheumatoid arthritis. 	<ul style="list-style-type: none"> • To Control acute episodes of Inflammatory bowel disease. • Refractory diarrhea unresponsive to other agents. 	
Adverse effects:	<ul style="list-style-type: none"> • <u>Mainly due to sulfapyridine (sulfonamide):</u> → drug allergy, bone marrow depression and megaloblastic anemia (avoided by giving folic acid). 		

Traveler's diarrhea (TD):

- One of the **most common illnesses** faced by travelers to a new environment with poor hygiene or sanitation.
- Transmission of infection is through **contaminated food or water**.
- Usually, it's due to **exposure to bacteria** such as *Escherichia coli*, *Campylobacter* and *Shigella* are the most frequent causes.
- **Prevention:** bismuth subsalicylate. **MCQ**
- **Treatment:** **MCQ**
 - Oral Rehydration Solution (ORS)
 - Loperamide ± bismuth subsalicylate
 - Azithromycin or Fluoroquinolones (e.g., ciprofloxacin)

4. Probiotics

- Probiotics are **live micro-organisms (bacteria and yeasts)** that when ingested in adequate doses, provide a benefit to digestive system.
- **Probiotics are believed to work by:**
 - Improving the balance of **gut microorganisms**.
 - Enhancing **immune function**.
 - Reducing **inflammation**.
- **These mechanisms can help** support gut health and alleviate symptoms of gastrointestinal disorders such as diarrhea, bloating and gas.

