

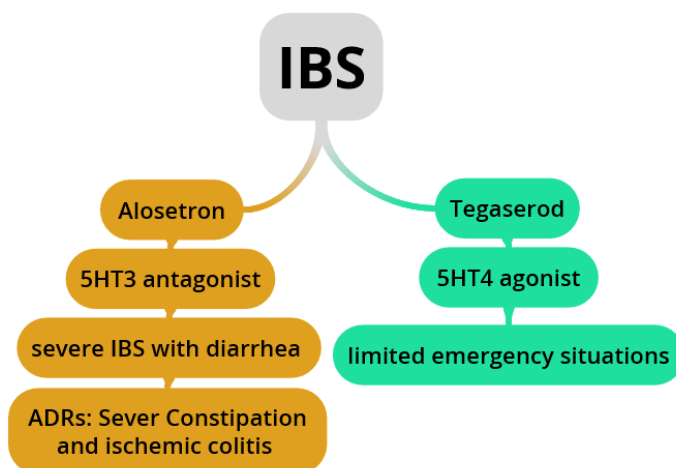
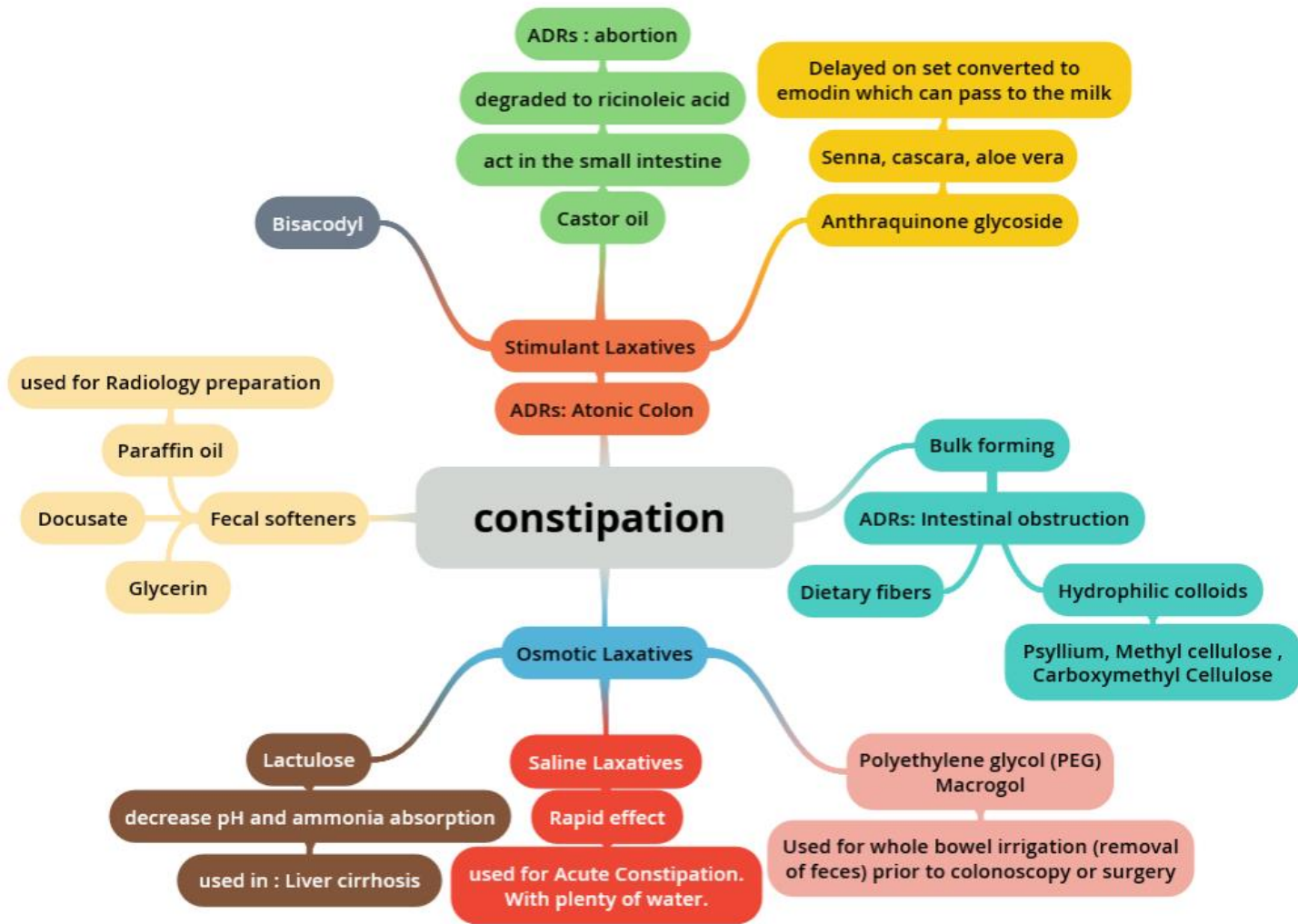
## Drugs used in treating constipation and

### Objectives: **IBS**

1. Define constipation
2. Know the different symptoms of constipation
3. Know the different lines of treatment of constipation
4. Identify the different types of laxatives
5. Discuss the pharmacokinetics, dynamics, side effects and uses of laxatives
6. Discuss the difference between different treatment including bulk forming laxatives, osmotic
7. laxatives, stimulant laxatives And stool softeners (lubricants).
8. Define bowel syndrome (IBS).
9. Identify the pharmacokinetics, dynamics, side effects and uses of drugs used for IBS.

Editing File

# Mind Maps



# Constipation

**infrequent defecation**, often with straining and the passage of hard, uncomfortable stools.

May be accompanied by other symptoms:

- Loss of appetite
- Flatulence
- Abdominal and rectal pain
- Lethargy
- Depression

## Causes of constipations

### Decreased motility in colon:

Decrease in water and fiber contents of diet.

### Difficulty in evacuation:

-Local painful conditions:  
anal fissures, piles  
- Lack of muscular exercise

### Drug-induced:

-Anticholinergic agents  
-Opioids  
-Iron  
-Antipsychotics

## Treatment of Constipation

- Adequate fluid intake.
- High fiber contents in diet.
- Regular exercise
- Regulation of bowel habit.
- Avoid drugs causing constipation.
- **Use drugs (laxatives or purgatives)**

## Medications used in constipations

Drugs that hasten the transit of food through the gastrointestinal tract are called laxatives or purgatives

# Classification of laxatives

## 1. Bulk forming laxatives

Increase volume of non-absorbable solid residue.

## 2. Osmotic laxatives

Increase water content in large intestine.

## 3. Stimulant or irritant laxatives

Act by direct stimulation of nerve endings in colonic mucosa.

## Stool softeners (lubricants)

Alter the consistency of feces easier to pass.

# 1-Bulk forming laxatives

### Includes

#### Dietary fibers:

- Indigestible parts of vegetables & fruits.
- Bran powder.

#### Hydrophilic colloids:

- **Psyllium** seed (powder)
- Methyl cellulose
- Carboxymethyl Cellulose (CMC)

### M.O.A

Dietary fibers and hydrophilic colloids are non-absorbable substances → Increase the bulk of intestinal contents by water retention → increase mechanical pressure on the walls of intestine stimulation of stretch receptors → **increase peristalsis** → evacuation of **soft** stool.

### ADRs

- **Delayed onset of action** (1-3 days).
- **Intestinal obstruction (should be taken with enough water).**
- Bloating, flatulence, distension.
- Interfere with other drug absorption e.g. iron, cardiac glycosides.

## Osmotic Laxatives

- are water soluble compounds
- Poorly absorbable compounds (salts or sugars)
- They remain in the bowel, attract and retain water by **osmosis** thereby increasing the volume of feces → ↑ peristalsis → evacuation of stool.

### Osmotic Laxatives includes:

- Sugars : lactulose
- Salts (Saline laxatives):
  1. Magnesium sulphate or hydroxide
  2. Sodium or potassium phosphate.
- Polyethylene glycol (PEG)

## 2-Osmotic Laxatives

Drug	<b>lactulose</b>
P.K	<ul style="list-style-type: none"> <li>• Semi synthetic disaccharide of fructose &amp; galactose.</li> <li>• Non absorbable.</li> <li>• In the colon, metabolized by bacteria to fructose &amp; galactose.</li> <li>• These sugars are fermented into lactic acid &amp; acetic acid that function as osmotic laxatives (<b>they cause acidification of the colon</b>)</li> </ul>
Indications	<ul style="list-style-type: none"> <li>• Prevention of chronic constipation</li> <li>• Hemorrhoids</li> <li>• <b>Hepatic encephalopathy (Hyperammonemia)</b></li> <li>• <b>Liver cirrhosis</b></li> </ul> <p>Why lactulose is used in Liver cirrhosis &amp; Hyperammonemia?            increases the H<sup>+</sup> concentration in the gut, This favors the formation of the non-absorbable NH<sub>4</sub><sup>+</sup> from NH<sub>3</sub>, trapping NH<sub>3</sub> in the colon and reducing its back diffusion into blood.</p> <ol style="list-style-type: none"> <li>1. Acidification of the colon (increases the H<sup>+</sup> concentration) by lactic acid &amp; acetic acid causes increase of H<sup>+</sup> concentration, this will cause NH<sub>3</sub> (ammonia-lipid soluble absorbed easily) trapping by the formation of NONabsorbable NH<sub>4</sub><sup>+</sup> (ammonium-polar "water soluble" poorly absorbed) and thus reducing absorption.</li> <li>2. Simply: Lactulose = Lactic acid + Acetic acid Acidification of the colon ↓ ammonia absorption (NH<sub>4</sub><sup>+</sup>)</li> </ol>
ADRs	<ul style="list-style-type: none"> <li>• Delayed onset action (2-3 Days)</li> <li>• Abdominal cramps &amp; flatulence.</li> <li>• Electrolyte disturbance.</li> </ul>
Dose	15 ml for constipation & 30 ml for Liver cirrhosis.

## 2-Osmotic Laxatives

Drug	Saline Laxatives
P.K	<ul style="list-style-type: none"> <li>-Are poorly absorbable salts</li> <li>-Increase evacuation of <b>watery</b> stool.</li> <li>-Magnesium sulphate (<b>Epson's salt</b>).</li> <li>-Magnesium hydroxide (<b>milk of magnesia</b>).</li> <li>-Sodium phosphate or potassium phosphate.</li> <li>-have rapid effect (<b>within 1-3 h</b>).</li> <li>-Isotonic or hypotonic solution should be used.</li> </ul>
Indications	<p>Treatment of acute constipation. (used With plenty of water)</p>
ADRs	<ul style="list-style-type: none"> <li>-Disturbance of fluid and electrolyte balance.</li> <li>-May have systemic effects.</li> </ul>
C.I	<p>Sodium salts in congestive heart failure</p> <p>Magnesium salts are contraindicated in:</p> <ul style="list-style-type: none"> <li>● Renal failure</li> <li>● Heart block</li> <li>● CNS depression</li> <li>● Neuromuscular block</li> <li>● (also can not be combine with Aminoglycosides)</li> </ul>

### Balanced Polyethylene Glycol (PEG) (Macrogol)

- ❖ Isotonic solution of polyethylene glycol & electrolytes (NaCl, KCl, Na bicarbonate).
- ❖ Is a colonic lavage solution
- ❖ Used for whole bowel irrigation prior to colonoscopy or surgery (4L over 2-4 hours).
- ❑ **Advantages**
  - Limited fluid or electrolyte imbalance
  - less flatulence and cramps

## 3-Stimulant Laxatives

Drug	Bisacodyl	Castor oil	Anthraquinone derivatives <i>(senna, cascara, aloes)</i>
<b>M.O.A</b>	act via direct stimulation of enteric nervous system $\Rightarrow$ increased peristalsis & purgation. They are the most powerful group among laxatives and should be used with care.		
<b>P.K</b>	-Is given orally, acts on colon -Onset of action = orally (6-12 h)/ per rectum (1 h) - Type: Diphenylmethane	-Given orally -5-20 ml on empty stomach in the morning. -acts in small intestine -Vegetable oil degraded by lipase $\rightarrow$ ricinoleic acid + glycerin $\rightarrow$ -Ricinoleic acid is very irritating to mucosa. -Onset of action = 2-6 h.	-Act in colon -Hydrolyzed by bacterial colon into sugar + emodin (The absorbed emodin has direct stimulant action ). -Emodin may pass into milk. -Delayed onset of action (8-12 h). -Bowel movements in 12 h (orally) or 2 h (rectally as suppository). -Given at night.
<b>ADRs</b>	<ul style="list-style-type: none"> <li>❖ Abdominal cramps may occur.</li> <li>❖ Prolonged use: dependence &amp; destruction of myenteric plexus leading to atonic colon.</li> </ul>		
<b>C.I</b>	-	in pregnancy: reflex contraction of uterus $\rightarrow$ abortion.	<b>Senna is contraindicated in breastfeeding.</b>



## Common stimulant purgatives

Drugs	Type	Site of Action	Onset of Action
Cascara	Anthraquinone	colon	8-12 hours
Senna	Anthraquinone	colon	8-12 hours
Aloe vera	Anthraquinone	colon	8-12 hours
Bisacodyl	Diphenylmethane	colon	6-8 hours
Castor Oil	ricinoleic acid	small intestine	2-6 hours

## Fecal softeners (Lubricants)/surfactants

- Non-absorbed drugs
- Act by either **decreasing surface tension** (by some chemical action) or by **softening the feces** thus promoting defecation.
- Treat constipation in patient with hard stool or specific condition and for people who should avoid straining.

### 4- Fecal softeners

Drug	<b><u>Docosate</u></b> (sodium dioctyl sulfosuccinate)	<b>Paraffin oil</b>	<b>Glycerin</b>
<b>M.O.A</b>	<ul style="list-style-type: none"> <li>• Surfactant, act by <u>decreasing</u> surface tension of feces</li> <li>• Increase water penetration into the stool thus softening of feces and make it easier to move through the G.I.T.</li> </ul>	Mineral oil , Acts as lubricant thus softening the feces and promote defecation	Lubricant
<b>P.K</b>	Given orally(12-72h) or enema <b>rectumform</b> (5-20 min)	Given orally (not palatable) <b>Bad taste</b>	Given rectally (suppository)
<b>Indications</b>	often used as <b>prophylaxis</b> rather than acute treatment, - especially in hospitalized patients-because of delayed onset when given orally.	Good for <b>radiology preparation.</b>	-
<b>ADRs</b>	-	Impairs absorption of fat soluble vitamins <b>A,K,E,D</b>	-
<b>Note</b>	Stool softeners used for prevention of straining after rectal surgery and in acute peri-anal disease		



<b>Purgatives</b>	<b>Site of Action</b>	<b>Onset of Action</b>
<b>Bulk purgatives</b>	<b>Small &amp; large intestine</b>	<b>12-72 hours</b> <b>Delayed</b>
<b>Saline purgatives</b>	<b>Small &amp; large intestine</b>	<b>1-3 hours</b> <b>Rapid</b>
<b>Lactulose</b>	<b>colon</b>	<b>12-72 hours</b> <b>Delayed</b>
<b>Mineral oil</b>	<b>colon</b>	<b>6-8 hours</b>
<b>Docusate</b>	<b>Small &amp; large intestine</b>	<b>Enema :5-20 hours</b> <b>Orally :12-72 hours</b>
<b>Stimulants</b>	<b>Small intestine</b> <b>colon</b>	<b>See the previous table</b>

# Irritable bowel syndrome (IBS)

Chronic bowel disorder characterized by: **common in women , related to stress.**

1. Abdominal discomfort (bloating, pain, distension, cramps)
2. Alteration in bowel habits (diarrhea or constipation or both)

## :Symptomatic treatment of IBS

-Low dose of tricyclic **antidepressant** e.g. amitriptyline or SSRIs → TCAs acts via:

- ↓ GI motility because of **anticholinergic action**.
- ↓ **visceral afferent sensation**.
- **Antispasmodics** e.g. Mebeverine **Act by relaxing the smooth muscle**
- **Laxatives** in IBS with constipation
- **Antidiarrheal** in IBS with diarrhea (diphenoxylate , loperamide)
- **Tegaserod** in IBS-C
- **Alosetron** in IBS-D

## IBS drugs

Drug	Alosetron	Tegaserod
<b>M.O.A</b>	<ul style="list-style-type: none"> <li>• Selective <b>5HT<sub>3</sub></b> antagonist. (Pharmacologically can be used for vomiting, but clinically it is not approved yet.)</li> <li>• 5-HT<sub>3</sub> receptor antagonism of the enteric nervous system of the GIT results into:                             <ul style="list-style-type: none"> <li>• Inhibition of colon motility.</li> <li>• Inhibition of unpleasant visceral afferent pain sensation (nausea, pain, bloating).</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>5HT<sub>4</sub></b> agonist.</li> <li>• Stimulation of 5HT<sub>4</sub> of enteric nervous system of GIT and that will increase peristalsis.</li> </ul>
<b>Indications</b>	<ul style="list-style-type: none"> <li>• Used in severe IBS with diarrhea in women who have not had success with any other treatment.</li> </ul>	<ul style="list-style-type: none"> <li>• Short term treatment of IBS with constipation in women &lt;55 year old <b>with no history of heart problems</b>.</li> <li>• May still be used in <b>limited emergency situations</b>.</li> </ul>
<b>ADRs</b>	<ul style="list-style-type: none"> <li>• Constipation and ischemic colitis may occur.</li> </ul> <p>People taking alosetron <b>must sign a consent form</b> before starting to take the medicine.</p>	<ul style="list-style-type: none"> <li>• CVS side effects.</li> </ul>

# Summary

## Bulk forming laxatives

Drug	Dietary fibers	Hydrophilic colloids
MOA	Increase the bulk of intestinal contents by water retention	
Use	Acute and chronic constipation	
ADRs	<ul style="list-style-type: none"> <li>• Delayed onset of action (1-3 days).</li> <li>• Intestinal obstruction (should be taken with enough water ).</li> <li>• Interfere with other drugs absorption (iron, cardiac glycosides)</li> </ul>	

## Osmotic laxatives

Drug	Sugars(lactulose)	Saline	Polyethylene glycol (PEG) Macrogol
P.K	Acidification of colon due to conversion of NH <sub>3</sub> to NH <sub>4</sub> "NH <sub>3</sub> trapping" → ↓PH	-poorly absorbed(90% NOT absorbed). -Increase evacuation of watery stool.	-isotonic solution of PEG & electrolytes. -it's a colonic lavage solution.
Uses	Use as as prophylactic therapy in Hepatic encephalopathy in people with Liver cirrhosis.	Short term Treatment of moderate to severe Acute Constipation. used With plenty of water.	whole bowel irrigation prior to colonoscopy or surgery (4L over 2-4 hours).
ADRs	Delayed onset of action(2-3 days)	-Disturbance of fluid and electrolyte balance. -May have systemic effects.	May cause Hypokalemia.

## Stimulant laxatives

Drug	Bisacodyl	Castor oil	Anthraquinone
M.O.A	They act via direct stimulation of enteric nervous system → increase peristalsis & purgation.		
P.k	-Act on colon. -Onset of action (6-12h) Per rectum (1h).	-Acts on Small intestine. -Vegetable oil degraded by lipase—→ ricinoleic acid + glycerin. -Ricinoleic acid is very irritating to mucosa.	-Act on colon. -Hydrolyzed by bacterial colon into sugar + emodin (The absorbed emodin has direct stimulant action ). -Emodin may pass into milk.

# Summary

<b>ADRS</b>	-Abdominal cramps may occur. -Prolonged use— — —>dependence & destruction of myenteric plexus leading to <b>atonic colon</b> .		
<b>C.I</b>	—	in pregnancy— — —>reflex contraction of uterus— — —> abortion.	Senna is contraindicated in breastfeeding.

Fecal softeners			
Drug	Docusate(sodium dioctyl phospho sulphate)	Paraffin oil	Glycerin
<b>M.O.A</b>	-Surfactant act by <b>decreasing</b> surface tension of feces. -Increase water penetration into the stool thus softening of feces and make it easier to move through the G.I.T.	-Mineral oil , Acts as lubricant thus softening the feces and promote defecation.	-Lubricant.
<b>P.k</b>	Given <b>orally</b> (12-72h) or <b>enema rectum form</b> (5-20 min)	Given orally ( <b>not palatable</b> )	Given rectally ( <b>suppository</b> )
<b>ADRs</b>	-	Impairs absorption of fat soluble vitamins <b>A,K,E,D</b> .	-

IBS treatments		
Drug	Alosetron	Tegaserod
<b>MOA</b>	Selective <b>5HT3</b> antagonist	<b>5HT4</b> agonist
<b>Use</b>	Used severe IBS <b>with diarrhea</b>	Used severe IBS <b>with constipation</b>
<b>ADRs</b>	Constipation and ischemic colitis may occur.( <b>People taking alosetron must sign a consent form before starting to take the medicine.</b> )	<b>CVS</b> side effect

# MCQs:

Q1- Female patient who is diagnosed with severe irritable bowel syndrome associated with diarrhea. Which of the following could be used ?

- A- Tegaserod  
B- Alosetron  
C- Lactulose  
D- Bisacodyl

Q2- Patients must sign a consent form before administering which drug?

- A- Docusate  
B- Castor oil  
C- Alosetron  
D- Tegaserod

Q3 33 years old male who use atracurium as muscle relaxants, if he had constipation, which one of the following drugs should not be used in his case ?

- A- Senna  
B- Bisacodyl  
C- Sodium phosphate  
D- Magnesium Sulphate

Q4-Anthraquinone"senna" is contraindicated in breast-feeding ladies due to which compound?

- A- Emodin  
B- Diphenylmethane  
C- Ricinoleic acid  
D- glycerin

Q5-Which of the following is used to treat liver cirrhosis?

- A- Saline laxatives  
B- Lactulose  
C- Senna  
D- Sodium salts

Q6- Which of the following drugs may cause iron deficiency?

- A- Bulk forming laxatives  
B- Osmotic laxatives  
C- Stimulant laxatives  
D- Stool softeners

Q7- Which of the following drugs often used for radiology preparation ?

- A-Glycerin  
B- Anthraquinone  
C- Castor oil  
D-Paraffin oil

Q8- Patient was prescribed Paraffin oil, which of the following will decrease in his serum?

- A- Iron  
B- Vitamin B12  
C- Vitamin K  
D- Calcium

# SAQ:

Answers:  
1-B  
2-C  
3-D  
4-A  
5-B  
6-A  
7-D  
8-C

**Case 1: A 34yo patient is going to have a colonoscopy. A-which drug should be used for emptying his colon ?**

Polyethylene glycol (PEG)

**B-List 2 advantages for using the drug**

1-Limited fluid & electrolyte imbalance. 2-Less flatulence & cramps.

**2- mention 2 indications for using lactulose**

1-Prevention of chronic constipation 2-Hemorrhoids 3-Hepatic encephalopathy (Hyperammonemia)  
4-Liver cirrhosis

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## References:

✓ Doctors' slides and notes



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