

## Gastrointestinal Block

Pharmacology Team 439

### Color index:

Main Text

Important

Dr's Notes

Female Slides

Male Slides

Extra

# Drugs Used In Treating Constipation & IBS

### Objectives:

- 1- Classify laxatives
- 2- Discuss the pharmacological properties of different classes of laxatives, their pharmacokinetics, uses and side effects
- 3- Define/Outline drugs used to treat irritable bowel syndrome

# Constipation

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

**Epidemiology:** Constipation affects all age groups, The elderly are most susceptible, There is high incidence of females, Formula-fed baby are more likely to have constipation, Over 700 drugs have constipation as a side effect

## Causes:

Female slides only

1

### Decreased motility in colon:

Decrease in water and fiber contents of diet.

Most common cause

2

### Difficulty in evacuation:

- Local painful conditions: anal fissures, piles (Hemorrhoids)
- Lack of muscular exercise.

3

### Drug-induced: (Chronic use)

- Anticholinergic agents
- Opioids
- Iron
- Antipsychotics

## May be Accompanied by These Symptoms:

Female slides only

Loss of appetite

Flatulence

Abdominal & rectal pain

Lethargy\*

Depression

\*fatigue, sleepiness, and it can lead to depression.

## Treatment of Constipation General Measures:

Female slides only

In treatment of constipation, we do not prescribe drugs right away. First, we try to change habits and take the general measures.

1. Adequate **fluid intake**
2. **High fiber** contents in diet (fruit, vegetables, nuts)
3. Regular exercise
4. Regulation of bowel habit.
5. Avoid drugs causing constipation.
6. Use drugs (laxatives or purgatives): Drugs that hasten the transit of food through GIT

## Classification Of Laxatives:

Click [here](#) to see the picture of classification in **male's** slides

1. Bulk forming laxatives

2. Osmotic laxatives

3. Stimulant/Irritant laxatives

4. Stool softeners (lubricants)

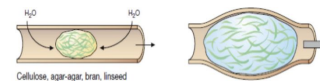
5. Serotonin (5-HT<sub>4</sub>) agonists

6. Intestinal secretagogues (Chloride secretion activators)

7. Opioid receptor antagonists

# 1. Bulk Forming Laxatives

	Dietary fibers	Hydrophilic colloids	Synthetic fibers
Types	<ul style="list-style-type: none"> <li>Indigestible parts of vegetables &amp; fruits</li> <li>Bran powder النخالة في الخبز البر</li> </ul>	<ul style="list-style-type: none"> <li>Psyllium seed* (natural plant products)</li> <li>Methyl cellulose (semisynthetic)</li> <li>CarboxyMethyl cellulose (CMC)</li> </ul>	<ul style="list-style-type: none"> <li>Polycarbophil</li> </ul>
M.O.A	Dietary fibers and hydrophilic colloids are <b>non absorbable substances</b> (hydrophilic colloids absorb water) → ↑ the bulk of intestinal contents by <b>water retention</b> (keep water in intestine), <b>Increase volume of non-absorbable solid residue</b> → ↑ mechanical pressure on the walls of intestine ( <b>distend the colon</b> ) → <b>stimulation</b> of stretch receptors → ↑ peristalsis → evacuation of soft stool.		
ADRs	<ul style="list-style-type: none"> <li>Delayed onset of action (1-3 days) so we can't use it in acute constipation, only chronic.</li> <li>Intestinal obstruction (should be taken with enough water).</li> <li>Bloating, flatulence, distension (Digestion of plant fibers by bacteria → bloating, flatus)</li> <li>Interfere with other drug absorption e.g. iron, cardiac glycosides (digoxin &amp; digitalis).</li> </ul>		



\*Fermented by the bacteria to yield some fatty acids, which nourish the intestine and improve its kinetics. It must be prescribed with plenty of water, otherwise it will solidify and occlude the bowel. For this reason, it is **contraindicated** with dehydrated patients and renal patients, and **indicated** with patients who have watery diarrhea.

## 2. Osmotic Laxatives

Are **water soluble BUT poorly absorbable compounds** (non-absorbable salts or sugars).

**MOA:** They remain in the bowel, attract and retain water by **osmosis** thereby increasing the volume of feces & **water content in large intestine** → ↑ peristalsis → evacuation of stool, ↑ **stool liquidity**.

(same mechanism as bulk forming laxatives, but by the **action of osmosis**)

### Osmotic Laxatives Include 3 Classes:

#### A. Sugars:

- Lactulose
- Sorbitol

#### B. Salts (Saline laxatives):

- Magnesium sulphate ( $MgSO_4$ ) or hydroxide ( $Mg(OH)_2$ )
- Sodium ( $Na_3PO_4$ ) or Potassium phosphate ( $K_3PO_4$ )

#### C. Polyethylene glycol (PEG)

## A. Sugars

	Lactulose
P.k	<ul style="list-style-type: none"> <li>Semi synthetic <b>disaccharide of fructose &amp; galactose</b></li> <li>Non absorbable</li> <li>In the colon, metabolized by bacteria into fructose &amp; galactose.</li> <li>These sugars are fermented into <b>lactic acid &amp; acetic acid</b> that function as osmotic laxatives</li> </ul>
Uses	<ul style="list-style-type: none"> <li>Prevention of <b>chronic</b> constipation</li> <li>Hepatic encephalopathy (<b>hyperammonemia</b>: high ammonia in blood)</li> <li>Hemorrhoids (piles)</li> <li>Liver cirrhosis</li> <li>Constipation caused by vincristine (anti cancer)</li> <li>Opioid encephalopathy</li> </ul> <div style="border: 1px dashed red; padding: 5px; margin-top: 10px;"> <p><b>Why is lactulose commonly used in liver cirrhosis?</b></p> <p><b>Mechanism:</b></p> <p>Lactulose → Lactic acid + Acetic Acid →</p> <p>acidification of the colon → ↓ ammonia absorption (<math>NH_4^+</math>)</p> </div> <p><b>Why is lactulose used in Liver cirrhosis &amp; Hyperammonemia?</b></p> <p>It increases the <math>H^+</math> concentration in the gut (by formation of lactic acid &amp; acetic acid), this favors the formation of the non-absorbable <math>NH_4^+</math> from <math>NH_3</math>, trapping <math>NH_3</math> in the colon and reducing its back diffusion into blood.</p> <p>It increases acidity → trap <math>NH_3</math> → converts it to <math>NH_4^+</math> (non-absorbable) = end result is decreased <math>NH_3</math> in blood → Hyperammonemia is treated!</p>
ADRs	<ul style="list-style-type: none"> <li>Delayed onset action (2-3 Days) Hence use in chronic</li> <li>Electrolyte disturbance (common osmotic ADR)</li> <li>Abdominal cramps &amp; flatulence (metabolized by colonic bacteria severe flatus &amp; cramps)</li> </ul>
Dose	15 ml for constipation & 30 ml for <b>Liver cirrhosis &amp; portal hypertension.</b>

## B. Salts (Saline laxatives)

Drug	Magnesium Sulphate & Citrate (Epsom salt) Magnesium hydroxide (milk of magnesia)	Sodium phosphate Potassium phosphate
P.k	<ul style="list-style-type: none"> <li>Poorly absorbable salts</li> <li>Increase evacuation of watery stool</li> <li>Have <b>rapid</b> effect (within 1-3 h)</li> <li>Isotonic or hypotonic solution should be used (hypertonic is not used because it causes vomiting &amp; dehydration)</li> </ul>	
Uses	<ul style="list-style-type: none"> <li>Treatment of <b>acute constipation</b></li> <li><b>Magnesium sulphate &amp; citrate:</b> treatment of acute constipation, cleanse the bowel</li> <li><b>Magnesium hydroxide:</b> treatment of <b>acute and chronic constipation</b></li> <li>Short-term treatment of moderate-to-severe constipation, bowel preparation for colonoscopy</li> </ul>	
ADRs	<ul style="list-style-type: none"> <li>Disturbance of fluid and electrolyte balance</li> <li>May have systemic effects</li> </ul>	
	<ul style="list-style-type: none"> <li><b>Magnesium Sulphate &amp; Citrate:</b> patient should maintain adequate hydration.</li> <li><b>Magnesium Hydroxide:</b> Prolonged use in patients with renal insufficiency → hypermagnesemia</li> </ul>	<b>Sodium Phosphate:</b> <ul style="list-style-type: none"> <li>May cause hyperphosphatemia, hypernatremia, <b>hypokalemia</b></li> <li>Cardiac arrhythmias</li> <li>Acute renal failure → deposition of calcium phosphate (nephrocalcinosis)</li> </ul>
C.I	<b>Magnesium salts:</b> it affects excitability 1- Renal failure (Hypermagnesemia) decrease excretion 2- Heart block* 3- CNS depression* 4- Neuromuscular block* *Because magnesium is the physiological antagonist of calcium	<b>Sodium salts:</b> congestive heart failure

## C. Balanced Polyethylene Glycol (PEG)

Drug	Polyethylene Glycol (PEG)	
P.k	<ul style="list-style-type: none"> <li><b>Isotonic solution</b> of polyethylene glycol (PEG) &amp; electrolytes (Na sulfate, NaCl, KCl, Na bicarbonate)</li> <li>A colonic lavage solution (used to empty the colon before procedures)</li> </ul>	
Uses	<ul style="list-style-type: none"> <li>Used for whole bowel irrigation <b>prior to colonoscopy or surgery</b> (4L over 2-4 hours)</li> <li>Safe for all patients</li> <li>For optimal cleansing 1-2 litres ingested rapidly over 1-2 hrs on evening before the procedure &amp; 4-6 hrs before the procedure</li> <li>For chronic constipation PEG mixed with juice (no cramps or flatus)</li> </ul>	
Advantage	<ul style="list-style-type: none"> <li>Limited fluid or electrolyte imbalance</li> <li>Less flatulence and cramps "Ideal laxative"</li> </ul>	

### 3. Stimulant/Irritant Laxatives

Click [here](#) for classification found only in female slides.

Drug	Anthraquinone derivatives	Diphenylmethane* Derivatives	Castor oil زيت الخروع
Types	<ul style="list-style-type: none"> <li>● Senna</li> <li>● Cascara</li> <li>● Aloe vera</li> </ul>	<ul style="list-style-type: none"> <li>● Bisacodyl</li> </ul> <p>*Written as "Diphenomethane" in male slides</p>	
MOA	<p>★ The most powerful group among laxatives and should be used with care</p> <ul style="list-style-type: none"> <li>● Act via <b>direct stimulation</b> of nerve endings of <b>enteric nervous system</b> in colonic mucosa → increased peristalsis &amp; purgation (↑ bowel movement)</li> <li>● ↑ electrolyte and fluid secretion</li> </ul>		
P.k	<ul style="list-style-type: none"> <li>● Orally, bowel movements 6-12hrs</li> <li>● Rectally (as suppository), bowel movements 2hrs</li> <li>● Given at night</li> <li>● Act in colon</li> <li>● Delayed onset of action (8-12 h)</li> <li>● Hydrolyzed by bacterial colon into sugar + emodin (The absorbed emodin has direct stimulant action)</li> <li>● Emodin may pass into milk. It should be avoided in lactating women</li> <li>● occur naturally, poorly absorbed</li> </ul>	<ul style="list-style-type: none"> <li>● Given orally</li> <li>● Acts on colon</li> <li>● Onset of action = orally (6-12 h)/per rectum (1h)</li> <li>● Hydrolysed in the gut, absorbed, conjugated to glucuronic acid in the liver acid &amp; secreted with bile</li> <li>● Oral administration is followed after 6-8 h by discharge of soft stool</li> </ul>	<ul style="list-style-type: none"> <li>● Given orally</li> <li>● 5-20 ml on empty stomach in the morning</li> <li>● Onset of action = 2-6 h</li> <li>● Acts in <b>small intestine</b></li> <li>● Vegetable oil degraded by lipase → ricinoleic acid + glycerin</li> <li>● <b>Ricinoleic acid</b> is very irritating to mucosa.</li> <li>● Castor oil is obtained from the seeds of <i>Ricinus communis</i></li> <li>● Oral administration of 10-30ml is followed by a discharge of watery stool within 0.5-3hrs</li> </ul>
Specific Uses	Prolonged use → brown pigmentation of the colon "Melanosis coli" benign		Could be employed after oral ingestion of a toxin
Uses	<ul style="list-style-type: none"> <li>● In patients who are neurologically impaired because it stimulates ENS</li> <li>● In bed-bound patients in long-term care facility</li> </ul>		
ADRs	<ul style="list-style-type: none"> <li>● Abdominal cramps may occur</li> <li>★ Prolonged use → <b>dependence</b> &amp; destruction of myenteric plexus leading to <b>atonic colon</b> (loss of motility)</li> </ul>		
C.I	Senna: breastfeeding		pregnancy → reflex contraction of uterus → <b>abortion</b>
Dependance	Click <a href="#">here</a> to see the doctor's explanation and picture about stimulant laxatives dependence in male's slides		

### 5. Serotonin 5-HT<sub>4</sub>-Receptor Agonists

Male slides only

Drug	Prucalopride
MOA	<ul style="list-style-type: none"> <li>● Stimulation of 5-HT<sub>4</sub> receptors (agonist) → ↑ release of neurotransmitters ↑ second order enteric neurons</li> <li>● Enterokinetic activities (Enteric neurons stimulates proximal bowel contraction &amp; distal bowel relaxation)</li> </ul>
Uses	<ul style="list-style-type: none"> <li>● used for chronic constipation in women</li> <li>★ Advantage: Lack CVS side effects</li> </ul>

## 4. Fecal Softeners (Lubricants)/Surfactants

Drug	Docusate	Glycerin Suppositories	Paraffin/Mineral Oil
<b>MOA</b>	<ul style="list-style-type: none"> <li>• Non absorbed drugs</li> <li>• Act by either <b>decreasing surface tension</b> (surfactant) allowing water to interact with the stool <b>OR</b> by <b>softening the feces</b> thus promoting defecation (alter the consistency of feces → easier to pass)</li> </ul>		
<b>P.k</b>	<ul style="list-style-type: none"> <li>• Sodium dioctyl sulfosuccinate</li> <li>• One type of surfactants</li> <li>• Act by decreasing surface tension of feces</li> <li>• is given orally (12-72 hours) or enema (5-20 min)</li> </ul>	<ul style="list-style-type: none"> <li>• Lubricant</li> <li>• Given rectally (suppository)</li> </ul>	<ul style="list-style-type: none"> <li>• A mineral oil, given orally</li> <li>• Acts as lubricant thus softening the feces and promoting defecation</li> <li>• Lubricate stool ↓ water absorption from the stool</li> <li>• Inhibit water absorption</li> </ul>
<b>Specific Uses</b>	<p>Used In hospitalized patients → ↓constipation &amp; straining. Straining: exerting very high force to evacuate, this is why we use this drug after rectal surgery and for hemorrhoids</p>		<ul style="list-style-type: none"> <li>• Good for <b>radiology preparation</b></li> <li>• To prevent fecal impaction* in children &amp; debilitating adults *formation of very solid stool which you can't pass</li> </ul>
<b>Uses</b>	Treat constipation in patients with <b>hard stool</b> or specific conditions and for people who should <b>avoid straining</b> (after surgeries/hernia when patients can't push hard, to avoid rupture)		
<b>ADRs</b>			<ul style="list-style-type: none"> <li>• Not palatable (bad taste, if aspired it can cause Lipoid pneumonia)</li> <li>• <b>Impairs absorption of fat soluble vitamins</b> (Vit. A, D, E, K) on long-term use</li> <li>• May leak out from anal sphincter which can be embarrassing</li> </ul>

## 6. Chloride Secretion Activators

Male slides only

Drug	Lubiprostone	Linacotide
<b>MOA</b>	It stimulates type 2 chloride in the small intestine → ↑ Cl and $\text{HCO}_3^-$ -rich fluid, → intestinal motility → shortens intestinal emptying <ul style="list-style-type: none"> <li>• No loss of efficacy with long-term use</li> </ul>	Stimulates chloride secretion through activation guanylate cyclase C
<b>Uses</b>	<ul style="list-style-type: none"> <li>• <b>Lubiprostone</b>: designated category C for pregnancy</li> <li>• Used for chronic constipation &amp; IBS-C</li> </ul>	
<b>ADRs</b>	After discontinuation, constipation may return to pretreatment	Most common ADR is diarrhea

# 7. Opioid Receptor Antagonists

Male slides only

Drug	Methylnaltrexone	Alvimopan
MOA	μ- receptor antagonist 1	
P.k	doesn't cross the BBB (peripheral, doesn't affect central analgesic drugs)	
Uses	★ <b>Opioid-induced</b> constipation in patients receiving palliative care for advanced illness e.g. cancer patients taking opioids	★ Short term to shorten the period for postoperative ileus

## Irritable Bowel Syndrome

Idiopathic Chronic bowel disorder characterized by abdominal discomfort (bloating, pain, distention, cramps) associated with alteration in bowel habits (diarrhea or constipation or both).

### Symptomatic Treatment of IBS:

Female slides only

- **Alosetron (IBS with diarrhea)**
- **Tegaserod (IBS with constipation)**
- Antispasmodics e.g. mebeverine (Smooth muscle relaxant to treat spasm of GIT)
- Laxatives in IBS with Constipation e.g. Chloride Secretion Activators
- Antidiarrheals in IBS with diarrhea (**diphenoxylate, loperamide**)  
more details in treatment of dysentery & amoebiasis lecture
- Low doses of TCA (amitriptyline) act via: Anticholinergic action, reduce visceral afferent sensation (much lower dose than what's used in depression)

- For patients with predominant **diarrhea** → antidiarrheal, loperamide
- For patients with predominant **constipation** → Fibers are used, may cause bloating. Osmotic (milk of magnesia).
- For chronic **abdominal pain** → low dose of tricyclic antidepressants

This table was found in male slides only

<b>IBS-C Agents</b>
Linaclotide, Lubiprostone, <b>Tegaserod</b>
<b>IBS-D Agents</b>
<b>Alosetron</b>
<b>Agents for IBS-C and IBS-D</b>
Dicyclomine, Hyoscyamine

# Symptomatic Treatment of IBS

Click [here](#) for pictures of MOA of Alosetron and Tegaserod found in [male](#) & [female](#) slides

Drug	Alosetron
MOA	<ul style="list-style-type: none"> <li>● Selective 5-HT<sub>3</sub> <b>antagonist</b> (it bind with high affinity &amp; dissociate slowly from the receptor) Theoretically, it can be used as antiemetic (-setron)</li> <li>● 5-HT<sub>3</sub> receptors antagonism of the enteric nervous system of the gastrointestinal tract <b>results into</b>:               <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>
P.k	<ul style="list-style-type: none"> <li>● Rapidly absorbed from GIT, 50-60% bioavailability, half life= 1.5 h</li> <li>● Undergoes extensive CYT P450 metabolism</li> </ul>
Uses	★ Use <b>restricted in IBS with severe diarrhea</b> in women who have not had success with any other treatment
ADRs	★ <b>Severe constipation and ischemic colitis may occur.</b> (People taking alosetron must sign a consent form before starting to take the medicine)

Drug	Tegaserod
MOA	<ul style="list-style-type: none"> <li>● 5-HT<sub>4</sub> <b>agonist</b></li> <li>● Stimulation of 5-HT<sub>4</sub> of enteric nervous system of GIT → <b>increases peristalsis</b></li> </ul>
Uses	<p>Short term treatment of <b>IBS-associated with constipation</b> in women &lt;55 years old with <u>no history</u> of heart problems</p> <p>May still be used in limited emergency situations</p>
ADRs	Tegaserod has <b>CVS side effects</b> , unlike prucalopride, which was also a 5-HT <sub>4</sub> agonist

Male slides only

Drug	Hyoscine	Dicyclomine
MOA	Antispasmodics (anticholinergics) Inhibit muscarinic cholinergic receptors in enteric plexus and smooth muscle	
Uses	Efficacy questionable	



# Case From Male's Slides

Q

A 70-year-old woman who was previously very active but whose mobility has recently been limited by osteoarthritis on the knees & hips sees her general practitioner because of a recent **change in bowel habit** from once daily to **once every three days**. Her current medication includes regular **co-codamol (paracetamol + codeine)** for her osteoarthritis, **oxybutynin** for urinary frequency, **aluminum hydroxide** p.r.n for dyspepsia, and **bendroflumethiazide & verapamil** for hypertension. Following bowel evacuation by a phosphate enema, proctoscopy & colonoscopy are reported as normal.

1

**What general approach should be employed to this patient?**

- Adequate fluid intake.
- High fiber contents in diet.
- Regular exercise.

2

**What are the possible contributing causes of her constipation?**

- Immobility
- Old Age
- Gender (female)

3

**Which of these patient's medications may contribute to her constipation?**

**Drugs that can cause constipation:**

- **Aluminum hydroxide**
- **Anticholinergics** (older antihistamines) (oxybutynin)
- Diltiazem
- **Verapamil**
- **Diuretics** (bendroflumethiazide)
- **Opioids** (Codeine)
- Tricyclic antidepressants
- Iron preparations
- Disopyramide
- Amiodarone

4

**What pharmacologic & non-pharmacologic approaches would be appropriate to this patient?**

First we want quick relief, so for example Stimulant Laxatives, then we use drugs for prevention like Lactulose (Osmotic laxative)

# Summary

Drug	P.k.	Uses	ADRs
<b>1. Bulk Forming Laxatives</b>			
Dietary fibers	<b>MOA:</b> Dietary fibers and hydrophilic colloids are <b>non absorbable substances</b> → ↑ the bulk of intestinal contents by <b>water retention</b> → ↑ mechanical pressure on the walls of intestine ( <b>distend the colon</b> ) → <b>stimulation</b> of stretch receptors → ↑ peristalsis → evacuation of soft stool		<ul style="list-style-type: none"> <li>• Delayed onset of action (1-3 days)</li> <li>• Intestinal obstruction (should be taken with enough water). So, not used for patients in which water intake is restricted like heart failure, Kidney failure</li> <li>• Bloating, flatulence, distension</li> <li>• Interfere with other drug absorption e.g. iron, cardiac glycosides</li> </ul>
Hydrophilic colloids			
Synthetic fibers			
<b>2. Osmotic Laxatives</b>			
<b>MOA:</b> They remain in the bowel, attract and retain water by <b>osmosis</b> thereby increasing the volume of feces → ↑ peristalsis → evacuation of stool			
Lactulose	<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 <b>lactic acid &amp; acetic acid</b> that function as osmotic laxatives</li> </ul>	<ul style="list-style-type: none"> <li>• Prevention of chronic constipation (and opioid induced constipation)</li> <li>• Hemorrhoids</li> <li>• Hepatic encephalopathy (Hyperammonemia)</li> <li>• Liver cirrhosis</li> </ul>	<ul style="list-style-type: none"> <li>• Delayed onset action (2-3 Days)</li> <li>• Electrolyte disturbance.</li> <li>• Abdominal cramps &amp; flatulence.</li> </ul>
Magnesium sulphate/Citrate (Epsom salt) Magnesium hydroxide (milk of magnesia)	<ul style="list-style-type: none"> <li>• Are poorly absorbable salts</li> <li>• Increase evacuation of watery stool</li> <li>• have rapid effect (within 1-3 h)</li> <li>• Isotonic or hypotonic solution should be used</li> </ul>	<ul style="list-style-type: none"> <li>• Treatment of <b>acute and chronic constipation (Magnesium hydroxide)</b></li> <li>• Treatment of acute constipation, <b>cleanse of bowel (Magnesium sulphate/Citrate)</b></li> </ul>	<ul style="list-style-type: none"> <li>• Disturbance of fluid and electrolyte balance</li> <li>• Dehydration</li> <li>• May have systemic effects.</li> <li>• Sodium phosphate:               <ul style="list-style-type: none"> <li>◦ May causes Hyperphosphatemia, hypernatremia, <b>hypokalemia</b>.</li> <li>◦ Cardiac arrhythmias</li> <li>◦ Acute renal failure → deposition of calcium phosphate "nephrocalcinosis"</li> </ul> </li> </ul>
Sodium phosphate Potassium phosphate			<b>C.I:</b> <b>Magnesium salts:</b> 1- Renal failure (Hypermagnesemia) 2- Heart block 3- CNS depression 4- Neuromuscular block  <b>Sodium salts:</b> congestive heart failure
Polyethylene Glycol (PEG)	<ul style="list-style-type: none"> <li>• Isotonic solution of polyethylene glycol &amp; electrolytes (Na sulfate, NaCl, KCl, Na bicarbonate)</li> <li>• A colonic lavage solution</li> </ul>	<ul style="list-style-type: none"> <li>• Used for whole bowel irrigation prior to colonoscopy or surgery (4L over 2-4 hours)</li> <li>• For optimal cleansing 1-2 litres ingested rapidly over 1-2 hours on evening before the procedure &amp; 4-6h before the procedure</li> <li>• Used For chronic constipation PEG mixed with juice</li> </ul>	<b>Advantages:</b> <ul style="list-style-type: none"> <li>• Limited fluid or electrolyte imbalance</li> <li>• Less flatulence and cramps</li> </ul>

# Summary

Drug	M.O.A	Uses	ADRs
<b>3. Stimulant Laxatives/Irritant</b>			
<b>Anthraquinone derivatives</b>	<ul style="list-style-type: none"> <li>★ The most powerful group among laxatives and should be used with care</li> <li>● Act via direct stimulation of enteric nervous system → increased peristalsis &amp; purgation</li> </ul>	<ul style="list-style-type: none"> <li>● In patients who are neurologically impaired</li> <li>● in bed-bound patients in long-term care facility</li> </ul>	<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> <p><b>C.I:</b> Castor oil in pregnancy</p>
<b>Diphenyl methane derivatives</b>			
<b>Castor oil</b>			
<b>4. Fecal Softeners (Lubricants)/Surfactants</b>			
<b>Docusate</b>	<ul style="list-style-type: none"> <li>● Non absorbed drugs</li> <li>● Act by either decreasing surface tension allowing water to interact with the stool or by softening the feces thus promoting defecation</li> </ul>	Treat constipation in patients with hard stool or specific conditions and for people who should avoid straining  <b>Paraffin:</b> Good for radiology preparation	<ul style="list-style-type: none"> <li>● Impairs absorption of fat soluble vitamins (Vit.A,D,E,K)</li> <li>● May leak out from anal sphincter which can be embarrassing</li> </ul>
<b>Glycerin</b>			
<b>Paraffin oil</b>			
<b>5. Serotonin 5-HT<sub>4</sub>-Receptor Agonists</b>			Male slides only
<b>Prucalopride</b>	<ul style="list-style-type: none"> <li>● Stimulation of 5-HT<sub>4</sub> receptors → ↑ release of neurotransmitters ↑ second order enteric neurons</li> <li>● with enterokinetic activities (Enteric neurons stimulates proximal bowel contraction &amp; distal bowel relaxation)</li> </ul>	<ul style="list-style-type: none"> <li>● Chronic constipation in women</li> <li>★ Advantage: Lack CVS side effects</li> </ul>	
<b>6. Chloride Secretion Activators</b>			Male slides only
<b>Lubiprostone</b>	It stimulates type 2 chloride in the small intestine → ↑Cl <sup>-</sup> fluid rich fluid, → intestinal motility → shortens intestinal emptying	<ul style="list-style-type: none"> <li>● Designated category C for pregnancy (Lubiprostone)</li> <li>● Used for chronic constipation &amp; IBS-C</li> </ul>	After discontinuation, constipation may return to pretreatment
<b>Linacotide</b>	Stimulates chloride secretion through activation guanylate cyclase C		Most common ADR is diarrhea
<b>7. Opioid Receptor Antagonists</b>			Male slides only
<b>Methylnaltrexone</b>	μ- receptor antagonist 1	★ Opioid-induced constipation in patients receiving palliative care for advanced illness.	<b>P.k:</b> does not cross the BBB
<b>Alvimopan</b>		★ Short term to shorten the period for postoperative ileus	

# Summary

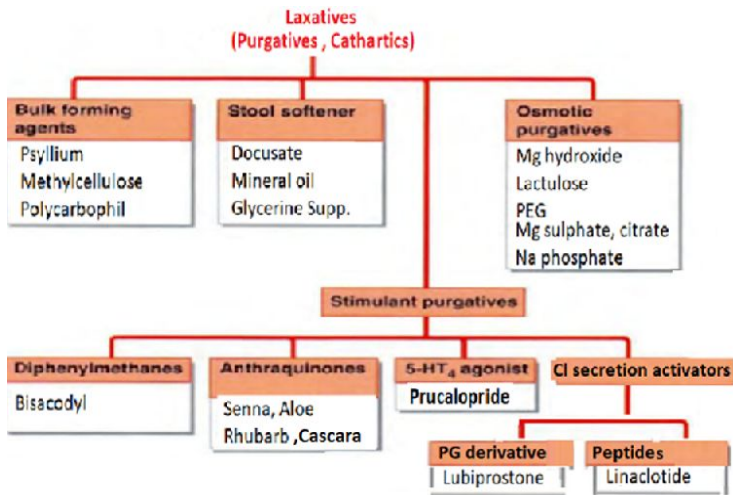
Drug	M.O.A	Uses	ADRs
<b>Symptomatic Treatment of IBS</b>			
<b>Alosetron</b>	<ul style="list-style-type: none"> <li>• Selective 5-HT<sub>3</sub> antagonist ( it bind with high affinity &amp; dissociate slowly from the receptor)</li> <li>• 5-HT<sub>3</sub> receptors antagonism of the enteric nervous system of the gastrointestinal tract 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>	<p>★ Use restricted in IBS with severe diarrhea in women who have not had success with any other treatment</p>	<p>★ Severe Constipation and ischemic colitis may occur (People taking alosetron must sign a consent form before starting to take the medicine)</p>
<b>Tegaserod</b>	<ul style="list-style-type: none"> <li>• 5-HT<sub>4</sub> agonist</li> <li>• Stimulation of 5-HT<sub>4</sub> of enteric nervous system of GIT → increases peristalsis</li> </ul>	<p>Short term treatment of IBS-associated with constipation in women &lt;55 years old with no history of heart problems</p> <p>May still be used in limited emergency situations</p>	<p>Tegaserod has CVS side effects</p>
<b>Hyoscine*</b>	<p>Antispasmodics (anticholinergics) Inhibit muscarinic cholinergic receptors in enteric plexus and smooth muscle</p>	<p>Efficacy questionable</p>	
<b>Dicyclomine*</b>			

## Summary From **Female's** Slides

<b>Bulking agents</b>	Oral, 48-72 hours	Acute and chronic constipation
<b>Stool softeners</b>	Oral, 24-72 hours; Rectal, 5-20 minutes	Prevention of straining after rectal surgery and in acute perianal disease
<b>Osmotic laxatives (lactulose)</b>	Oral, 24-72 hours	<ul style="list-style-type: none"> <li>• Chronic constipation</li> <li>• Hepatic encephalopathy</li> <li>• Opioid constipation</li> </ul>
<b>Saline laxatives</b>	Oral, 0.5-3 hours; Rectal, 30 minutes	short -term treatment of moderate-to-severe constipation; acute constipation; bowel preparation for colonoscopy

# Pictures found in Dr.'s Slides

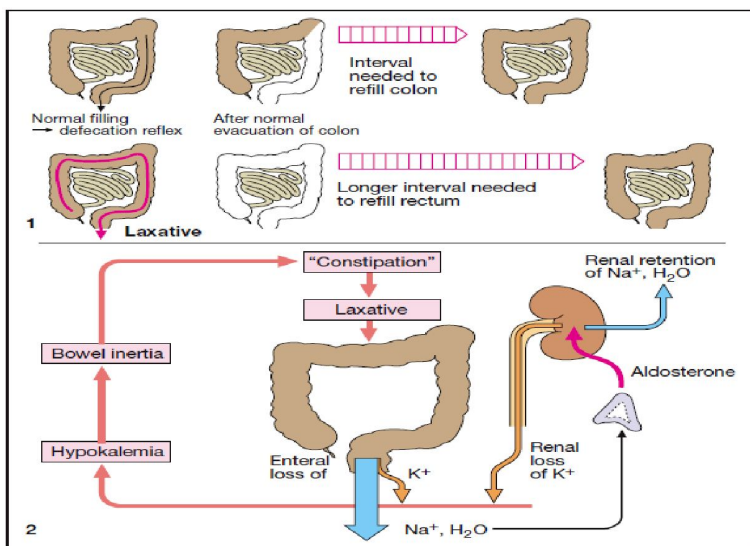
## Classification of laxatives



## Classification of stimulant laxatives

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

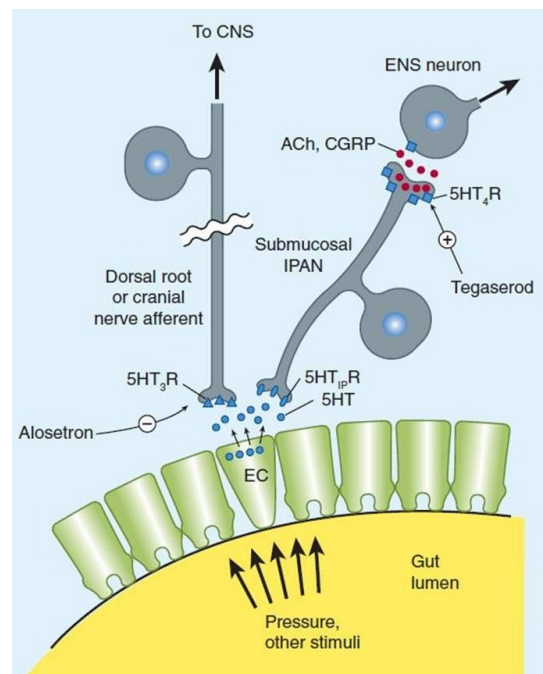
## Stimulant laxative dependence



There is a slide talking about stimulant laxatives **dependence**, this is how the doctor clarified it:

"Normally, the **descending colon ONLY** gets evacuated, until it gets filled again, and so on. Laxatives help in evacuating the **WHOLE colon**, not only the descending part. So the filling will take longer time and the patient might take another dose of the drug thinking he still has constipation, which can cause increase loss of water, leading to **aldosterone secretion, which causes sodium and water retention**, but increases potassium **excretion (loss)**. Increased potassium excretion (**hypokalemia**) leads to **decreased bowel inertia** (the ability of the bowel to initiate peristalsis) thus, leading to constipation and irresponsibility to laxatives."

## Symptomatic treatment of IBS MOA



# MCQs

Q1: Which of the following drugs may cause iron deficiency?			
A- Bulk forming laxatives	B-Osmotic laxatives	C-Stimulant laxatives	D-Stool softeners
Q2: Which of the following is used to treat liver cirrhosis?			
A- Senna	B-Lactulose	C-Sodium salts	D- Saline laxatives
Q3: 44-year-old female patient who has severe constipation and he has a history of cardiovascular diseases which drug should be avoided?			
A- docusate	B-linaclotide	C-tegaserod	D-lubiprostone
Q4: 34-year-old woman has irritable bowel syndrome with diarrhea that is not responsive to conventional therapies, Despite the small risk of severe constipation and ischemic colitis,the patient decides to begin therapy with alosetron. Alosetron has which of the following receptor actions?			
A- 5-HT <sub>3</sub> agonist	B- 5-HT <sub>3</sub> antagonist	C- 5-HT <sub>4</sub> agonist	D- 5-HT <sub>4</sub> antagonist
Q5: which of the following is NOT related to Lactulose uses?			
A- liver cirrhosis	B- hyperammonemia	C-hemorrhages	D-hemorrhoids
Q6: 4-year-old child has chronic constipation with <b>hard stool</b> which drug should be used?			
A- Sodium salts	B-Mg hydroxide	C-castor oil	D-glycerin
Q7: 57-years male patient who received multiple regimen of drugs for advanced disease causing opioid-induced-constipation ,What is the appropriate drug for this condition?			
A- prucalopride	B-Methylnaltrexone	C-Lactulose	D-Linaclotide
Q8: Sodium phosphate may cause:			
A- hyponatremia	B-hypomagnesemia	C-hyperkalemia	D-hyperphosphatemia

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

# SAQ

Q1) Mention 2 indications for using lactulose

Q2) 40-year-old patient is going to have a colonoscopy.

A- Which drug should be used for emptying his colon ?

B- List 2 advantages for using the drug

Q3) 35 years women present to the hospital with severe constipation and She has History of myocardial diseases, which drug should be used ?

Q4) mention M.O.A for the previous drug

Q5) mention the specific uses of paraffin oil

## Answers

A1) 1- Prevention of chronic constipation

2- Hemorrhoids

3- Liver cirrhosis

A2) A) Polyethylene glycol (PEG)

B) 1- Limited fluid & electrolyte imbalance.

2- Less flatulence & cramps.

A3) Prucalopride

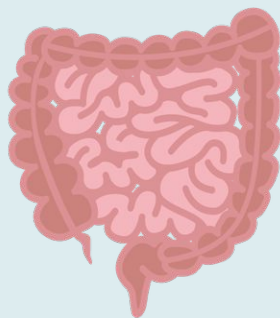
A4) Stimulation of 5-HT<sub>4</sub> receptors → ↑ release of neurotransmitters ↑ second order enteric neurons

A5) 1- good for radiology preparation

2- to prevent fecal impaction in children and debilitating adults



Feedback Form



# Gastrointestinal Block

Pharmacology Team 439

## Leaders

Banan AlQady

Ghada AlOthman

Nawaf Alshahrani

## Organizers

- Ghada Aljedaie
- Hind Almotywea
- Mais Alajami
- Norah Alasheikh
- Nouf Alsubaie
- Sadem Alzayed
- Shatha Aldhohair
- Shayma Alghanoum
- Tarfa Alsharidi

## Note Takers

- Duaa Alhumoudi
- Homoud Algadheb
- Mishal Althunayan
- Omar Alhalabi
- Yasmine Alqarni

## Reviser

- Dana Naibulharam
- Mishal Althunayan
- Omar Alhalabi

## Members

- Abdulaziz Alderaywsh
- Abdulaziz Alghuligah
- Abdulrahman Almebki
- Abdulrhman Alsuhaibany
- Aljoharah Albnyan
- Aljoud Algazlan

- Arwa alqahtani
- Feras Alqaidi
- Lama Alahmadi
- Maha Alanazi
- Manal Altwaim
- Mona Alomiriny

- Norah Almasaad
- Noura Bamarei
- Rand AlRefaei
- Rawan Bakader
- Salem Alshihri
- Shahd Almezel

