


King Saud University
College of Medicine
2nd Year, 2nd Block

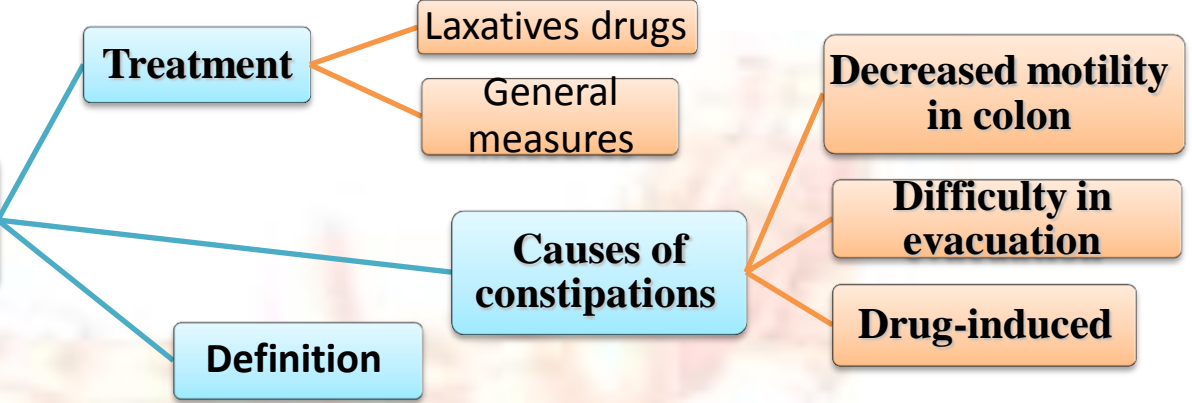
GIT BLOCK



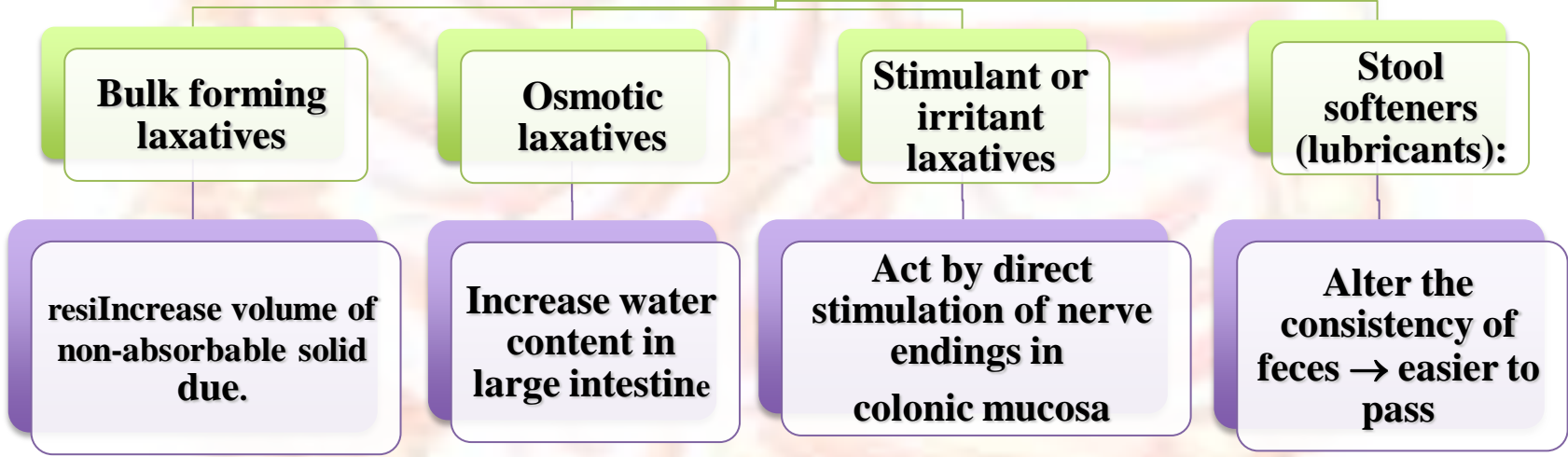
L4 Drugs used in treating
constipation and IBS

Mind map

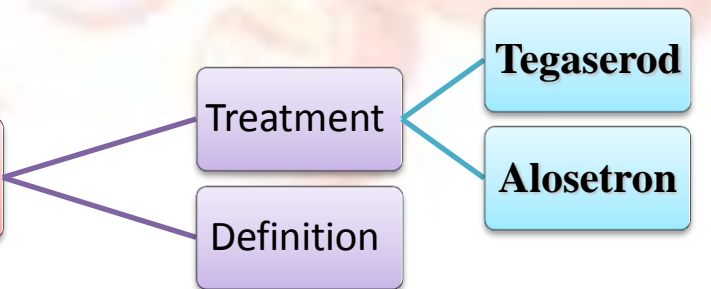
A. constipation



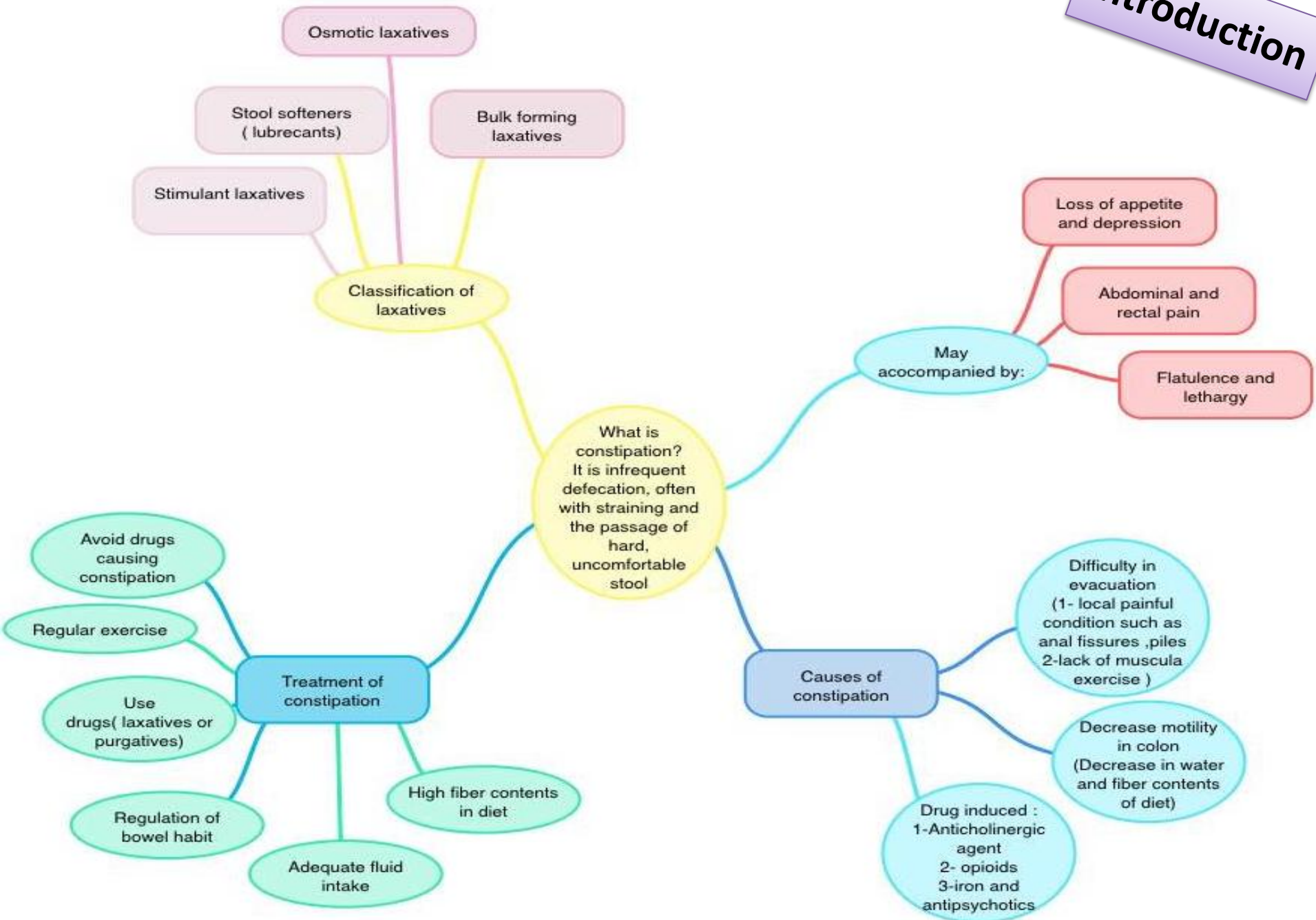
Classification of laxatives or purgatives



B. Irritable bowel syndrome



introduction



A.CONSTIPATIONS

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

4-Stool softeners (lubricants):

Alter the consistency •
of feces → easier to pass

Note: most of the drugs are non absorbed.

1-Bulk (fiber) Laxatives

Types

1-Dietary fibers:

- Indigestible parts of vegetables & fruits
- Bran powder

2-Hydrophilic colloids

- Psyllium seed
- Methyl cellulose
- Carboxymethyl cellulose (CMC)

M.O.A

act on **Small & large intestine**

- Delayed** Onset of action **12-72 h**
- Dietary fibers and hydrophilic colloids are Non absorbable substances** → Increase 1-The bulk of intestinal contents by water retention → ↑ mechanical pressure on the walls of intestine. And then stimulation of stretch receptors → ↑ peristalsis → evacuation of soft Stool.

S.E

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

2-Osmotic Laxatives

Type

1-Sugars : e.g. lactulose

2-Salts (Saline laxatives):

- Magnesium sulphate (Epson's salt).
- Magnesium hydroxide (milk of magnesia).
- Sodium or potassium phosphate.

3-Polyethylene glycol (PEG)

M.O.A

They remain in the bowel, attract and retain water by **osmosis** thereby increasing the volume of feces → ↑ **peristalsis** → evacuation of stool

are water soluble compounds
Poorly absorbable compounds
(salts or sugars)

Lactulose

Saline Laxatives

Balanced Polyethylene Glycol (PEG)

1-Semisynthetic **disaccharide** of fructose and galactose
 2-Non absorbable
 3-In **colon**, metabolized by bacteria into fructose and galactose
 4-These sugars are fermented into **lactic acid and acetic acid** that function as **osmotic laxatives**

1-Are poorly absorbable salts
 2-Increase evacuation of watery stool.
 3-**have rapid effect** (within 1-3 h).
 4-**Isotonic** or hypotonic solution should be used.
 5-**act in Small & large intestine**

1-**Isotonic solution of polyethylene glycol & electrolytes** (NaCl, KCl, Na bicarbonate).

2-**Is a colonic lavage solution**

Uses
 1-**for chronic constipation** (always natural drugs for chronic constipation)
 2-**Hepatic encephalopathy** (Hyperammonemia)
 3- **Hemorrhoids**

for acute constipation

for whole bowel irrigation prior to colonoscopy or surgery
 (4L over 2-4 hours)

M.O.A
 Lactulose increases the H⁺ concentration in the gut, This favors the formation of the non-absorbable NH₄⁺ from NH₃, trapping NH₃ in the colon and reducing its back diffusion into blood.

M.O.A

M.O.A

S.E
 1-Delayed onset of action (2-3 days)
 2-Abdominal cramps and flatulence.
 3-**Electrolyte disturbances**

1-**Disturbance of fluid and electrolyte balance**
 2--May have systemic effects.

S.E

Why Lactulose is commonly used in liver cirrhosis?

Lactulose → Lactic acid + Acetic Acid
 → acidification of the colon ↓ Ammonia absorption

Contraindications:
 1-**Sodium salts in congestive heart Failure**
 2-**Magnesium salts are contraindicated in:**
 - Renal failure
 - Heart block
 - CNS depression
 -Neuromuscular block

Advantages
Limited fluid or electrolyte imbalance
less flatulence and cramps

Note: Even the drug is sugar but still approved for diabetic patient because the sugar **not absorbed to the blood**

3-Stimulant Laxatives

are the most powerful group among laxatives and should be used with care

drugs	Bisacodyl (Diphenylmethane)	Castor oil (ricinoleic acid)	Anthraquinone derivatives (senna, cascara, aloe vera)
M.O.A	act via direct stimulation of enteric nervous system → increased peristalsis & purgation.		
Pharmacokinetics	<ul style="list-style-type: none"> -given orally. -<u>acts on colon.</u> -Onset of action = A-orally (6-12h)/ B-per rectum (1 h). 	<ul style="list-style-type: none"> -Given orally -5-20 ml on empty stomach in the morning. -acts in <u>small intestine</u> -Vegetable oil degraded by lipase → ricinoleic acid + glycerin. -<u>Ricinoleic acid</u> is very irritating to mucosa. -Onset of action = 2-6 h. 	<ul style="list-style-type: none"> -<u>Act in colon.</u> -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). -Given at night.
Side Effects	<ul style="list-style-type: none"> *Abdominal cramps may occur. *Prolonged use → dependence *the patient won't be able to pass stool unless he takes the drug & destruction of myenteric plexus leading to <u>atonic colon</u>. 		
Contraindications	<ul style="list-style-type: none"> *Senna is contraindicated in lactation *Castor oil #in pregnancy → reflex contraction of uterus → abortion. 		

4-Fecal Softeners (Lubricants)/surfactants

- Are non absorbed drugs.
- Act by either **1-decreasing surface tension** or by **2-softening** the feces thus promoting defecation.
- Treat constipation in patients **with hard stool** or specific conditions and for people who should avoid **straining** (doing an effort during defecation).

drugs	Docusate	Glycerin	Paraffin oil
Pharmacokinetics & uses	<ul style="list-style-type: none"> -Sodium dioctyl sulfosuccinate. -One type of surfactants- -Act in Small and large intestine by decreasing surface tension of feces. -given orally (1-3 days) or enema (5-20 min). 	<ul style="list-style-type: none"> -Lubricant. -Given rectally (suppository). 	<ul style="list-style-type: none"> -Is a mineral oil. -given orally. -acts as lubricant thus softening the feces and promoting defecation. -Good for radiology preparation
Side Effects	-----	-----	<ul style="list-style-type: none"> -impairs absorption of fat soluble vitamins. -not palatable *طعم غير مستساغ

B.IRRITABLE BOWEL SYNDROME (IBS)

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

Antispasmodics e.g.
mebeverine

Low doses of tricyclic antidepressants
(amitriptyline) act via

Laxatives, Tegaserod in IBS-Constipation

Antidiarrheals, Alosetron in IBS-diarrhea

Anticholinergic action

Reduce visceral afferent sensation

Alosetron :anti-diarrhea associated with IBS

M.O.A	<ul style="list-style-type: none">-Selective 5HT₃ antagonist.-block 5-HT₃ receptors of the enteric nervous system of the gastrointestinal tract.-inhibition of colon motility.-inhibition of unpleasant visceral afferent pain sensation (nausea, pain, bloating).
Uses	severe IBS with diarrhea in women <u>who have not had success with any other treatment.</u>
ADRs	<ul style="list-style-type: none">▪ Constipation▪ ischemic colitis may occur. <p>People taking alosetron must sign a consent form before starting to take the medicine</p>

Tegaserod:anti-constipation associated with IBS

M.O.A	<ul style="list-style-type: none">-5HT₄ agonist.-Stimulation of 5HT₄ of enteric nervous system of GIT → increases peristalsis.
Uses	Short term treatment of IBS-associated with constipation in women <55 years old with no history of heart problems
ADRs	<ul style="list-style-type: none">▪has CVS side effects▪may still be used in limited emergency situations.

S U M M A R Y

Drug/Category	Examples	Side Effects	Onset + site of action
Bulk forming laxatives	Dietary fibers: Indigestible parts of vegetables & fruits, Bran powder	<ol style="list-style-type: none"> 1. Delayed onset of action (1-3 days). 2. Intestinal obstruction (should be taken with enough water). 3. Bloating, flatulence, distension. 4. Interfere with other drug absorption e.g. iron, cardiac glycosides. 	Onset of action : Oral, 48–72 hours Site of action: Small & large intestine
	Hydrophilic colloids: Psyllium seed, Methyl cellulose, Carboxymethyl cellulose (CMC)		

Drug/Category	Examples	M.O.A	Uses	Site of action	Onset of action
Stool softeners (lubricants)	Docusate	Act by decreasing surface tension of feces (allow more water to get in)	Treat constipation in patients with hard stool or specific conditions and for people who should avoid straining . (as in after surgery or acute perianal disease	Small and large intestine	Enema 5-20 minutes Orally 12 – 72 h
	Glycerin	Lubricant . Given rectally.			
	Paraffin oil	acts as lubricant thus softening the feces and promoting defecation.		Colon	6 – 8 hours

Drug/Category	Examples	Side Effects	Contraindications	Site of action + onset of action
Stimulant laxatives	Bisacodyl	<ol style="list-style-type: none"> 1. Abdominal cramps may occur. 2. Prolonged use → dependence & destruction of myenteric plexus leading to atonic colon. 	<ol style="list-style-type: none"> 1. Senna is contraindicated in lactation because it pass into milk. 2. Castor oil is contraindicated in pregnancy it may cause abortion. 	<ol style="list-style-type: none"> 1. acts on colon . 2. Onset of action : orally (6-12 h)/ per rectum (1 h)
	Castor oil “Given orally”			<ol style="list-style-type: none"> 1. acts on small intestine . 2. Onset of action: 2-6 h.
	Anthraquinone derivatives (senna, cascara, aloes)			<ol style="list-style-type: none"> 1. Acts on colon 2. Onset of Action 12 h (orally) or 2 h (rectally).

S U M M A R Y

Drug/Category	Examples	Uses	Side Effects
Osmotic laxatives	Sugars : e.g. Lactulose “ have delayed action 12-72 h “ “acts on Colon”	1. Prevention of chronic constipation 2. Hepatic encephalopathy (Hyperammonemia) as in liver cirrhosis. 3. Hemorrhoids 4. opioid constipation	1. Delayed onset of action (2-3 days) 2. Abdominal cramps and flatulence. 3. Electrolyte disturbances.
	Salts (Saline laxatives) “have rapid effect (within 1-3 h).” “Acts on Small & large intestine”	Treatment of acute constipation . short term treatment of moderate-to-severe constipation; chronic constipation; bowel preparation	1. Disturbance of fluid and electrolyte balance 2. May have systemic effects.
	Polyethylene glycol (PEG)	Is a colonic lavage solution Used for whole bowel irrigation prior to colonoscopy or surgery (4L over 2-4 hours).	1. Limited fluid or electrolyte imbalance 2. less flatulence and cramps

Drug/Category	Alosetron	Tegaserod
M.O.A	<ul style="list-style-type: none"> ▪ Selective 5HT₃ antagonist ▪ block 5-HT₃ receptors of the enteric nervous system of the gastrointestinal tract. ▪ inhibition of colon motility. ▪ inhibition of unpleasant visceral afferent pain sensation (nausea, pain, bloating). 	<ul style="list-style-type: none"> ▪ 5HT₄ agonist. ▪ Stimulation of 5HT₄ of enteric nervous system of GIT → increases peristalsis
Uses	Used in severe IBS- D “with diarrhea” <u>in women who have not had success with any other treatment.</u>	Short term treatment of IBS- C “with constipation” <u>in women <55 years old with no history of heart problems</u>
Side Effects	Constipation and ischemic colitis	CVS side effects

Quiz yourself

1. A patient was taking a laxative for long time. He suddenly developed atonic colon. What is the medication he was taking ?

- A) Saline laxatives.
- B) Tegaserod.
- C) Senna
- D) Paraffin oil

4. A patient was using a drug and suddenly he developed Neuromuscular Block. Which of the following he was taking ?

- A) Magnesium salts
- B) Sodium salts
- C) Bisacodyl
- D) Docusate

7. Which of the following is used in colonic lavage ?

- A) Balanced Polyethylene Glycol (PEG)
- B) Sodium salts
- C) Lactulose
- D) Anthraquinone glycosides

2. Which of the following is used in treatment of Hepatic encephalopathy ?

- A) Lactulose
- B) Magnesium salts
- C) Sodium salts
- D) Bisacodyl

5. Which of the following is contraindicated in pregnant women ?

- A) Castor oil
- B) Senna
- C) Docusate
- D) Bulk purgatives

8. Which of the following Act by decreasing surface tension of feces ?

- A) Bisacodyl
- B) Docusate
- C) Lactulose
- D) Paraffin oil

3. Which of the following drugs is acting on small intestine ?

- A) Bisacodyl
- B) Castor oil
- C) Lactulose
- D) Paraffin oil

6. Which of the following is contraindicated in lactating women?

- A) Castor oil
- B) Senna
- C) Docusate
- D) Bulk purgatives

9. A patient with IBS was treated by a drug and after a while he developed ischemic colitis . What was the drug he took ?

- A) Tegaserod
- B) Anthraquinone glycosides
- D) Alosetron
- C) Balanced Polyethylene Glycol (PEG)



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It always seems impossible until it is done

BEST OF LUCK



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