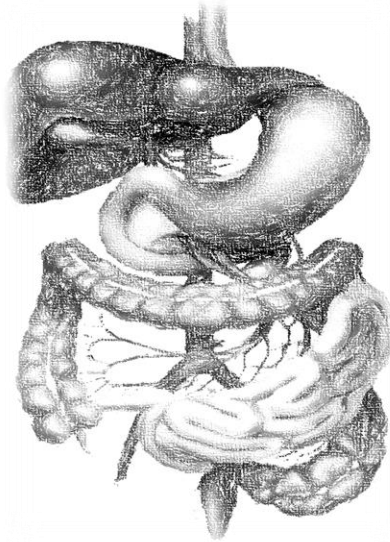




MEDICINE
KING SAUD UNIVERSITY



Drugs used in treating constipation and IBS

Objectives

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

Color index

● extra information and further explanation

● **important**

● **doctors notes**

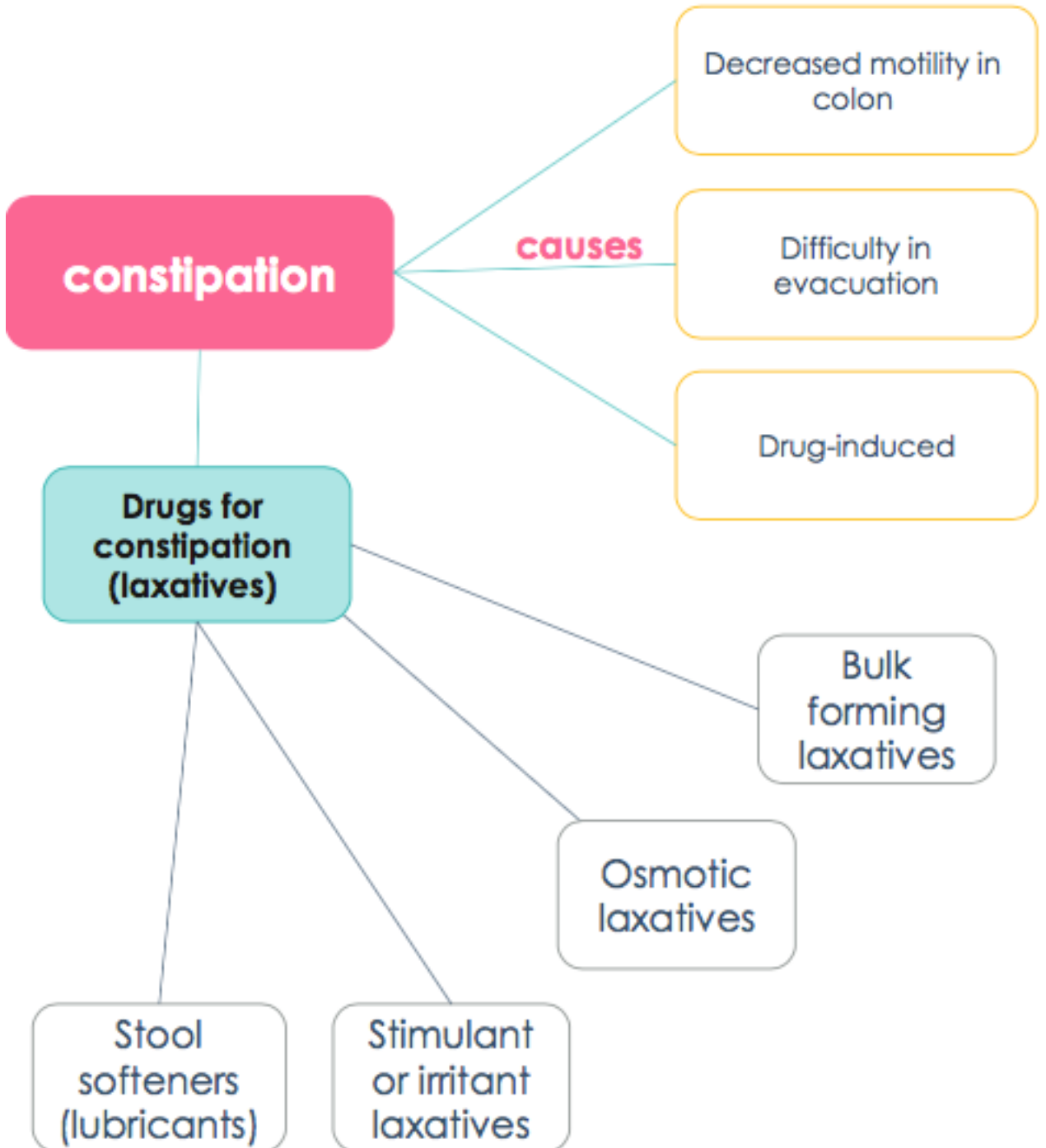
● **Drugs names**

● **Mnemonics**



[Kindly check the editing file before studying this document](#)

Introduction



To understand !

What is constipation?



Very useful.
Don't miss it

Infrequent defecation, often with straining and the passage of hard, uncomfortable stools.
- **May be accompanied by other symptoms:** Abdominal discomfort and rectal pain, Flatulence, Loss of appetite, Lethargy & Depression.

Causes of constipations:

Decreased motility in colon:

Decrease in water and fiber contents of diet.
"Unbalanced diet"

Difficulty in evacuation:

1. Local painful conditions: anal fissures, piles.
2. Lack of muscular exercise.

Drug-induced:

1. Anticholinergic agents
2. Opioids
3. Iron
4. Antipsychotics.
5. Anti-depressant, anti-histamine, has anticholinergic effect

Treatment by general measures

Adequate fluid intake

Use drugs (laxatives or purgatives *more watery effect*)

Regular exercise

High fiber contents in diet

Regulation of bowel habit.

Avoid drugs causing constipation.

Medications used in constipations

- Drugs that hasten the transit of food through the gastrointestinal tract are called **laxatives** (ملينات) or **purgatives** (محرکات) (Or we say the drugs that increase GI motility)
- Loosen stools and increase bowel movement

Classification of Laxatives or Purgatives:

Bulk forming laxatives (increase the size of stool)

- Increase volume of non-absorbable solid residue.

Osmotic laxatives (cause water withdrawal by sugar or salt)

- Increase water content in large intestine.

Stimulant or irritant laxatives (cause irritation to intestinal mucosa to increase the motility)

- Act by direct stimulation of nerve endings in colonic mucosa.

Stool softeners (lubricants)

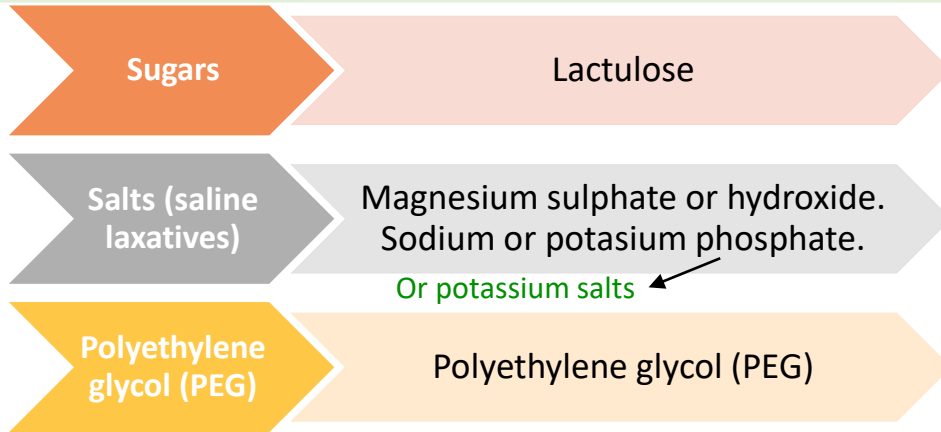
- Alter the consistency of feces → easier to pass

Bulk forming laxatives taken orally

Include	<p><u>Dietary fibers:</u></p> <ul style="list-style-type: none"> • Indigestible parts of vegetables (broccoli) & fruits. • Bran powder (نخالة) • Whole grains (female's slides only) 	<p><u>Hydrophilic colloids</u></p> <p>(They absorb water and increase the volume.)</p> <ul style="list-style-type: none"> • Psyllium seed (powder) "natural" • Methyl cellulose "semisynthetic" • Carboxymethyl Cellulose (CMC)
Mech. Of action	<p>Dietary fibers and hydrophilic colloids are non-absorbable substances (main mechanism of action) → Increase the bulk of intestinal contents by water retention → ↑mechanical pressure on walls of intestine → the stimulation of stretch receptors → ↑peristalsis → evacuation of soft stool.</p> <p>الفكرة اننا نبي نوصل للأمعاء انك مليانه ولازم تتحركين بأننا نزيد الكتلة بالماء مو المواد اللي تطع مع الغائط)) نقدر نشبهها بحلى الجلي، بالبداية تكون على هيئة بودرة ولما نضيف عليها ماء تبدأ تتشكل وتصير صلبة ولها وزن وثقل</p>	
use	Acute and chronic constipation	
ADRs	<ul style="list-style-type: none"> • Delayed onset of action (1-3 days) • Intestinal obstruction (should be taken with enough water) it is not absorbed and it is a powder so it need a water for the action and also to prevent the obstruction • Bloating, flatulence, distension. • Interfere with other drug absorption (if taken at the same time) e.g. iron , cardiac glycosides. 	

Osmotic Laxatives

- They are **Water soluble** compounds, **poorly absorbed** “high percentage is not absorbed”
- They remain in the bowl
- Attract water by **osmosis** (water retention in the bowel) → **increase the volume of feces** → increase peristalsis & evacuation
- It has a **hygroscopic effect**.
- Give with water to prevent the dehydration.



DRUG	Lactulose	
P.K	<ul style="list-style-type: none"> ○ Semisynthetic disaccharide of fructose & galactose. Increase water content (osmotic effect) ○ Non absorbable. ○ Lactulose retains water in colon (osmotic effect) ○ In the colon metabolized by bacteria to fructose & galactose. These sugars are fermented into lactic acid & acetic acid & formic acid thus lowering the PH. Acidification 	
INDICATIONS	<ul style="list-style-type: none"> • Prevention (prophylaxis) of chronic constipation in patients as a long-term treatment. Because its well tolerated, it can be used with elderly patient and chronically. • Hemorrhoids (بواسير) • Hepatic encephalopathy in people with Liver cirrhosis as prophylactic therapy • Opioid constipation <p>→ Why lactulose is used in Liver cirrhosis & Hyper-ammonemia ?</p> <p>* Acidification of the colon (increase of the H⁺ concentration) by lactic acid & acetic acid causes increase of H⁺ concentration in gut, this will cause non-polar NH₃ (ammonia) trapping (which is non-charged = lipid soluble= easily absorbed), by favors the formation of NON- absorbable (polar=easily excreted) NH₄⁺ (ammonium) and thus reducing absorption.</p> <p>* Simply: Lactulose → Lactic acid + Acetic acid + formic acid → Acidification of the colon → ↓ ammonia absorption (NH₄⁺) (ammonium salt “polar” will be excreted in feces) .</p>	
ADRS	<ul style="list-style-type: none"> • Delayed on set action(2-3Days) • Abdominal cramps & flatulence. • Electrolyte disturbance. 	<p style="color: green; text-align: center;">In pt. of cirrhosis → may cause diarrhea due to high dose</p>
DOSE	15 ml for constipation & 30 ml for Liver cirrhosis.	

Osmotic Laxatives (cont.)

DRUG	Saline Laxatives	Polyethylene glycol (PEG) Macrogol.
DRUGS	<ul style="list-style-type: none"> • Magnesium sulphate (Epson's salt) • Magnesium hydroxide (milk of magnesia) • Sodium phosphate/potassium phosphate • potassium phosphate 	<ul style="list-style-type: none"> ○ Osmotically active laxative. ○ Isotonic solution of polyethylene glycol & electrolytes (NaCl, KCl, Na bicarbonate) they balance the effect of electrolytes by adding salt.
P.K	<ul style="list-style-type: none"> ○ Poorly absorbed (90% NOT absorbed) ○ Rapid effect (1-3h) acute situations (emergency) ○ Isotonic or hypotonic solution should be used. If you used hypertonic solution it will cause dehydration by ↑ vomiting. ○ It increases evacuation of watery stool. 	<ul style="list-style-type: none"> ○ Is a colonic lavage solution. Cause complete evacuation . <p>Role of electrolytes in macrogol: (NaCl, KCl , Na bicarbonate) help mitigate the possibility of electrolyte imbalance & dehydration.</p>
Advantage	-	<ul style="list-style-type: none"> ○ Limited fluid & electrolyte imbalance. ○ Less flatulence & cramps.
Uses	Short term Treatment of moderate to severe Acute Constipation. used With plenty of water.	Used for whole bowel irrigation (removal of feces) prior to colonoscopy or surgery. It should be ingested rapidly (4L over 24h)
ADRS	<p>in case of repeated administration:</p> <ul style="list-style-type: none"> ○ Disturbance of fluid & electrolyte balance. ○ May have systemic effects. 	<p>We have a colonies of this macro-organism</p> <p>May cause Hypokalemia</p>
Contraindication	<ul style="list-style-type: none"> ○ Sodium salts in: <ul style="list-style-type: none"> • Congestive heart failure. ○ Magnesium salt in: <ul style="list-style-type: none"> • Renal failure (little % excreted by the kidney) • Heart blockers. • CNS depression. • Neuromuscular blockers (e.g. curium) • (also can not be combine with <u>Aminoglycosides</u>) 	-

Stimulant Laxatives

البسكوييت يحمس الواحد يأكله

Bisacodyl

تحمس / يحمس = Stimulant Laxatives

roller coaster ride تحمس الواحد يجربها

Castor oil

السنة النبوية تحمس الواحد بسويها عشان الأجر

Anthraquinone

(Senna, cascara, aloes)

هذي الماسكارا تحمس الواحد يجربها

- Are the **most powerful groups** among laxative & should be used with care. **Not for prolonged use.**
- **Mechanism of action:** They act via **direct stimulation of enteric nervous system** → increase peristalsis & purgation.

DRUG	Anthraquinone glycoside (Senna, cascara, aloe vera) Natural products	Castor oil زيت الخروع	Bisacodyl
P.K	<ul style="list-style-type: none"> ○ Delayed on set of action (8-12h) ○ Bowel movements in 12h (orally) or 2h (rectally) as suppository) ○ Given at night. ○ Hydrolyzed by bacterial colon into sugar + emodin (The absorbed emodin has direct stimulant action) ○ Act on colon ○ Emodin may pass into milk. <p>نتخيل الطفل يقول "أمي أديني الحليب" ○ Senna is useful in treating opioid induced constipation.</p>	<ul style="list-style-type: none"> ○ Onset of action(2-6h) ○ Given orally,5-20ml on empty stomach in the morning ○ Act in small intestine ○ Vegetable oil degraded by lipase → ricinoleic acid + glycerin. ○ Castor change to ricinoleic acid by bacterial action. ○ Ricinoleic acid is very irritating to mucosa. 	<ul style="list-style-type: none"> ○ Given orally. Before sleep because the delayed onset of action. ○ Onset of action (6-12h) Per rectum (1h). Rapid onset of action. ○ Act on colon ○ Type: Diphenylmethane
ADRS	<ol style="list-style-type: none"> 1. Abdominal cramps 2. Dependence & destruction of myenteric plexus leading to Atonic Colon due prolonged use (the patient can't go to the bathroom without these drugs because his/her bowel movement is Addicted to the drug!!) 3. May cause Apoptosis to the intestinal mucosal cells 	<p>roller coaster ride تحمس الواحد يجربها وتخليه يدمن عليها</p>	<p>البسكوييت هذا يخلي الواحد يدمن عليه</p>
Contraindication	<p>الطفل الرضيع اذا طلع سنه يبدأ يزجج الأم وهي ترضعه</p> <p>Senna is contraindicated in breast feeding (lactation) But we can use Lactulose is safer</p>	<p>In pregnancy (causes reflex contraction of uterus this will lead to abortion!!)</p> <p>The pregnant women should not play roller coaster ride</p>	<p>—</p>

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.

Drug	<u>Docusate</u> (sodium dioctyl sulfosuccinate)	Paraffin oil	Glycerin
Mech. of action	<p>صدمت لما عرفت إن دي أختك ، سولفوا لي عنها وعن نجاحاتها</p> <ul style="list-style-type: none"> • Surfactant act by <u>decreasing</u> 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. 	<p>Mineral oil , Acts as lubricant thus softening the feces and promote defecation</p> <p>زي الواحد لما يحط صابون ويتزحلق بس هنا يكون زيت</p>	Lubricant
P.K	Given orally(12-72h) or enema rectum form (5-20 min)	Given orally (not palatable) طعمه مش حلو	Given rectally (suppository)
Indications	often used as prophylaxis rather than acute treatment, - especially in hospitalized patients-because of delayed onset when given orally.	Good for radiology preparation .	—
ADRs	—	Impairs absorption of fat soluble vitamins A,K,E,D . AKED I like this perfume(Paraffin)	—
Note	Stool softeners used for prevention of straining after rectal surgery and in acute peri-anal disease		

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 :



4:16 for better understanding

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
In severe case
Alosetron
in IBS-D

Alosetron

M.O.A	<ul style="list-style-type: none"> ○ Selective 5HT₃ antagonist. Pharmacologically can be used for vomiting, but clinically it is not approved yet. ○ 5-HT₃ receptor antagonism of the enteric nervous system of the GIT results into: <ul style="list-style-type: none"> • Inhibition of colon motility → means there is time for the water to be absorbed → thus hardening of stool. • Inhibition of unpleasant visceral afferent pain sensation (nausea, pain, bloating).
Uses	Used in severe IBS with diarrhea in women who have not had success with any other treatment. ”ألو، الست الحديدية ماتت” (Alo-set-ron) , (diarrhea)
ADRs	○ Severe Constipation and <u>ischemic colitis</u> “ high risk → not preferable ” may occur. (People taking alosetron must sign a consent form before starting to take the medicine)

Tegaserod

M.O.A	<ul style="list-style-type: none"> ○ 5HT₄ agonist. ○ Stimulation of 5HT₄ of enteric nervous system of GIT → increase peristalsis (Constipation)Patient say to his doctor ma tegaser (Tegaserod)
Uses	<ul style="list-style-type: none"> ○ Short term treatment of IBS with constipation in women <55 year old with no history of heart problems. ○ May still be used in limited emergency situations.
ADRs	CVS side effects

Summary

Constipation treatments

Non-absorbable	Bulk forming	<ul style="list-style-type: none"> Dietary fibers Hydrophilic colloids 	
	Osmotic laxatives	Sugars (Lactulose)	
		Saline	
PEG			
The most potent	Stimulant laxatives	<p>They act via direct stimulation of enteric nervous system → increase peristalsis & purgation.</p> <p>Dependence & destruction of my enteric plexus leading to Atonic Colon due prolonged use</p>	Bisacodyl
		Castor oil	
		Anthraquinone	
	Fecal softeners	Glycerin	
		Paraffin oil	
		Docosate	

- **Increase the bulk of intestinal content by water retention.**
- Orally , has Delayed onset.
- **Interfere with other drugs absorption** (iron, cardiac glycosides)

- **Retains water in colon by osmotic effect.**
- Acidification of colon due to conversion of NH₃ to NH₄ "NH₃ trapping" → ↓PH
- **Use as prophylactic therapy in Hepatic encephalopathy in people with Liver cirrhosis**

- **Result in watery stools** by osmotic effect.
- **Rapid effect , treat acute constipation.**
- C.I.s: (Na salt → CHF) (Mg salt → RF, HB CNS dep. , Nm block & aminoglycosides)*

- ↑water content by osmotic effect.
- **Used for complete evacuation of colon prior to colonoscopy or prior to surgery.**
- Given with Electrolytes to compensate the deficiency.

- Orally / rectally "faster" acts on colon, at night

- Orally on empty stomach , **degraded in small intestine by lipase into ricinoleic acid which is very irritating to mucosa.**
- Most rapidly in oral form
- **In pregnancy (causes reflex contraction of uterus this will lead to abortion)**

- Acts on colon & given at night
- **Hydrolyzed into emodin which may pass into milk → C.I breast-feeding mom (especially Senna)**
- Delayed onset & may cause dependence

- Lubricant , rectally (suppository)

- Lubricant , promote defecation
- **For Radiology preparation**
- **Impairs absorption of fat soluble vitamins (A,K,E,D).**

- **Sodium dioctyl sulfosuccinate**
- **Surfactant (decrease surface tension)**
- **Allow water mixing with stool for easier movement in the GIT**

*RF → renal failure

HB → heart block

Nm block → neuromuscular

MCQs

7- Which of following stimulant laxatives act on small intestine & degraded into ricinoleic acid ?

A. Senna

B. Bisacodyl

C. castor oil

8- If we have patient with sever acute constipation and he need rapid effect. Which of the following has the fastest onset of action?

A. Saline Purgative

B- Osmotic Purgative

C- Fecal softeners

9- Which of the following laxative classes is the most powerful?

A. Saline Purgative

B- Osmotic Purgative

C- Stimulant Purgative

10- 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. Docusate

B. Magnesium Sulphate

C. Sodium phosphate

11- 21 years old male who has infection and use gentamycin, if he had constipation, which one of the following drugs should not be used in his case ?

A. Docusate

B. Magnesium Sulphate

C. Sodium phosphate

12- Alcoholic patient who has liver cirrhosis and he may develop hepatic encephalopathy, to prevent that, which one of the following could be used ?

A. Lactulose

B. Bisacodyl

C. Macrogol

13- A patient was assigned a surgery the next day with colonoscopy, which of these is used to evacuate the colon and should be taken night before ?

A. Macrogol

B. Bisacodyl

C. Docusate

14- Which one of the following laxatives is not recommended to be taken before sleep ?

A. Cascara

B. Bisacodyl

C. Magnesium sulphate

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

A. Mebeverine

B. Alosetron

C. Tegaserod

16- Which of these drugs allow the water to be incorporated into the stool and decrease the surface tension?

A. Docusate

B. Macrogol

C. Lactulose

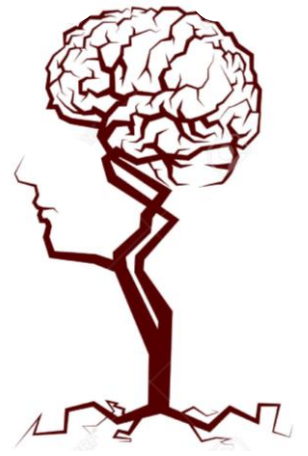
17- Patients must sign a consent form before administrating which drug?

A. Mebeverine

B. Alosetron

C. Tegaserod

7)	C
8)	A
9)	C
10)	B
11)	B
12)	A
13)	A
14)	C
15)	B
16)	A
17)	B



إِنَّ فِي ذَلِكَ لَآيَاتٍ لِّقَوْمٍ يَتَفَكَّرُونَ ﴿٣﴾

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