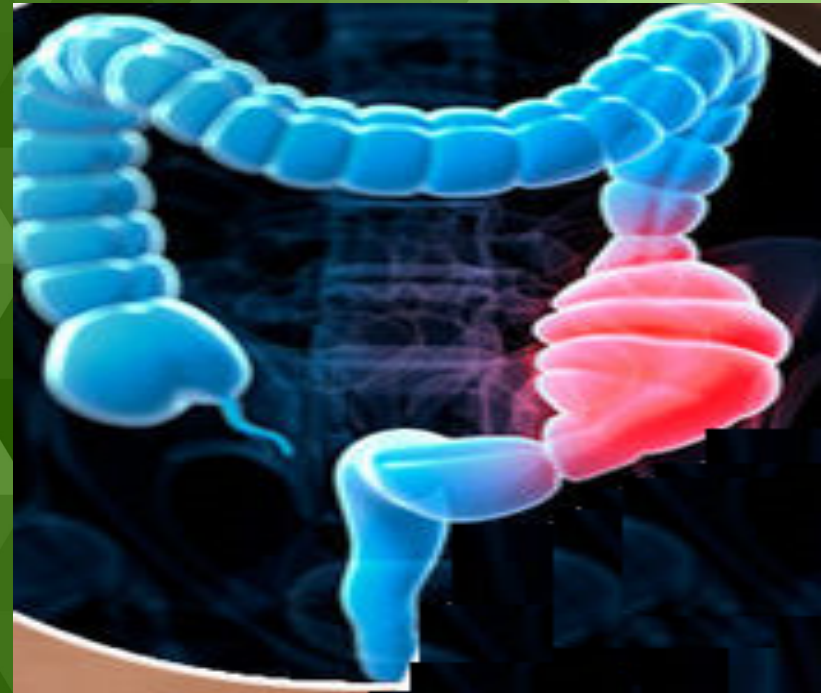


CONSTIPATION & IBS



CONSTIPATION & IBS

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

CONSTIPATION & IBS

ILOS

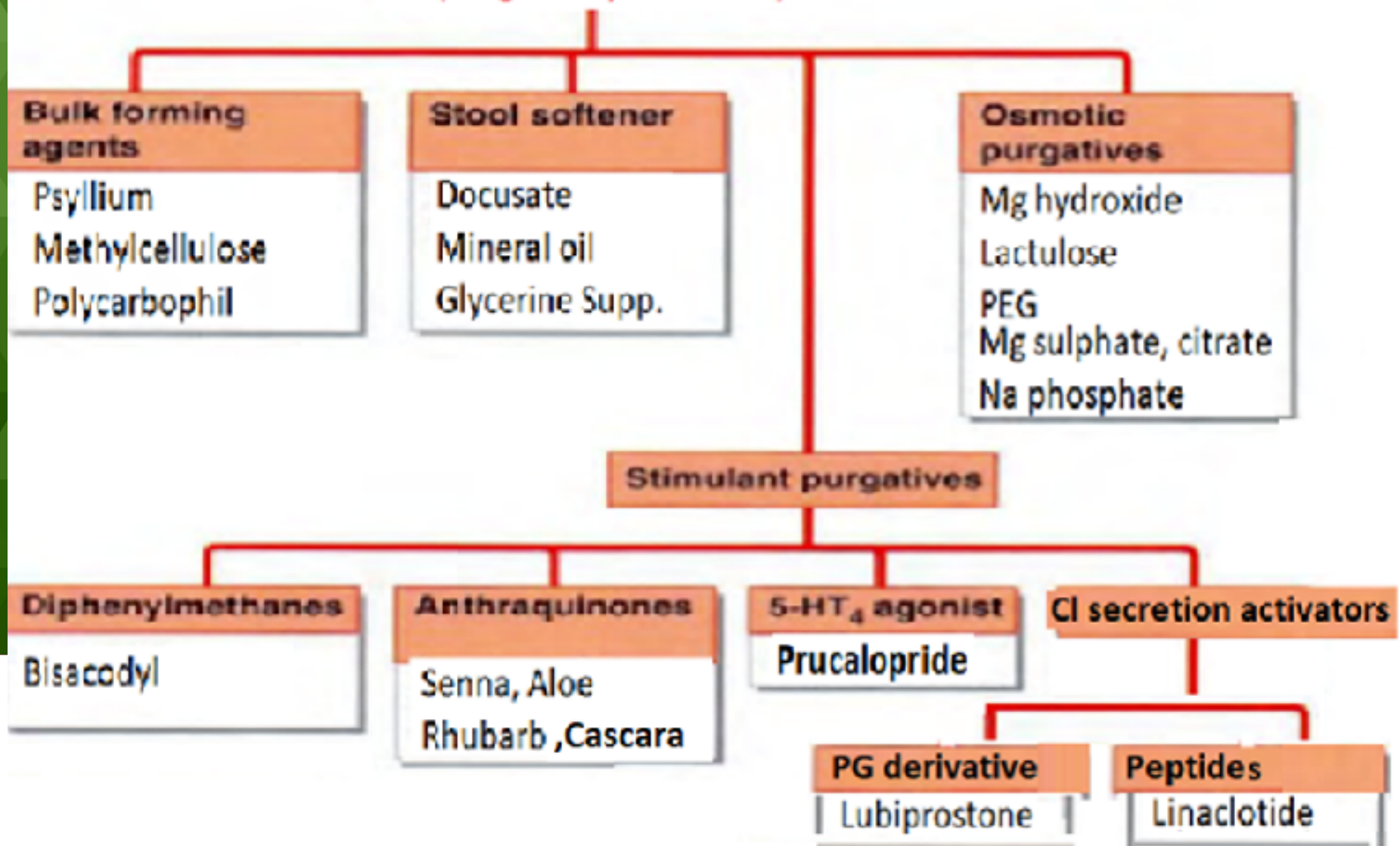
Classify Laxatives

Discuss the pharmacological properties of different classes of laxatives

Outline drugs used to treat irritable bowel syndrome

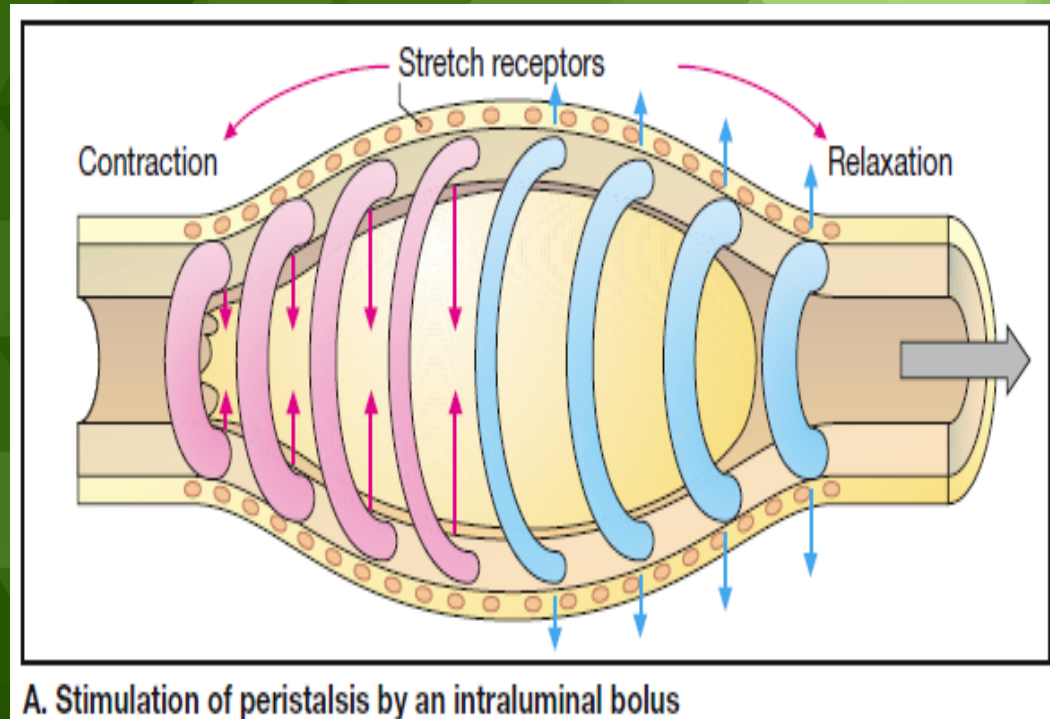
CLASSIFICATION

Laxatives (Purgatives, Cathartics)



1-BULK-FORMING LAXATIVES

**Indigestible
hydrophilic colloids
absorb water →
distend the colon →
promote peristalsis**

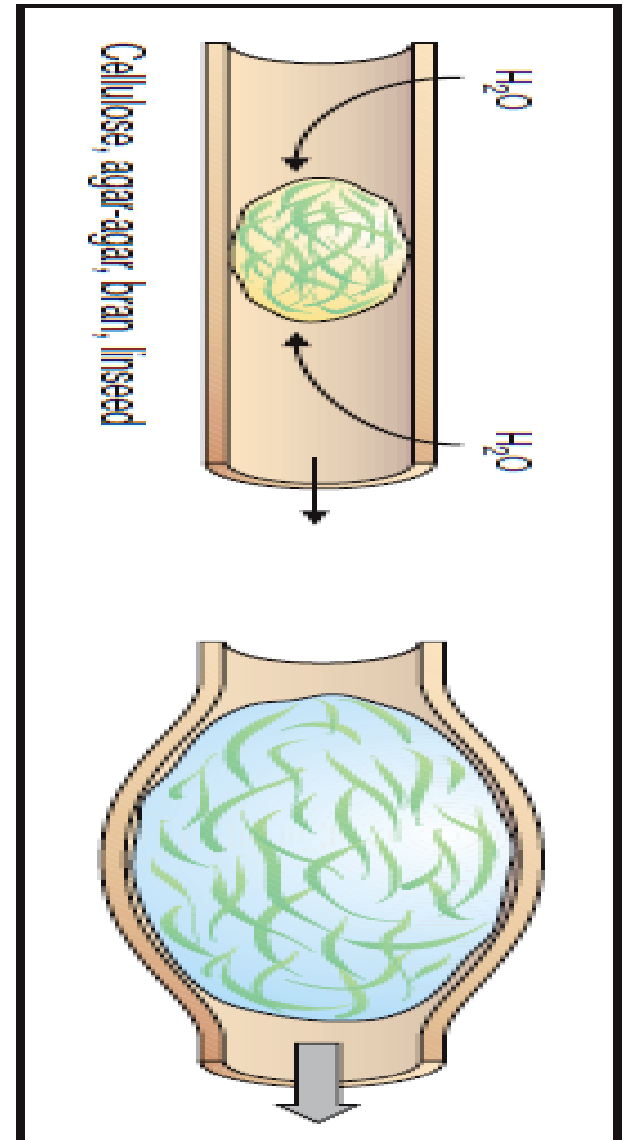


BULK-FORMING LAXATIVES

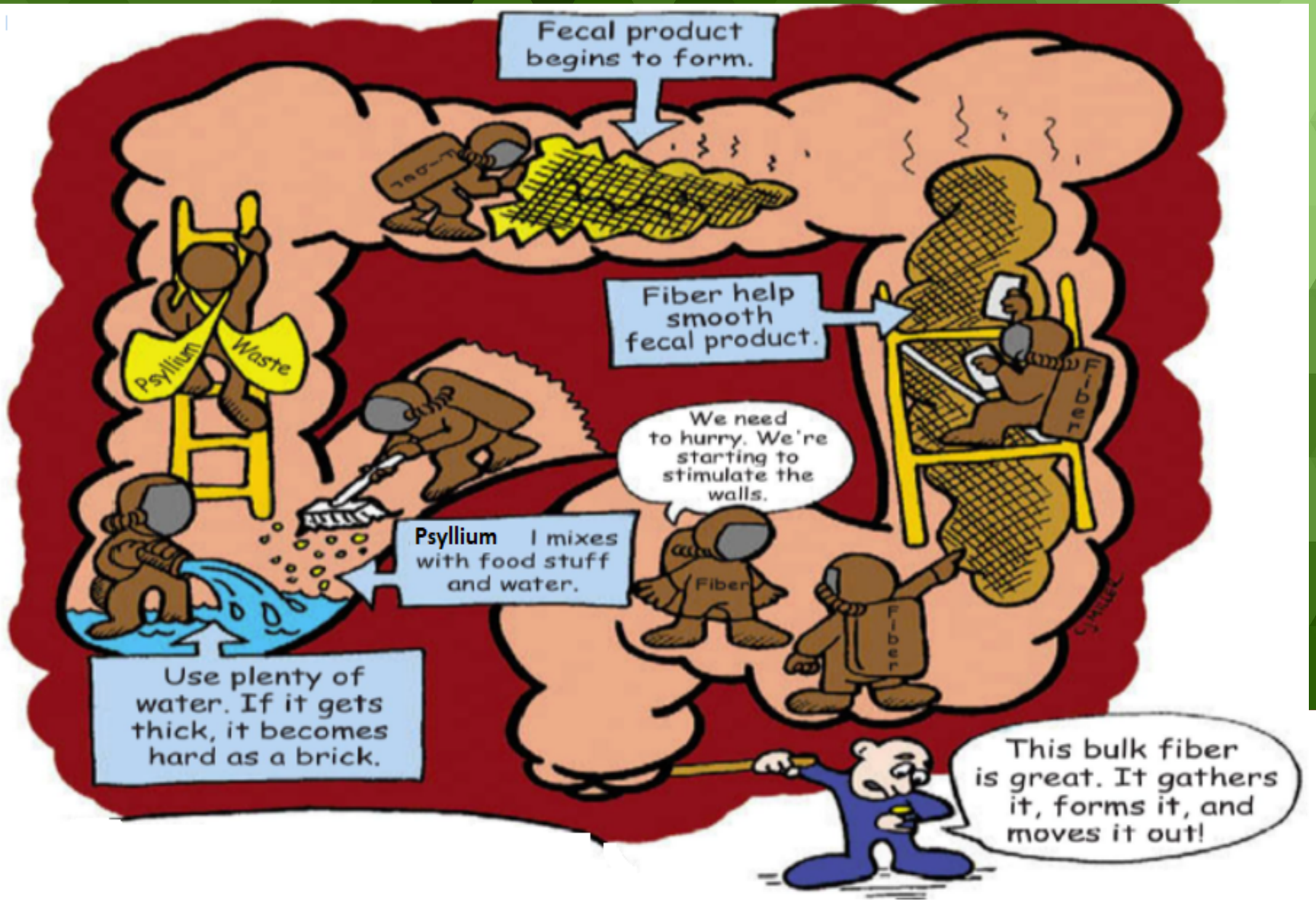
- **Natural plant products**
Psyllium,
 - **Semisynthetic**
methylcellulose
 - **Synthetic fibers**
Polycarbophil

- **Digestion of plant fibers by bacteria** → bloating, flatus

B. Bulk laxatives



PSYLLIUM



2-STOOL SOFTENERS

Lower surface tension allowing water to interact with the stool

- **A-Docusate**
- Oral or enema
- In hospitalized patients
→ ↓ constipation & straining

B-Glycerin suppositories

C-Mineral oil

Lubricate stool ↓ water absorption from the stool

To prevent fecal impaction in children & debilitated adults

Not palatable

Long- term use → deficiency of fat-soluble vitamins

What the heck happened?

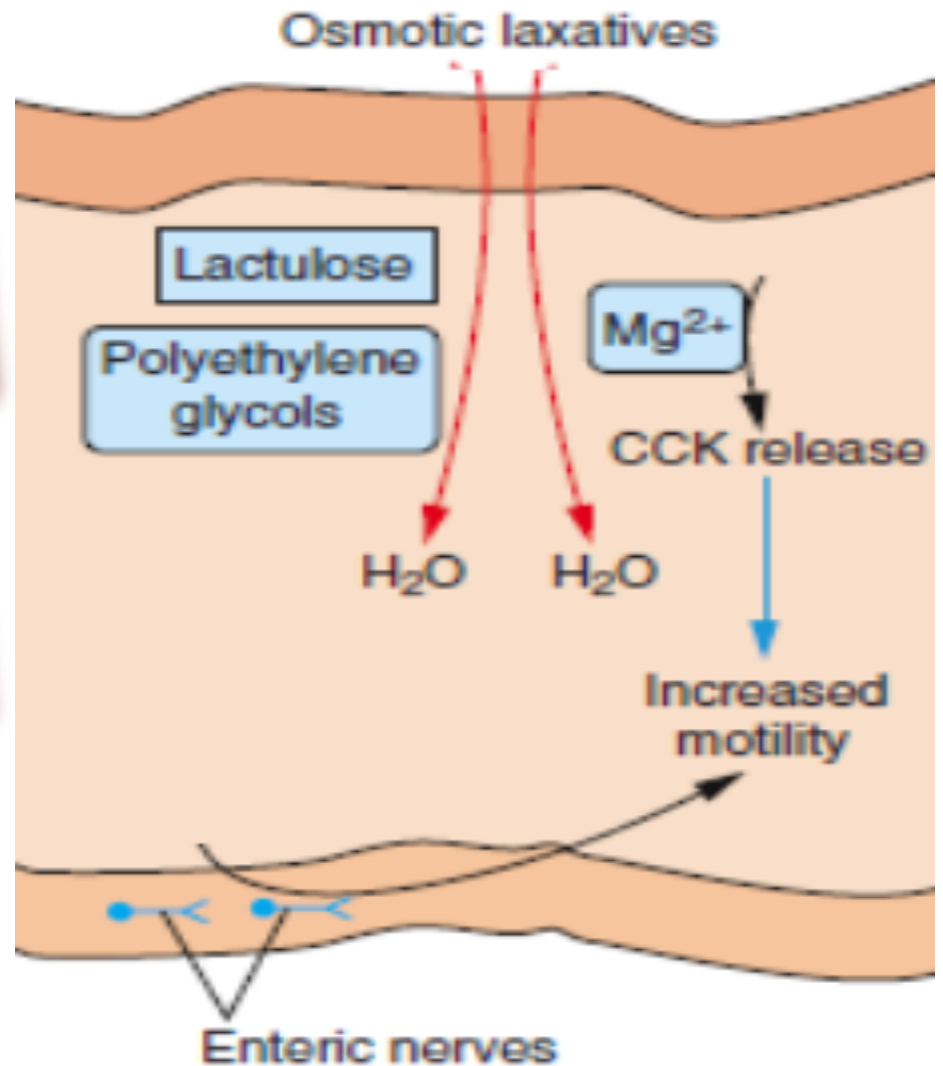
Someone slipped a stool softener in my drink!



3-OSMOTIC LAXATIVES

Soluble non absorbable compounds → ↑ stool liquidity

Non- absorbable sugars & salts



OSMOTIC LAXATIVES

A-Magnesium hydroxide

Used in acute & chronic constipation

Prolonged use in patients with renal insufficiency → hypermagnesemia

Mg salts contraindicated in kidney failure, heart block, neuromuscular block, CNS depression.

MAGNESIUM HYDROXIDE (MILK OF MAGNESIA)



OSMOTIC LAXATIVES

B- Lactulose

Chronic constipation

Metabolized by colonic bacteria severe flatus & cramps

LACTULOSE

You have portal hypertension. Your liver is not working right. Here is some lactulose to help flush out the ammonia in your intestinal tract.



OSMOTIC LAXATIVES

C-Magnesium sulphate & citrate

Severe purgative for acute constipation, cleanse the bowel

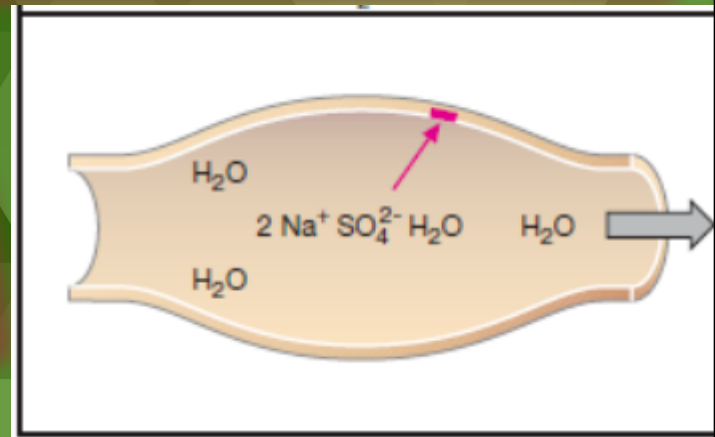
Patient should maintain adequate hydration

D-Sodium Phosphate

May cause hyperphosphatemia, hypernatremia, hypokalemia

Cardiac arrhythmias

Acute renal failure → deposition of calcium phosphate
"nephrocalcinosis"



E-BALANCED POLYETHYLENE GLYCOL

Isotonic solution containing PEG, sodium sulphate, sodium chloride, sodium bicarbonate, potassium chloride

Safe for all patients

For optimal bowel cleansing 1-2 litres ingested rapidly over 1-2 hours on the evening before the procedure & 4-6h before the procedure

For chronic constipation PEG powder mixed with juice (no crams or flatus)

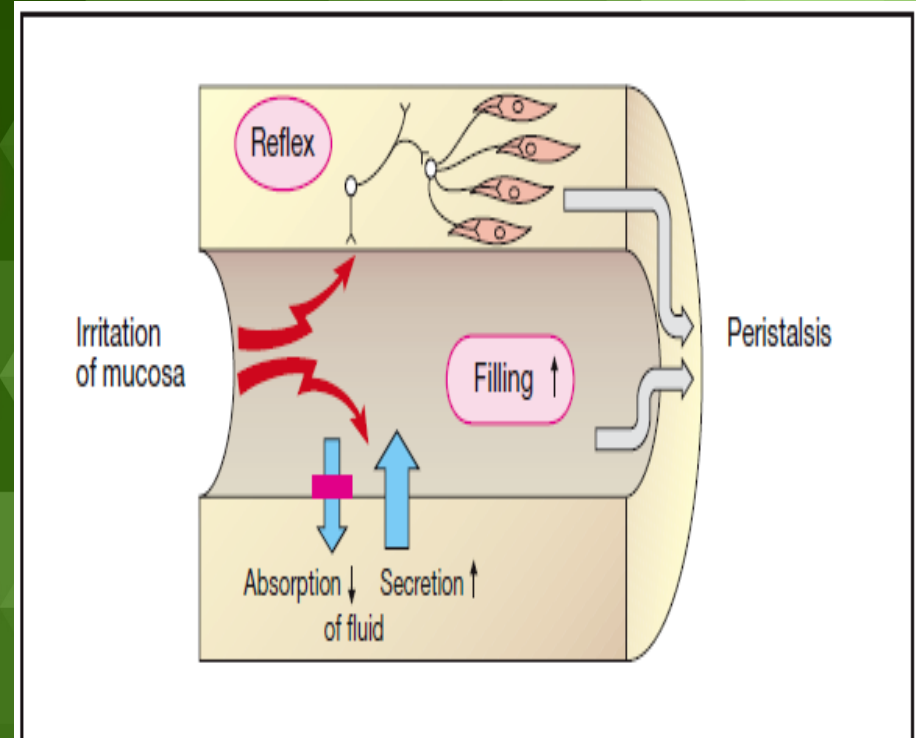
4-STIMULANT LAXATIVES

By stimulating enteric nervous system \rightarrow \uparrow bowel movement

Increase electrolyte & fluid secretion

In patients who are neurologically impaired

Bed-bound patients in long-term care facility



A. Stimulation of peristalsis by mucosal irritation

A-ANTHRAQUINONE DERIVATIVES

Senna



Rhubarb



Aloe



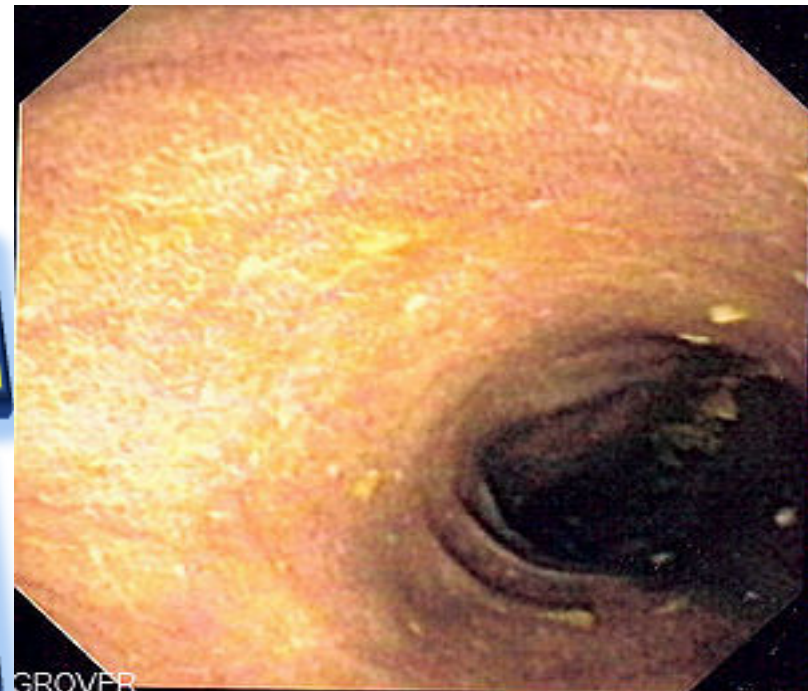
Cascara sagrada

Occur naturally, poorly absorbed

Orally , bowel movement 6-12hrs.
Rectally 2hrs

Prolonged use → brown pigmentation of the colon
"Melanosis coli"

FAB

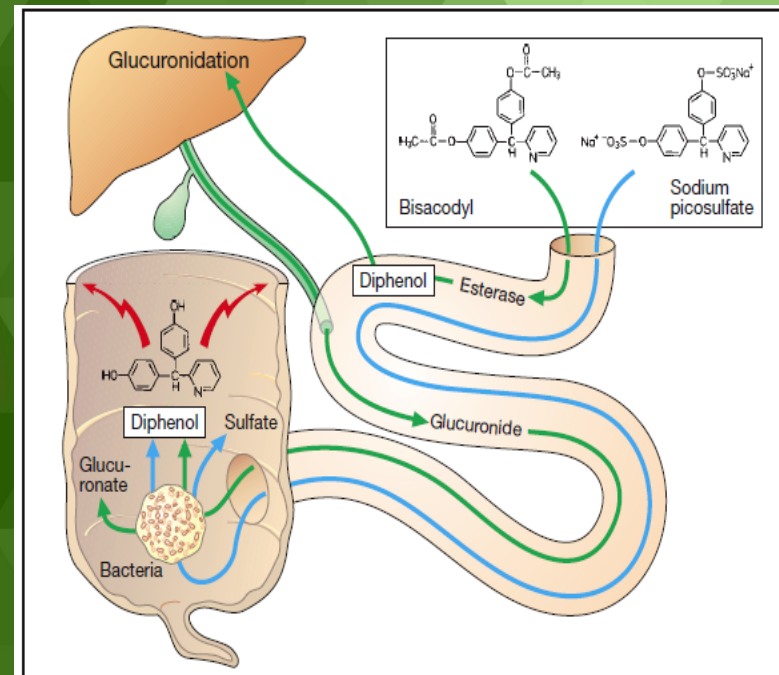


B-DIPHENOMETHANE DERIVATIVES

Bisacodyl

Hydrolysed in the gut, absorbed, conjugated to glucouronic acid in the liver acid & secreted with bile

Oral administration is followed after 6-8 h by discharge of soft stool



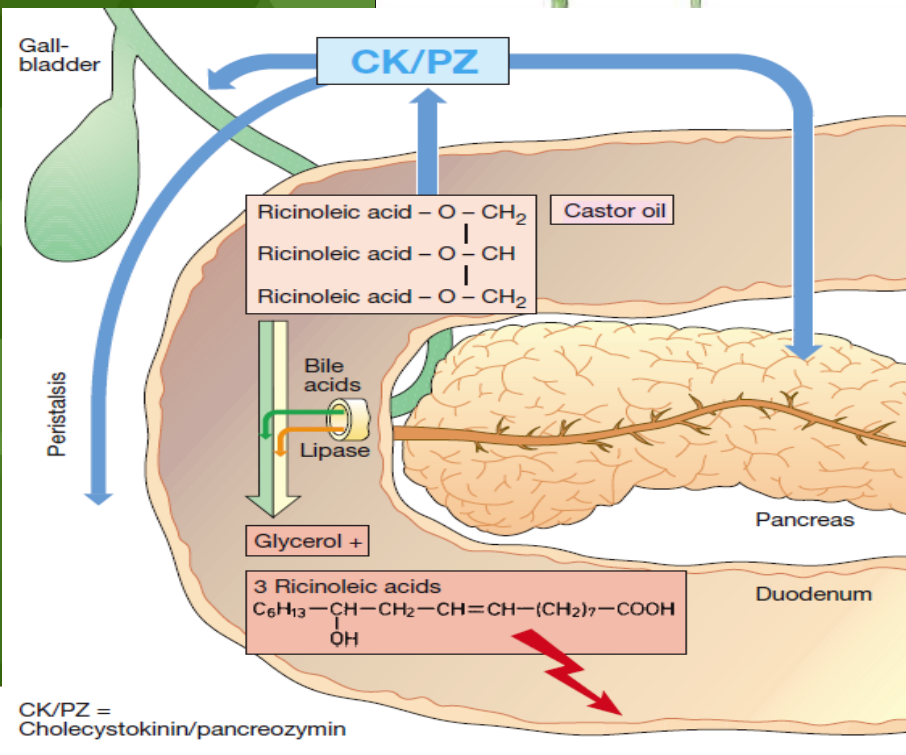
B. Large-bowel irritant laxatives: diphenylmethane derivatives

C-CASTOR OIL

Castor oil is obtained from the seeds of *Ricinus communis*

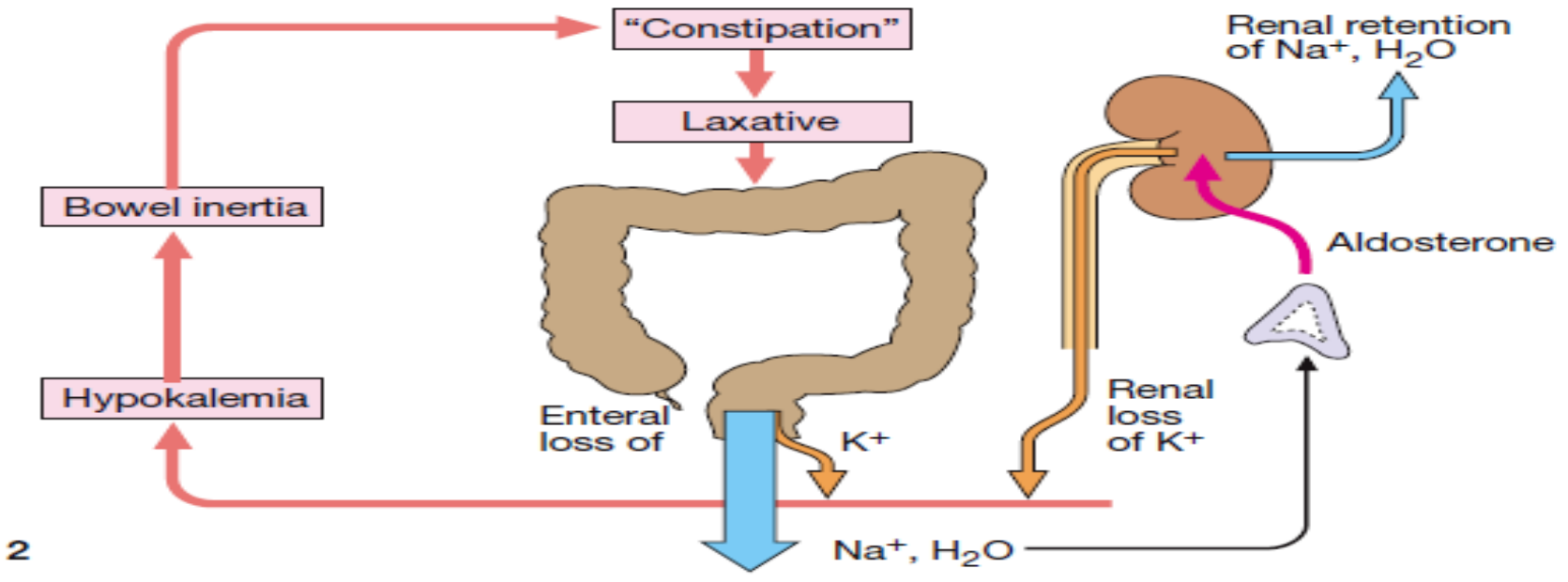
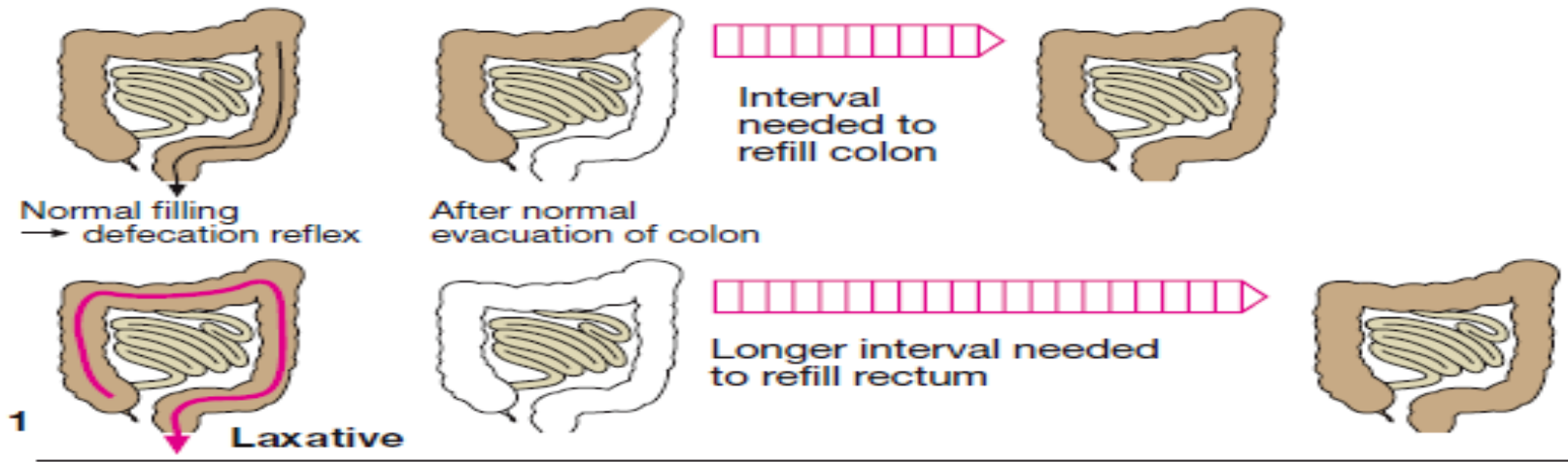
Oral administration of 10-30ml is followed by a discharge of watery stool within 0.5-3hrs.

Could be employed after oral ingestion of a toxin



. Small-bowel irritant laxative: ricinoleic acid

STIMULANT LAXATIVE DEPENDENCE

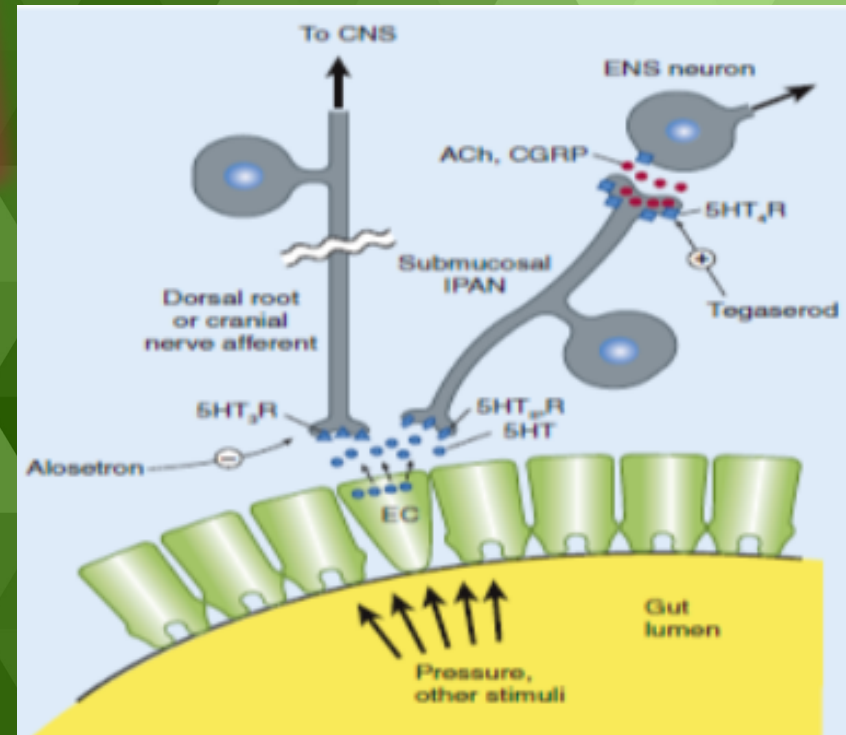


B. Causes of laxative habituation

D-SEROTONIN 5HT₄-RECEPTOR AGONISTS

Stimulation of 5HT₄ receptors → ↑ release of neurotransmitters ↑ second order enteric neurons

Enteric neurons stimulates proximal bowel contraction & distal bowel relaxation



Prucalopride is used for chronic constipation in women

E-CHLORIDE SECRETION ACTIVATORS

Lubiprostone used for chronic constipation & IBS-C

It stimulates type 2 chloride in the small intestine → ↑Cl – fluid rich fluid, → intestinal motility, shortens intestinal emptying

No loss of efficacy with long-term use

After discontinuation, constipation may return to pretreatment

Designated category C for pregnancy

E-CHLORIDE SECRETION ACTIVATORS

Linacotide stimulate chloride secretion through activation guanylate cyclase C

Approved for chronic constipation & IBS-C.

Most common ADR is diarrhea

OPIOID RECEPTOR ANTAGONISTS

Acute & chronic treatment with opioids is accompanied with constipation

Methylnaltrexone & alvimopan are μ -receptor antagonist which do not cross the BBB

Methylnaltrexone is used in opioid induced constipation in patients receiving palliative care for advanced illness

Alvimopan is used for short term to shorten the period for post operative ileus

FAB



"I'm prescribing a laxative pill and a sleeping pill. Never, never take them together."

DRUGS USED FOR IBS

Idiopathic chronic relapsing disorder characterized by pain, bloating, distension, cramps with alteration in bowel habit

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

IBS-C AGENTS

Linaclotide

Lubiprostone

Tegaserod

IBS-D AGENTS

Alosetron

AGENTS FOR IBS-C AND IBS-D

Dicyclomine

Hyoscyamine

ANTISPASMODICS (ANTICHOLINERGICS)

Dicyclomine & hyoscine

Inhibits muscarinic cholinergic receptors in enteric plexus & smooth muscle

Efficacy questionable

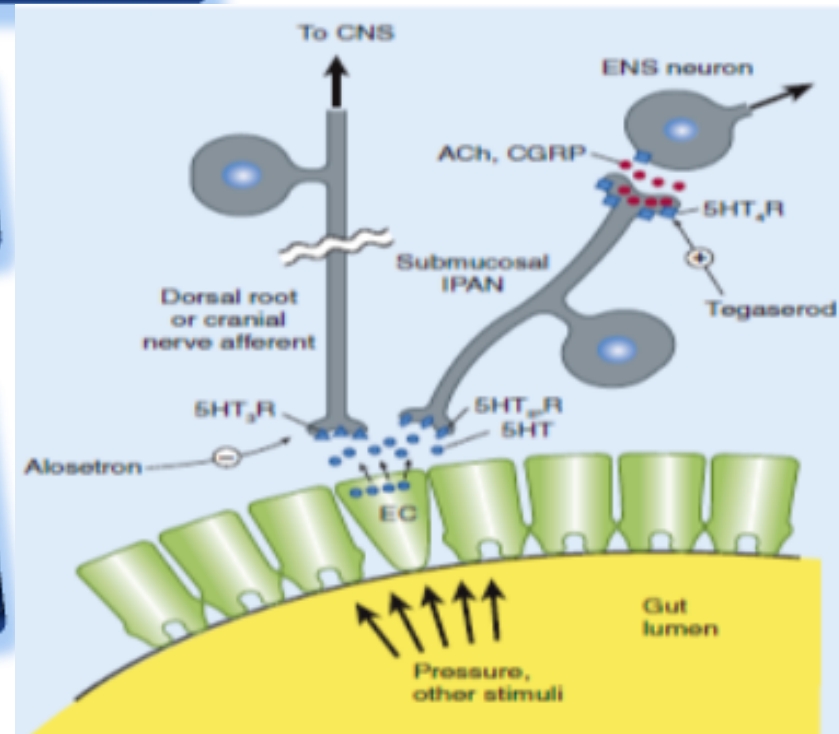
5-HT₃ -RECEPTOR ANTAGONISTS

5HT₃ receptors in the GIT activate visceral afferent pain sensation

Inhibition of 5-HT₃ receptors reduce nausea, bloating & pain

Alosetron 5-HT₃ receptor antagonist used in patients with severe IBS with diarrhea

Rapidly absorbed from the GIT , 50-60% bioavailability, $t_{1/2}$ 1.5h



5-HT_{2A} -RECEPTOR ANTAGONISTS

Undergoes extensive cytochrome P450 metabolism

It binds with high affinity & dissociate slowly from the receptor

Indicated in Irritable Bowel Syndrome

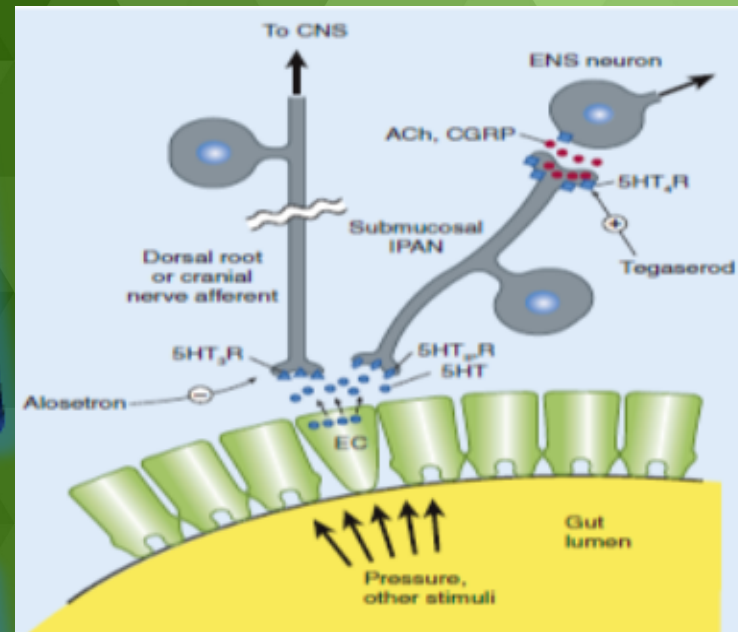
Use restricted in women with severe diarrhea-predominant IBS who have not responded to other therapies

TEGASEROD

▪ Stimulation of $5HT_4$ of enteric nervous system of GIT → increases peristalsis.

▪ Short term treatment of IBS-associated with constipation in women <55 years old with no history of heart problems.

▪ Tegaserod has CVS side effects



Case

- 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, oxybutynine for urinary frequency, aluminum hydroxide prn for dyspepsia, and bendrofluazide and verapamil for hypertension. Following bowel evacuation by a phosphate enema, proctoscopy & colonoscopy are reported as normal.



Case

1-What general approach should be employed to this patient?

Drugs that can cause constipation

- Aluminium hydroxide
- Amiodarone
- Anticholinergics (older antihistamines)
- Diltiazem
- Disopyramide
- Diuretics
- Iron preparations
- Opioids
- Tricyclic antidepressants
- Verapamil

2-What are the possible causes of her constipation?

3-Which of these drugs may contribute to her constipation?

4-What pharmacological approaches would be appropriate to this patient?

