CONSTIPATION & IBS

CONISTIPATION & 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

CONISTIPATION & IBS

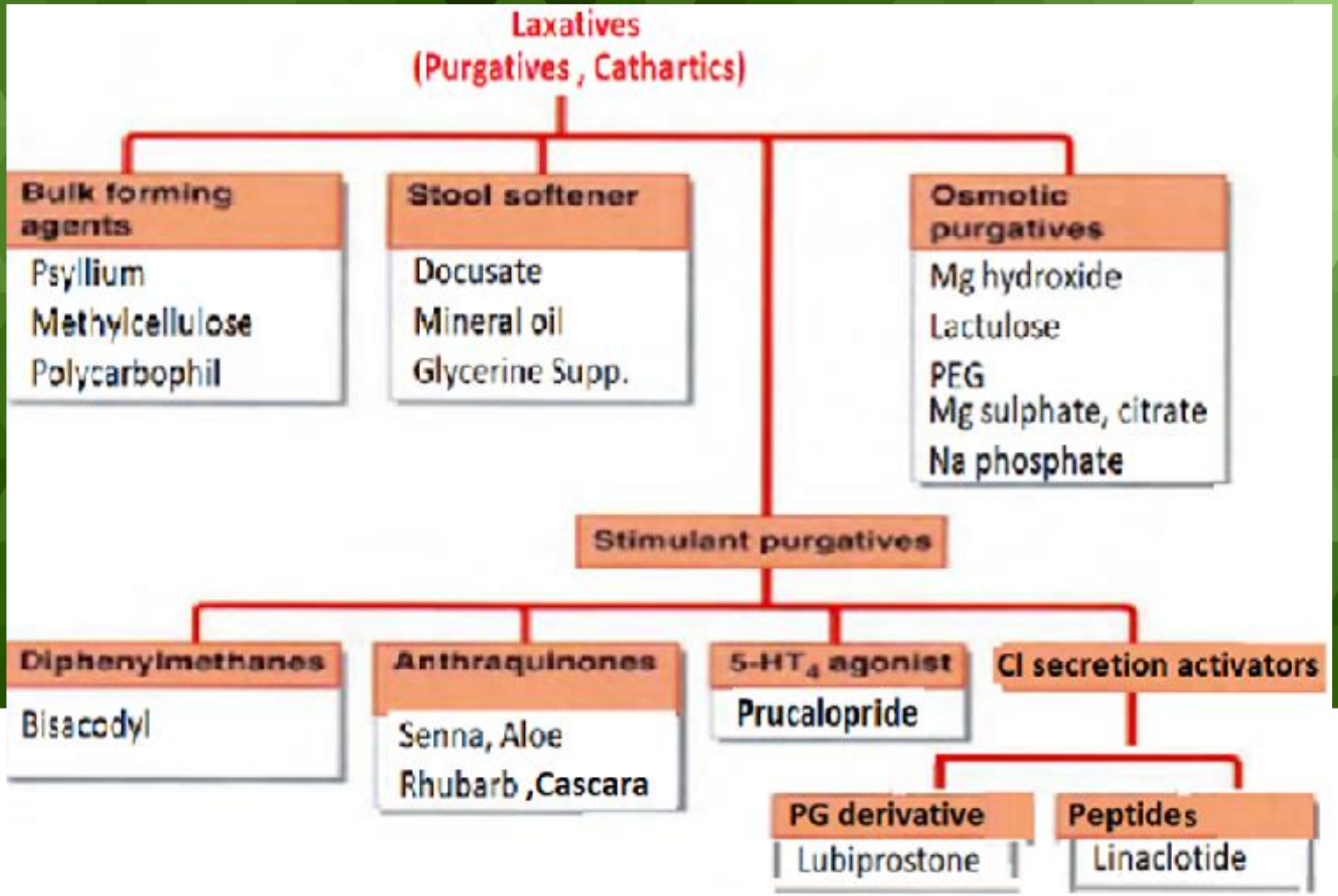
ILOS

Classify Laxatives

Discuss the pharmacological properties of different classes of laxatives

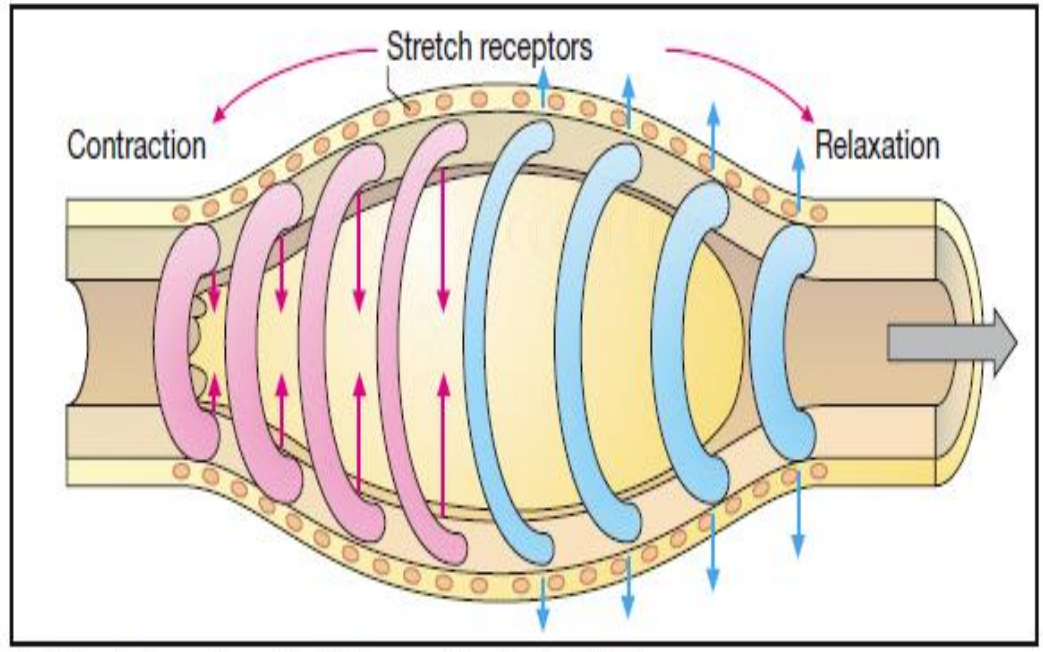
Outline drugs used to treat *irritable bowel syndrome*

CLASSIFICATION



1-BULK-FORMING LAXATIVES

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

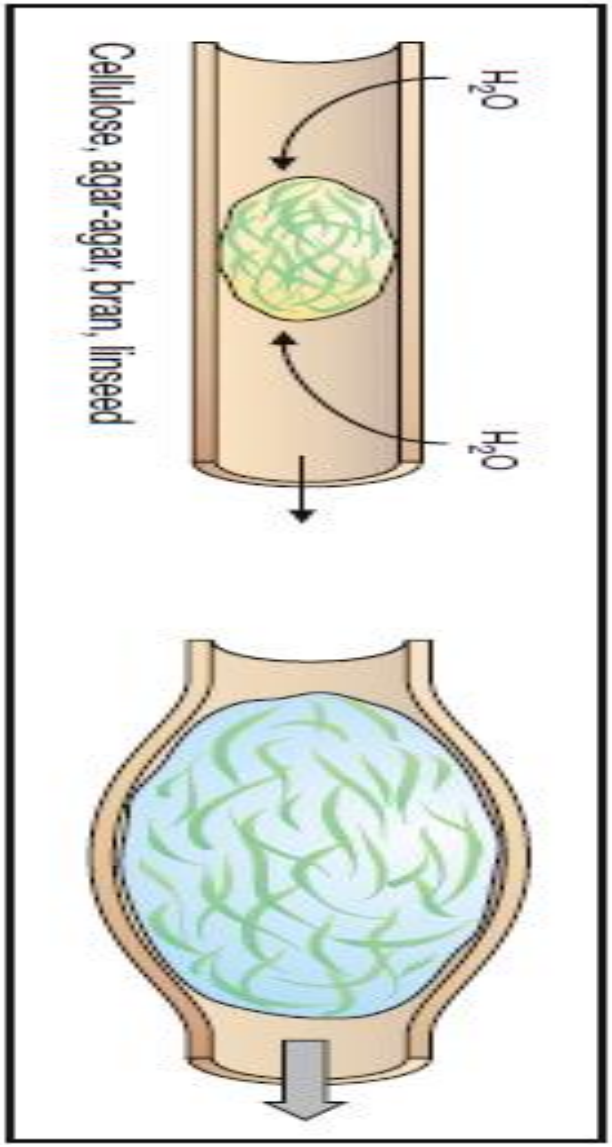


A. Stimulation of peristalsis by an intraluminal bolus

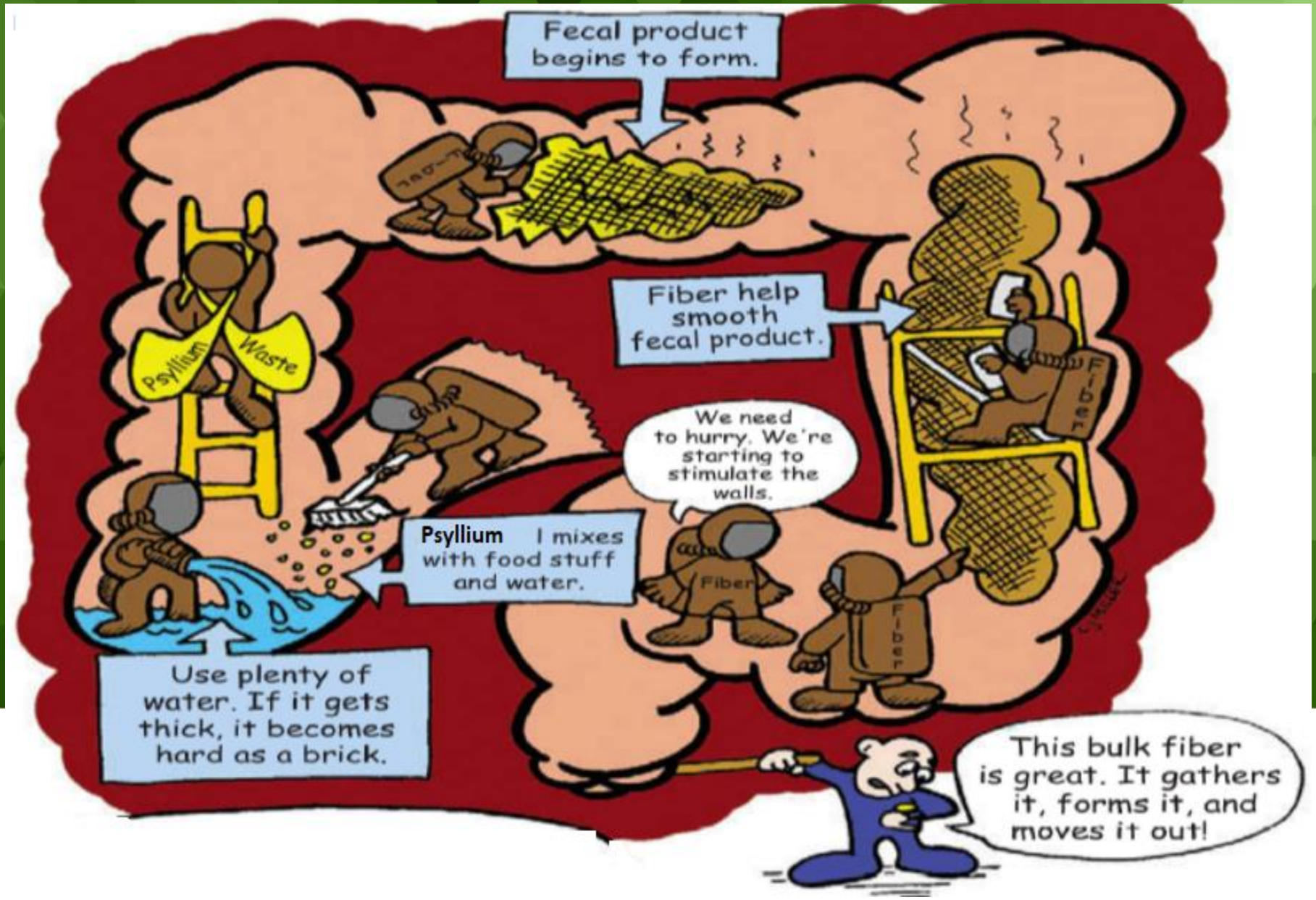
BULK-FORMING LAXATIVES

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

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



PSYLLIUM


Fecal product begins to form.
Fiber help smooth fecal product.
We need to hurry. We're starting to stimulate the walls.
Psyllium
Waste
Psyllium I mixes with food stuff and water.
Use plenty of water. If it gets thick, it becomes hard as a brick.
Fiber
Fiber
Fiber
This bulk fiber is great. It gathers it, forms it, and moves it out!

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

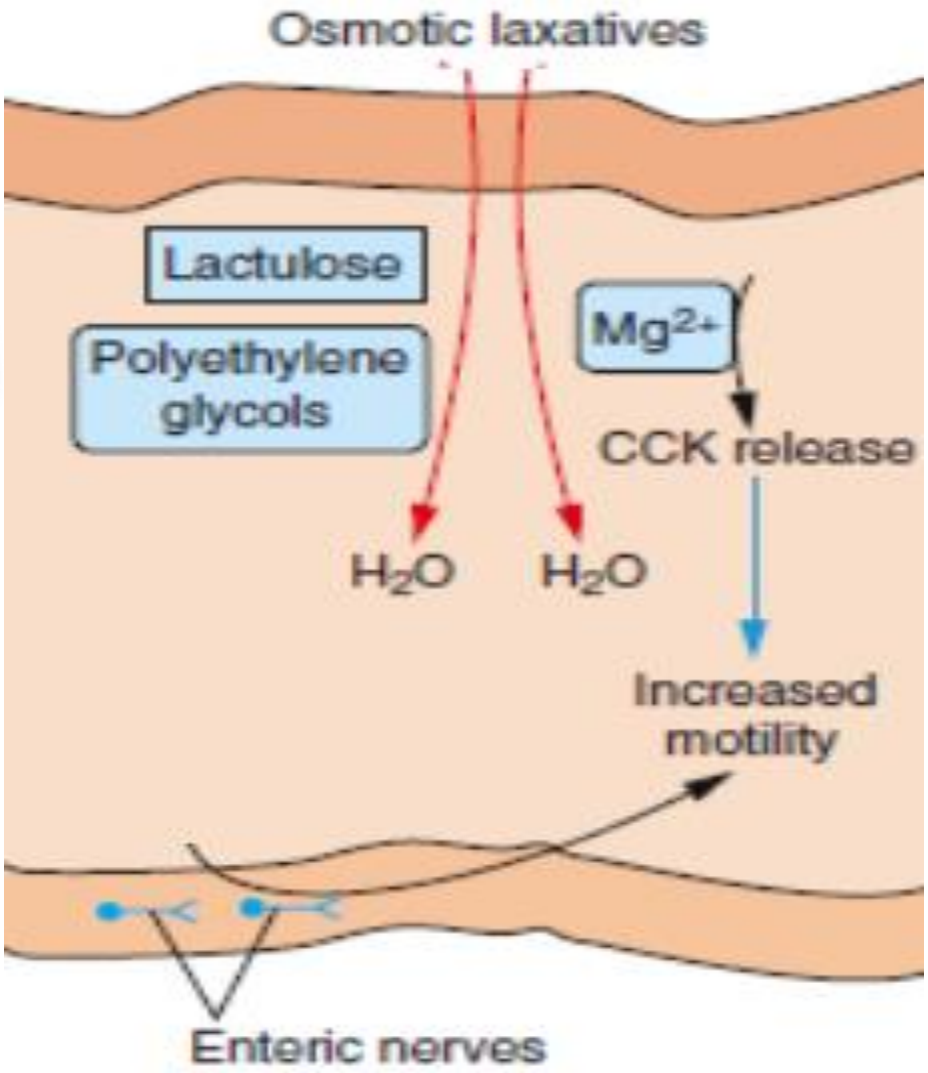
Not palatable

Long- term use→ deficiency of fat-soluble vitamins

3-OSMOTIC LAXATIVES

Soluble non absorbable compounds→↑ stool liquidity

Non- absorbable sugars & salts



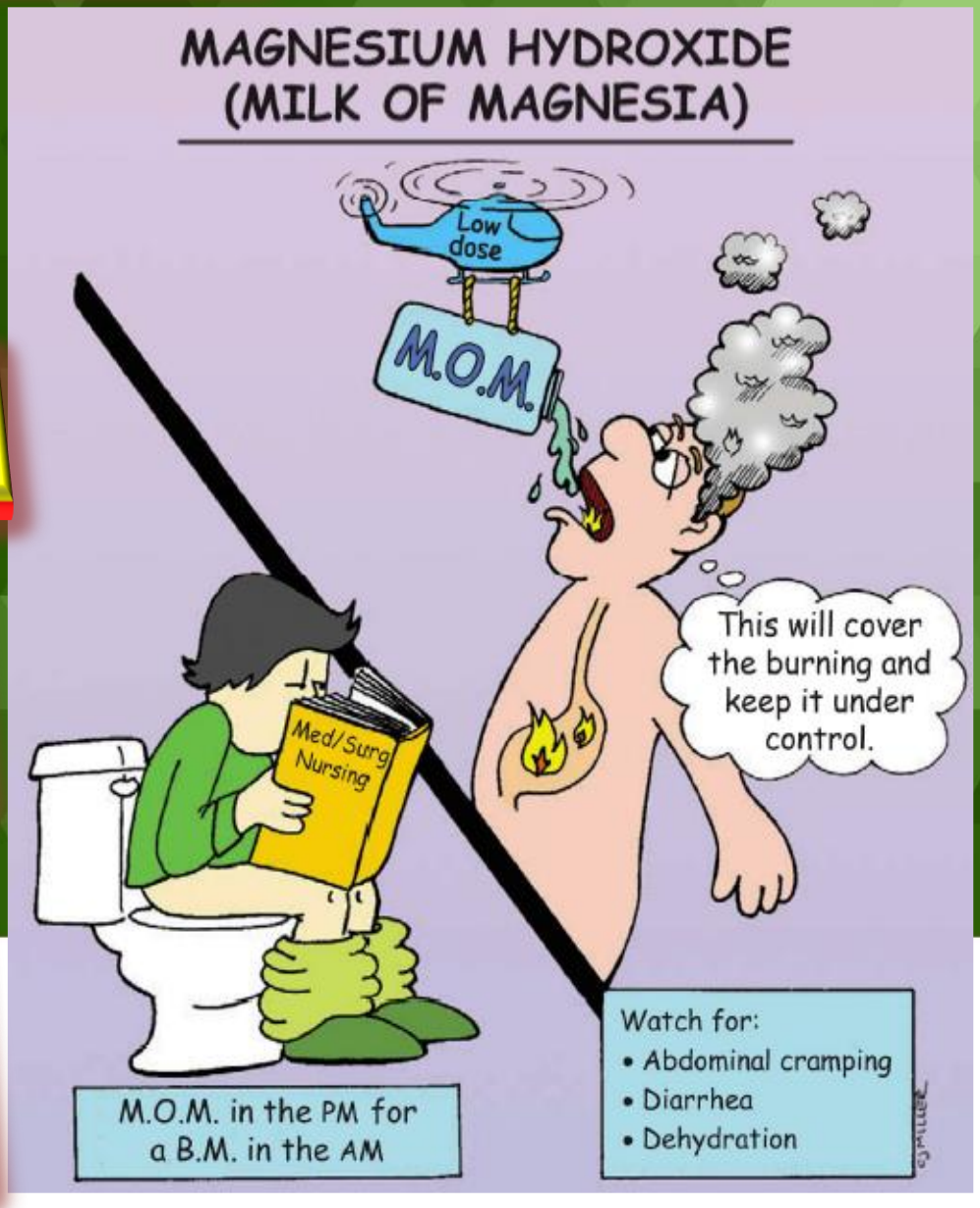
OSMOTIC LAXATIVES

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.

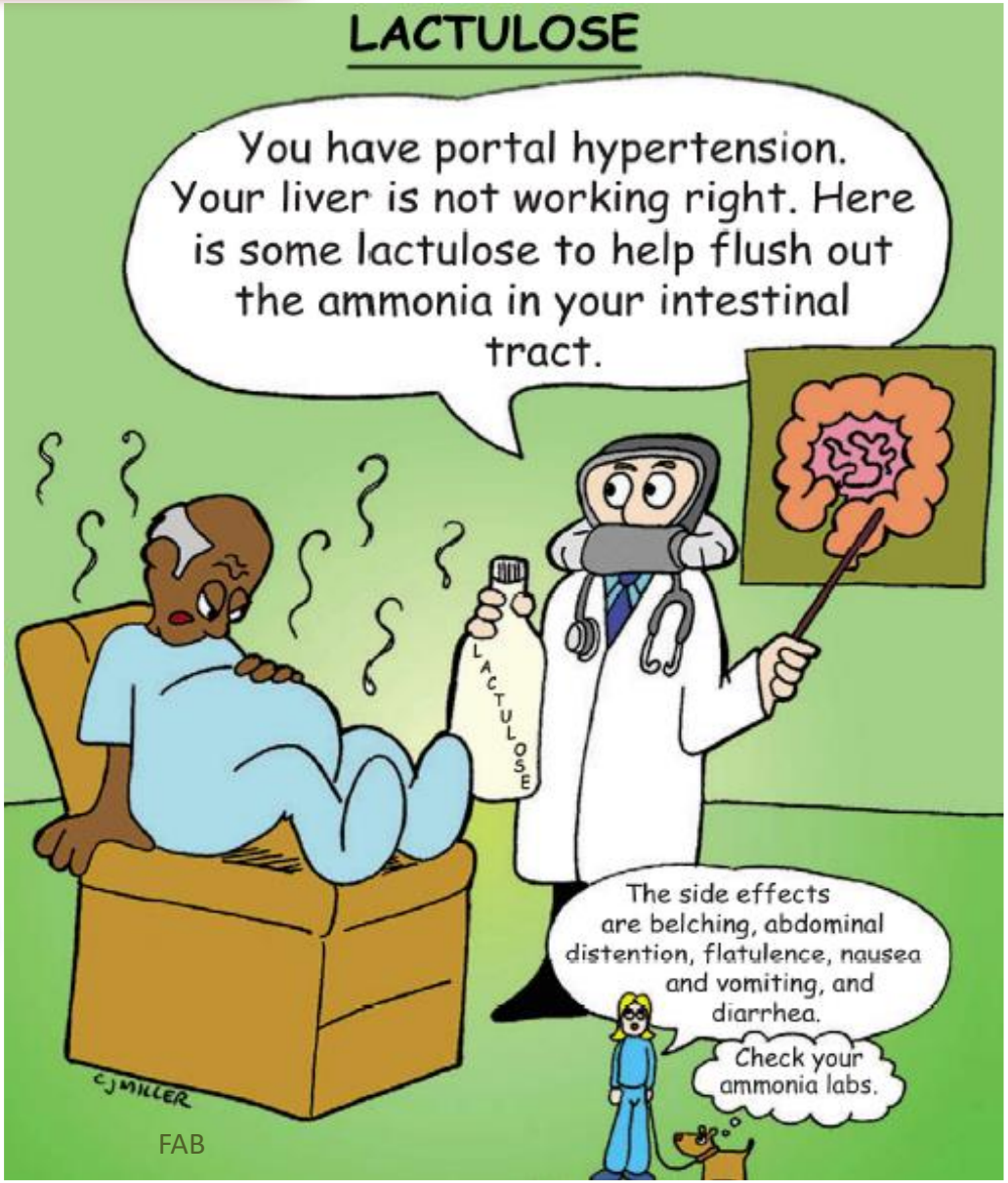


OSMOTIC LAXATIVES

B- Lactulose

Chronic constipation

Metabolized by colonic bacteria severe flatus & cramps



OSMOTIC LAXATIVES

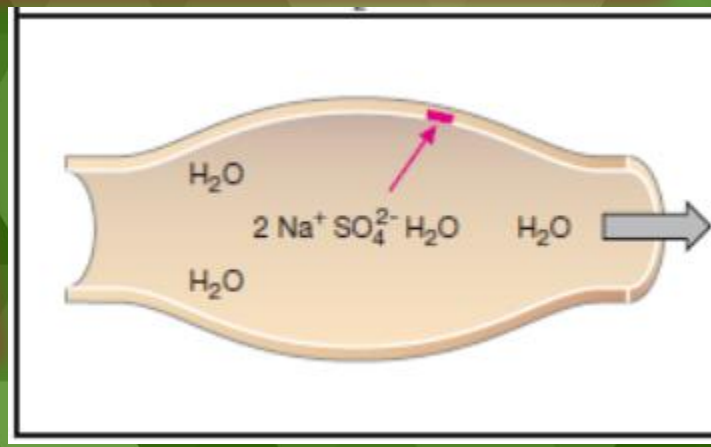
C-Magnesium sulphate & citrate

Severe purgative for acute constipation, cleanse the bowl

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 bowl cleansing1-2litres 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)

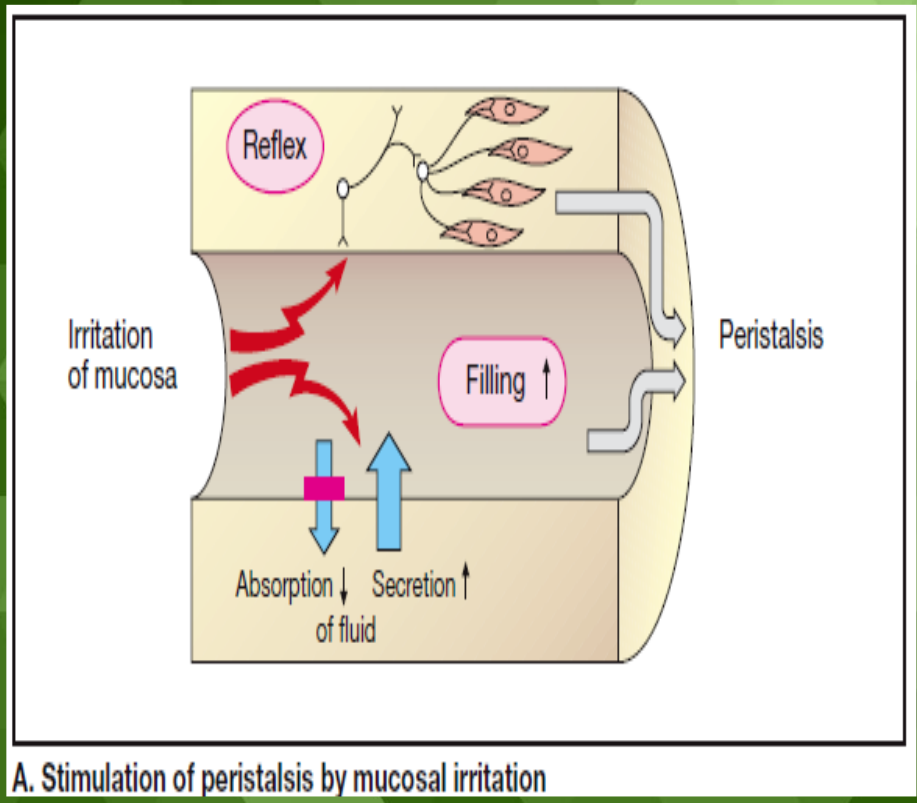
4-STIMULANT LAXATIVES

By stimulating enteric nervous system→↑bowl movement

Increase electrolyte & fluid secretion

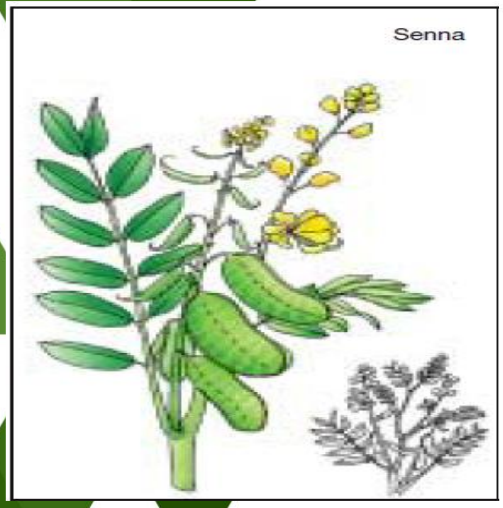
In patients who are neurologically impaired

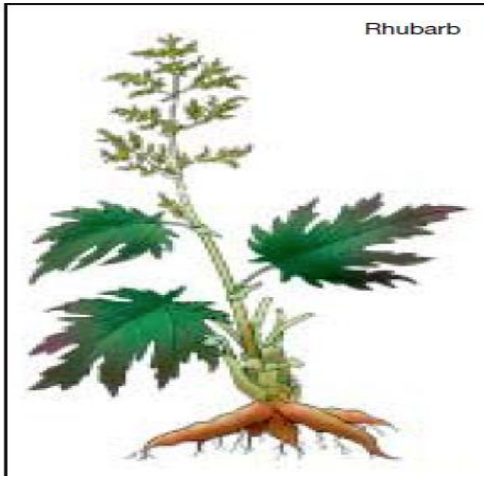
Bed- bound patients in long- term care facility

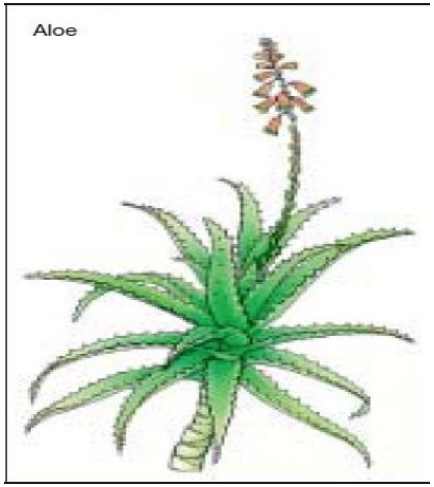


A. Stimulation of peristalsis by mucosal irritation

A-ANTHRAQUINONE DERIVATIVES





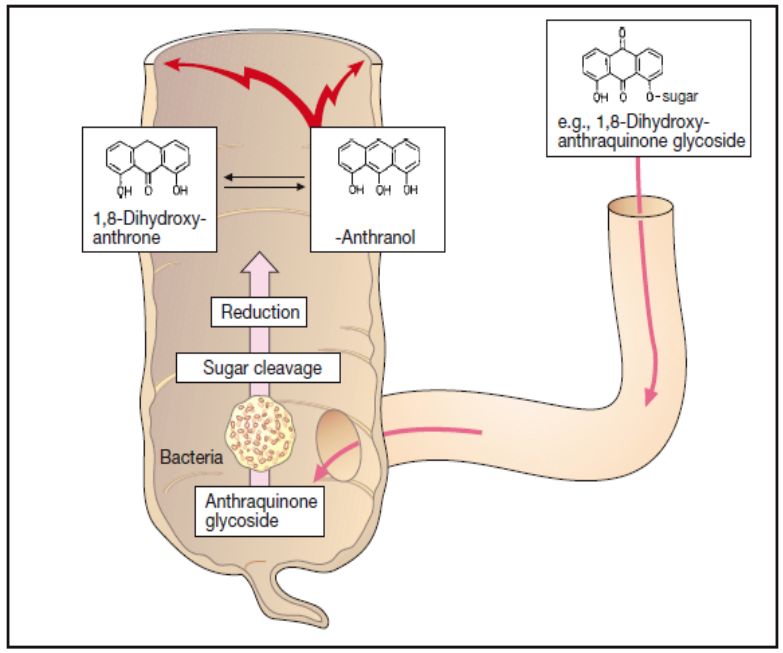


Cascara sagrada

Occur naturally, poorly absorbed

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

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



A. Large-bowel irritant laxatives: anthraquinone derivatives

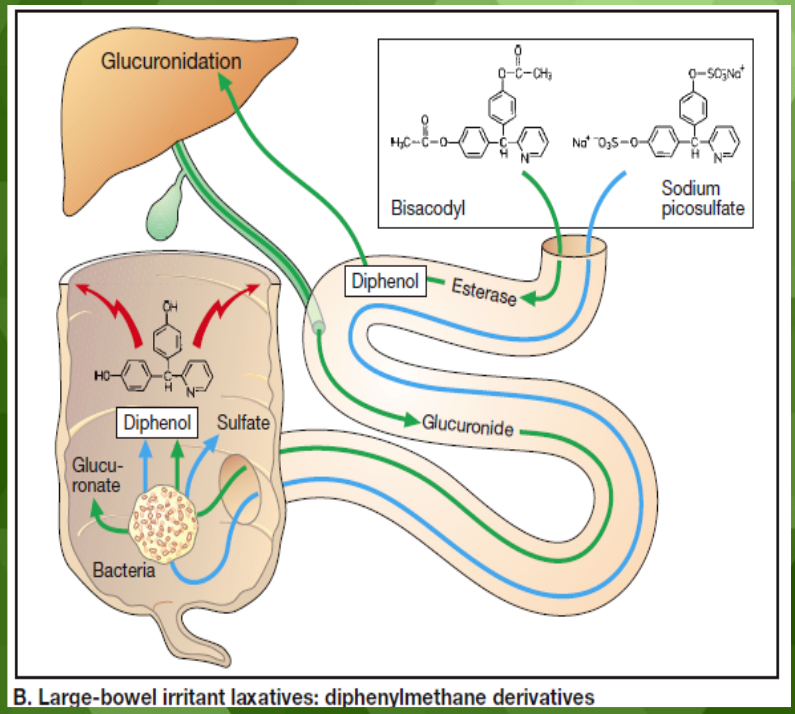
FAB

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



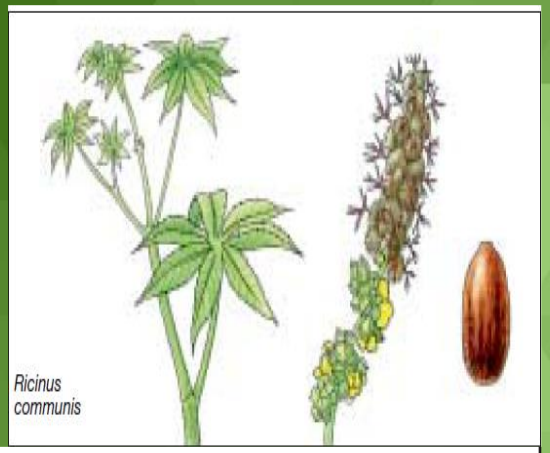
B. Large-bowel irritant laxatives: diphenylmethane derivatives

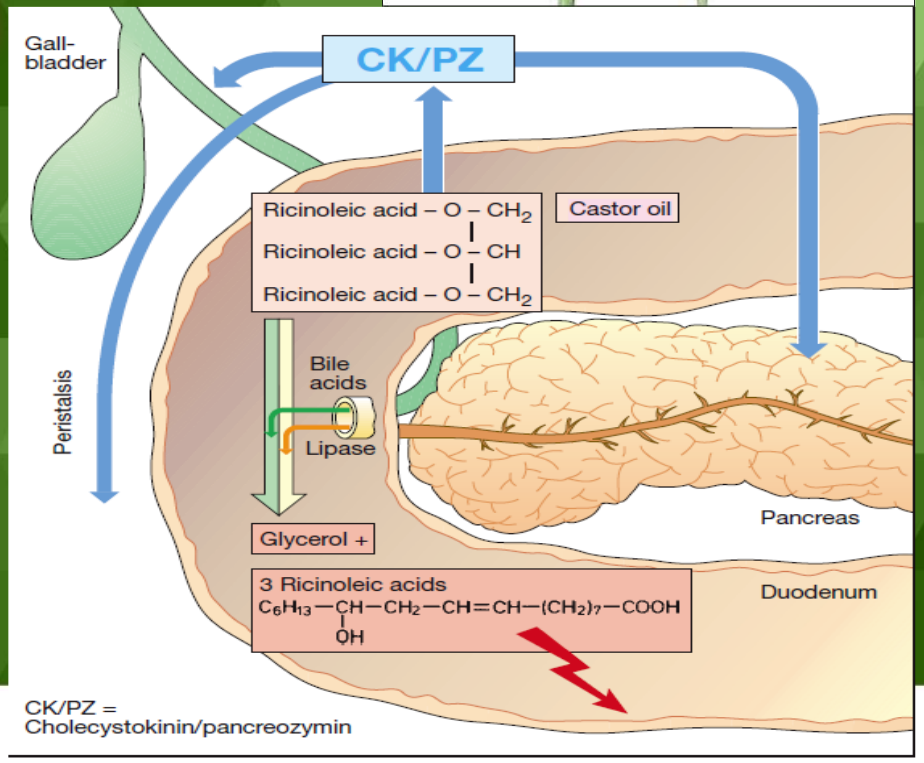
C-CASTOR OIL

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.

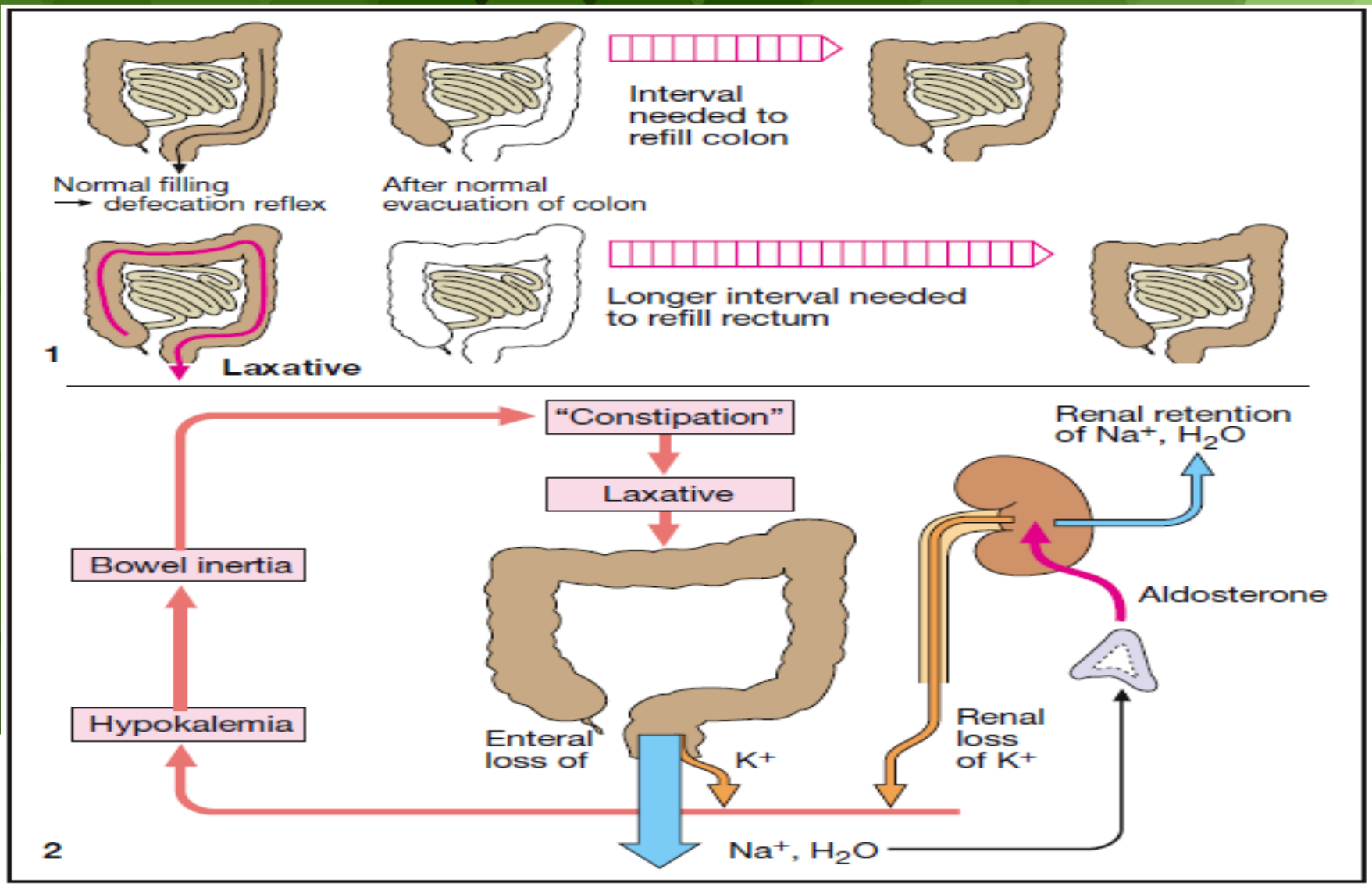
Could be employed after oral ingestion of a toxin





. Small-bowel irritant laxative: ricinoleic acid

STIMULANT LAXATIVE DEPENDENCE

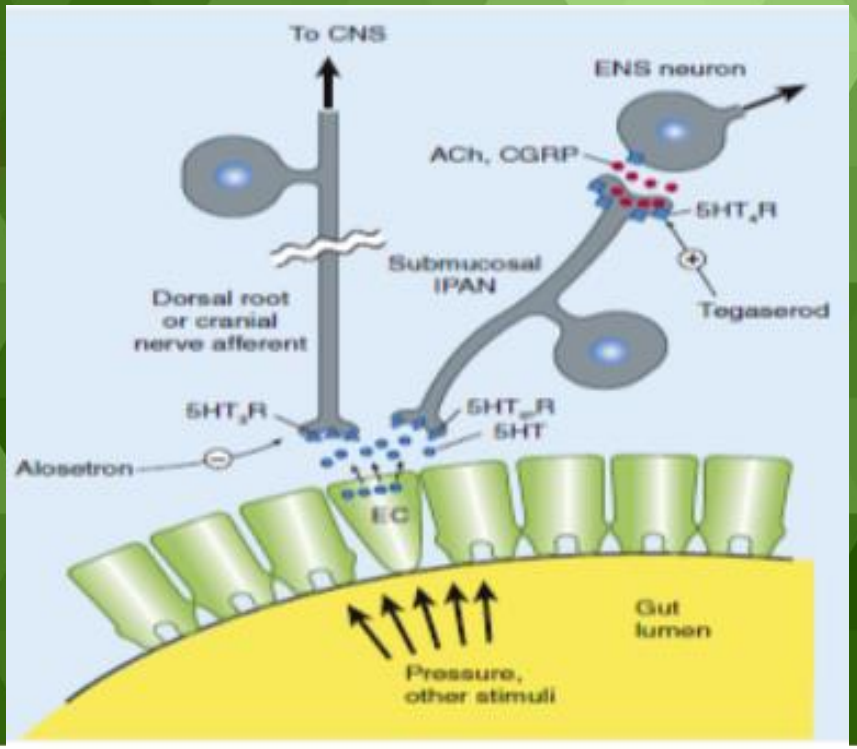


B. Causes of laxative habituation

D-SEROTONIN 5HT4-RECEPTOR AGONISTS

Stimulation of 5HT 4 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

Linaclotide *stimule chloride sececretion through activation guanaylate cyclase C*

Both agents are approved for chronic constipation & IBS-C.

Most common ADR is diarrhea

OPIOID RECEPTOR ANTAGONISTS

Acute & chronic treatment with opioids is accompanied with constipation

Methylnaltrexone & alivimopan are μ- receptor antagonist which don 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

"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 bowl 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

FAB

ANTISPASMODICS (ANTICHOLINERGICS)

Dicyclomine & hyoscine

Inhibits muscarinic cholinergic receptors in enteric plexus & smooth muscle

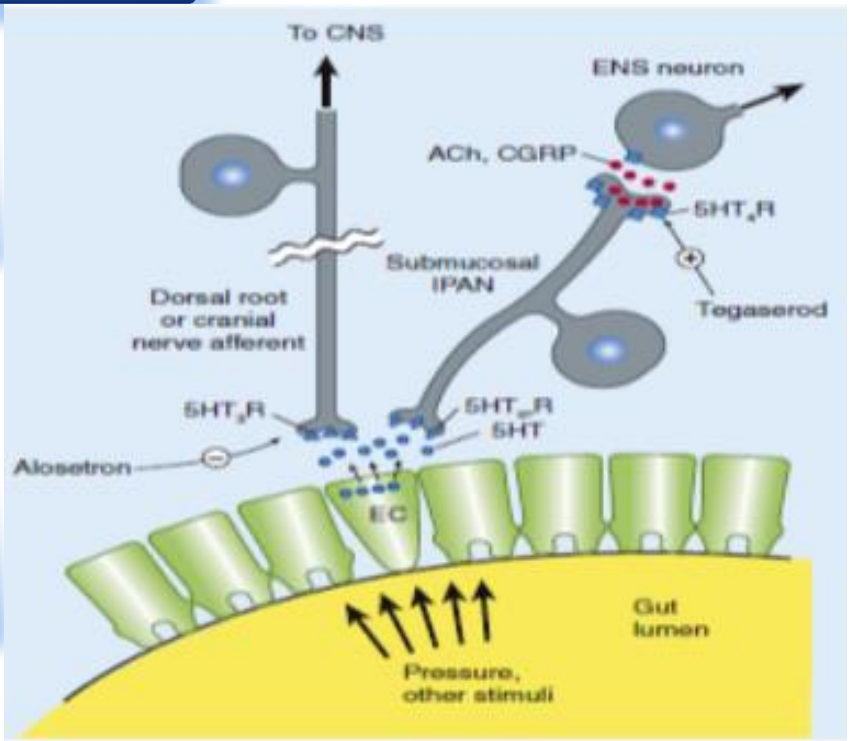
Efficacy questionable

5HT3 –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, t½ 1.5h

5HT3 –RECEPTOR ANTAGONISTS

Undergoes extensive cytochrome P450 metabolism

It binds with high affinity & dissociate slowly from the receptor

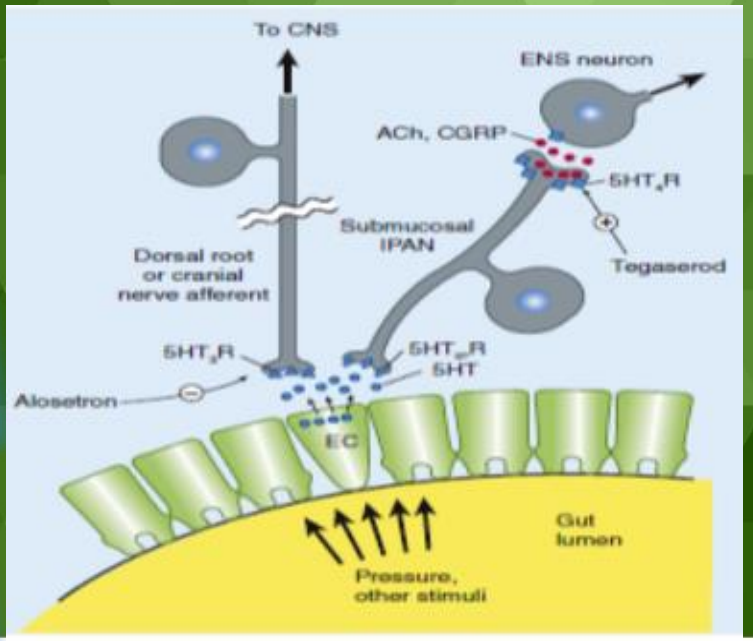
ADRs: severe constipation, ischemic colitis

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, aluminuim 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 pa

2-What are the pos causes of her const

3-Which of these may contribute to

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

Drugs that can cause constipation

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