

# Drugs Used in Constipation and Diarrhoea



Website



Videos

# DRUGS FOR CONSTIPATION

LAXATIVES → These are the drugs that promote evacuation of bowels.

- ↳ a) Laxatives or Aperient → Milder action, elimination of soft, but formed stools
- ↳ b) Purgatives or Cathartics → Stronger action resulting in more fluid & force evacuation

## DRUG CLASSIFICATION

1) Bulk Forming Agent → Dietary Fibres, Ispaghula, methyl Cellulose

2) Stool Softner → Docusates, Liquid paraffin

3) Osmotic Purgative →  $MgSO_4$ ,  $Mg(OH)_2$ ,  $Na_2SO_4$ ,  $Na_3PO_4$ , Sod. Pot. tartarate, Lactulose, Lactitol

4) Stimulant Purgatives →

A) Diphenylmethanes - Bisacodyl, Sod. picosulphate

B) Anthraquinones (Emodins) → Senna, Cascara - Sagrada

- c)  $5HT_4$  Agonist → Prucalopride
- D) PG-Analogue → Lubiprostone

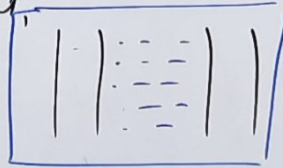
## Mechanism of Action of Purgative

↳ All purgative increase the water content of faeces by -

A) A hydrophilic or Osmotic action  
↳ Retain water & electrolyte in intestine and ↑ colonic content → Easy to

B) ↓ Intestinal Absorption Propell of water

C) ↑ propulsive Action



## MOA OF LAXATIVE

↳ Alter the fluid dynamic of mucosal cell & accumulate fluid in gut lumen by →

↳ ↓  $Na^+K^+ATPase$  in villous cells

↳ (+) AC in crypt cells → ↑ water/electrolyte secretion

↳ ↑ mucosal PG synthesis → ↓

↳ ↑ NO synthesis → ↓

↳ structural injury in mucosa → ↓ water absorption





## STIMULANT PURGATIVES

- ↳ These are strong purgatives
- ↳ Mode of Action → 1) ↑ gut motility by acting on myenteric plexus neurons.
- 2) ↑ accumulati<sup>n</sup> of water & electrolyte in gut lumen by altering abs. & sec. activity.
  - ↳ ↓ Na<sup>+</sup>K<sup>+</sup>ATPase on villous cells
  - ↳ (+) cAMP pathway on crypt cells
  - ↳ ↑ PG Synthesis & NO Synthesis
- ↳ Larger dose may cause → Excessive purgation → Electrolyte imbalance → Hypokalemia & colonic atony may occur.

### "BISACODYL"

- ↳ Synthetic diphenylmethane deriv. purgatives
- ↳ 5-10 mg orally/suppositories, excreted in bile to undergoes partial enterohepatic circulation
- ↳ Shows irritative effects on colonic mucosa, → ↑ fluid secretion and also ↑ motility
- ↳ 1 or 2 semiformal motion b/w 6-8 h
- ADR → ↳ Rectal inflammation by suppository,  
↳ Orally - Allergic Reactn, "Stevens-Johnson Syndrome"

### "ANTHRAQUINONES"

- ↳ Senna, "Cassia sps" → Glycoside, Emodines
  - ↳ unabsorbed in intestine → Liberate active anthrol by microbial flora → act either locally or absorbed into circulation → Excreted into bile & act on small intestine.
- ↳ It can be secreted into milk (not used in lactating mother)
- ↳ Purgative action is similar to diphenylmethane derivatives
- ↳ Onset of action - 6-8 h, taken bed time
- ADR - Skin Rashes, Fixed drug eruption  
Regular use (4-12 months) may cause colonic atony & mucosal pigmentation

"Stimulant purgatives are generally contraindicated in Pregnancy"



# DIARRHOEAS

- ↳ frequent passage of poorly formed stool
- ↳ It can be either acute self limiting episode or severe chronic illness

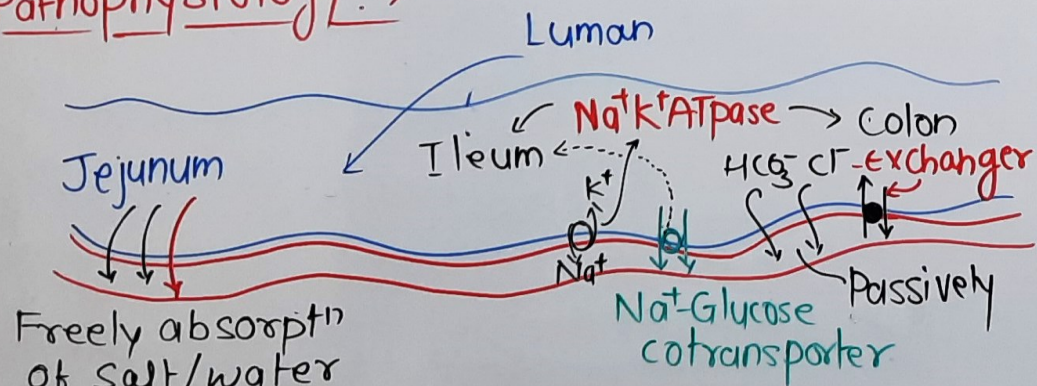
↳ WHO,  $\geq 3$  loose & watery stool within 24h

- ↳ **FACTORS**  $\rightarrow$  Excess water in faeces by
  - $\rightarrow$   $\downarrow$  absorption of electrolyte & water
  - $\rightarrow$   $\uparrow$  secretion by intestinal mucosa
  - $\rightarrow$   $\uparrow$  Luminal osmotic load
  - $\rightarrow$  Mucosal inflammation
  - $\rightarrow$   $\uparrow$  GI motility

$\rightarrow$  According to UNICEF data  $\rightarrow$  1400 young children die every day worldwide

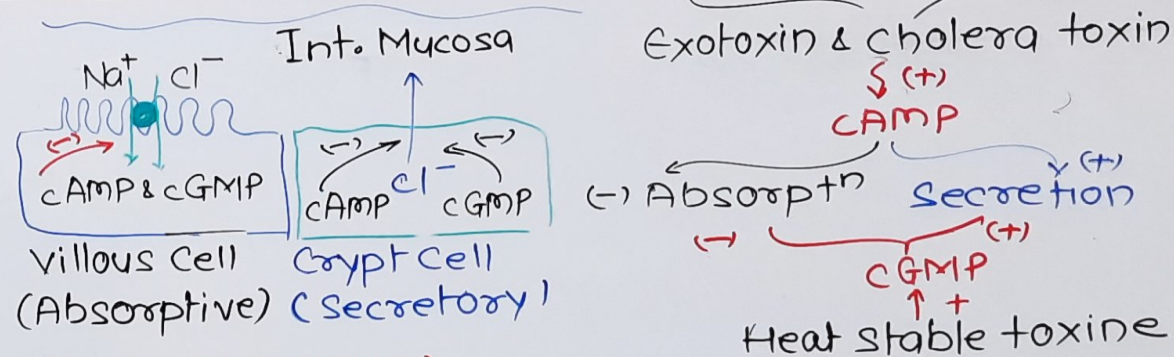
$\rightarrow$  Ministry of Health  $\rightarrow$  13 children/h (die), India

## Pathophysiology: $\rightarrow$



Freely absorpt<sup>n</sup> of salt/water (Passively)  $\Delta$  Secondary to Nutrients

$\checkmark$  e.coli, Salmonella, S. aureus



- $\checkmark$  Carcinoids ( $\uparrow$  5HT)
- $\checkmark$  Medullary carcinoma of thyroid ( $\uparrow$  Calcitonin)
- $\checkmark$  Clostridium, E. histolytica
- $\checkmark$  IBD  $\checkmark$   $\uparrow$  GI Motility  $\checkmark$  Drug induced

## PRINCIPLE MANAGEMENT

- Treatment of fluid depletion, Shock and Acidosis
- Maintenance of Nutrition "REHYDRATION"
- Drug Therapy  $\rightarrow$ 
  - $\hookrightarrow$  Antimicrobial
  - $\hookrightarrow$  Antimotility
  - $\hookrightarrow$  Probiotics / Prebiotic
  - $\hookrightarrow$  Immunosuppressants
  - $\hookrightarrow$  Antisecretory



# ANTI-DIARRHOEAL DRUGS

## REHYDRATION

- ↳ To prevent and reverse salt and water depletion
- ↳ It can be done orally and iv.

A) Intravenous → It is needed only when fluid loss is severe (> 10% of BW) → If not corrected, it will lead to shock and death  
 → If patient is losing > 10 ml/kg/h, or is unable to take enough fluids orally.

### Recommended Composition (Dhaka Fluids) →

NaCl - 85 mM = 5 g	} in 1L water or s/l glucose solution	133 mM Na <sup>+</sup>
KCl - 13 mM = 1 g		13 mM K <sup>+</sup>
NaHCO <sub>3</sub> - 48 mM = 4 g		98 mM Cl <sup>-</sup> 48 mM HCO <sub>3</sub> <sup>-</sup>

Alternate → Ringer Lactate Solution #  
 Na<sup>+</sup> = 130, Cl<sup>-</sup> = 109, K<sup>+</sup> = 4, lactate 28 mM

## B) ORAL REHYDRATION THERAPY (ORT)

- ↳ Used in mild (5-7%) to Moderate (7.5-10%) loss
- ↳ Salt + Glucose → Na-Glucose → ↑ absorption
- ↳ Principle governing composition of ORS are
  - It should isotonic or little hypotonic total osmolarity - 200-310 mOsm/L plasma ≈ 290 mOsm/L

b) molar ratio of Glucose, should be equal to Na<sup>+</sup>  
 • Not exceed 110 mM

c) K<sup>+</sup> = 15-25 mM, HCO<sub>3</sub><sup>-</sup> = 8-12 mM

↳ New WHO ORS composition →

NaCl	2.6 g	Na <sup>+</sup> - 75 mM
KCl	1.5 g	K <sup>+</sup> - 20 mM
Trisod. Citrate	2.9 g	Cl <sup>-</sup> - 65 mM
		Citrate - 10 mM
Glucose	13.5 g	Glucose - 75 mM
Water	1 L	Total Osmolarity = 245 mOsm/L

Old Formula	
Na <sup>+</sup>	90 mM
K <sup>+</sup>	20 mM
Cl <sup>-</sup>	80 mM
Citrate	10 mM
Glucose	110 mM
= 310 mOsm/L	

Administration → every 1/2-1 h interval, in case of 5-7.5% loss.

children - 5 ml/kg/h for 2-4 h

Uses - Diarrhoea, Dehydrat<sup>n</sup>, Heat shock, Post-surgical loss.

Zinc in pediatric Diarrhoea → Zinc Supplements with low osmolarity ORS may effectively reduce the acute diarrhoea in children (< 5y)

dose - 10 mg/day → 0-6 month  
 20 mg/day → 6-60 month For 10-14 days

→ ↓ cAMP dependent Intestinal Cl<sup>-</sup> Secret<sup>n</sup>