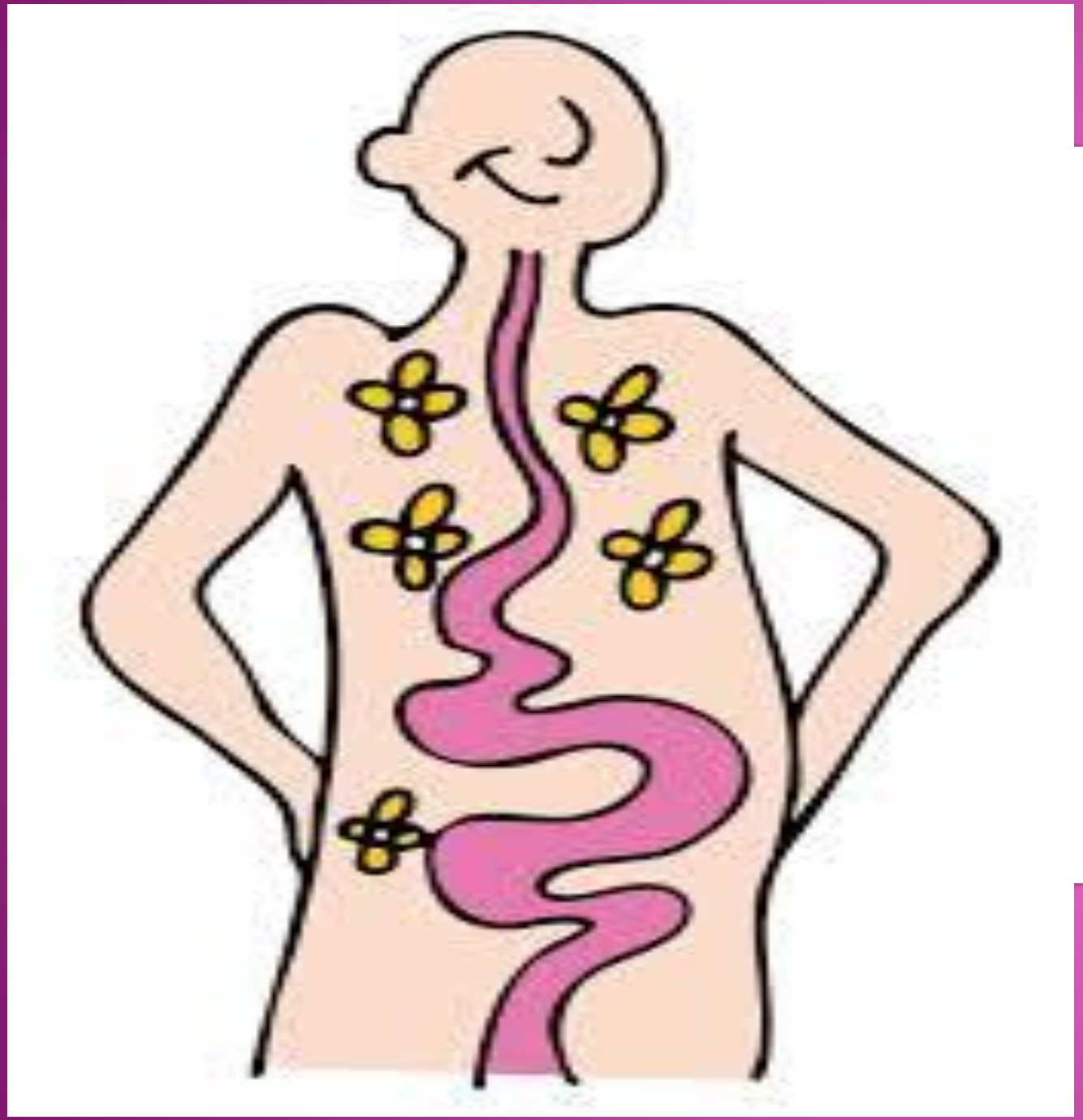

DRUGS AFFECTING GIT MOTILITY

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Drugs affecting git motility

INCREASES

upper GI

Prokinetics

in Large + small intestine

laxatives

for constipation

DECREASES

antispasmodic

in upper GI

from stomach to duod..

antidiarrheal

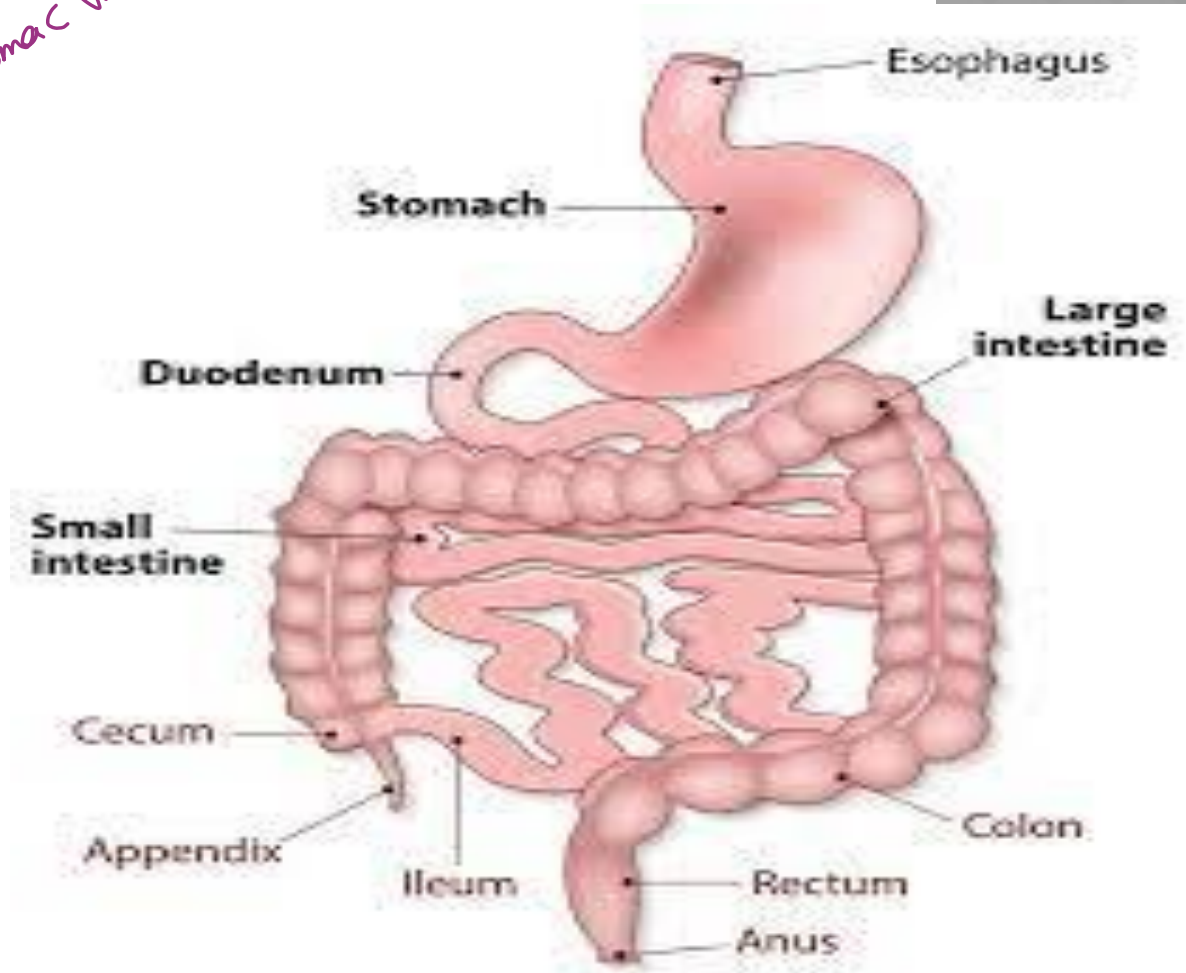
lower GI

Prokinetic drugs

Stimulate → in upper GI

↓ from esophagus until Stomach ↳

- **Drugs that selectively stimulate gut motor function.**



* The systems that modulate motility in GI are 2:

Enteric Nervous System (Enteric plexus)

↳ Interneurons modulate the action of sympathetic + paras... (autonomic NS) in GIT

The 2 systems that done by enteric plexus are related to

1- Serotonin
↓
① work on 5-HT$_4$ Receptors
↓
↑↑ contraction

② 5-HT$_3$ Receptors
↓
↓↓ special mediators that cause relaxation so contraction occurs. + ↑ motility

2- Dopamine → from sympathetic Nerve supply in GI.
↓
on D$_2$ Receptors
↓
↓↓ Ach in GIT

1.Dopamine (D_2) antagonists: inhibitory → decrease inhibitory

- Metoclopramide.
- Domperidone.
- Sulpiride.

2. Serotonin receptor modulators: stimulatory → increase Ach release

- Tegaserod Maleate (Zelnorm), partial 5-HT_4 agonist.
- Cisapride (Proplusid), 5-HT_4 agonist.

3. Muscarinic receptor agonist : Bethanechol

3. Directly stimulate motilin receptors Macrolides

Dopamine (D_2) antagonists: Metoclopramide

powerful

D_2

Pharmacokinetic:

- Rapidly absorbed.
- Half life 4-6 hrs.
- Distributed rapidly to most tissues (bl. brain barrier, placenta, milk).
- Hepatic metabolism (sulfation & glucuronidation).
- Excreted in urine.

➲ Mechanism of action:

- ***D_2 receptor antagonist.***
- Promotes release of Ach from myenteric plexus (***5-HT_4 agonist***)
- ***5-HT3 antagonists.***

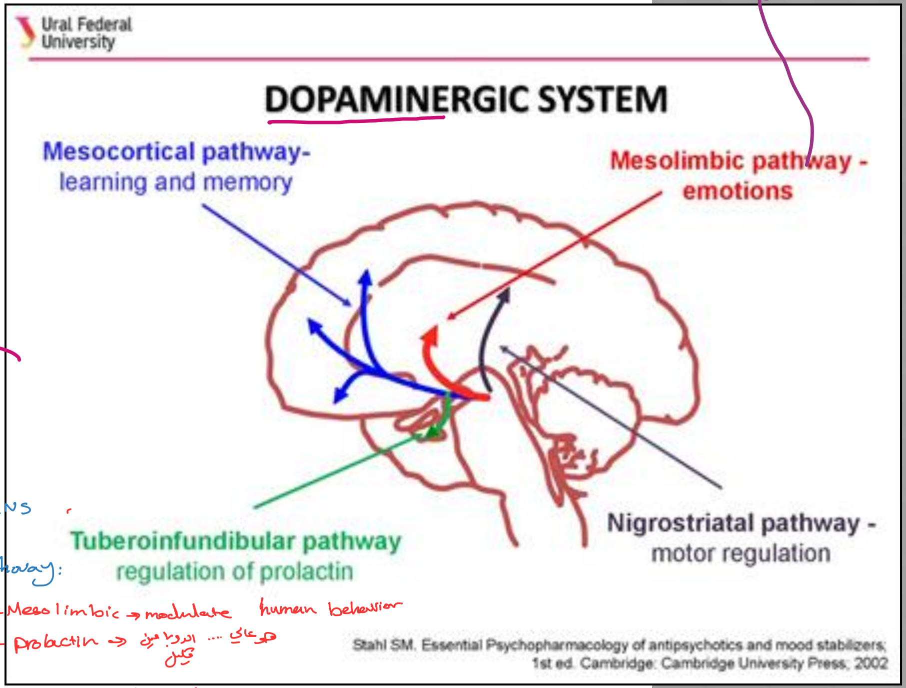
Pharmacological effects:

- **1. C.N.S.**: D_2-blocker.
  - Antiemetic. (CTZ)
  - Hyperprolactinemia.
  - Extrapyramidal symptoms. (basal ganglia)
- **2. G.I.T.** : ↑esophageal peristaltic amplitude, ↑ LESP, and enhances gastric emptying (upper digestive tract) but has no effect upon small intestine or colonic motility

D2 Receptors found in vomiting center in CNS

occurs just with Metoclopramide
because it can pass CNS (High lipid soluble)
→ Block D2 in CNS

D2 → have 5 pathway:
1- Vomiting center
2- Motor coordination
3- Mesolimbic → modulate human behavior
4- prolactin →
5- Nigostriatal pathway



➲ Uses:

1. Antiemetic (potent antiemetic).
2. Prokinetic action:
   A. GERD (Gastroesophageal reflux disease) (rarely used).
   B. Gastric hypomotility & postoperative ileus.
   C. To facilitate intubation procedure (nasoenteric feeding tube) and radiological examination of gut.
   D. To empty the stomach before emergency surgery

➲ Side effects:

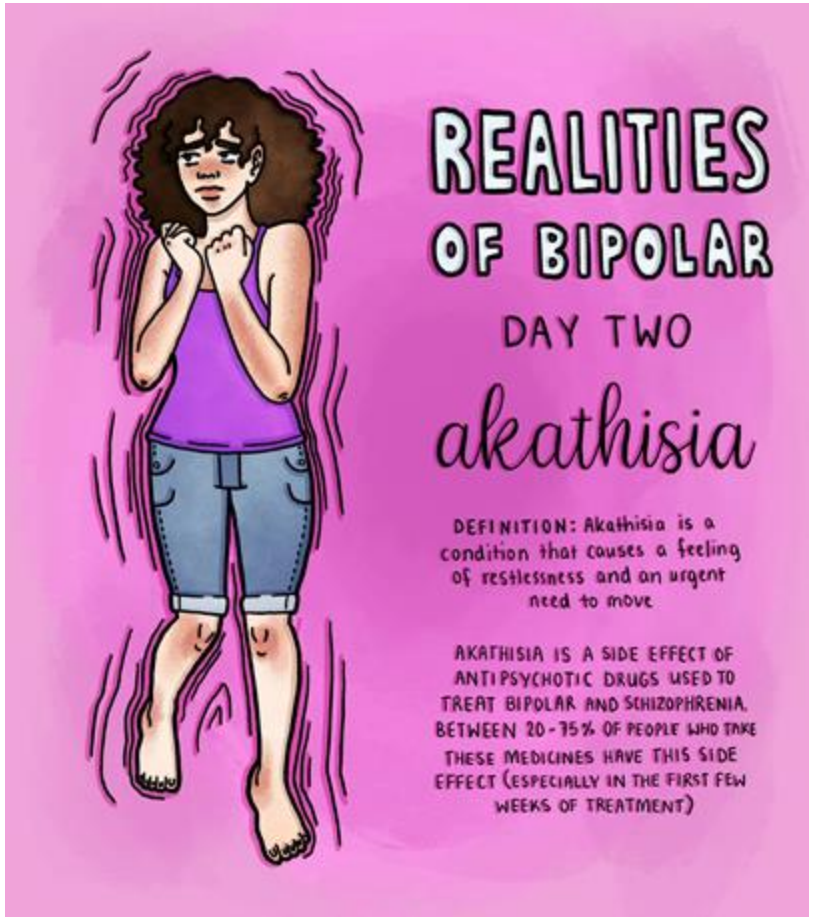
1. Restlessness, drowsiness, insomnia, anxiety & agitation (10-20%, especially the elderly).

2. Extrapyramidal effects (dystonia, akathisia, parkinsonian features).

- 25% in high doses & 5% in long term therapy.
- Tardive dyskinesia, sometimes irreversible (in long term therapy).
- Long term use should be avoided unless absolutely necessary, especially in the elderly.

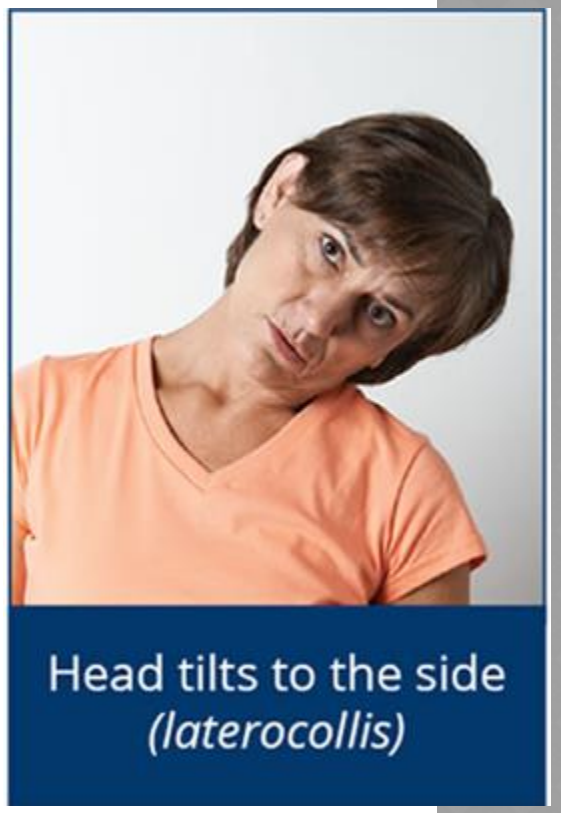
3. Stimulates prolactin release → Galactorrhea, gynecomastia, impotence & menstrual disorders.

Akathisia



Tardive dyskinesia

dystonia



DOMPERIDONE (MOTILIUM)

↳ can't pass CNS

- **Pharmacokinetics:**
  - Rapidly absorbed.
  - Half-life 7-8 hrs.
  - Excreted in feces.
  - ***Rarely crosses bl. brain barrier*** (rare extra-pyramidal reactions).
  - Hyperprolactinaemia.
- **Mechanism of action:** D_2-blocker.
- **Pharmacological effects:** As Metoclopramide

CISAPRIDE (PREPULSIDE)

only on serotonergic system

- **Mechanism of action**: Release of myenteric Ach ($5HT_4$ agonist).
- **Pharmacological effect:** Acts on both upper and lower gut.
- **Uses:**
  - Prokinetic.
  - Chronic idiopathic constipation and colonic hypomotility.
- **Side effects:**
  - Diarrhea.
  - Arrhythmia (due to inhibition of cardiac hERG K^+ channels, which results in QT prolongation in some patients).

MACROLIDES

- ➲ Directly stimulate **motilin** receptors on G.I.T. smooth muscle and promote the onset of a migrating motor complex.
- ➲ **Uses:**
  - 1. IV erythromycin in gastroparesis, however tolerance rapidly develops.
  - 2. Acute upper GIT hemorrhage to promote gastric emptying of blood prior to endoscopy.


Thank You!
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