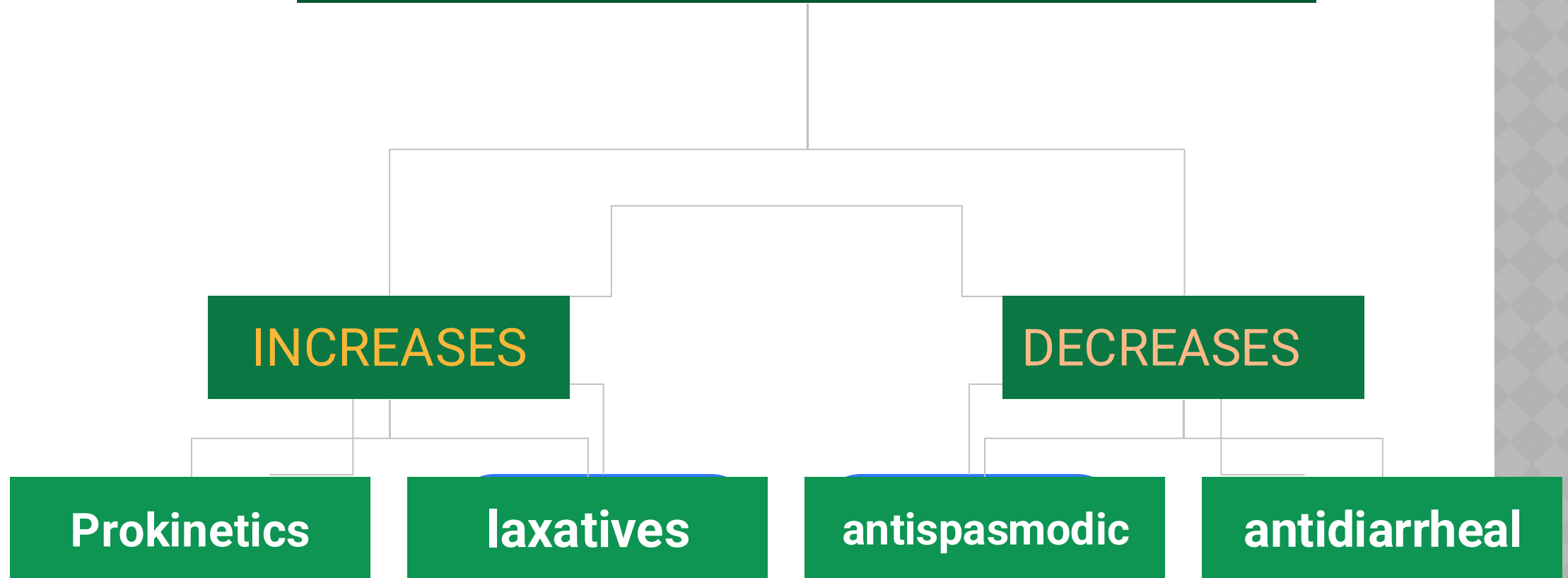


DRUGS AFFECTING GIT MOTILITY

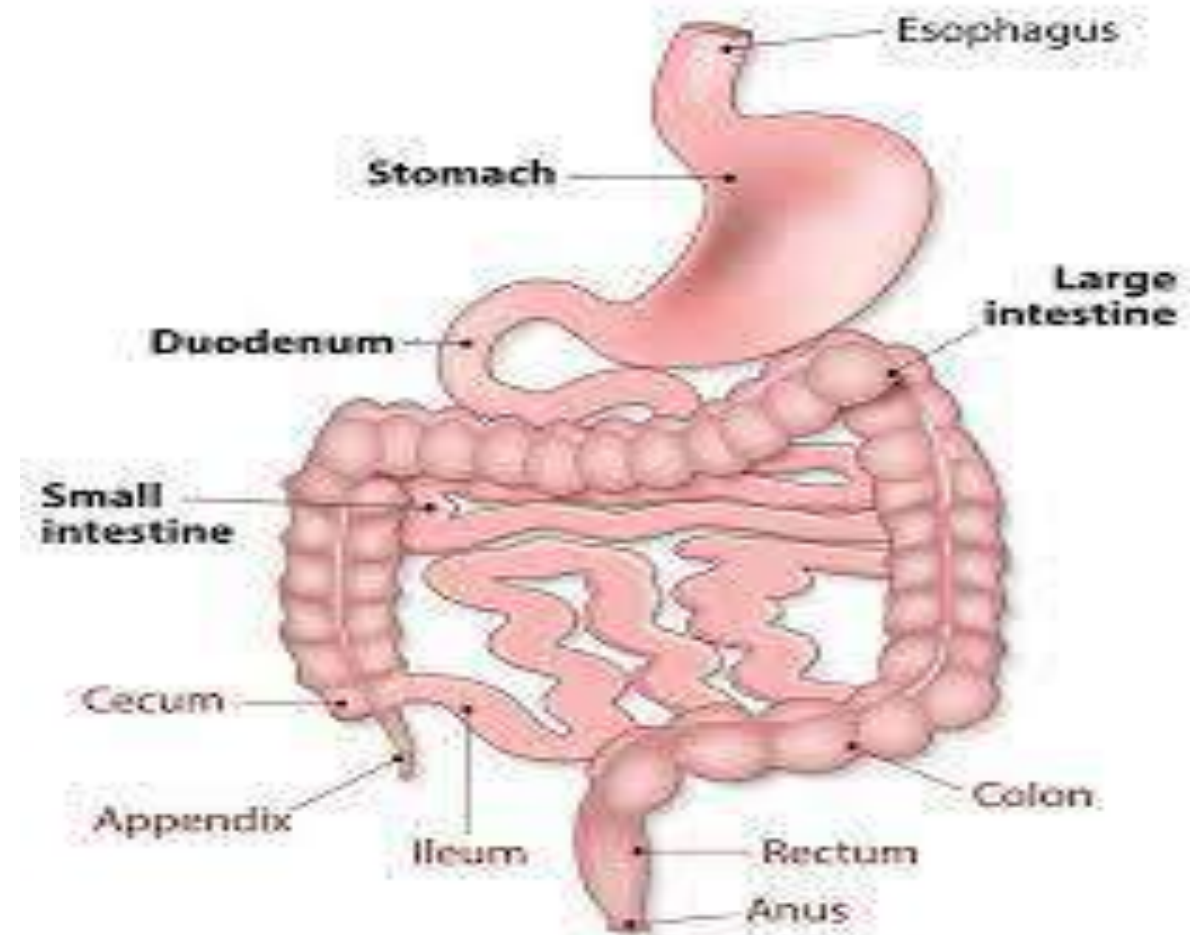
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Drugs affecting git motility



Prokinetic drugs

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



1. Dopamine (D_2) antagonists:

- Metoclopramide. ■ Domperidone. ■ Sulpiride.

2. Serotonin receptor modulators:

- 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

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:

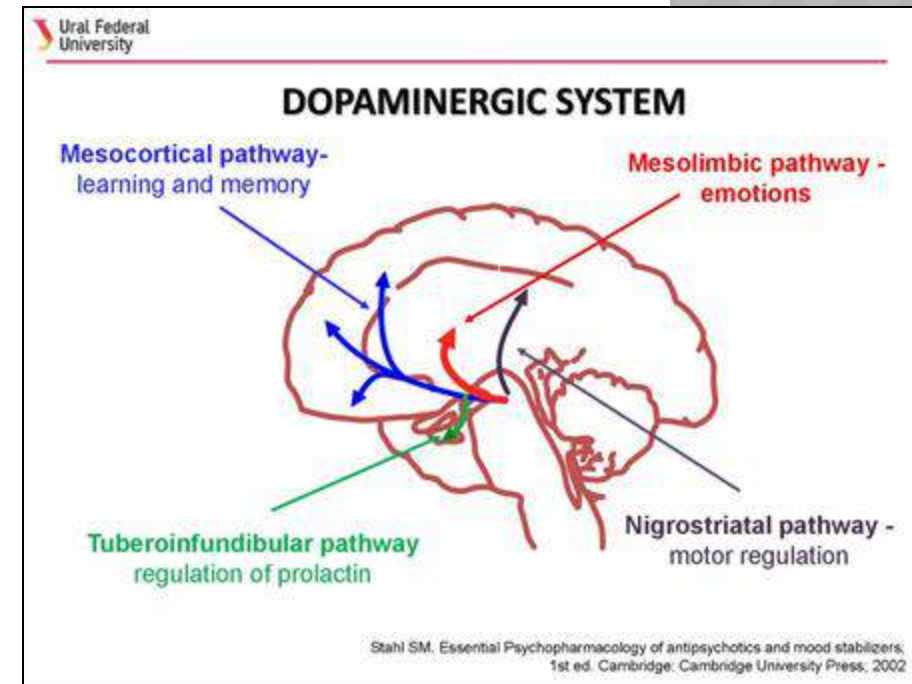
- *D_2 receptor antagonist.*
- Promotes release of Ach from myenteric plexus (*$5-HT_4$ agonist*)
- *$5-HT_3$ antagonists.*

Pharmacological effects:

■ 1. C.N.S.: D₂-blocker.

- Antiemetic. (CTZ)
- Hyperprolactinemia.
- Extrapyrasidal 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



➤ 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 (nasogastric feeding tube) and radiological examination of gut.
- D. To empty the stomach before emergency surgery

➤ Side effects:

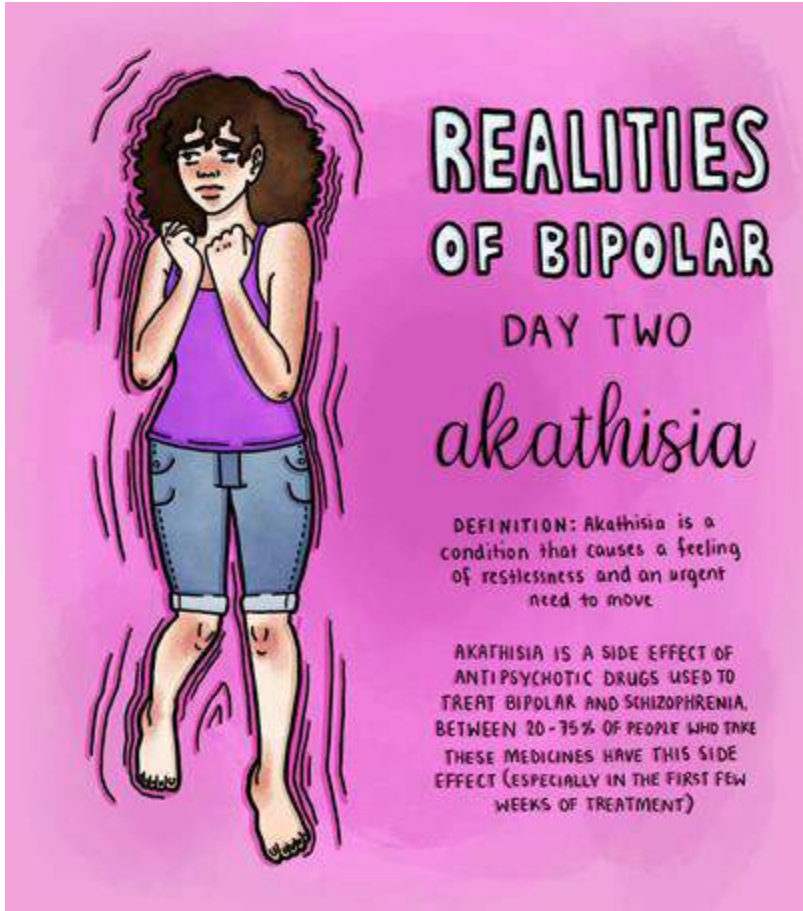
1. Restlessness, drowsiness, insomnia, anxiety & agitation (10-20%, especially the elderly).

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

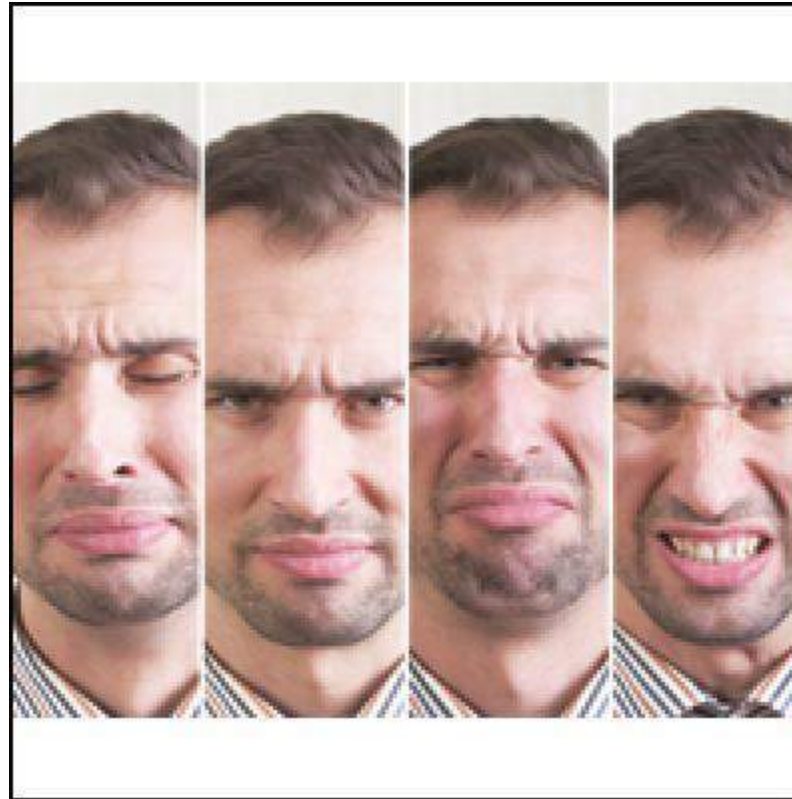
- 25% in high doses & 5% in long term therapy.
- Tardive dyskinesia, sometimes irreversible (in long term therapy).
- Long term use should be avoided unless absolutely necessary, especially in the elderly.

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

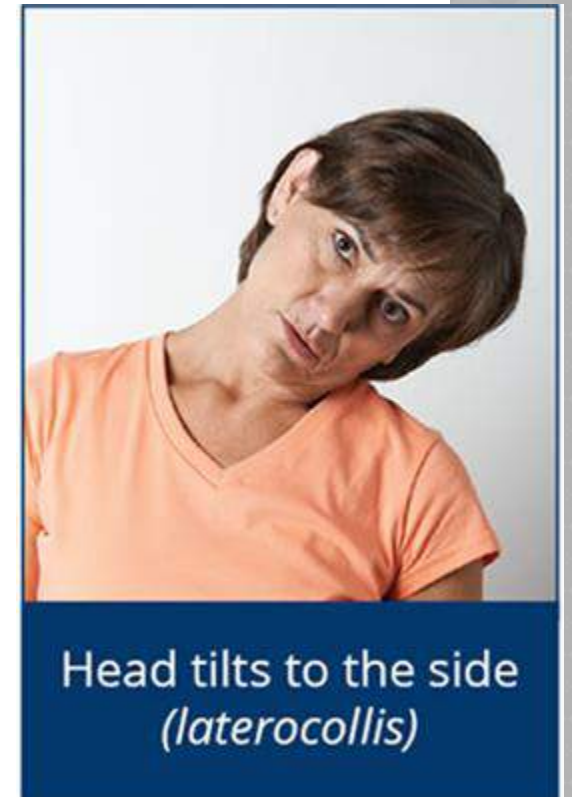
Akathisia



Tardive dyskinesia



dystonia



DOMPERIDONE (MOTILIUM)

⦿ ➤ Pharmacokinetics:

- Rapidly absorbed. ■ Half-life 7-8 hrs.
- Excreted in feces.
- ***Rarely crosses bl. brain barrier*** (rare extra-pyramidal reactions).
- Hyperprolactinaemia.

⦿ ➤ Mechanism of action: D₂-blocker.

⦿ ➤ Pharmacological effects: As Metoclopramide



CISAPRIDE (PREPULSIDE)

- ⦿ ➤ **Mechanism of action:** Release of myenteric Ach (5HT₄ 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.

