

Drugs Affecting GI Motility

- A. **Drugs Stimulating GI Motility “Prokinetic Agents”**
- B. **Laxative Agents.**
- C. **Antidiarrheal Agents.**



Mucosa

Epithelium

Lamina Propria

Muscularis Mucosa

Submucosa

Meissner's (Submucosal) Plexus

Muscularis Propria

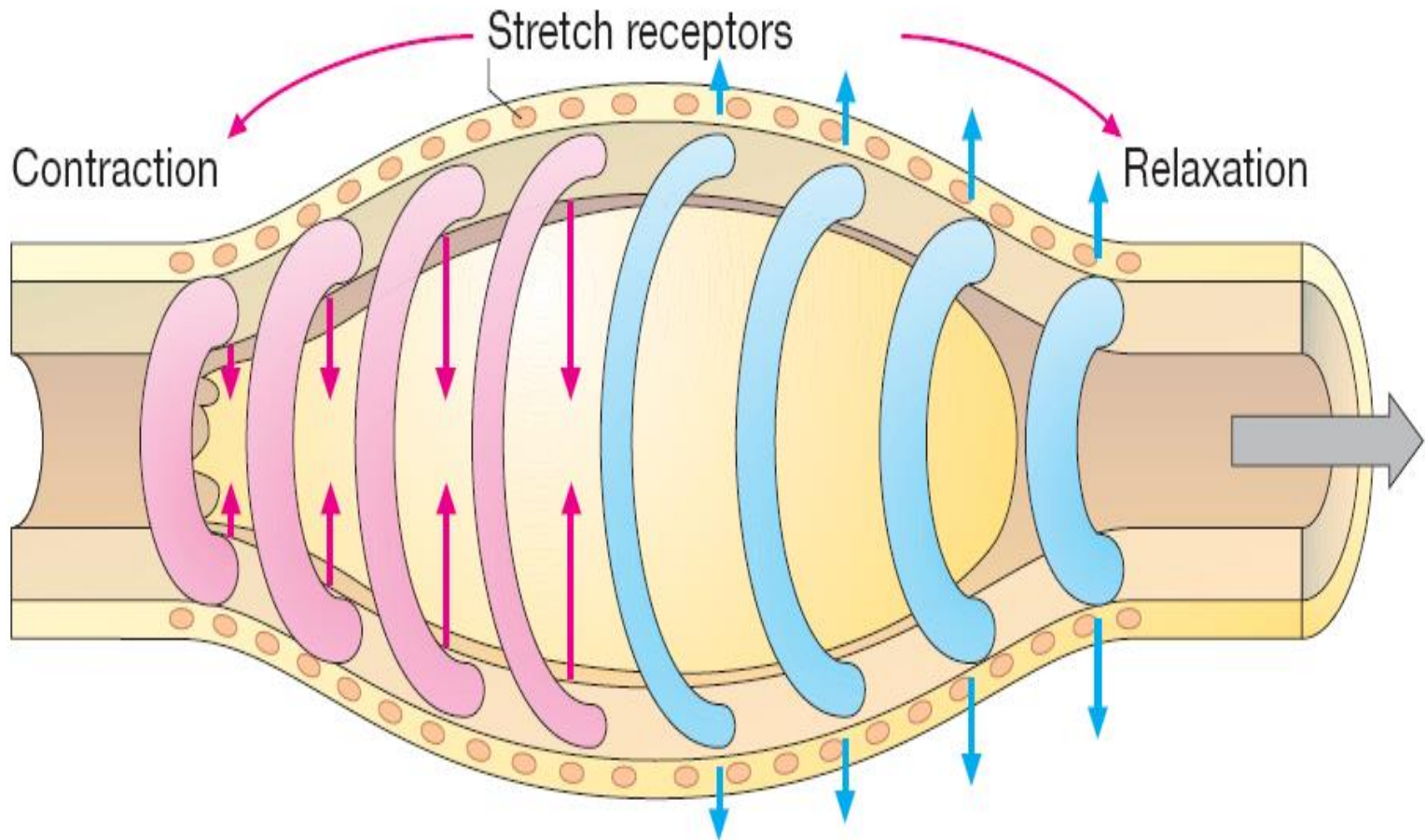
Circular Muscle

Auerbach's (Myenteric) Plexus

Longitudinal Muscle

Serosa or Adventitia

Peristaltic movement is due to reflex activation of proximal contraction and distal relaxation



A. Stimulation of peristalsis by an intraluminal bolus

Drugs Stimulating GI Motility ” Prokinetic Agents”

Potential Uses:

- Lower esophageal sphincter: GERD.
- Stomach: gastroparesis and postsurgical gastric emptying delay.
- Small intestine: Postoperative ileus.
- Colon: constipation.



” Prokinetic Agents”

Cholinomimetic Agents:

Bethanecol:

Stimulates M₃ receptors on muscle cells and myenteric plexus synapses.

Was used in GERD and gastroparesis.

Neostigmine:

AChase inhibitor.

”Acute Colonic Pseudo-obstruction”: IV can result in rapid evacuation of flatus and feces.

Can cause cholinergic effects.

” Prokinetic Agents”

Dopamine Receptor Antagonists:

Metoclopramide

Domperidone.

D₂ antagonists.

Dopamine inhibits cholinergic action on smooth muscle.

Have actions on esophagus and stomach, but not the small or large intestine.

Also inhibit the chemoreceptor trigger zone(Area Postrema).

” Prokinetic Agents”

Uses of Dopamine Receptor Antagonists:

1. GERD:

Not effective with erosive esophagitis.

Not superior to antisecretory agents.

Used in combination with antisecretory drugs.

2. Gastroparesis:

Postsurgical: vagotomy and antrectomy.

Diabetic.

Advancement of feeding nasoenteric tubes.

” Prokinetic Agents”

Other Uses of Dopamine Receptor Antagonists:

3. Nonulcer dyspepsia.

4. Antiemetic agents.

5. Postpartum lactation stimulation.



” Prokinetic Agents”

Adverse Effects of Dopamine Receptor Antagonists:

Metoclopramide crosses BBB so can cause:

Restlessness, drowsiness, insomnia, anxiety, agitation, extrapyramidal symptoms (dystonia, akathisia, parkinsonian features) and tardive dyskinesia.

Domperidone does not cross the BBB, so does not cause CNS effects

Both drugs can elevate serum prolactin levels causing galactorrhea, gynecomastia, impotence and menstrual disorders.



” Prokinetic Agents”

Macrolide Antibiotics:

Directly stimulate motilin receptors in the GIT.

Gastroparesis: given IV, but tolerance develops rapidly.

Acute upper GIT bleeding: to promote emptying of blood before endoscopy.



” Prokinetic Agents”

Chloride Channel Activator:

Lubiprostone:

PG analog.

Can be used in chronic constipation.

Stimulates chloride channel opening in GIT.

This increases liquid secretion in the intestine.

Delays gastric emptying leading to nausea.



Antiemetic Agents

- Afferent Inputs to the Vomiting Center:
 - Chemoreceptor trigger zone: DA₂, 5-HT₃, NK1, and opioid receptors.
 - Vestibular system involved with motion sickness through cranial nerve VIII. Rich in M and H₁ receptors.
 - Pharyngeal irritation through the vagus.
 - GIT afferents through the vagus and spinal afferent nerves, rich in 5-HT₃ receptors.
 - Central mechanisms due to psychiatric disorders, stress, and anticipatory vomiting of cancer chemotherapy (5-HT₃).

Antiemetic Agents

- Serotonin 5-HT₃- Receptor Antagonists:

- Ondansetron.

- Granisetron.

- Dolasetron.

- Palonosetron.

- 5-HT₃ receptors are involved in three out of the five inputs involved with vomiting.

- Activity restricted to vomiting due to vagal stimulation and chemotherapy.

- Motion sickness is poorly controlled.

Antiemetic Agents

- Serotonin 5-HT₃- Receptor Antagonists:
 - Used before chemotherapy, activity enhanced by dexamethasone and NK₁ antagonist.
 - Can also be used in postoperative and post radiation vomiting.
 - Safe drugs but can cause headache, dizziness and constipation.
 - Also prolong QT interval(i.e. **proarrhythmic**).

Antiemetic Agents

- Neurokinin Receptor(NK1) Antagonists:
 - Apripetant:
 - Central blockade in the area postrema.
 - Used in combination with 5-HT₃ antagonists.
 - Can cause fatigue, dizziness and diarrhea.



Antiemetic Agents

- Antipsychotic drugs:
 - Prochlorperazine.
 - Promethazine.
 - Droperidol.
 - Inhibit dopamine and muscarinic receptors.
 - Can cause extrapyramidal effects, hypotension and prolong QT interval.



Antiemetic Agents

- Antihistamines and anticholinergic Drugs:
 - Diphenhydramine
 - Meclizine.
 - Hyoscine (scopolamine).
 - Particularly useful in **motion sickness**.
 - Can cause dizziness, sedation, confusion, dry mouth, cycloplegia, and urinary retention.
 - Hyoscine can be used as a transdermal patch.



Antiemetic Agents

- Benzodiazepines:
 - Lorazepam.
 - Diazepam.
 - Antianxiety-hypnotic drugs
 - Reduce anticipatory vomiting caused by anxiety.



Antiemetic Agents

- Cannabinoids:
- Dronabinol.
- Nabilone.
 - Delta-9- tetrahydrocannabinol from marijuana is useful for chemotherapy-induced vomiting.
 - Mechanism not understood.
 - Can cause euphoria, dysphoria, sedation, hallucinations, dry mouth, and increased appetite(**the munchies**).
 - Also, hypotension, tachycardia, and conjunctival injection.

Emetic Agents

- Many drugs.
- Hypertonic saline.
- Apomorphine.
- Ipecac syrup.

