GI Pharma

rebound effect, CO_2 production

1) Antacids → Aluminum, Magnesium, Calcium Carbonate, Sodium bicarbonate

Aluminum & Magnesium → Cause Constipation / diarrhea → given in combination

Sodium bicarbonate → Counteract diuretic therapy for hypertension

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50% first-pass metabolism

2) H_2-Receptor Antagonist → Cimetidine, Ranitidine, Famotidine, Nizatidine

GERD, Non-Ulcer dyspepsia, Stress Related Gastritis, Peptic Ulcer

Stress Related Gastritis → IV

Peptic Ulcer → ✗ H. pylori & ✗ NSAID is continued

IV Cimetidine

Adverse effects: GI symptoms (diarrhea, headache, fatigue ...), CNS (confusion, hallucinations)

⊖ estradiole metabolism, ↑ prolactin levels, cross placenta, bradycardia and hypotension

↳ Cimetidine

Drug interactions: Cimetidine → ⊖ Cytochrome P450 enzymes (↑ $t_{1/2}$ of many drugs)

Ranitidine → bind 4-10 times less

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3) PPI → Omeprazole (oral), Rabeprazole, Lanzoprazole, Pantoprazole, Esmoprazole (oral + IV)

(prodrug formulation)

GERD, Nonulcer Dyspepsia, Stress-Related Gastritis, Gastrinoma, Peptic ulcer disease

Stress-Related Gastritis → oral PPI (omeprazole) by nasogastric tube; ✗ Nasogastric tube

IV H_2 antagonist

Peptic ulcer disease → H. pylori (Triple ⊖ PPI + Clarithromycin + Amoxicillin or Metronidazole)

✓ NSAID associated ulcers

✓ Rebleeding ulcers (oral or IV)

Synthetic form of vitamin B12

Adverse effects: Diarrhea, headache, ↓ Cyanocobalamine absorption, ↑ gastrin levels, Chronic inflammation in gastric body, Atrophic gastritis (Hyperplasia of ECL Carcinoid tumors)

Drug interactions: Affect → absorption → digoxin, ketoconazole

→ Metabolism → diazepam, phenytoin

Omeprazole

Laxatives

1) Bulk forming laxatives → Natural plant products ⇒ Psyllium, Sterculia, Methylcellulose
→ Synthetic fibers ⇒ polycarbophil

* Can cause bloating and flatus

2) Stool surfactant agents → Docusate, Glycerin suppository, Mineral oil
→ Aspiration can cause lipoid pneumonia → can impair absorption of fat-soluble vitamins

3) Osmotic Laxative (Purgatives) → Magnesium Oxide, Sorbitol, lactulose, balanced polyethylene Glycol
rapid bowel evacuation within 1–3 hrs
Can cause purgation which may lead to volume depletion
⇒ cause severe flatus and cramps

4) Stimulant Laxatives (Cathartics) → enteric system activation ⇒ neurologically impaired patients
→ bed-bound patients

Anthraquinone derivatives (Aloe, Senna, Cascara)
⇒ cause brown pigmentation of colon (Melanosis), poorly absorbed

Castor oil → hydrolized → ricinoleic acid (local irritant)
⇒ clean colon before procedures

5) Tegaseroid → Serotonin 5-HT4 Partial agonist → Presynaptic receptor of IPANs → Neurotransmitter release
⇒ Chronic constipation, Nonulcer dysplasia, Gastroparesis, IBS
Adverse effects ⇒ diarrhea (9% of patients) → hypomotility of GI
proximal bowel contraction and distal relaxation

Antidiarrheal Agents → Mild to moderate acute diarrhea, Chronic diarrhea, IBS, inflammatory bowel syndrome

1) Opioid agonists → ⊖ Cholinergic nerves, ↑ Colonic transit time (Constipating effects)
* Can have CNS effects and addiction potential (+ Atropine to reduce dependence)

→ Loperamide, Diphenoxylate → Can have CNS effects
↳ analgesic or addiction potential
(Doesn't cross BBB)

2) Kaolin and pectin → Combined = Kaopectate
Aluminum Silicate = indigestible carbohydrate (from apples)

3) Bile Salt-binding resins: Cholestyramine, Colistipol
Can cause bloating, flatulence, constipation and fecal impaction

4) Octreotide = Synthetic octapeptide (similar action to Somatostatin)
→ ⊖ of endocrine tumor effects
→ Diarrhea due to vagotomy or dumping syndrome
→ Pituitary tumors and GI bleeding
→ Can stimulate motility in small bowel bacterial overgrowth, intestinal pseudo-obstruction (IPO) → not physical
↳ in low doses! (it typically slow down GI motility) at higher doses
↳ Caused by Scleroderma

Drugs used for Irritable bowel syndrome (متلازمة القولون العصبي)

1) Antispasmodic or Anticholinergic → Dicyclomine, Hyoscyamine

2) Serotonin 5 HT3 - Receptor antagonist → Alosetron → Women with severe IBS and diarrhea is the prominent symptom
↓
Can cause ischemic colitis
↳ extrinsic Sensory nerves (gut → CNS)
↳ terminal of enteric cholinergic neurons

3) Serotonin 5 HT4 - Receptor agonist → Tegaserod → Constipation

Antiemetic drugs

1] Serotonin 5H-3 Antagonist (Ondansetron, Granisetron)

Central → Area postrema
Peripheral → GIT receptors

↘ acute chemotherapy-induced nausea and emesis and postoperative nausea and vomiting
(Combined with dexamethasone and NK1-receptor antagonist)

Adverse effect: Headache, dizziness and constipation

2] NK1 Receptor Antagonists (Aprepitant)

area postrema

→ prevention of acute and delayed nausea and vomiting
(Combined with 1] and Corticosteroids)

3] Cannabinoids (Dronabinol, Nabilone)

→ Chemotherapy-induced vomiting
→ psychoactive agents

Adverse effects: Euphoria, dysphoria, Sedation, hallucinations, dry mouth, increase apetite

4] Antipsychotic drugs (Prochlorperazine, Promethazine, Droperidol)

→ block dopamine and muscarinic receptors
→ Can block H_1 receptors → Antihistamine activity ↘ Sedative effects

5] Benzodiazepines (Lorazepam, Diazepam)

Reduce vomiting caused by anxiety

Antiprotozoal drugs → Antimalarial drugs (Chloroquine, Quinine, Artemisinin, Doxycycline, Pyrimethamine)
→ miscellaneous antiprotozoals (Metronidazole, tinidazole, nifuratel)

→ Metronidazole → extraluminal amebiasis (kill trophozoites but not cysts), anaerobic bacteria
inactive → activated by reduction → disrupt replication and transcription and ⊖ DNA repair
↳ pyruvate-ferredoxin oxidoreductase enzyme (in anaerobic organisms)

Adverse effects: Nausea, headache, dry mouth, metallic taste (common), Vomiting, diarrhea, insomnia (أرق), weakness, dizziness (infrequent)
Rare: Pancreatitis, CNS toxicity (Tinidazole is better tolerated)
* best avoided in pregnant or nursing women

→ Tinidazole → Similar but better toxicity profile, Can be given in a single dose

→ Nifuratal → Alternative to metronidazole or tinidazole in treatment of trichomoniasis

→ Amebiasis → Asymptomatic → lumenal amebicide (Diloxanide furoate, Iodoquinol, Paromomycin)

Amebic Colitis → lumenal amebicide + Metronidazole
→ Tetracyclines + erythromycin (✗ extraintestinal disease)
→ Dehydroemetine or emetine (best to avoid due to toxicity)

Metronidazole is not effective against lumenal parasites

→ Giardiasis → Metronidazole → 90% efficacy after a single treatment, Tinidazole is equally effective

→ Trichomoniasis → Metronidazole → Single dose of 2g

→ Chloroquine → acute attack (oral, IV, IM), Resistance develops

Adverse effects: Nausea, headache, teratogenic

→ Quinine → Oldest drug (from Cinchona tree), toxic, No resistance

→ Artemisinin → New drug (from Sweet wormwood (الشيح))
→ Doxycycline → Antiprotozoal but is also used for treating bacterial infection
→ Same thing to Metronidazole

Anthelmintics → exert their antiparasitic effect by interference with:
1) energy metabolism
2) neuromuscular coordination
3) microtubular function
4) cellular permeability

For nematodes:

1) **Piperazine** (Vermizine) ⇝ heterocyclic ring → hyperpolarization
→ agonist at chloride gated channels on the parasite muscle → reversible flaccid paralysis → expulsion of the worm

→ Prolonged treatment and might need a purgative
↳ So that paralyzed worms are quickly expelled

2) **Diethylcarbamazine**
→ Interfere with the metabolism of arachidonic acid and block the production of prostaglandins
→ resulting in capillary vasoconstriction and impairment of the passage of the microfilara
↳ treat filariasis

3) **Mebendazole** (Vermox) → Wide spectrum, safe drug
Threadworm → Hookworm (Ankylostomiasis) → Roundworm
(Enterobius vermicularis) — 2 tablets for 3 days — (Ascaris lumbricoidis)
Single dose, can be repeated after 3 weeks

For cestodes (Flatworms):

1) **Niclosamide** (Dichlorinated Salicylamide)
⇝ ⊖ anerobic incorporation of inorganic phosphate into ATP → ↓ ATP production
→ detachment of the scolex from intestinal wall → evacuation of cestodes

For trematodes

1) **Praziquantel** (Biltricide)

↑ Ca^{+2} permeability through parasite specific ion channels → muscle cell accumulate Calcium → ↑ parasitic motility
hidden antigens are exposed ← the drug alters the parasite's surface structure ← spastic paralysis ←
↳ disruption of lipid bilayer →
(tegumental antigens, lipid anchored protein, actin) → Host immune recognition → Antibodies and Complement-mediated assult