

Drugs Used for Gastric and Duodenal Ulcers

- **Acid secretion:** (+) → Histamine, Ach and Gastrin.
(-) → SS and PGE2
- Drugs are used to **relieve pain, accelerate healing** and **prevent recurrences**.

Drugs for lowering acid concentration	1- Antacids	a- Absorbable <i>(Not recommended for long time use)</i>	NaHCO_3	<ul style="list-style-type: none"> - Na^+ ions remain even with the presence of alkaline pancreatic secretions (HCO_3^-), which are then absorbed into the blood causing metabolic alkalosis. - It is avoided in case of hypertension, edema and cardiac failures.
		b- Non- absorbable	CaCO_3 Al(OH)_3 Mg(OH)_2	<ul style="list-style-type: none"> - Ions dissolve in the process of neutralization. Basic groups are mixed with alkaline pancreatic secretions (HCO_3^-) causing precipitation. They are then excreted with feces. - Excessive CaCO_3 → Hypercalcemia. - Al(OH)_3 → Constipation, hypophosphatemia and drug-drug interactions with tetracyclines. - Mg(OH)_2 → Diarrhea, releases CCK. ⇒ $\text{Al(OH)}_3 + \text{Mg(OH)}_2$ are used in combination as a last line therapy. This neutralizes HCl, relieves pain and promote healing.
	2- Inhibitors of acid production	a- M1 Anticholinergic	Pirenzepine Dicyclomine	<ul style="list-style-type: none"> - Used in adjuvant therapy for peptic ulcer and Zollinger-Ellison syndrome (ZES). - Limited usage due to side effects of cardiac arrhythmia, dry mouth, constipation and urinary retention.
		b- H2 Antihistaminic (-idine)	Cimetidine Ranitidine Nizatidine Famotidine	<ul style="list-style-type: none"> - Inhibit basal/food-stimulated acid secretion and acute stress ulcer. - Diminish responsivity to gastrin (in ZES). - Cimetidine was withdrawn from markets due to side effect.
		c- PPIs (-prazole)	Omeprazole Lansoprazole Pantoprazole Rabeprazole	<ul style="list-style-type: none"> - Omeprazole can cause maximal inhibition of HCl secretion. - These agents are prodrugs, with acid-resistant capsules removed in the duodenum to be absorbed into the blood to act on parietal cells inhibiting H^+/K^+ pump. - Long term treatment (ZES) and prevents recurrences. Reduce bleeding from NSAIDs and helps in H. pylori eradication. - Long term usage: Gastrin carcinoid tumor, Vit. B12 deficiency, superinfection by C. difficile and incomplete Ca^{+2} absorption. - Drug-drug interactions: Warfarin, diazepam, cyclosporine and phenytoin.

Mucosal protective drugs	1- Sucralfate	<ul style="list-style-type: none"> - Contains Al(OH)₃ residues but its not an antacid; fails to lower acidity. - Sucralfate binds to protein components forming a gel which adheres to mucosal defects creating a protective barrier. - It stimulates PGE₂ release and bicarbonate output. - It is taken on an empty stomach but may cause constipation. - It requires low pH to be active, thus, it is not used with antacids and H₂ blockers. - It interferes with drug absorptions, and Al⁺³ absorption may cause heavy metal toxicity.
	2- Misoprostol	<ul style="list-style-type: none"> - PGE₂ analog; inhibits HCl, stimulates mucus and bicarbonate secretion. - It attenuates the adverse effect (<i>protective</i>) of NSAIDs on the mucosa. - It is contraindicated for pregnant women.
H. pylori eradication	Bismuth compounds	<ul style="list-style-type: none"> - It is no longer recommended due to heavy metal exposure.
	Omeprazole + Amoxicillin + Clarithromycin	<ul style="list-style-type: none"> - If Amoxicillin and Clarithromycin cannot be tolerated, Metronidazole serves as a substitute. Therapy is taken for 7 days.

Extra notes in the slides:

- Therapeutic approaches of peptic ulcers are:
 - a- Lowering gastric acidity by neutralizing or decreasing proton output and slowing gastric emptying.
 - b- Increase protective forces by means of muco-protectants.
 - c- Eradicate Helicobacter pylori by Antibiotics.
 - d- Support psychotherapy (sedatives and tranquilizers).
 - e- Slowing gastric motility (emptying) by anticholinergics.
 - f- Treatment of complications such as bleeding, due to NSAIDs or COX inhibitors, (by blood transfusion) and perforation (by surgery).
- Acid neutralization depends on:
 - a- The antacid capacity to neutralize HCl.
 - b- Stomach food intake, food delay, and stomach emptying allowing more time for antacid reaction.
- CaCO₃ reacts with HCl in the stomach forming CO₂ and CaCl₂. It may also be used as supplements for the treatment of osteoporosis.
- Aluminum containing antacids can lead to precipitation in the gut lumen causing side effects, such as reduced absorption of other drugs, or phosphate depletion of the body with excessive intake.
- Mg(OH)₂ produces a laxative effect (osmotic action, and release of cholecystokinin by Mg²⁺).
- The laxative effect of Mg(OH)₂ is deleted by the constipation effect of Al(OH)₃.
- H₂ antihistamines reduces intracellular concentration of cAMP and thus decreases the secretion of HCl.
- Cimetidine rarely cause CNS disturbances such as confusion, gynecomastia, decreased libido and impotence in men. It also inhibits the hepatic biotransformation of many other drugs. Other antihistamines cause only headache, dizziness, diarrhea, and muscular pain.

Anti-Emetic Drugs

- **Medullary center** for emesis can be activated by many stimuli; vestibular, visual, olfactory, gustatory inputs, viscerosensory afferents and psychic experiences. Motion sickness and pregnancy vomiting have unclear mechanisms.
- Polar substances **cannot** reach the emetic center due to the BBB, they activate chemoreceptors in the **area postrema** or vagal nerve endings inducing emesis.
- **Area postrema has:** Dopamine D2, opioid, serotonin 5-HT₃ and NK1 receptors, thus blocking them reduce emesis.
- Antiemetic drugs are used to **prevent** kinetosis (*motion sickness*), pregnancy/cytotoxic drug-induced/ radiation/ postoperative vomiting.

Motion Sickness	Parasympathetic Scopolamine	<ul style="list-style-type: none"> - Drugs should be taken 30mins before travelling, repeated every 4-6 hours. - Scopolamine transdermally is protective for up to 3 days.
	H1 Antihistamines. (Diphenhydramine, Meclizine)	
Pregnancy vomiting	Antihistamines	<ul style="list-style-type: none"> - Pregnancy vomiting occur in the first trimester coinciding with the period of maximal fetal vulnerability. - Drugs are only used when continues vomiting threatens to disturb electrolytes and water balance placing the fetus at risk.
	Neuroleptics	
Drug-induced vomiting	5-HT₃ antagonists	<div style="text-align: center;">Ondansetron Granisetron Tropisetron</div> <ul style="list-style-type: none"> - To prevent vomiting during anti-cancer therapy (cisplatin), 5-HT₃ antagonists are used +/- GCS (methylprednisolone, dexamethasone). - They are effective against cytotoxic drug-induced emesis both at the start and during the therapy.
	Dexamethasone	
Anxiolytic drugs	Fluoxetine	<ul style="list-style-type: none"> - Anti-depressant by blocking serotonin re-uptake. - Psychomotor stimulation and appetite depression.
	Buspirone	
Anticipatory nausea	Benzodiazepine (Lorazepam)	<ul style="list-style-type: none"> - Anticipatory nausea and vomiting results from uncontrolled emesis in cytotoxic chemotherapy patients.
Dopamine-induced nausea	D2-receptor antagonist (Domperidone, sulpiride)	<ul style="list-style-type: none"> - In parkinsonian patients.
Miscellaneous	Metoclopramide	<ul style="list-style-type: none"> - Effective in nausea of GI origin (<i>5-HT₄ agonism</i>). - At high dosage, used for chemotherapy and radiation induced sickness (<i>5-HT₃/ D₂ antagonism</i>).
	Phenothiazine (-zine) (Levomepromazine, Trimeprazine, Perphenazine)	<ul style="list-style-type: none"> - Suppress postoperative, opioids, GI irritation, uremia and elevated intracranial pressure nauseas.
	Cannabinoids (Dronabinol, Nabilone)	<ul style="list-style-type: none"> - Antiemetic effects for cancer and AIDs patients.
	LSD	<ul style="list-style-type: none"> - Psychedelic (<i>hallucination</i>) by binding to 5-HT_{2A}.
	Sumatriptan	<ul style="list-style-type: none"> - It is an antimigraine drug, acts on 5-HT_{1D}.
	Cisapride	<ul style="list-style-type: none"> - Prokinetic drug (<i>control acid reflux, fast emptying</i>).