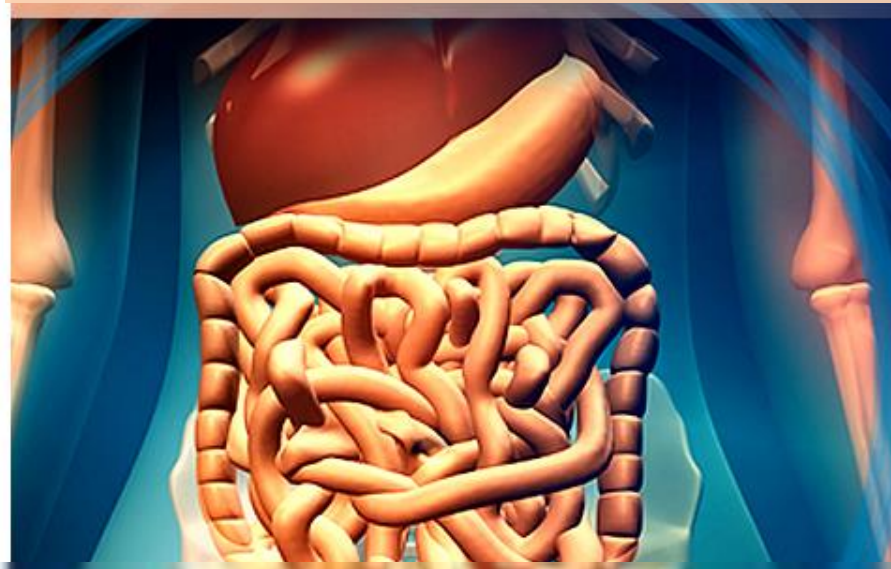
King Saud University
College of Medicine
2nd Year, 2nd Block

GIT BLOCK

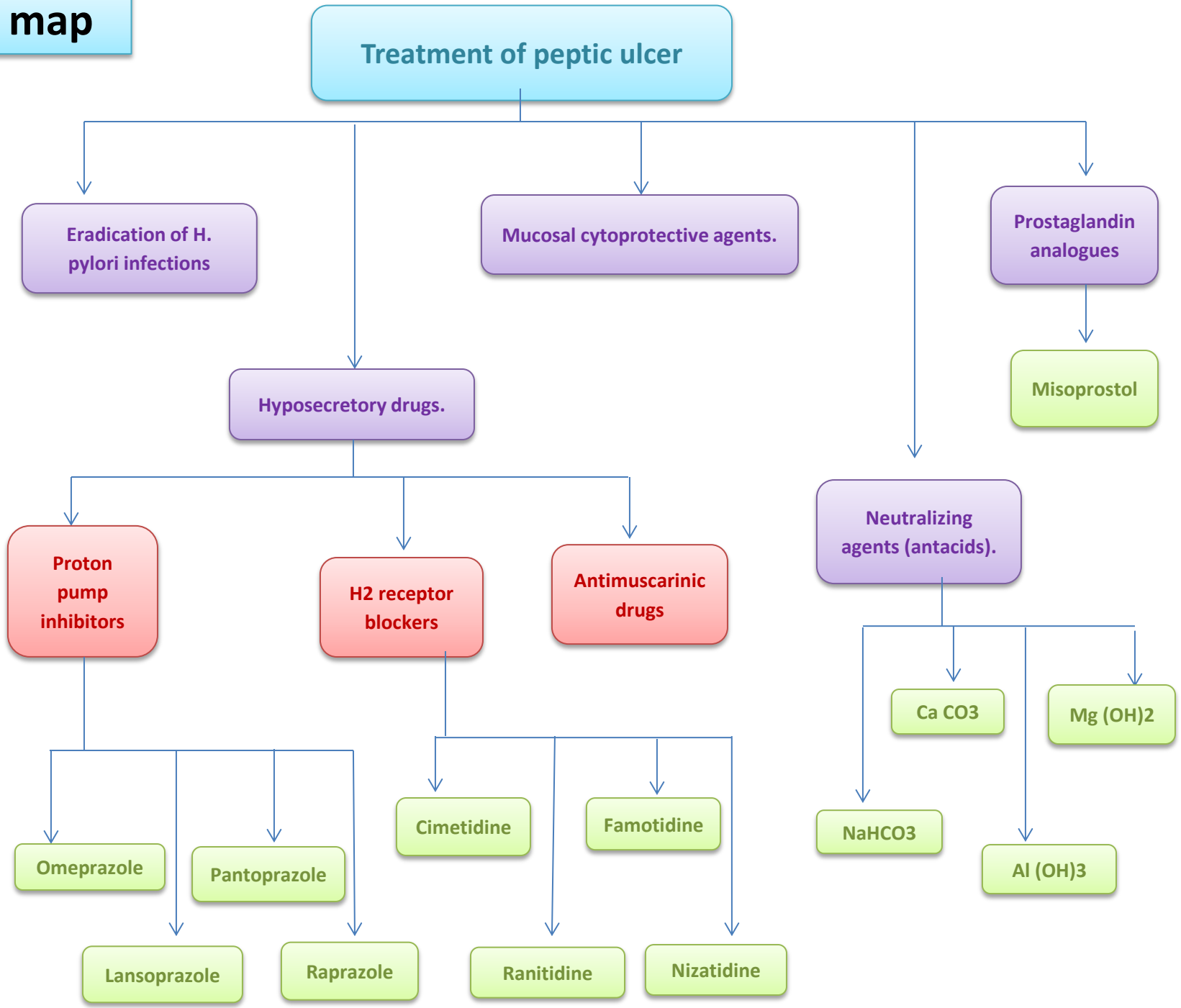
PHARMACOLOGY 433

MED 433 Teams



L2 - H2 blockers and proton pump inhibitors

Mind map


Treatment of peptic ulcer
Eradication of H. pylori infections
Mucosal cytoprotective agents.
Prostaglandin analogues
Misoprostol
Hyposecretory drugs.
Proton pump inhibitors
H2 receptor blockers
Antimuscarinic drugs
Neutralizing agents (antacids).
Ca CO3
Mg (OH)2
NaHCO3
Al (OH)3
Omeprazole
Pantoprazole
Lansoprazole
Raprazole
Cimetidine
Famotidine
Ranitidine
Nizatidine

introduction

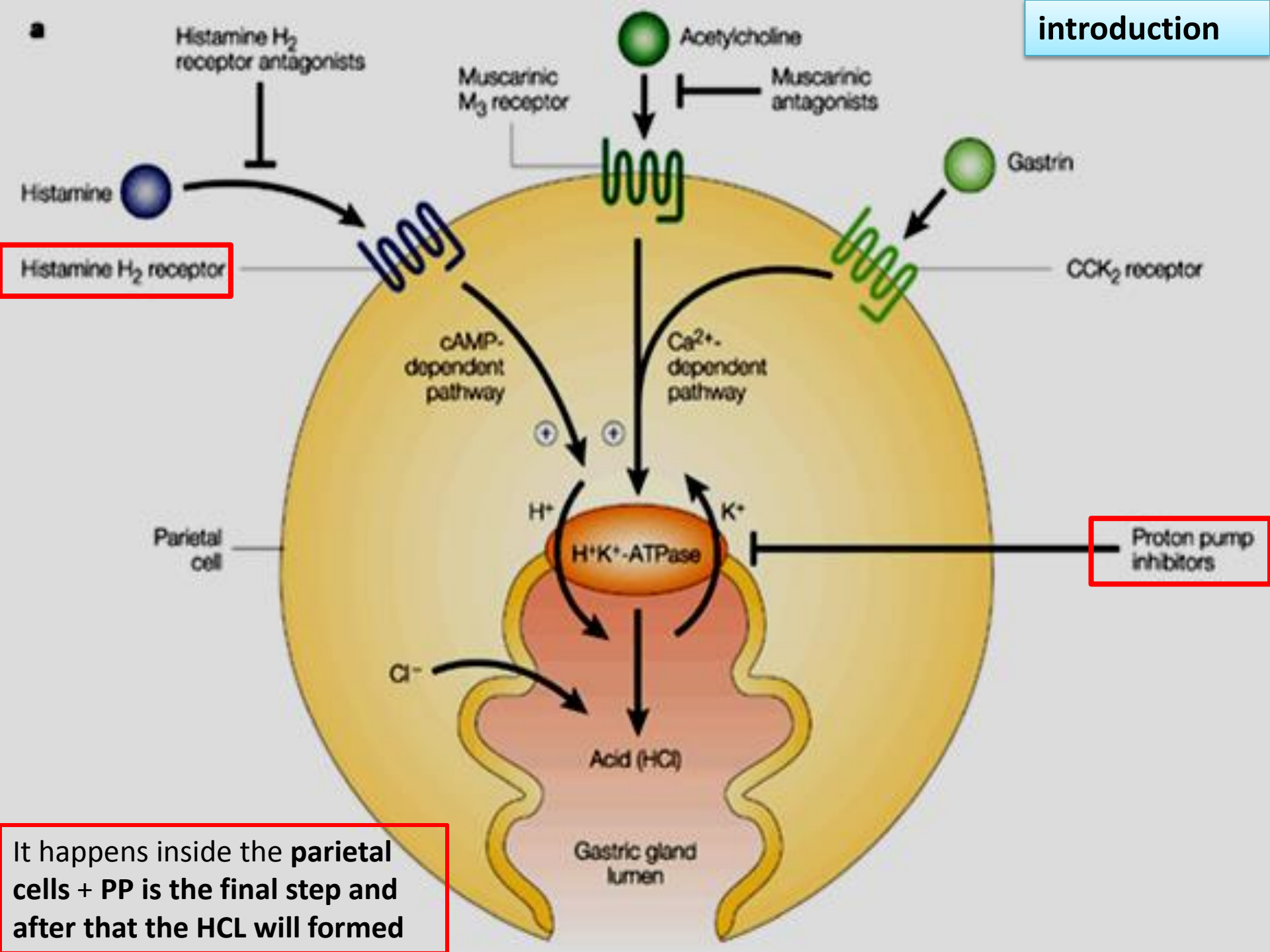
Peptic ulcer

Definition	Pathophysiology	Etiology	Treatment
▪ a localized lesion of the mucous membrane of the stomach (gastric ulcer) or duodenum (duodenal ulcer), typically extending through the muscularis mucosa.	is imbalance between aggressive factors (acid & pepsin) And Defensive factors (e.g. prostaglandins, mucus & bicarbonate layer)	• H. pylori infection • Alcohol • Smoking • Caffeine • Genetic factors*group O • Diet • Hypersecretory states "hypersecretion of HCL" (Zollinger Ellison syndrome) • Drugs (e.g.) NSAIDs.	• Eradication of H. pylori infections • Hyposecretory drugs. 1. Proton pump inhibitors 2. H_2 receptor blockers 3. Antimuscarinic drugs. • Mucosal cytoprotective agents: Prostaglandin analogues. • Neutralizing agents (antacids)

Gastric secretions

Types	Regulation	Gastric hyposecretory drugs
1. HCl and intrinsic factor (Parietal cells). 2. Pepsinogens (Chief cells). 3. Mucus, bicarbonate (mucus-secreting cells)	Parietal cells secrete acid in response to: 1. Histamine (local hormone): H_2 receptors 2. Gastrin (hormone): CCK_2 receptors 3. Ach (neurotransmitter): M_3 receptors 4. Proton pump (H^+/ K^+ ATPase)	1. Proton pump inhibitors 2. H_2 receptor blockers 3. Antimuscarinic drugs Hyposecretory drugs decrease gastric acid secretion ➔ Promote healing & relieve pain.

slide | doctor's note | important | explanation



It happens inside the **parietal cells** + **PP is the final step and after that the HCL will formed**

1-Proton Pump Inhibitors (PPIs)

examples	Omeprazole	Lansoprazole	Pantoprazole	Raprazole
M.O.A	Acts by irreversible inhibition of proton pump (H+/ K+ ATPase) that is responsible for final step in gastric acid secretion from the parietal cell. (Carbonic anhydrase involved in bicarbonate production)			
Pharmaco dynamics	They are the most potent inhibitors of acid secretion available today. Produce marked inhibition of basal & meal stimulated-acid secretion (90-98%). Reduce pepsin activity. Promote mucosal healing & decrease pain			
Pharmaco kinetics	▪Given orally as enteric coated capsules* (unstable in acidic medium in stomach). *It means not dissolved unless reaching the intestine *Are pro-drugs (it get activated after administered). *Dose reduction is required in severe liver failure ▪rapidly absorbed from the intestine. ▪In the acidic medium of parietal cell canaliculi, they are activated. ▪Should not combined with H_2 blockers or antacids.*because H2 blockers+antacid they decrease acidity and PPIs need an acid medium to get activated ▪At neutral pH, PPIs are inactivated. Have long duration of action (> 12 h-24 h) ▪Once daily dose is sufficient Given 1 h before meal. ▪Bioavailability is reduced by food. metabolized in the liver by Cyt-P450.			

slide doctor's note important explanation

2- Proton Pump Inhibitors (PPIs)

Uses	• **Eradication of H. pylori (combined with antimicrobial drugs).** • **Resistant sever peptic ulcer (4-8) weeks.** • **Reflux esophagitis.** • **Hypersecretory conditions as Zollinger Ellison syndrome and gastrinoma* (First choice)**
Adverse effects	• **Headache, diarrhea & abdominal pain.** **Long term use:** • **Achlorhydria (gastric acid in stomah is decreased or absent)** • **Hypergastrinaemia* (the presence of an excess of gastrin in the blood) *consequences to decreased HCL.** • **Gastric mucosal hyperplasia** • **Increased bacterial flora** • **Increased risk of community-acquired respiratory Infections& nosocomial pneumonia** ***Long term use:** **1) vitamin B12 deficiency.** **2) increased risk of hip joint fractures.**

*Zollinger Ellison syndrome (for your information)

Gastrin -secreting tumor of the pancreas.

Gastrin produces:

- Parietal cell hyperplasia (trophic factor).
- Excessive gastric acid production

slide | doctor's note | important | explanation

2- H2- Histamine receptors blockers

Such as	- Cimetidine - Ranitidine- Famotidine - Nizatidine
MOA	They competitively and reversibly block H_2 receptors on the parietal cells.
Pharmacokinetics	❖ Good oral absorption, given I.V in ER ❖ Given before meals. ❖ Famotidine is the most potent drug. ❖ Exposed to first pass metabolism (except nizatidine that has 100 % bioavailability). ❖ Duration of action (4-12 h). ❖ Metabolized by liver and excreted mainly in urine.
Pharmacological actions	✓ Reduce basal and food stimulated-acid secretion ✓ better to be given before night sleep because Block 90% of nocturnal acid secretion (which depend largely on histamine) & 60-70% of total 24 hr acid secretion. ✓ Promote mucosal healing & decrease pain

Uses	❖ GERD (heartburn/ dyspepsia). ❖ Acute ulcer healing in moderate duodenal ulcer (6-8 weeks) and benign gastric ulcer (8-12 weeks). ❖ Pre-anesthetic medication (to prevent aspiration pneumonitis). ❖ Prevention of bleeding from stress-related gastritis. ❖ Post–ulcer healing maintenance therapy (in absence of H.pylori).
ADRs	➢ CNS effects: Headache – confusion, GIT disturbances (Nausea & Vomiting). ➢ Elderly: hepatic dysfunction, renal dysfunction. ➢ Bradycardia and hypotension (rapid I.V.) * Special ADRs for Cimetidine 1. inhibits CYT-P45 leads to decrease metabolism of some drugs e.g.warfarin,phenytoin and benzodiazepines. 2. drugs interaction. 3. Dose reduction for elderly. *centrally acting so high 4. Endocrine effects: A- Galactorrhea (Hyperprolactinemia) B- Antiandrogenic actions (gynecomasteia –impotence) due to inhibition of dihydrotestosterone binding to androgen receptors.

slide doctor's note important explanation

3- Antacids:

These drugs are mainly inorganic salts they counteract the acidity
e.g.:

- **NaHCO3: ADR Systemic alkalosis**
- **Ca CO3 : ADR milk alkali syndrome (hypercalcemia , renal failure)**
- **Al (OH)3 : ADR constipation;**
- **Mg (OH)2 : ADR Diarrhea**

1) **acts by direct chemical neutralization of HCL and may decrease pepsin activity.**
2) **used to: A) relief pain of peptic ulcer*not for long time , B) dyspepsia.**
3) **All antacids ↓ absorption of some drugs e.g tetracycline, fluoroquinolones, iron.**

4- Prostaglandin analogues (PGE1)

Drug as	Misoprostol*not used any more because of it's short half life
MOA	1) ↓ HCL secretion 2) ↑ protective measures (↑ mucous/bicarbonate & gastric mucosal blood flow).
Pharmacokinetics	Orally, must be taken 3-4 times/day
Uses	NSAIDS-induced peptic ulcer.
ADRs	▪ Abdominal cramps; diarrhea ▪ Uterine contraction (dysmenorrhea or abortion);vaginal bleeding. *contraindicated in pregnancy.

Summary

	Drugs	M.O.A	USES	Adverse effects
PPI	Omeprazole Lansoprazole Pantoprazole Raprazole	Acts by irreversible inhibition of proton pump (H+/ K+ ATPase) that is responsible for final step in gastric acid secretion from the parietal cell.	*Eradication of H. pylori + antimicrobial drugs *Resistant severe peptic ulcer (4-8 weeks). *Reflux esophagitis. *Hypersecretory conditions as Zollinger Ellison syndrome and gastrinoma (First choice).	*Headache, diarrhea & abdominal pain. *Achlorhydria *Hypergastrinaemia. *Gastric mucosal hyperplasia. *Vitamin B_{12} deficiency & increased risk of hip fractures (Long term use)
H2 Blockers	Cimetidine Ranitidine Famotidine Nizatidine	They competitively and reversibly block H_2 receptors on the parietal cells.	*GERD ((heartburn/ dyspepsia). *Acute ulcer healing in moderate cases *Pre-anesthetic (prevent aspiration pneumonitis). *Prevention of bleeding from stress-related gastritis. *Post–ulcer maintenance therapy.	*GIT disturbances & CNS effects *Bradycardia and hypotension *CYT-P450 inhibition + Endocrine effects (Only Cimetidine): Galactorrhea (Hyperprolactinemia) Antiandrogenic actions (gynecomasteia –impotence) *Precautions: Dose reduction of H_2 RAs in severe renal or hepatic failure and elderly.
Antacids	$NaHCO_3$ $Ca\ CO_3$ $Al\ (OH)_3$ $Mg\ (OH)_2$	acts by direct chemical neutralization of HCL and as a result may decrease pepsin activity	used to relief pain of peptic ulcer & for dyspepsia	*↓ absorption of some drugs *Systemic alkalosis (NaHCO3) *Diarrhea(Mg (OH)2) *milk alkali syndrome (hypercalcemia, renal failure) (Ca CO3) *constipation (Al (OH)3)
Prostaglandin analogues	Misoprostol	↓ HCL secretion. ↑ protective measures (↑ mucous/bicarbonate & gastric mucosal blood flow).	Used for NSAIDS-induced peptic ulcer.	*Abdominal cramps; diarrhea *Uterine contraction (dysmenorrhea or abortion);vaginal bleeding.

Quiz yourself

answers 1.B 2.C 3.A 4.B 5.A 6.B 7.C 8.B 9.A

1.Prostaglandin used in the treatment of peptic ulcer as:

A. Hyposecretory agent
B .Mucosal cytoprotective
C. antioxidant

2.A peptic ulcer patient was prescribed with a drug, after long time he developed VB12 dificiency , the drug is ?

A .Nizatidine
B. Cimetidine
C. Pantoprazole

3.The 1st drug of choice in the treatment of hepersecretory conditions as Zollinger Ellison syndrome is?

A. Pantoprazole
B. Ranitidine
C. NaHCO3

4.Which of the following drugs used to prevent aspiration pneumonitis ?

A. Pantoprazole
B. Ranitidine-
C. Misoprostol

5. A patient was using warfarin, and he developed peptic ulcer and started the treatment he suddenly develped warfarin toxicity, the drug is ?

A. Cimetidine
B. NSAIDs
C. prostaglandin

6. 83 years old man developed peptic ulcer, which one of the following drugs is used with Precautions in this case ?

A. NSAIDs
B. Nizatidine
C. Raprazole

7. M.O.A of Antacids :

A. inhibition of proton pump (H+/ K+ ATPase)
B. block H2receptor
C. Chemical neutralization of HCL and as a result decrease pepsin activity.

8.A pateint has an infection condition and was treated with NSAIDs, he suddenly developed peptic ulcer, the treatment is ?

A. Cimetidine
B. Misoprostol
C. Raprazole

9.The most potent inhibitor of acid secretion nowadays is ?

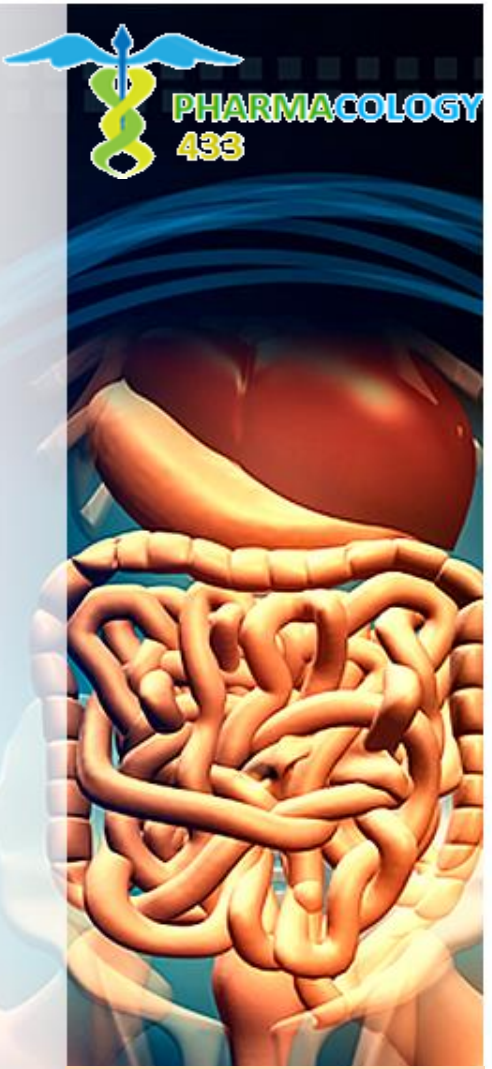
A. Omeprazole
B. Famotidine
C. Misoprostol

Done by

Raneem Alotaibi	Ahmed Aldakhil
Awatif alenazi	Omar Aldhas
Rawan Alotaibi	Faroq Abdulfattah
Noura Alrayes	

It always seems impossible until it is done

BEST OF LUCK



Contact us:-

Pharma_433@yahoo.com

@pharma_433