Peptic ulcer Disease

→ Gastritis → inflammation / irritation
Erosions.
Peptic ulcer.
} Upper G.I. tract.
Require gastric acid for their formation.

→ mucosa/membrane lining the stomach becomes inflamed.

→ Peptic ulcer differs from Gastritis & Erosions is ulcers typically extend deeper into muscularis mucosa.

→ PUD is a break in the lining of the stomach.
I part of small intestine.
occassionally the lowel palt of Esophagus.

Ulcer in the stomach. - Gastric ulcer.
First part of the intestine - Duodenal ulcer.

Three common forms of PUD

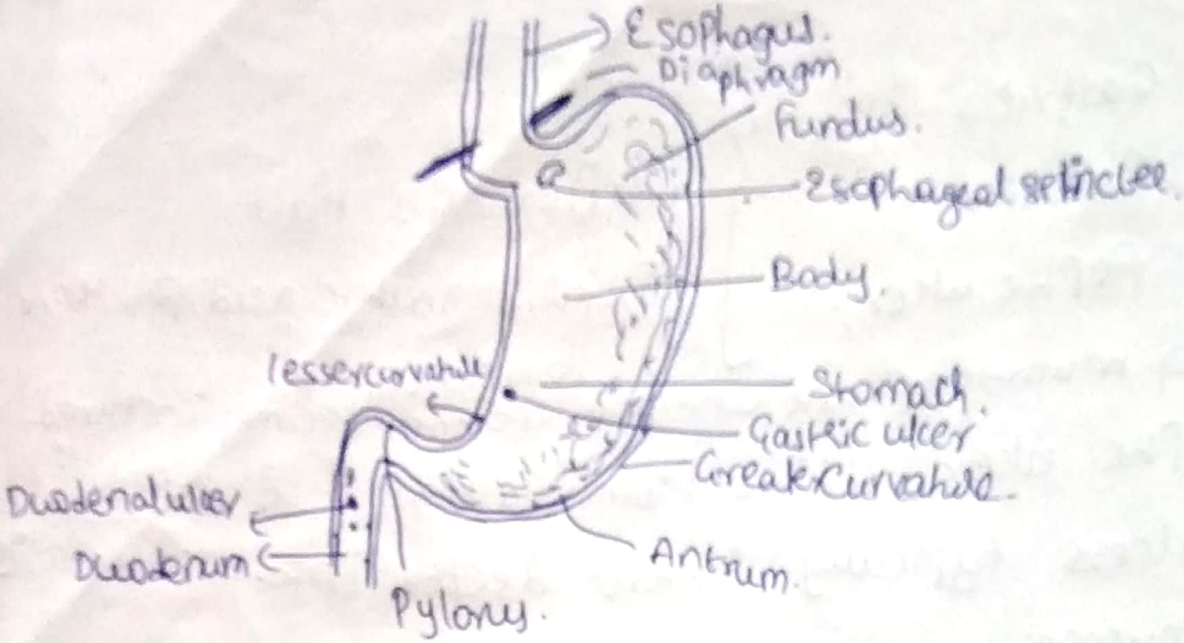
H. bacter pylori (+ve).
NSAIDs
} chronic ulcers.

Stress Related mucosal damage.
↳ Stress ulcers (or) Stress gastritis.

→ most commonly seen in ambulatory patients. in the stomach & Duodenum.

Etiology & Risk factors:

→ H. Pylori
→ NSAIDs.
→ Cigarette smoking.
→ Psychological Stress.
→ Dietary factors.



Anatomic Structure of the Stomach & Duodenum

Potential causes of peptic ulcer:

- → Idiopathic.
- → Hypersecretion of gastric acid. (Eg: zollinger Ellison Syndrome)
- → Viral infections.
- → Vascular Insufficiency.
- → Radiation therapy.
- → Chemotherapy.

Disease & mental conditions.

Cirrhosis.
Chronic Renal failure.
COPD.
Cardiovascular Disease.
Organ transplantation.

Heparin induced thrombocytopenia:-

-) It is an immune-mediated reaction to heparin and Platelet factor 4 (PF4) complexes resulting in a hypercoagulable state of Platelet activation & thrombin genelation.

Immune mediated.
↓
Heparin & PF_4.
↓
Result in Platelet activation
↓
Thrombin genelation.

Pathophysiology:-

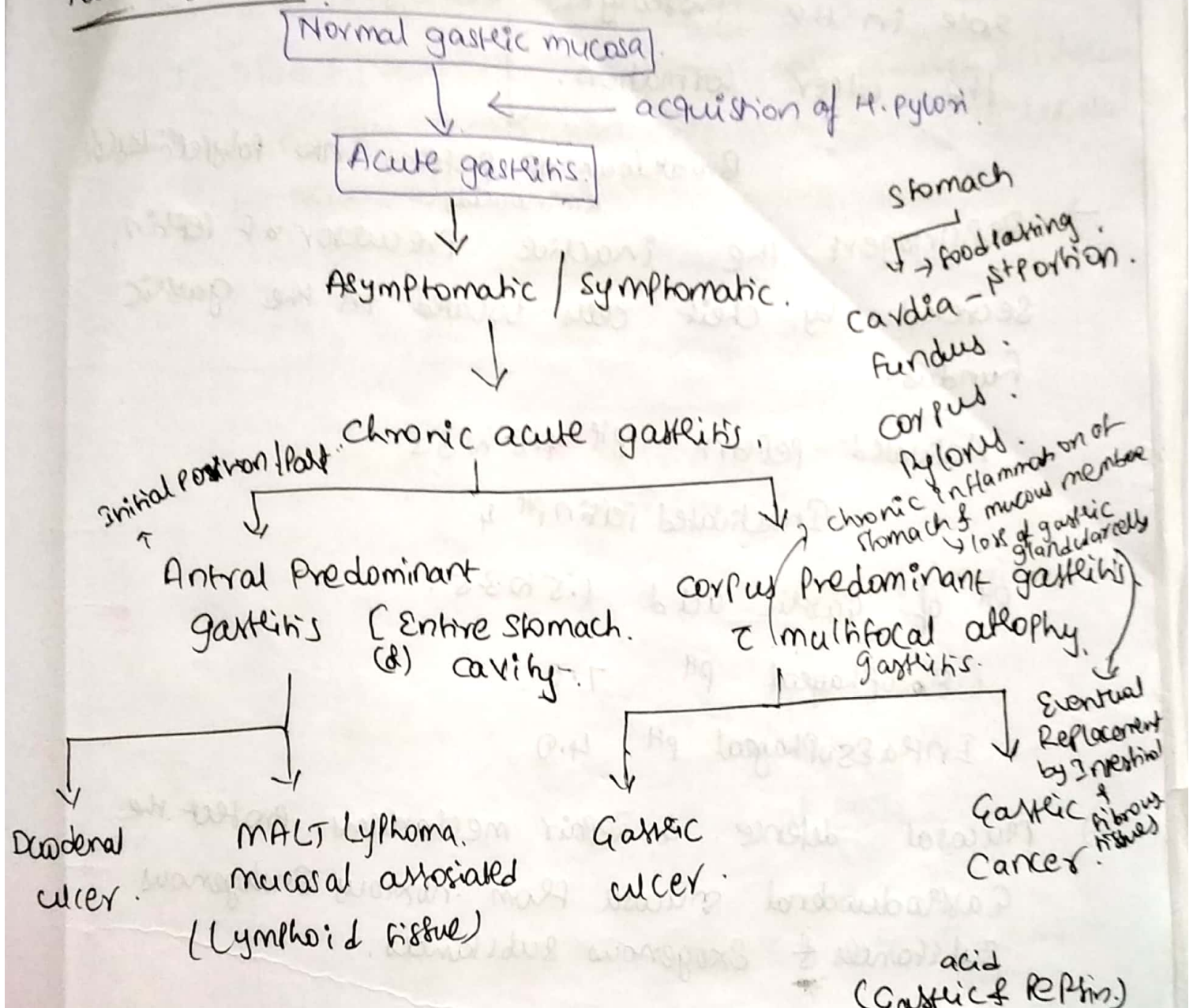
PF_4 + Heparin → PF_4-Heparin complex → IgG antibody.

IgG antibody → PF_4-Heparin-IgG. immune complex.

PF_4-Heparin-IgG. immune complex → Platelet → Platelet activation → PF_4 release → Endothelium injury.

Natural History of H.Pylori infection.

Pathophysiology:



→ Physiological imbalance b/w the aggressive & acid (Gastric & Peptic) Protective factors. (mucosal defense & Repair) remains an important issue in Pathophysiology.

→ Gastric acid is secreted by Parietal cells.

→ Acid secretion is Expressed as the amount. acid secreted under Basal or fasting conditions.

BAO (Basal acid output)

MAO (maximal acid output).

sucralfate

→ Pepsin is an important cofactor that plays a role in the proteolytic activity. Involved in the ulcer formation.

↓

Breakdown of proteins into polypeptides (or) aminoacids.

→ Pepsinogen the inactive precursor of pepsin. Secreted by chief cells located in the gastric fundus.

Activated pepsin pH 1.8 to 3.5

Inactivated pepsin pH 4.

pH of gastric acid 1.5 to 3.5.

Esophageal pH 7.0.

Intra Esophageal pH 4.0.

→ Mucosal defense & Repair mechanisms protect the gastroduodenal mucosa from noxious Endogenous substances & Exogenous substances.

→ H. Pylori is a gram-ve bacterium. That resides blw mucus layer & surface Epithelium of stomach. (or) any location where. Epithelium is found.

NSAIDs Induced PUD

-) Cause mucosal damage by two mechanisms.

1) Direct / topical irritation of gastric epithelium
2) Systemic inhibition of endogenous mucosal Prostaglandin synthesis.

Back diffusion of acids.

Acid, bilesalt, Aspirin, NSAIDS.
ischemia, H. Pylori.
↓
Breakdown of gastric mucosal Barrier.
↓
Acid back diffusion into mucosa.
↓
Destruction of mucosal cells.
↓
↑Acid & Pepsin Release. ← Histamine.
↓
→ Further mucosal Erosion.
→ Destruction of blood vessels.
→ Bleeding.
↓
ulceration.

Histamine.
↓
↑vasodilation.
↓
↑Capillary permeability
↓
loss of Plasma Proteins into gastric lumen
Mucosal Edema.

Clinical Presentation:

Signs & symptoms:

→ wt. loss ∵ nausea, vomiting & Anorexia (loss of appetite for food)
→ mild Epigastric Pain.
→ Abdominal Pain.
→ Heart burn
→ Belching (noisy sound from the stomach through mouth)
→ Bloating. (Become swollen with fluid & gas)
→ Anorexia.

Diagnostic tests:

1) Hematocrit & Hb are low ∵ bleeding & stool.
Hemoccult tests (presence of hidden blood in pt. stool) are positive.

2) Test for H. Pylori.

Endoscopy tests:

1) Histology - Microbiologic Examination using various stains
2) Culture - culture of biopsy.
(Removal of stomach tissue).
3) Biopsy urease - H. Pylori generates ammonia which causes color change.
4) Polymerase chain Reaction. → H. Pylori DNA detected in gastric tissue.

Non endoscopic tests:

1) Antibody Detection: Detects antibodies to H.Pylori in Serum using laboratory based enzyme-linked immunosorbent assay (ELISA) tests & latex agglutination techniques. - less sensitive.

2) Antibody detection: can be performed near Pt. Detects IgG antibodies to H.Pylori in whole blood or finger stick.

3) Urea Breathtest:
H.Pylori urease Breaks down ingested labeled C-urea, Patient Exhales labeled CO_2.

4) Fecal antigen:
Identifies H.Pylori antigen in stool by Enzyme immunoassay using Polyconal anti H.Pylori antibody.

→ Fiber-optic upper Endoscopy (esophagogastroduodenoscopy) detects more than 90% of peptic ulcers.

→ upper GI radiography with barium.

→ upper GI Endoscopy for suspected peptic ulcer.

Complications of Peptic ulcer Disease:

1) upper GI Bleeding. 4) Penetration
2) Perforation.
3) Gastric outlet obstruction.

→ occur with H.Pylori associated & NSAIDS. induced ulcers.

→ most serious, life threatening complication of Chronic PUD

→ G.I Bleeding is caused by the Erosion of an ulcer into an artery.

→ It may be occult (hidden) & insidious (or) may present as melena (black colowled stools).
Hematemesis (vomiting of blood).

→ use of NSAIDs is the major risk factor for GI Bleeding.

Perforation:

Ulcer related perforation into the peritoneal cavity generally considered as Sulgical Emelgency.

Pain of perforation is usually sharp, sudden & severe beginning first in the Epigastrium. but quickly spreading over the Entire abdomen

Penetration: (making a hole.)

→ Penetration occurs when an ulcer burrows into an adjacent structure (Pancreas, biliary tract, or liver) rather than opening freely into a cavity.

Gastric outlet obstruction:

→ Related to mechanical obstruction caused by scarring, muscular spasm. or Edema of the duodenal bulb resulting from Chronic ulceration.

Management of PUD:

Non Pharmacological:

→ Avoid smoking.

→ Reduce psychological stress.

→ avoid use of NSAIDS.

→ Avoid spicy foods & Beverages.

→ avoid alcohol.

→ vagatomy (truncal, selective or Paietal cell). inhibits Vagal stimulation of gastric acid.

Pharmacological therapy:

→ Drug Regimen used to Eradicate H. pylori 10-14 days is Recommended.

→ PHs ☐ NSAID induced ulcers should be tested for H.Pylori status

→ If H.pylori is +ve Heatment should be initiated with a PPI based three drug Regimen.

→ If H.Pylori is -ve Heatment should be. PPI or H_2RA or sucralfate. & avoid using of NSAIDS

→ If NSAID is continued Heatment should be initiated ☐ a PPI or PPI based threedrug Regimen.

→ Co therapy ☐ a PPI or misoprostol (200mcg) 4 times daily. or Switching to a selective Co x_2 inhibitor is Recommended for PHs at Risk of ulcer related complications.

Eradication of H.Pylori: 10-14 days Recommended

Drug #1	Drug #2	Drug #3	Drug #4
1) PPI Based Triple therapy			
PPI once or twice daily.	Clarithromycin 500mg twice daily	Amoxicilin 1g. twice daily (B) metronidazole 500mg twice daily	(1)
2) Bismuth Based Quadruple therapy:			
PPI (&) H_2RA once or twice Daily		Metronidazole 250-500mg 4 times daily	Tetracycline 500mg 4 times Daily.
		Bismuth Subsalicylate. 525mg 4 times daily.	
3) Sequential therapy			
PPI once (B) twice Daily	Amoxicilin 1g twice Daily on day 1-5.	metronidazole 250-500mg twice daily on days 6-10.	Clarithromycin 250-500mg 2 times Daily on days 6-10
i) 2nd line therapy for persistent infections:			
PPI (&) H_2RA once (B) twice daily.	Bismuth subsalicylate. 525mg 4 times daily.	metronidazole 250-500mg 4 times daily.	Tetracycline 500mg 4 times Daily.

→ maintenance therapy with a PPI or H_2RA should be limited to high risk PHs with ulcer complications

→ PHs who fail Eradication & those with H.pylori negative ulcers.

Misoprostol 100-200mcg 4 times Daily. 400-800mcg/day.

moderately inhibits acid secretion & Enhances mucosal defense.

Promote mucosal

AID

Oral Drug Regimen used to Heal Peptic ulcer & maintenance ulcer Healing.

Drug	Dose	Usual range mg/day Dose	MOA	Adverse Effects
PPIs				
omeprazole	40mg Daily	20-40mg/D	inhibits H^+K^+ ATPase enzyme ↓ H^+ & ions secretion ↓ acid secretion	Headache, Flatulence, Thrombocytopenia, neutropenia, Hypocalcemia, Liver function abnormalities, Renal impairement
Lansoprazole	30mg Daily	15-30mg/D		
Pantoprazole	40mg Daily	40-80mg/D		
Rabeprazole	20mg Daily	20-40mg/D		
Esomeprazole	40mg Daily	20-40mg/D		
Dexlansoprazole	30-60mg Daily	30-60mg/D		
H_2 Receptor Antagonist:				
Cimetidine	300mg-4times (8) 400mg-2times 800mg-once at Bedtime	800-1600mg/D	Supress the normal secretion of acid by Parietal cells & meal Stimulated secretion of acid.	Headache, Giddiness, Confusion, Constipation, Rash, Gynecomastia, loss of Libido, Impotence
Famotidine	20mg-2times. 40mg-at Bedtime.	20-40mg/D		
Nizatidine	150mg-2times. 300mg-once.	150-300mg/D		
Ranitidine	150mg twice. 300mg once	150-300mg/D	~~attaches to~~ Protein	
Promote mucosal Defense:			attaches to proteins on the surface of ulcers such as albumin & fibrinogen to form a cell stable insoluble complexes. ↓ Serves as protective barriers at the ulcer surface.	
Sucralfate	1g 4times daily 2g twice daily	1-2g/day	preventing further damage from acid, pepsin & bile	Insomnia, Backpain, mild itching skin rash
Prophylaxis for Stress related ulcer:				
Parenteral H_2RA's				
Cimetidine	300mg i.v loading dose. followed by 50mg/h as a continuous infusion or 300mg i.v every 6 to 8 hours			
Ranitidine	6.25mg/h as a continuous infusion (B) 20mg i.v every 12 hours			
Famotidine	1.7mg/h as a continuous infusion (B) 20mg i.v every 12hrs.			

Oral.

Omeprazole. 20-40mg daily.
Lansoprazole 30mg daily.
Pantoprazole 40mg daily.

Parenteral PPIs;
Pantoprazole. 40-80mg I.V every 12-24hrs.
Esomprazole 40mg I.V every 12-24 hours.

Probiotics; → live bacteria & yeasts.
→ a microorganism that when consumed maintains & restores beneficial bacteria to the GI tract.
→ (strains of Lactobacillus, & Bifidobacterium)

→ Probiotics & foodstuffs (Eg: cranberry & some milk proteins with bioactive components. have been used proactively to control H. Pylori. Colonization in at risk individuals.

→ alone probiotics does not Eradicate H. pylori. infection.

Strategies to Reduce the risk of NSAIDs ulcer & GI complications

Three therapeutic approaches to reducing the risk of NSAID ulcer.

① medical cotherapy : Either a PPI or misoprostol decrease ulcer risk & GI complications in high risk Pts

② use of selective cox-2 inhibitor instead of nonselective NSAID also use risk of ulcers & upper GI Event.

③ H_2 Receptor antagonist cotherapy.

Peptic ulcer Disease (1)

mucous membrane: → transportation absorption protection.

an epithelial tissue which secretes mucus.

→ covers the surface of internal organs.

Gastritis: It is an inflammation, irritation or erosion of the lining of the stomach.

→ It can occur suddenly (acute) or gradually chronic.

Erosion: Gradual destruction of tissue

muscularis mucosa: thin layer of muscle of the GI tract.

↳ present from the esophagus to the upper rectum composed of several thin layers of smooth muscle fibres.

Peptic ulcer:

It is a break in the lining of the stomach.

I part of small intestine

lower part of esophagus.

Ulcer in the stomach - Gastric ulcer

first part of the intestine - Duodenal ulcer.

Peptic ulcer differs from Gastritis. ulcers typically extend deeper into muscularis mucosa.

Three common forms of PUD

1) Helicobacter Pylori (Gram -ve bacteria)
   ↳ found in the mucus, on the inner surface of the epithelium.
2) NSAIDS
3) Stress Related mucosal damage

Etiology:

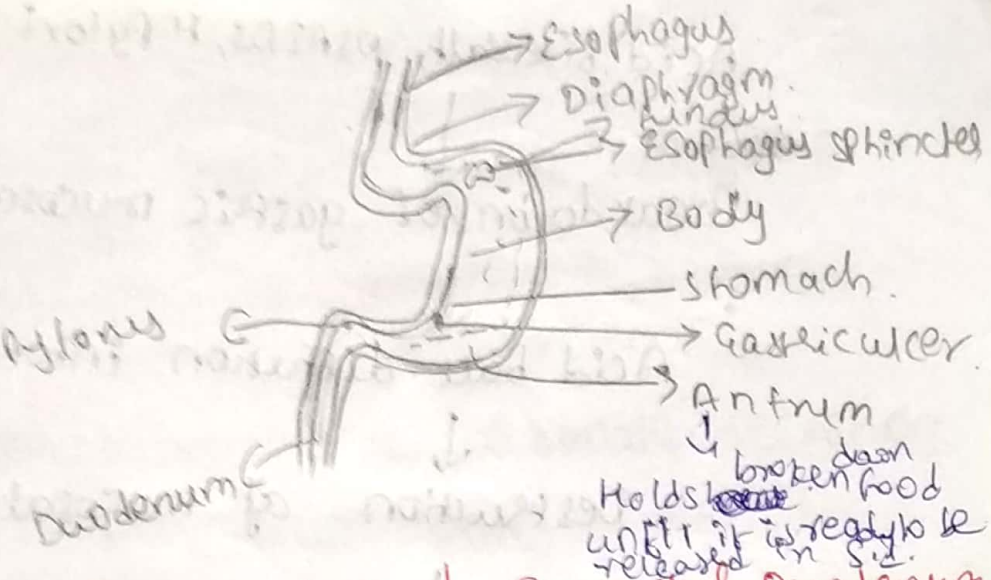
→ H. Pylori. → Gram -ve bacteria that resides the mucus layer & surface epithelium of Stomach
→ NSAIDS.
→ Cigarette smoking
→ Psychological Stress. (Reduction in mucosal blood flow → acid & pepsin imbalance) ↓ ulcer formation.
→ Dietary factors.

Pepsin: Endopephidase that breaks down proteins into smaller peptides.
→ Produced in the stomach.

Stomach acid does not digest protein so it activates an Enzyme called Pepsinogen → Pepsin. (pH 3.0 - 5.0) Requires acid to maintain that pH

→ Hypersecretion of gastrin.
→ Chronic Renal failure.
→ Organ Transplantation.
→ COPD.

(3)



Anatomic structure of Stomach & Duodenum

Pathophysiology:

→ Gastric acid secreted by Parietal cells.
↳ Epithelial cells that secrete HCl

→ Physiological imbalance blw the aggressive & Protective factors.
(Gastric acid & Pepsin) (mucosal defense & Repair)

→ mucosal defense & Repair mechanism Protect the Gastroduodenal mucosa from noxious Endogenous substances & Exogenous substances.

NSAIDS Induced:

→ mucosal damage by two mechanisms.

1) Direct / topical irritation of gastric Epithelium
2) systemic inhibition of Endogenous mucosal Prostaglandin Synthesis.

Acid, bile salt, NSAIDS, H. Pylori

↓

Breakdown of gastric mucosal Barrier

↓

Acid back diffusion into mucosa

↓

Destruction of mucosal cells.

↓

↑acid & Pepsin Release ← Histamine

↓

mucosal Erosion

↓

Destruction of blood vessels

↓

Bleeding

↓

ulceration.

Histamine ↓ ↑vasodilation ↓ ↑capillary Permeability ↓ Loss of plasma proteins into gastric lumen → mucosal Edema

↑ directly stimulate parietal cells

Histamine: Plays a role in gastric secretion by helping to induce the production of acid in the stomach.

Signs & symptoms:

- wt. loss.
- nausea & vomiting.
- Abdominal Pain.
- Heart burn.
- Belching
- Bloating.
- Anorexia.