PEPTIC ULCER DISEASE

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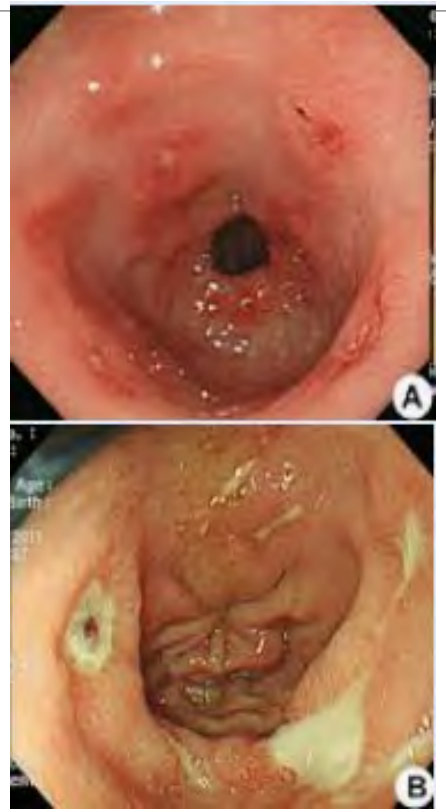
Introduction

An ulcer in the GI tract is a 5mm or larger break in the lining of the mucosa with appreciable depth on endoscopy and sub mucosal extension on histology.

Erosion <5mm

PUD includes ulcers and erosions in the stomach and duodenum.

Why ‘peptic’? Role of pepsinogen proteolytic activity in the pathogenesis regardless of inciting agent.



Epidemiology

Prevalence of PUD mimics Helicobacter pylori(Hp) infection which has been falling world wide.

Incidence of PUD in US 0.1-2.6% in hospital based case series in 2009.

Bleeding and mortality from PUD fell from 48 to 32 per 100,000 with a corresponding fall in case mortality.[1]

A recent systemic review published in 2024 showed a pooled prevalence of 15.2% inAfrica with DU(10%),GU(5.8%) and both in 0.6%.[2]

Southern Africa had the least prevalence 8%.

Incidence increases with age.

Male > Female with shifting dynamics

1 Laine et al.American Journal Of Gastroenterology.2012

2 Abdu et al.BMC Gastroenterology.2025

Etiology and pathogenesis

PU develop as a result of disruption of gastric mucosal protective factors by mostly Hp infection or NSAIDS.

Include:

Pre-epithelial Barrier (Mucus-Bicarbonate Layer)

Epithelial Barrier: Tight junctions between epithelial cells and rapid regeneration

Mucosal Blood Flow: Sustained sub mucosal blood flow acts as a buffer, removing H+ that have penetrated the epithelial barrier.

Prostaglandins and NO: stimulate mucus, bicarbonate, and phospholipid production, while promoting blood flow.

Growth Factors: These promote the repair and regeneration of the mucosa (re-epithelialization)

Etiology

Helicobacter pylori(HP) infection

NSAID use

Idiopathic (HP-negative, NSAID-negative ulcers)

Gastrinoma (ZES)

Viral infections (HSV,CMV)

Risk factors

Smoking-poor healing and high recurrence rate

Alcohol-damage to gastric mucosal barrier

Genetic factors- effect on cytokine production,CYP 450 polymorphism and metabolism of NSAIDS

Diet-protective effect of fruits and vegetables vs toxins in food

Stress- effect of stress on acid production and blood flow to the gut (fight or flight response).

Drugs (Corticosteroids, Bisphosphonates, Immune check point inhibitors)

Helicobacter Pylori infection(Hp)

Gram negative helical flagellated bacterium.

Strict tropism for gastric-type mucosa.

Typically causes diffuse antral gastritis with chronic active gastritis.

Infection occurs early in childhood with 50% prevalence in the world and up to 70% in developing countries.

In SA (Eastern Cape) serological prevalence ranges from 76-100% in healthy subjects and 66% in dyspeptic patients.[1,2]

Low Socio-economic status-higher prevalence and increases with age.

Gastro-oral and fecal-oral transmission dominant routes of transmission.

Iatrogenic transmission through inadequately disinfected endoscopes and endoscopic accessories reports.

1 Dube et al. Rev Environ Health. 2009

2 Tanih et al. SAMJ.2011

Pathogenesis

Hp leads to a persistent active inflammation with chronic inflammatory infiltrate despite robust host immune response and gastric low pH.

The virulence is related to both bacterial properties and pathophysiologic alterations in the host.

Bacterial factors

<u>Adherence</u>

Flagella- 6-8 Allow rapid migration to more favorable location below the gastric mucus layer

Outer inflammatory Protein A (OiPA)- facilitates adhesion and triggers inflammation by up regulating IL-8 expression

Blood group Antigen binding Adhesin(BAbA)-facilitates binding of fucosylated Lewis b blood group antigens on host cells.

May play a role in molecular mimicry and pathogenesis of Hp associated autoimmune gastritis.

Sialic acid binding adhesins (SabA)-binds glycoconjugates containing sialic acid in inflamed mucosa.Facilitates chronicity

Enzyme release: facilitate cellular damage and protect the bacteria

Urease: splits urea into CO2 and NH3 , NH3 reacts with H^+ to produce $NH4^+$ which provides favorable pH to Hp.

Phospholipase: alters phospholipid content of the gastric mucosal barrier leading to cell injury.

Catalase: protects bacterium from the toxic 0_2metabolites in the inflammatory gastric mucosa.

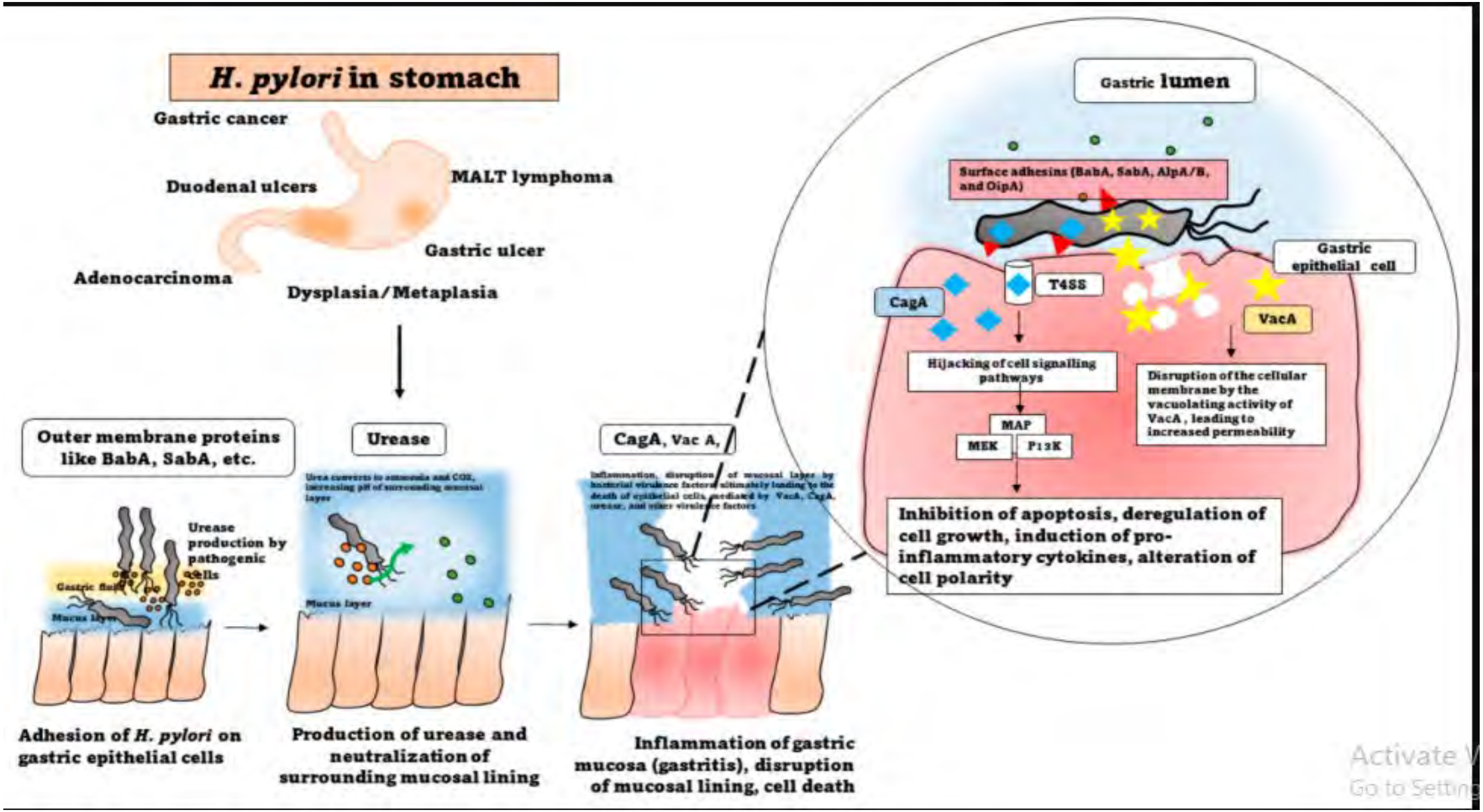
Virulence factors:

Vacuolating cytotoxin A(VacA)- All Hp express the gene, 50% produce the toxin. Increases gastric epithelium permeability by vacuolating activity

Cytotoxin-associated gene (CagA)- 50% of Hp

Tyrosine phosphorylation of the protein associated with increased IL-8 expression, mucosal inflammation, peptic ulceration and aptosis.

Increased pre-cancerous lesions and gastric adenocarcinoma.


H. pylori in stomach
Gastric cancer
Duodenal ulcers
MALT lymphoma
Gastric ulcer
Adenocarcinoma
Dysplasia/Metaplasia
Outer membrane proteins like BabA, SabA, etc.
Urease
CagA, Vac A,
Urease production by pathogenic cells
Gastric fluid
Mucus layer
Adhesion of H. pylori on gastric epithelial cells
Production of urease and neutralization of surrounding mucosal lining
Inflammation of gastric mucosa (gastritis), disruption of mucosal lining, cell death
Gastric lumen
Surface adhesins (BabA, SabA, AlpA/B, and OipA)
Gastric epithelial cell
T4SS
CagA
VacA
Hijacking of cell signalling pathways
Disruption of the cellular membrane by the vacuolating activity of VacA, leading to increased permeability
MAP
MEK
P13K
Inhibition of apoptosis, deregulation of cell growth, induction of pro-inflammatory cytokines, alteration of cell polarity

Host factors: Hp is non-invasive but stimulates robust inflammation in the acute phase

T cell response: Skewed towards Th1 and TH17. Promotes pro inflammatory cytokines(IL-8,TNF alpha, IFN Y) with resultant epithelial cell death, chronic infection and host immune escape.

IL-8- a potent chemotactic factor that activates neutrophils and recruits inflammatory cells. CagA/VacA-positive strains are potent IL-8 inducers.

Polymorphisms in the IL-8 gene associated with increased IL-8 expression are associated with increased inflammation and pre-malignant changes.

Antibody response: B cell response consists of the production of IgG and IgA antibodies.

Role in producing tissue injury or modulating inflammation controversial.

Prolonged stimulation of gastric B cells by activated T cells leads to **MALT lymphoma.**

Hp effect on gastric acid production

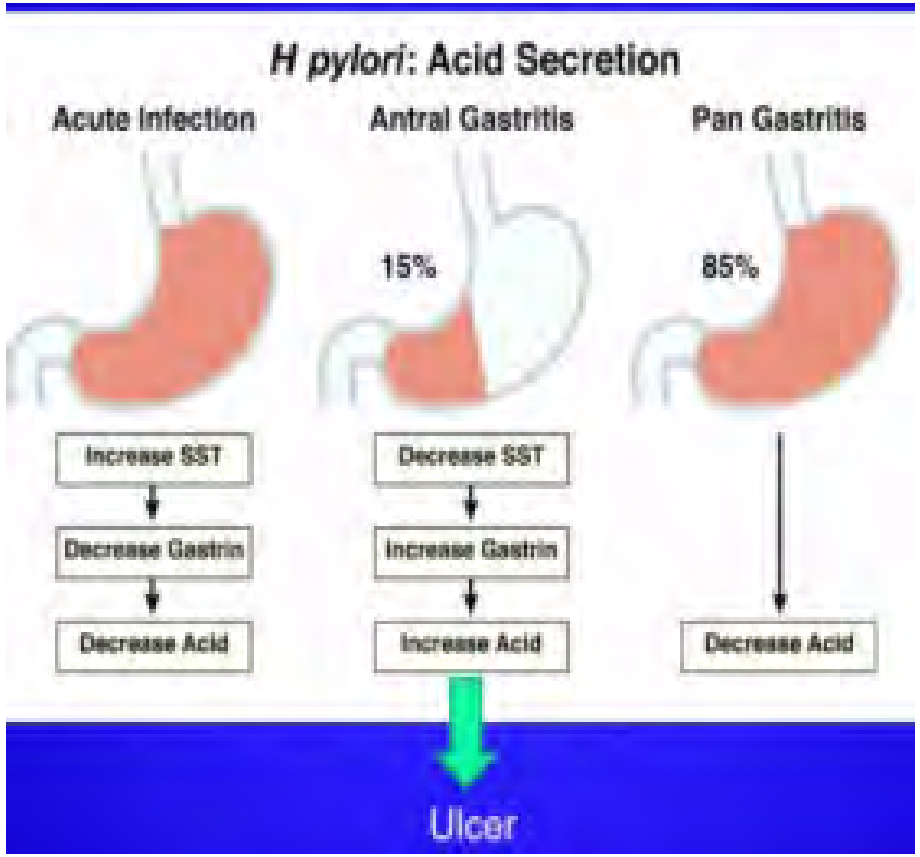
Acute infection: Transient hypochlorhydria to enable colonization.

Chronic infection: Varied patterns

Antrum-predominant gastritis - increased acidity and approximately 2x higher gastrin levels. Hp interrupts the physiologic feedback inhibition by luminal acid on gastrin release through effects on somatostatin-secreting D cells in the antrum.

Corpus-predominant and pan-gastritis-reduced acid secretion.

Results in hypochlorhydria and gastric atrophy from chronic gastric inflammation and increased levels of cytokines, such as TNF-alpha and IL-1



Disease spectrum

Asymptomatic- up to 80%

Gastritis- Acute gastritis which persists as chronic gastritis.

Can lead to gastric atrophy, gastric intestinal metaplasia (GIM), dysplasia and less commonly, gastric adenorcarcinoma.

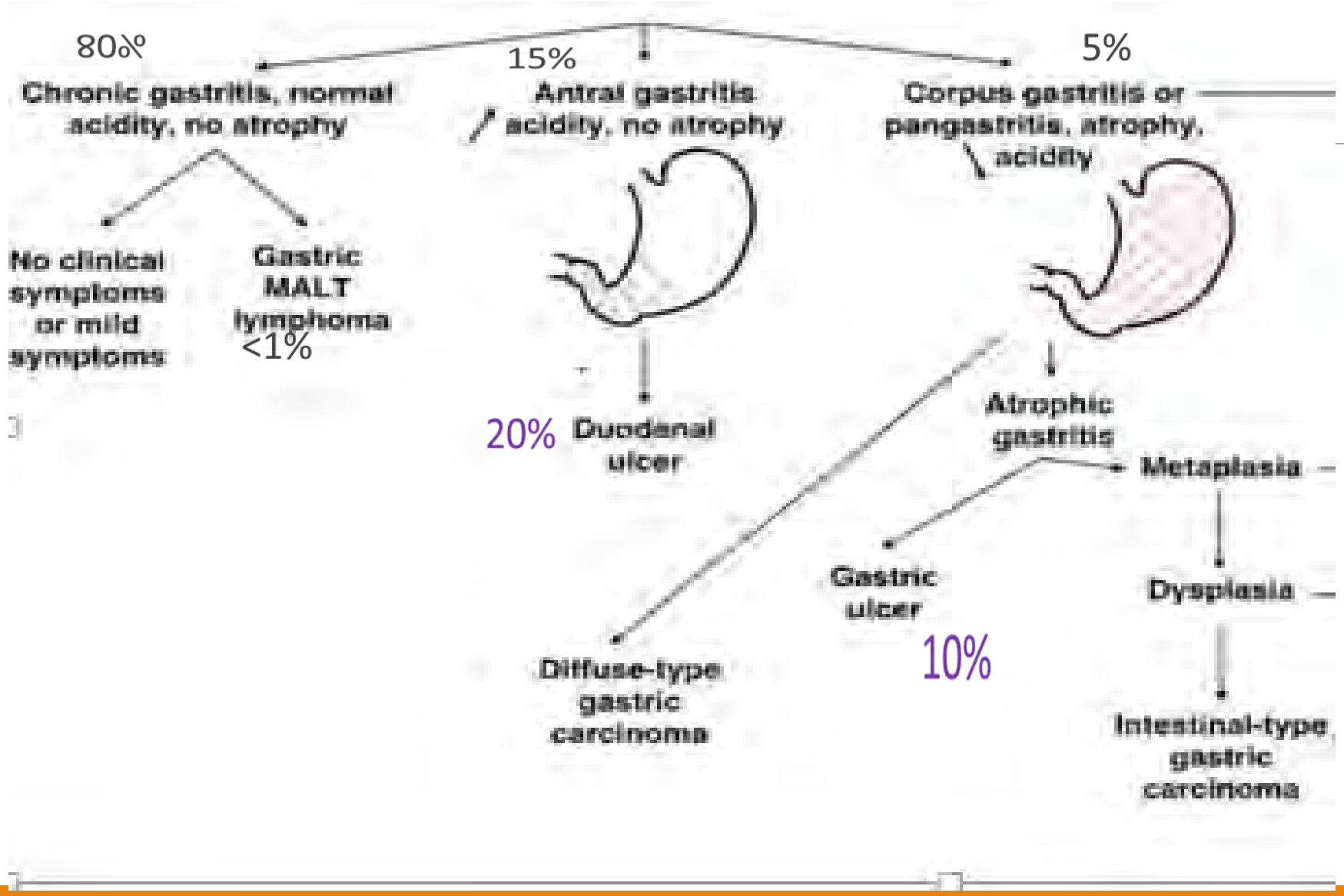
Dyspepsia.

Peptic ulcer disease

Iron deficiency anaemia

Immune thrombocytopenic purpura

HP Disease spectrum



Peptic Ulcer disease

Hp infection increases the likelihood of PUD, but only 10 -15% develop PUD.

Implicated in 90% of DU and 80% of GU

Environmental, microbial, and host genetic factors influence development of PUD.

Smoking, alcohol, NSAID and high-dose steroids have been implicated.

Hp increases risk of Peptic ulcer bleeding (PUB) by 1.79 fold, and by 6 fold with concomitant NSAID use.

Hp infection found in 72% of bleeding peptic ulcers with delayed testing,[1] Kgomo et al found Hp in 17% in bleeding GU and 24% in non-bleeding GU.[2]

Antral predorminant Hp results in high gastric acid with resultant gastric metaplasia in duodenum and subsequent duodenal ulceration.

Hp pangastritis, weakened mucosal defense mechanism rather than high acid, predisposes to GU.

- [1] Sanchez et al.American Journal of Gastroenterology.2011• [2] Kgomo et al.Journal of Bioanalysis & Biomedicine.2016

NSAID and Aspirin use related ulcers

There is increased use of aspirin for CVD prevention alone or in combination with a platelet adenosine diphosphate inhibitor.(DAPT)

11% of US population take NSAIDS on regular basis.

Local data not available but a large population on over the counter NSAIDS.

PUD in 10-30% of long term NSAID users.

NSAID use increases PUB by 5-6 fold.

Serious ulcer complications occur in 1-4% of NSAID users.

Hp infection increases the risk of PUD in patients taking NSAIDs.

Pathophysiology

NSAIDs cause PUD by suppression of prostaglandin (PG) synthesis.

COX-1 and COX-2 responsible for synthesis of PG.

COX-1-expressed in healthy stomach.

COX-2 expressed in response to cytokines in the inflammatory process.

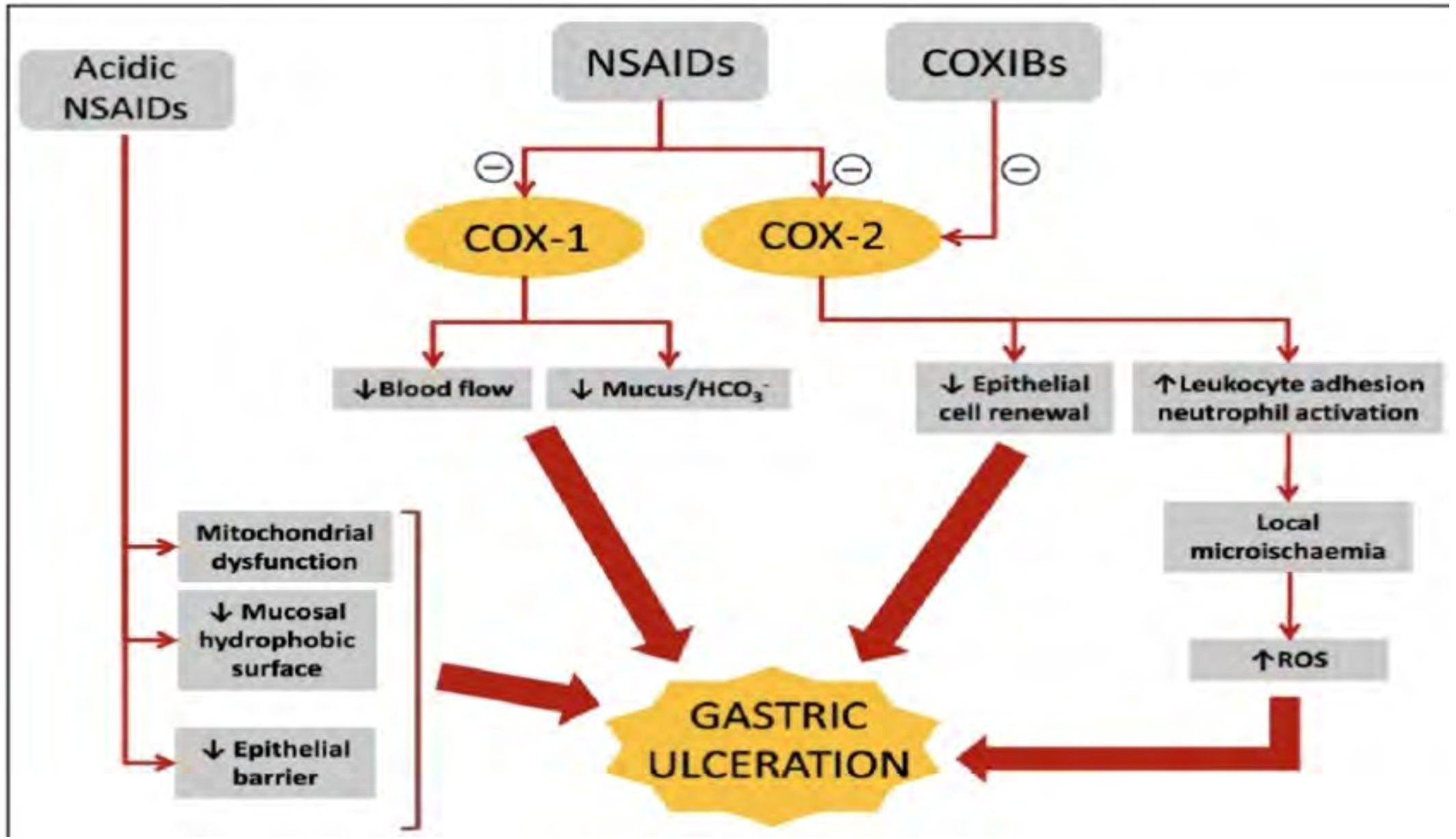
Non selective NSAIDS (brufen, diclofenac, naproxen), inhibit COX-1 and 2 almost equally.

Reduced COX-1 leads to impaired PG synthesis and disruption of gastric mucosal defense and integrity.

COX-2 inhibition leads to decreased epithelial renewal with increased neutrophil adherence.

Direct mucosal irritation with epithelial damage.

Gastric acid turns superficial mucosal lesions into deeper injury by interfering with platelet aggregation and impairing ulcer injury.


Acidic NSAIDs
NSAIDs
COXIBs
COX-1
COX-2
↓Blood flow
↓ Mucus/HCO_3^-
↓ Epithelial cell renewal
↑Leukocyte adhesion neutrophil activation
Mitochondrial dysfunction
↓ Mucosal hydrophobic surface
↓ Epithelial barrier
Local microischaemia
↑ROS
GASTRIC ULCERATION

Clinical features and diagnosis

Epigastric pain- associated with hunger, mostly at night, relieved by food and antacids.

Dyspeptic symptoms: bloating, abdominal fullness.

Heartburn

Upper GIT bleeding

Perforation – epigastric pain, tachycardia and rigidity

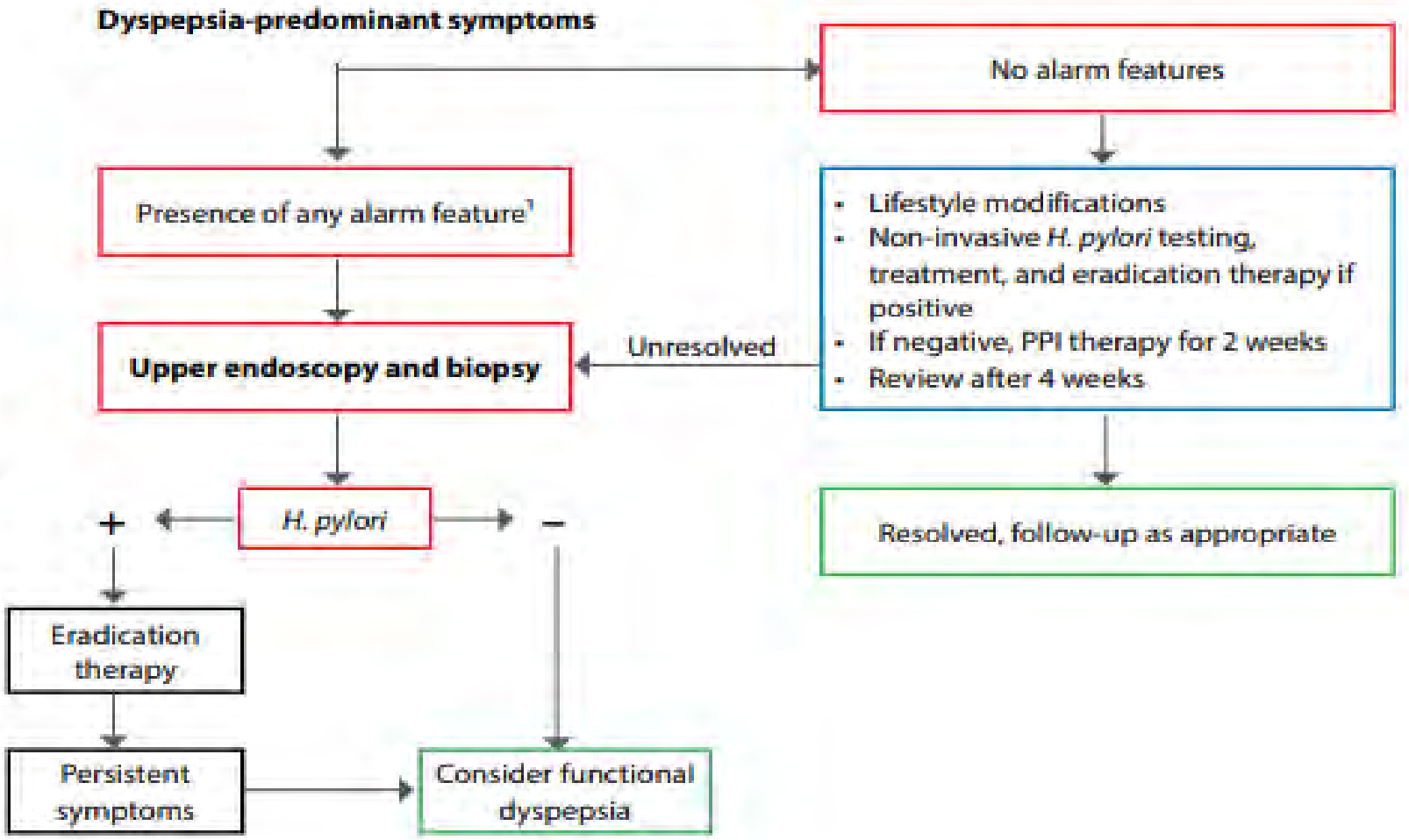
Esophagogastroduodenoscopy(EGD) is procedure of choice but is expensive and not without complications.

Decision to perform EGD as an initial test depends on presence of alarm features.

Biopsies taken from edges of GUs to rule out malignancy and from antrum and body for HP diagnosis(Sydney Protocol)

SAGES 2025 diagnostic algorithm for dyspepsia

1. Alarm features:
   - Age ≥ 50 years
   - Dysphagia/odynophagia
   - Family history of upper GI or relevant genetic syndromes
   - GI bleeding
   - Iron deficiency, with or without anaemia
   - Palpable abdominal mass
   - Severe or persistent abdominal pain
   - Pathological weight loss
   - Ulcerogenic medication (e.g. NSAIDs)



Diagnosis

Endoscopic tests

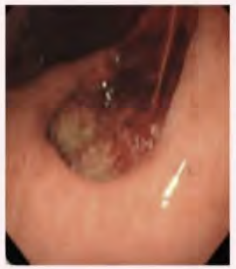
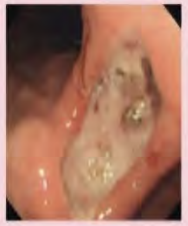
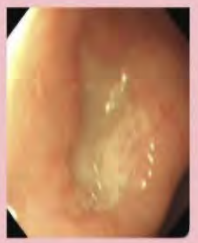
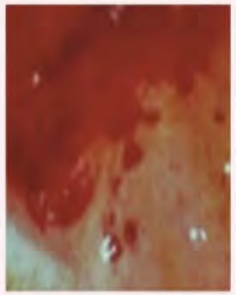
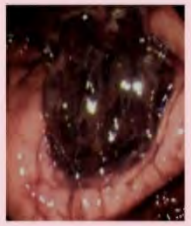
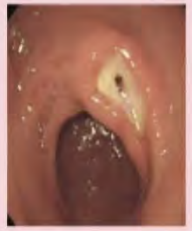
1. Biopsy urease test-negatively affected by blood, antibiotics, antisecretory drugs esp PPIs, bismuth(sens-95%, spe-100%)
2. Gastric mucosal histology- staining for HP and assessment of atrophic gastritis, and precancerous lesions.
3. Culture-Not routine-special media or in few drops of saline

Non endoscopic tests

1. Urea Breath Test (UBT) (sens-upto 95%,spec-95%) affected by PPIs, Bismuth cpds and antibiotics. Not accurate after gastric resection.
2. Stool antigen test-(sens 94%,Spe 97%) similar precautions as UBT
3. Serological tests-Detect IgG. Useful inlow prevalence as a negative predictive test.

PCR testing in biopsies, stool and water sources- not done routinely

Forrest Classification

Acute Hemorrhage	Signs of Recent Hemorrhage	Lesions without Active Bleeding
 **1a** **Active Spurting** *Rebleeding Risk:* 60 to 100%	 **IIa** **Non-Bleeding Visible Vessel** *Rebleeding Risk:* 40 to 50%	 **III** **Clean-Based Ulcer** *Rebleeding Risk:* 3 to 5%
 **1b** **Active Oozing** *Rebleeding Risk:* 50%	 **IIb** **Adherent Clot** Rebleeding Risk: 20 to 30%	
	 **IIc** **Flat Spot in Ulcer Base** Rebleeding Risk: 7 to 10%	

@enrrikke

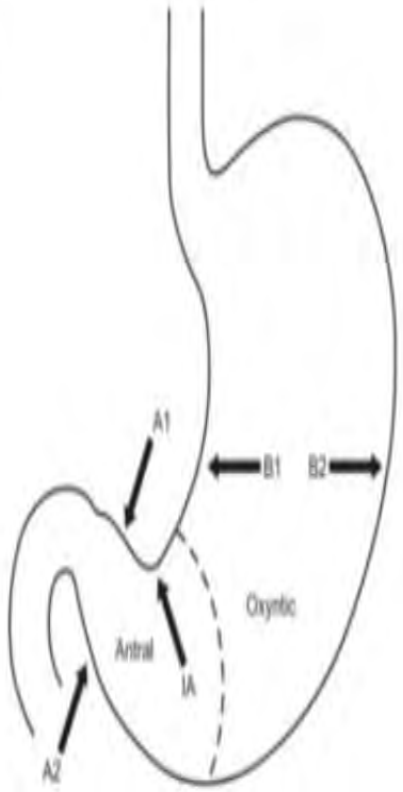
Images from Alzoubaidi, et al, 2018

- First described in 1974 by J.A. Forrest et al. in The Lancet
- Standardized classification system for endoscopists to describe peptic ulcers
- Helps prognosticate and risk stratify patients based on stigmata of recent hemorrhage and decide on discharge versus close inpatient monitoring

Sydney Protocol

- A1 – 3 cm from pylorus, greater curve
- A2 – 3 cm from pylorus, lesser curve
- IA – Incisura angularis
- B1 – Body, lesser curve
- B2 – Body, greater curve

- Place in separate bottles:
  - Antrum (A1, A2, IA)
  - Body (B1, B2)



Stanford MEDICINE

Medical therapy of active peptic ulcer

Pharmaceutical agents

Antacids- neutralize gastric acid, poor ulcer healing ability. Used to relieve dyspeptic symptoms.

Antisecretory agents:

Histamine 2 Receptor Antagonists (H2RAs)-suppress basal and meal stimulated acid secretion.

Effective in suppressing nocturnal acid secretion and healing of NSAID induced DU but not in those who continue to be on NSAIDs

Include: cimetidine, famotidine, nitazidine, ~~ranitidine~~

Absorption not affected by meals. Undergo first pass metabolism (bioavailability-35-60%) except nitazidine. Peak levels in 1-3 hrs.

Dose adjustment required in CKD

Tolerance develops.

A/Es: gynecomastia, impotence, inhibition of CYP 450

Proton pump inhibitors(PPIs) – decrease gastric acid secretion by inhibition of H+,K+ ATPase proton pump on parietal cells.

Include: esomeprazole, omeprazole, lansoprazole, dexlansoprazole, pantoprazole, rabeprazole

Pro drugs that need acid for activation.

Bind actively secreting pumps hence the requirement to be taken just before meals

Peak levels in 2-5hrs

Short half life of approx. 2 hrs but long duration of action due to covalent binding of proton pump.

Metabolised by liver; CYP 2C19 polymorphisms influences plasma levels except for rabeprazole.

Dexlansoprazole is a R-enantiomer of lansoprazole with dual delayed release with 2 peaks and not affected by meals. (pH 5.5-1-2 hrs P.roximal Duodenum, pH 6.8-4-5 hrs Distal ileum)

Superior healing in GERD and comparable to PPIs in HP eradication regimens

Potassium-competitive Acid Blockers (P-CABs)

Competes with K+ to bind H+,K+ ATPase.

Include: vonoprazan FDA approved

Acid stable, not a pro-drug, administration doesn't need to be meal timed.

Exerts near maximal acid suppression with 24 hr effect.

Mucosal protective agents

Sucralfate: complex aluminum salt of sulfated sucrose. Forms a protective paste that adheres to damaged mucosa creating a physical barrier.

1g QID of sucralfate comparable to H2RAs in healing DUs.

<5% systemic absorption.

Avoid in CKD

Colloidal Bismuth preparations- Modest effect in healing gastric ulcers.

Bismuth salts form complexes with mucus that appear to coat ulcer craters and have antimicrobial effect against Hp.

Used in Hp eradication regimens.

Misoprostol- PG E1 analog, enhances mucosal defense mechanisms and reduces acid secretion thro' inhibition of histamine mediated acid production.

Less effective than PPIs in healing GU and DU in patients on NSAIDs.

FDA approved for prevention of NSAID induced PUD.

Peak blood levels in 1.5 hrs. Metabolised in liver and excreted in kidneys. Dose adjustments not required in CKD.

A/Es: diarrhea ,Uterine contractions(avoid in pregnancy)

Non Pharmacological

Smoking cessation

Limit alcohol use (1 drink per day)

Discontinue NSAIDs unless when compelling indications exist

Evaluate for other causes

Hp associated ulcers

Account for 80-90% of DU

Testing of Hp mandatory by means of gastric biopsies.

Hp eradication sufficient to heal ulcers with a 14 day course.

Endoscopy to confirm healing not mandatory.

Non invasive methods can be used to confirm eradication.

GU 14 day course of eradication sufficient.

Whether prolonged anti-secretory therapy is required is controversial.

Patients with large or complicated GU, additional anti-secretory therapy can facilitate healing.

Follow up EGD to document healing, exclude malignancy and confirm eradication is recommended in GU.

Hp eradication therapy

First line treatment (SAGES 2025)

1.Low clathromycin resistance <15-20%

PPI+ clarithromycin+ amoxicillin triple therapy

PPI+ clarithromycin+ metronidazole therapy for patients with penicillin allergy

2. High clarithromycin resistance (> 20%) or unknown resistance:

- Bismuth-containing quadruple therapy (PPI, bismuth, metronidazole, and tetracycline).
- Non-bismuth concomitant quadruple therapy (PPI, amoxicillin,

clarithromycin, and metronidazole) if bismuth-containing quadruple therapy is unavailable.

Second line treatment

1. Bismuth containing quadruple therapy after failing clarithromycin based regimen.
2. Levofloxacin containing triple therapy (low quinolone resistance)
3. Levofloxacin plus bismuth-containing quadruple therapy(amoxillin, PPI)

Third line treatment

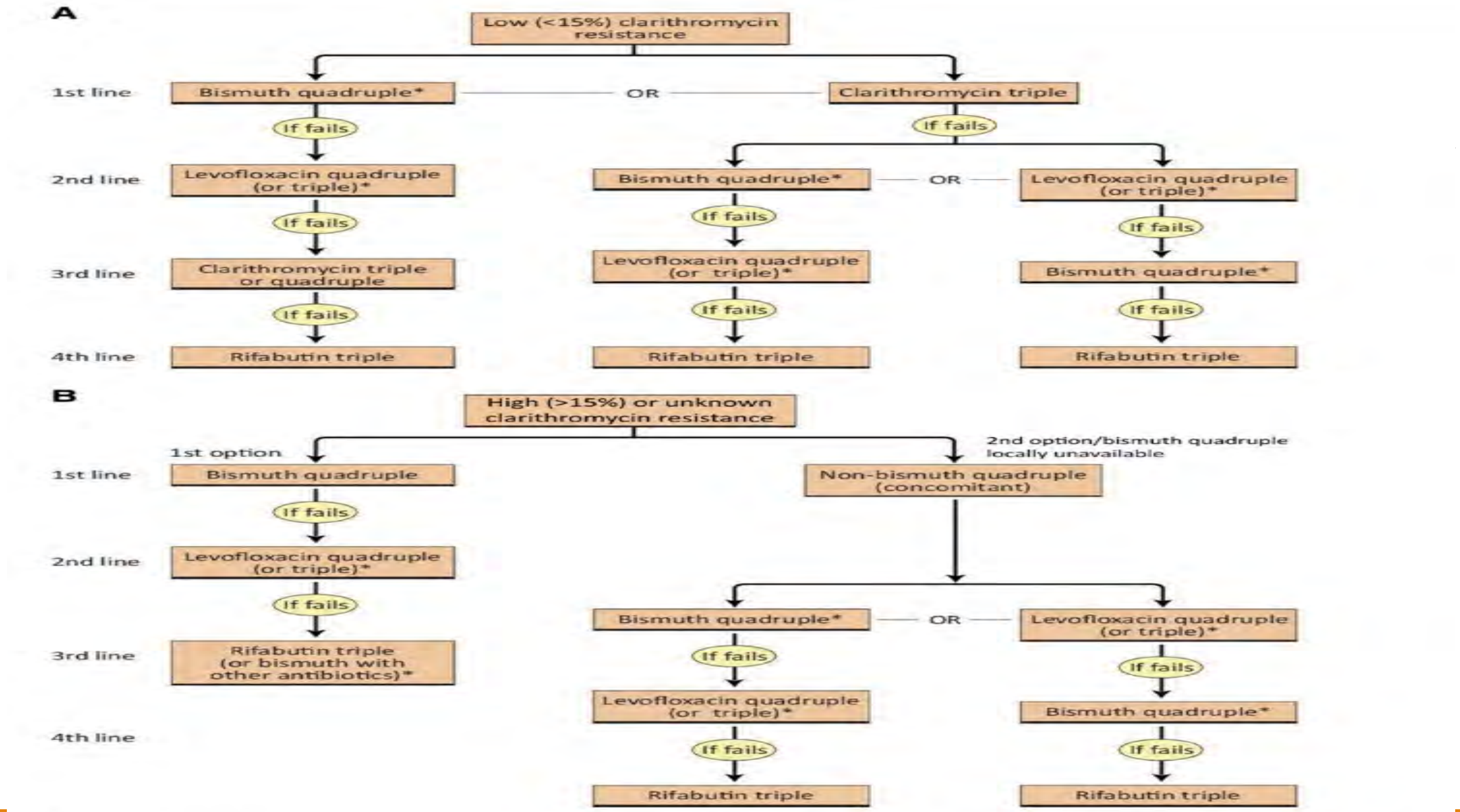
PPI+ Amoxicillin high dose dual therapy with >80% eradication rate (QID/TID)

Rifabutin- based therapy-(Amoxicillin, Rifabutin, PPI all TID)

ACG Clinical Guideline on the treatment of *Helicobacter pylori 2024*

Regimen	Drugs (doses)	Dosing frequency	FDA Approval	Recommendation
Optimized bismuth quadruple	PPI (standard dose)	b.i.d.	No	Strong (moderate quality of evidence)
	Bismuth subcitrate (120 - 300 mg) or subsalicylate (300 mg)	q.i.d.		
	Tetracycline (500 mg)	q.i.d.		
	Metronidazole (500 mg)	t.i.d. or q.i.d.		
Rifabutin triple (Talicia)	Omeprazole (10 mg)	4 capsules t.i.d.	Yes	Conditional (low quality of evidence)
	Amoxicillin (250 mg)			
	Rifabutin (12.5 mg)			
PCAB dual (Voquezna DualPak)	Vonoprazan (20 mg)	b.i.d	Yes	Conditional (moderate quality of evidence)
	Amoxicillin (1,000 mg)	t.i.d		
PCAB triple (Voquezna TriplePak)	Vonoprazan (20 mg)	b.i.d	Yes	Conditional (moderate quality of evidence)
	Clarithromycin (500 mg)			
	Amoxicillin (1,000 mg)			

Maastricht VI(2022)



Alternative regimens

Therapy	Description
Standard triple therapy	PPI*, 500 mg clarithromycin, and 1,000 mg amoxicillin (twice daily for 7–14 days)
Bismuth quadruple therapy**	PPI* (twice daily), 120–600 mg bismuth salt, 250–500 mg metronidazole, and 250–500 mg tetracycline (up to four times daily for 7–14 days)
Sequential therapy	PPI* and 1,000 mg amoxicillin (twice daily for 5–7 days) followed by PPI*, 500 mg clarithromycin, and 500 mg metronidazole (twice daily for 5–7 days)
Concomitant therapy	PPI*, 1,000 mg amoxicillin, 500 mg clarithromycin, and 500 mg metronidazole/tinidazole (twice daily for 7–14 days)
Hybrid therapy	PPI*, 1,000 mg amoxicillin (twice daily for 14 days) with 500 mg clarithromycin and 500 mg tinidazole (twice daily for the final 7 days)
Levofloxacin-based triple therapy	PPI*, 250 mg levofloxacin, and 1,000 mg amoxicillin (twice daily for 7–14 days)
Levofloxacin-based sequential therapy	PPI* and 1,000 mg amoxicillin (twice daily for 5 days) followed by PPI*, 250 mg levofloxacin, and 500 mg metronidazole (twice daily for 5 days)
Rifabutin-based triple therapy	PPI*, 1,000 mg amoxicillin, and 150 mg rifabutin (twice daily for 7–14 days)

Hp eradication in special groups

Penicillin allergy

Bismuth quadruple therapy recommended by most international societies.

Locally, Clarithromycin, metronidazole and PPIs.

Fluoroquinolone containing regimen is a viable option.

Failure of 1st line, penicillin allergy test <1% of population have true type 1 hypersensitivity.

Pregnancy

Hp infection associated with hyperemesis gravidarum, iron deficiency anaemia, fetal growth restriction, pre-eclampsia and ITP.

Asymptomatic patients don't need to be treated during the pregnancy.

Symptomatic patients: PPI, amoxicillin and metronidazole are safe.

Clarithromycin can be considered after 1st trimester.

Prescription guide

Good knowledge on local antibiotic resistance patterns and availability in local market.

BD dosing for all agents unless otherwise stated

14 days course unless 10 day course has been shown to be efficacious in local setting.

Confirmation using a non invasive method 4 weeks after completion of treatment.

Molecular resistance testing to guide further treatment after 2 treatment failures (can be considered if previous regimens unclear, prior antibiotic exposure and penicillin allergy)

No evidence to recommend use of probiotics to increase efficacy and tolerability of the various regimes.

NSAID related ulcers

Treatment with antisecretory medication.

PPIs mainstay of treatment.

Omeprazole 20-40mg OD 4-8 weeks depending on ulcer size(approx. 3mm per week)

PCABs (vonoprazan 20mg OD) was non inferior to lansoprazole 30mg OD in healing GU and DU and can be used when available.[1]

H2RAs more effective in treating DU than GU ulcers.

Not preferred in patients who need to be on NSAIDS

Misoprostol is less effective compared to PPIs and PCABs and hence it's hardly used for this indication.

- [1] Miwa et al.Alimentary Pharmacol therapeutics.2017

Non-HP, non NSAID ulcer

Account for approximately 20% of PUD in the USA

GU- omeprazole 20-40mg OD 8 weeks

DU – Omeprazole 20-40mg 4 weeks

Repeat endoscopy before discontinuing PPI.

Higher recurrence rate, 26% in Korean study[1] May need life long anti-secretory therapy.

Complicated Ulcers

Perforation, GOO, penetration(Bleeding discussed separately)

High dose PPI -omeprazole 40mg BD decreased to OD after 4 weeks

Duration: DU 4-8 weeks, GU 8-12 weeks

[1] Yoon et al.Gut liver.2013

Indications for repeat endoscopy

DU- routine endoscopy not recommended unless signs of ongoing bleeding

GU- Surveillance endoscopy after 8-12 with biopsies (if ulcer present) in patients with any 1 of the following

1. Persistent symptoms despite medical therapy including features of ongoing bleeding
2. Unclear etiology
3. Giant ulcer >2cm
4. Inadequate sampling during the index endoscopy(4 quadrant Biopsies)
5. Malignant appearing ulcers on index endoscopy(mass lesion, elevated irregular ulcer edges, abnormal mucosal folds) up to 5% of initially benign ulcers are malignant on repeat endoscopy
6. High risk of gastric cancer- >50 yrs, family Hx, East Asia origin, gastric atrophy, adenoma, dysplasia, intestinal metaplasia.

Refractory ulcers

Ulcer >5mm in diameter at 8-12 week endoscopy after anti-secretory (PPI) therapy.

May be symptomatic or asymptomatic

Up to 10% of PU

Etiology:

Giant ulcers >2 cm

Persistent Hp

Continued use of NSAIDs, glucocorticoids, bisphosphonates, cocaine, methamphetamine

Impaired ulcer healing-large fibrotic ulcers, smoking, CKD (uremia), cirrhosis, organ transplant

Poor adherence to anti-secretory therapy, rapid metabolism

Acid hypersecretory states: ZES, mastocytosis, hyperparathyroidism

Other underlying conditions: Crohns, sarcoidosis, lymphoma, EGID, syphilis, CMV, mesenteric ischaemia, TB, IgG4 sclerosing disease

Onging smoking

Evaluation and Management

Endoscopy, biopsies from ulcer and Sydney protocol forHp

Address etiology : Hp, drugs, gastrin levels, calcium levels

Antisecretory therapy: BD therapy if initially on OD

Consider changing PPI

PPI if on H2RAs

Vonoprazan has >80% healing rate of idiopathic ulcers and should be used when available.

Repeat endoscopy after 12 weeks with scar biopsies.

Indications for Surgery:

Failed BD therapy for 24 weeks and all etiology factors corrected (risk of malignancy)

Bleeding ulcer with failed endoscopic management

Perforation, obstruction

Prevention of ulcer disease

Mostly in patients on NSAIDs at moderate to high ulcer risk.

Indications

1. Relapsing idiopathic ulcers.
2. MDR Hp after multiple failed courses
3. > 2 recurrent PUD per year
4. Continued NSAID use

PPIs at standard daily doses significantly reduce risk of Pus to approx. 5%

Misoprostol at 800 mcg/day effective but usage limited by GI upset.

H2RAs at standard dose ineffective

Choice of NSAID: no significant difference in cardiothrombotic risk btwn COX-2 inhitors and non selective NSAIDs with exception of naproxen 500mg BD

Celecoxib 200mg/day non inferior to ibuprofen and naproxen in CV safety with lower GI events than both, and fewer renal events when compared with ibuprofen

TABLE 53.2 Recommendations for Reducing the Risk of NSAID Ulcers as a Function of GI and Cardiovascular Risk

	GI Risk*		
	Low	**Moderate**	**High**
Low CV risk	NSAID at the lowest effective dose	NSAID plus a PPI, or celecoxib alone	Celecoxib plus a PPI
High CV risk†	Naproxen or celecoxib, plus a PPI	Naproxen or celecoxib, plus a PPI	Celecoxib plus a PPI if simple analgesics failed

**Low GI risk* denotes no risk factors (see Table 53.1); *moderate GI risk* denotes 1 or 2 risk factors; *high GI risk* denotes ≥3 risk factors, prior complicated ulcer, or concomitant use of low-dose aspirin or anticoagulants. All patients with a history of ulcer who require NSAIDs should be tested for Hp, and if infection is present, eradication therapy should be given (see Chapter 52).

†*High CV risk* denotes the requirement for prophylactic low-dose aspirin for primary or secondary prevention of serious CV events.

CV, cardiovascular.

TABLE 53.1 Risk Factors for NSAID Ulcers*

Risk factor	Risk ratio
History of complicated ulcer	13.5
Use of multiple NSAIDs (including aspirin, COX-2 inhibitors)	9
Use of high doses of NSAIDs	7
Use of an anticoagulant	6.4
History of an uncomplicated ulcer	6.1
Age >70 years	5.6
Hp infection	3.5
Use of a glucocorticoid	2.2

*Not all NSAIDs pose the same risk.

PUD complications

Bleeding

Perforation

Penetration

Gastric outlet obstruction

Thank you