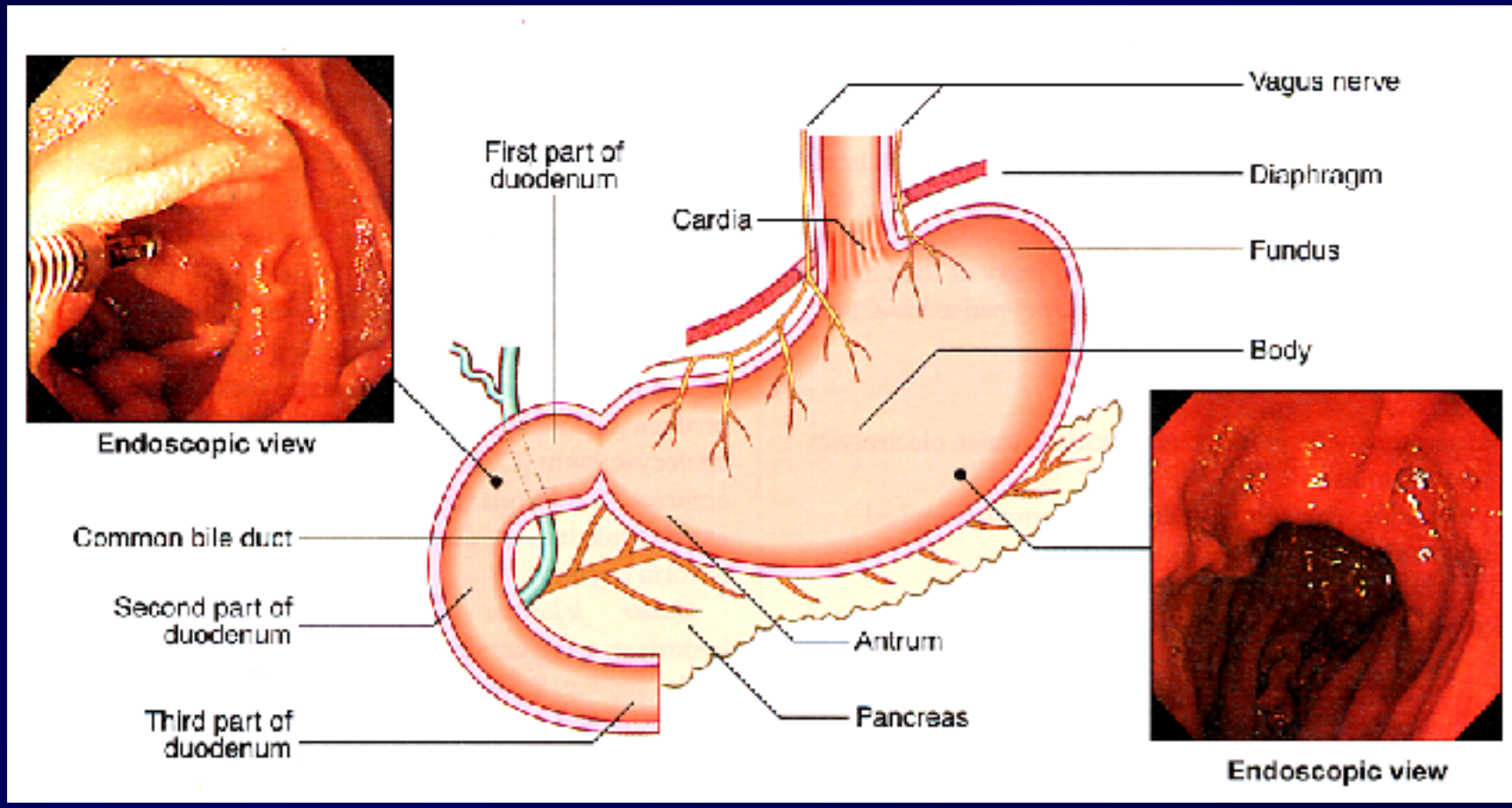
Diseases of the Stomach and Duodenum

Eman A. Sabet

Professor of Internal Medicine

2021

Structure of the stomach and doudenum



Structure of the stomach and doudenum

The stomach:

- Cardia, fundus, body, antrum and pylorus.
- The smooth muscle of the wall of the stomach has three layers: outer longitudinal, inner circular and innermost oblique layers.
- There are two sphincters, the gastro-oesophageal sphincter and the pyloric sphincter.

The doudenum:

- C-shaped and the pancreas sits in the concavity. It terminates at the duodenojejunal flexure.

Histological background

- ***Mucosal lining***
- ***Mucus-secreting cells*** :Are present throughout the stomach and secrete mucus (mucins) and bicarbonate. Secretion is stimulated by Prostaglandins.
- ***Mucosal barrier*** made up of the plasma membranes of mucosal cells and the mucus layer, protects the gastric epithelium from damage by acid and, for example, alcohol, aspirin, NSAIDs and bile salts.

Histological background

Upper 2l3 of the stomach:

- *Parietal cells* that secrete HCl & intrinsic factor.
- *Chief cells* that secrete pepsinogen

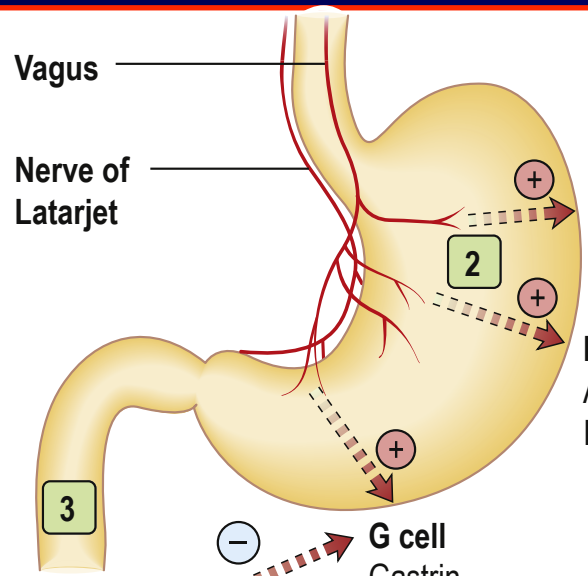
Antral mucosa

- *G cells*, secrete gastrin, stimulating acid production.
- *D cells secretes* Somatostatin, a suppressant of acid secretion

Duodenal mucosa

- Brunner's glands; secrete alkaline mucus. This, along with the pancreatic and biliary secretions, helps to neutralize the acid secretion

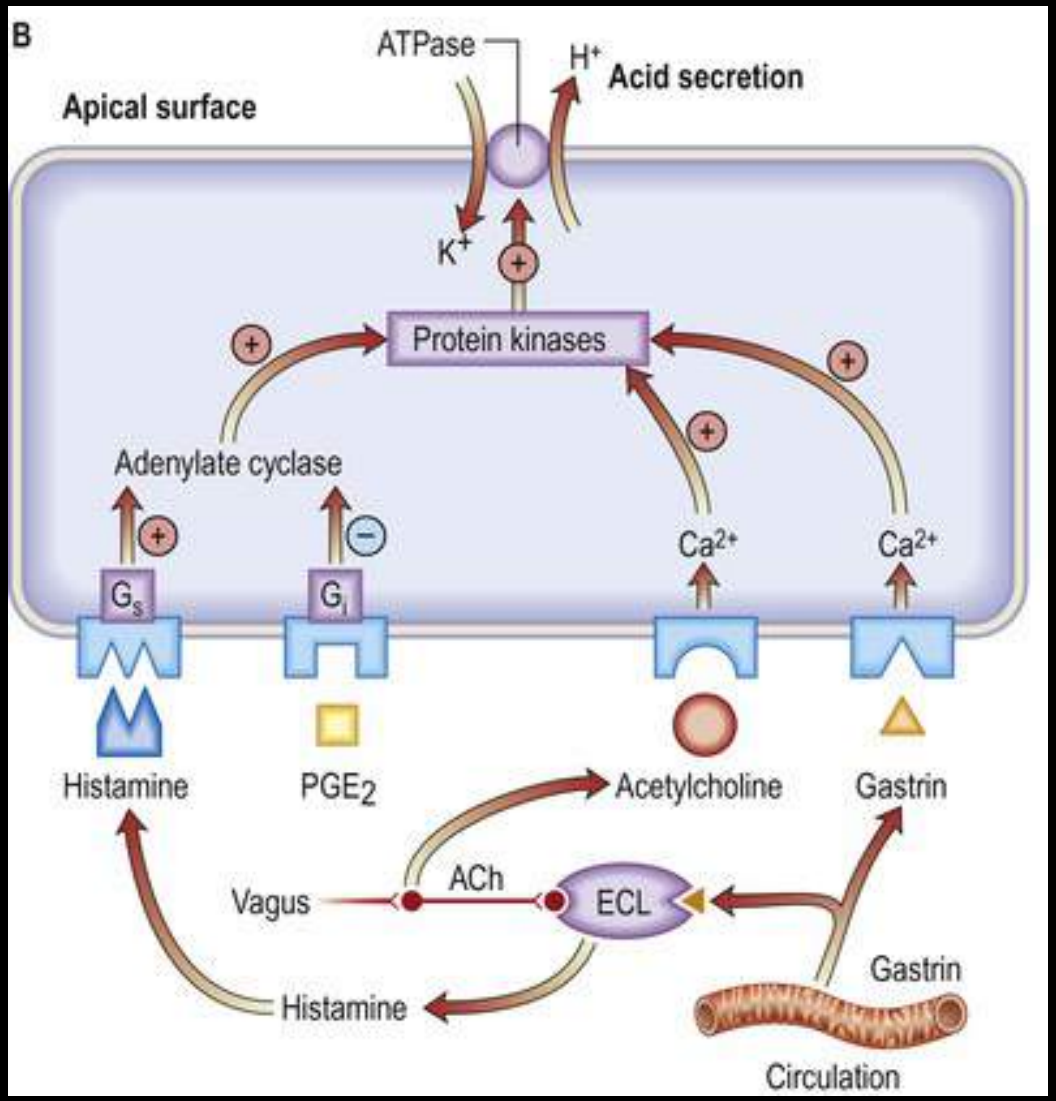
Physiology of Gastric Secretion



Phases of acid secretion

1. **Cephalic**
   Thought, sight and smell of food stimulate the vagus, producing acetylcholine
2. **Gastric**
   Distension by food directly stimulates secretory cells and gastrin release
3. **Intestinal**
   Passage of food into duodenum stimulates GI hormone release

Pathophysiology of gastric secretion



- Gastric Functions

1. Acid prevent some food- borne infections.
2. Reservoir for food
3. Emulsification of fat and mixing of gastric contents
4. Secretion of intrinsic factor
5. Absorption (of only minimal importance).

Symptoms of Gastroduodenal diseases

- Dyspepsia:

  A collective term of upper abdominal symptoms; Anorexia & nausea, heartburn or regurgitation, upper abdominal or lower chest pain, bloating or flatulence. Sometimes described as indigestion.

  Alarm features: Dysphagia, Weight loss, Anemia, heamatemesis or melena.
- Abdominal pain.
- Nausea & vomitting.
- Weight loss.
- Heamatemesis or melena.

Investigations of Gastroduodenal diseases

- Barium swallow, barium meal and double contrast study
- Abdominal Ultrasonography
- Upper Endoscopy
- Endoscopic Ultrasound
- CT
- MRI
- Positron emission tomography (PET).

Gastritis and gastropathy

'Gastritis' indicates inflammation associated with mucosal injury

'Gastropathy' indicates epithelial cell damage and regeneration, but there is no accompanying inflammation.

•Classifications of gastritis are controversial due to lack of correlation between endoscopic and histological findings.

Gastritis and gastropathy

Causes of gastritis:

1. H. pylori infection is the commonest cause of gastritis (80%).

2. Autoimmune gastritis is seen in 5%.

3. Other causes:

-Viruses (e.g. cytomegalovirus and herpes simplex).

-Specific causes, e.g. Crohn's, more common in children than adults.

Gastropathy

Etiology:

1. Irritants (drugs, NSAIDs and alcohol).

2. Portal hypertension (called portal gastropathy), chronic congestion

3. Hypovolaemia, shock.

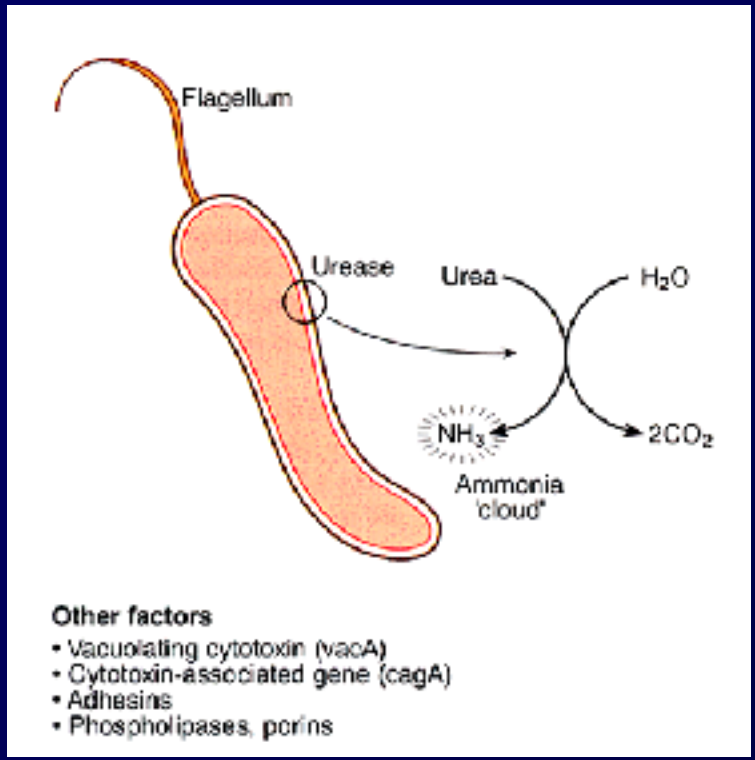
4. Severe stress (stress ulcers), secondary to burns (Curling ulcers) or trauma.

5. Renal failure

•The underlying mechanism for these ulcers is unknown but may be related to an alteration in mucosal blood flow.

Helicobacter Pylori infection

- Spiral-shaped, gram-negative urease producing bacterium.
- The prevalence of *H. pylori* is high in developing countries (80-90% of the population), and much lower (20-50%) in developed countries.
- Infection is usually acquired in childhood, The vast majority remain asymptomatic.



Pathogenesis of Hp infection

- The organism exclusively colonizes gastric-type epithelium and inhabiting the mucous layer.
- It adheres on the surface of gastric mucosal cells and causes gastritis in all infected subjects.
- Damage to the gastric epithelial cell is caused by the release of enzymes (urease) that enables the conversion of urea to ammonium and chloride, which are directly cytotoxic, and enhance the induction of apoptosis.
- Pathological effects depends not only on the virulence of the organism, but also, host genetic factors.

Possible results of Hp infection

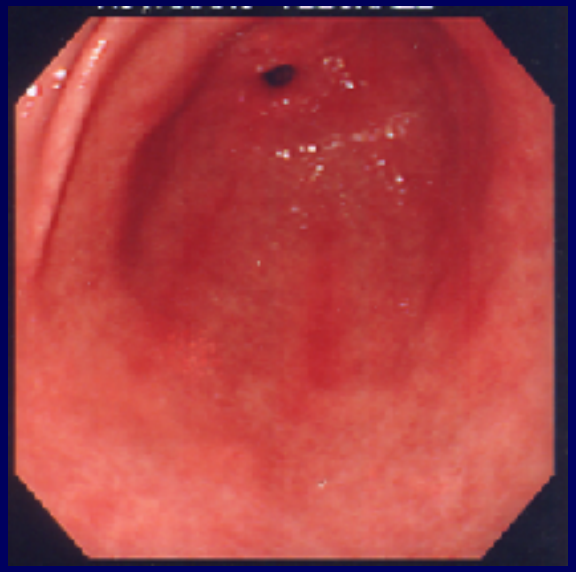
- ***Antral gastritis*** …..may progress to:

  Pan gastritis, Atrophic gastritis or Intestinal metaplasia
- ***Peptic ulcers*** (duodenal and gastric)
- ***Gastric adenocarcinoma***; H-pylori is recognized by WHO as a class I gastric carcinogen
- ***MALT lymphoma*** (mucosa-associated lymphatic tissue lymphoma; Over 70% of patients with gastric B cell lymphomas are infected with H-pylori, low grade lymphomas regress with H-pylori eradication.

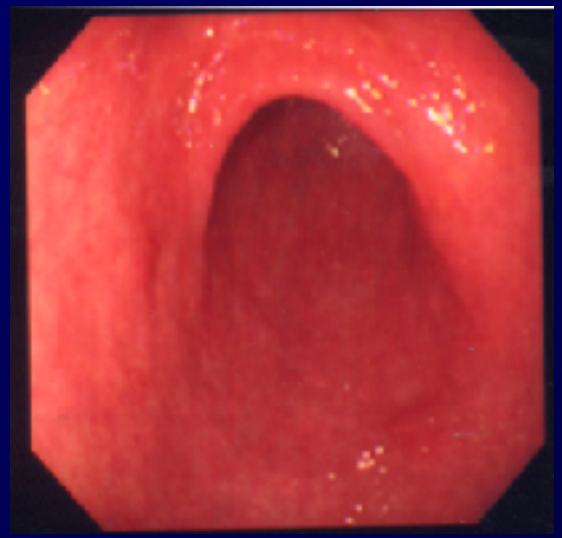
Antral Gastritis

- **It** is the usual effect of *H. pylori* infection. There is epithelial damage from local release of cytokines.
- It is usually asymptomatic.
- Sometimes dyspeptic symptoms that relieves after *Helicobacter* eradication.
- Chronic antral gastritis causes hypergastrinaemia due to gastrin release from antral G cells. The subsequent increase in acid output is usually asymptomatic, but can lead to duodenal ulceration.

- **Antral gastritis**
- Can gradually extend to involve the body of the stomach
- It may progress to chronic atrophic gastritis or intestinal metaplasia.



Antral gastritis; Endoscopically; reddened mucosa.



Chronic antral gastritis

Peptic Ulcer disease

1. ***A peptic ulcer*** consists of a break in the superficial epithelial cells penetrating down to the muscularis mucosa of either the stomach or the duodenum; there is a fibrous base and an increase in inflammatory cells.
2. ***Erosions***, by contrast, are superficial breaks in the mucosa alone.

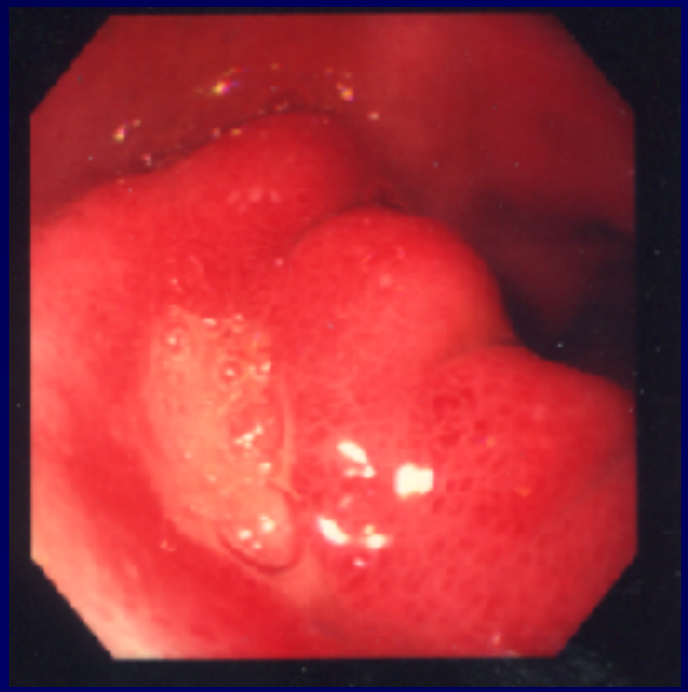
Epidemiology of peptic Ulcer disease

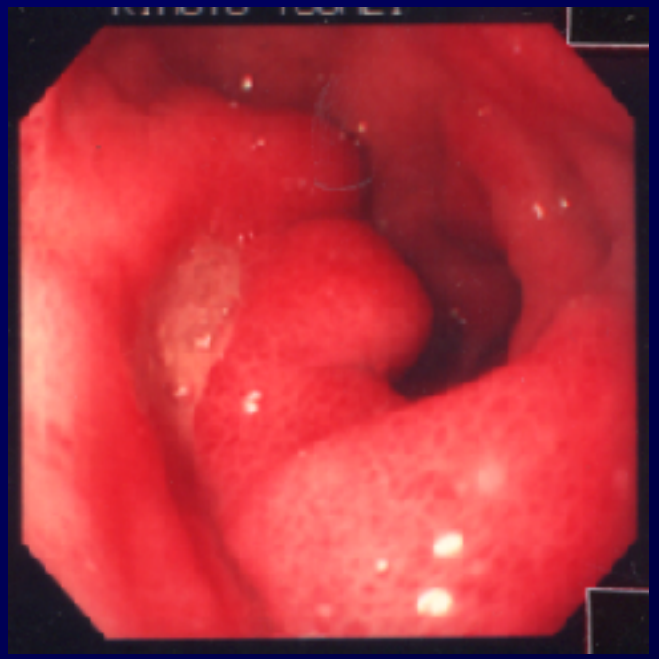
1. Duodenal ulcers:
   - Affect approximately 10% of H pylori- infected adults.
   - 2-3 times more common than gastric ulcers.
2. There is considerable geographical variation:
   - Prevalence in developing countries related to the high H. pylori infection.
   - In the developed world the percentage of NSAID-induced peptic ulcers is increasing.

Duodenal Ulcer

- Hp causally associated with DU disease because:

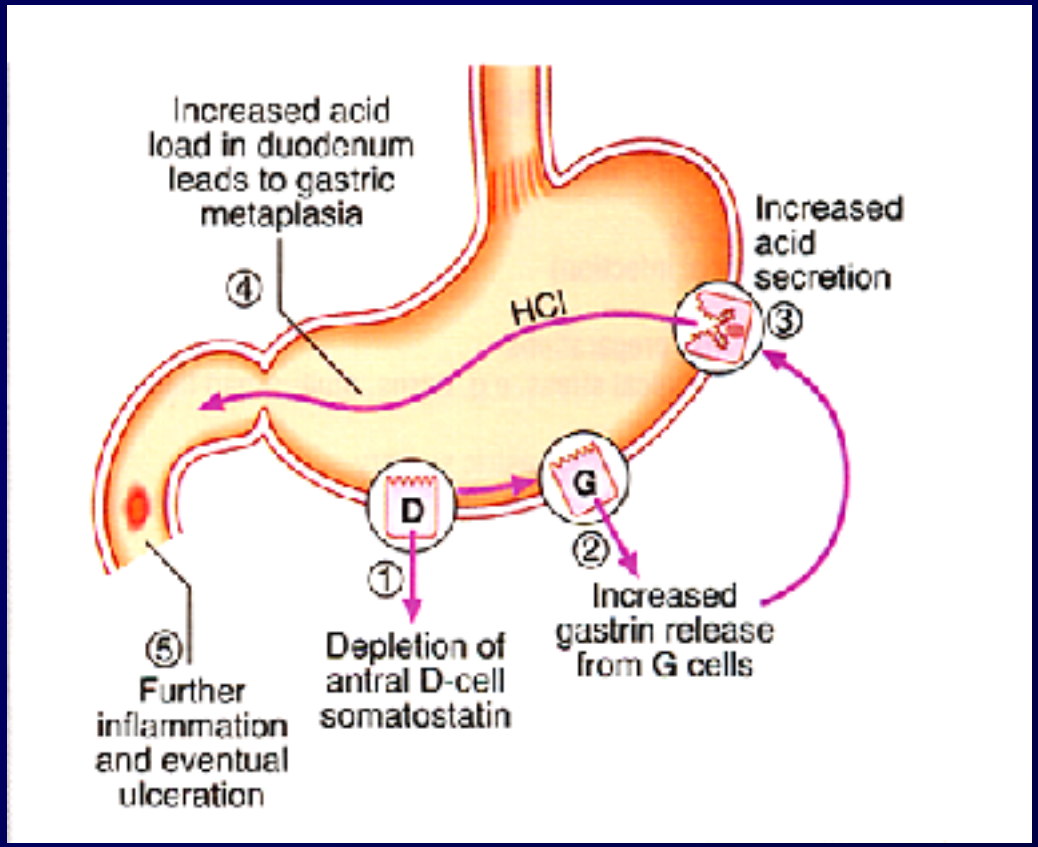
1. 95% are infected with Hp
2. Recurrence prevented by Hp eradication
3. the surrounding mucosa appears inflamed, hemorrhagic or friable (duodenitis).





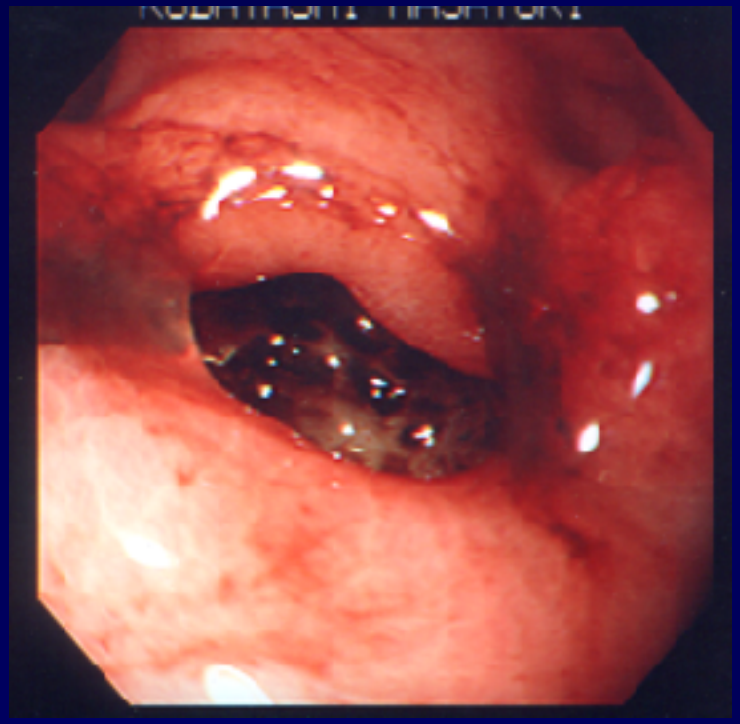
Factors implicated in DU disease

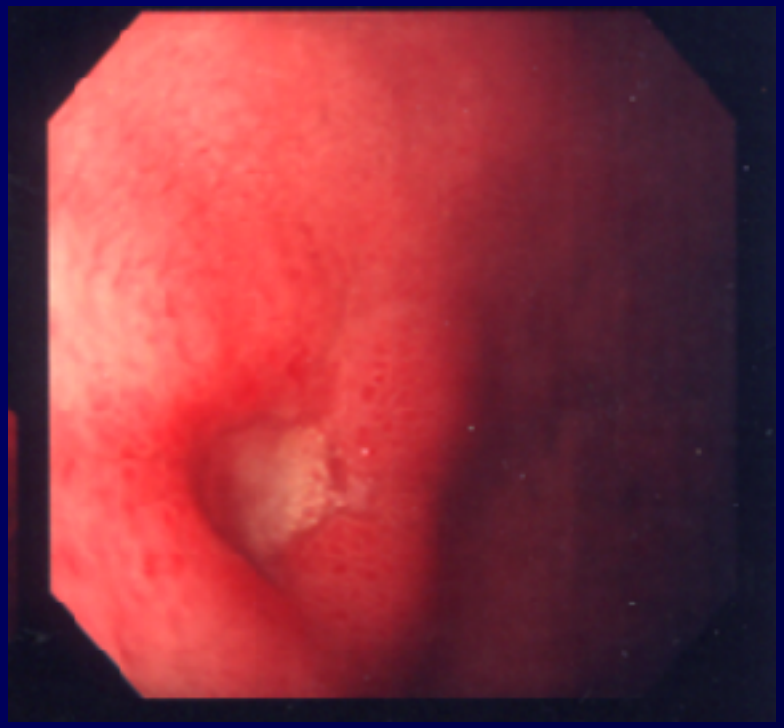
1. Increase acid secretion.
2. Decrease acid suppression
3. Smoking
4. Genetic susceptibility (Blood group O).
5. Virulence factors.



Gastric Ulcer

- The ulcer usually occur at the junction between antral-type and body–type mucosa.





Gastric Ulcer

- Associated with pangastritis causing parietal cell depletion and reduced acid production.
- The ulcers are thought to occur because of reduction of gastric mucosal resistance due to cytokine production by the infection or perhaps to alterations in gastric mucus.
- Acid secretion is normal or low

Clinical features of peptic Ulcer disease

1. Epigastric pain (Hunger pain, night pain, episodic)
2. Nausea & vomitting
3. Heart burn
4. Anorexia and weight loss
5. Hematemesis
6. Persistant severe pain suggests penetration.
7. Examination usually unhelpful.

Other Etiological factors for peptic ulcers

- ***NSAIDS:***

➢Cause damage of the gastric mucosal barrier.

➢Responsible for 30% of gastric ulcers but only small proportion of duodenal ulcers.

➢Mechanism : mostly due to inhibition of Prostaglandins

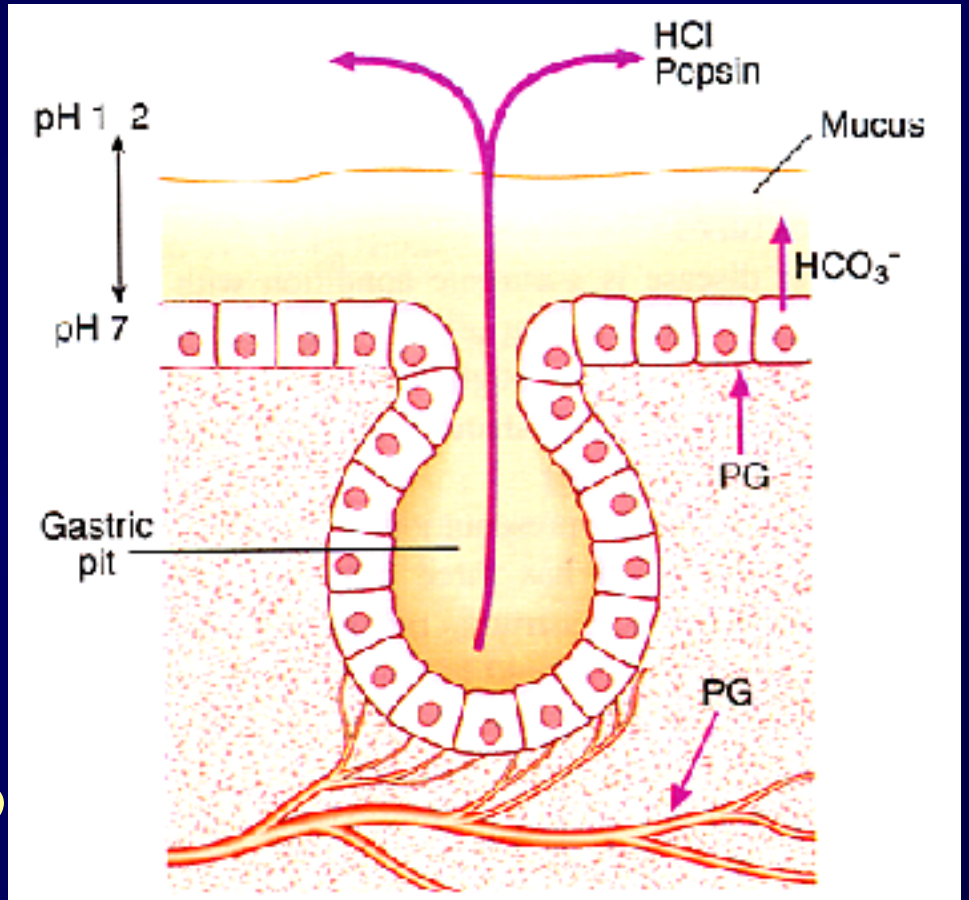


Fig. 9.28 Gastroduodenal mucosal protection. Prostaglandins (PG) stimulate bicarbonate and mucus secretion and increase mucosal blood flow. Bicarbonate ions are secreted into the unstirred mucus layer, neutralising hydrogen ions as they back-diffuse towards the epithelium. Rapid cell turnover and a rich mucosal blood supply are important protective elements.

NSAIDs, Helicobacter and ulcers

- Aspirin and other NSAIDs deplete mucosal prostaglandins by inhibiting the cyclo-oxygenase (COX) pathway
- Cyclo-oxygenase occurs in two main forms: COX-1, the constitutive enzyme; and COX-2, inducible by cytokine stimulation in areas of inflammation.
- COX-2-specific inhibitors have less effect on the COX-1 enzyme in the gastric mucosa
- They still produce gastric mucosal damage but less than with other conventional NSAIDs.
- Some 50% of patients taking regular NSAIDs will develop gastric mucosal damage and approximately 30% will have ulcers on endoscopy. Only a small proportion of patients have symptoms (about 5%)
- H. pylori and NSAIDs are independent and synergistic risk factors for the development of ulcers.

NSAIDS-induced Gastropathy

- **Treatment**
- Stop the ingestion of NSAIDs.
- A PPI should be given.
- H. pylori eradication therapy if positive.

Patients who can't stop NSAIDs use:

- A Cox-2 selective NSAID at lowest dose
- Prophylactic cytoprotective therapy, e.g. PPI or misoprostol (synthetic analogue of PG-E).

Diagnosis of peptic ulcer

Document the presence of ulcer:

1. Endoscopy
2. Double contrast study

Diagnosis of the cause of ulcer:

1. Diagnosis of *H pylori* infection.
2. History of other predisposing factors: e.g. NSAIDS intake, Smoking, Alcohol…
3. Rare causes as Zollinger-Ellison syndrome; usually causes intractable ulcers

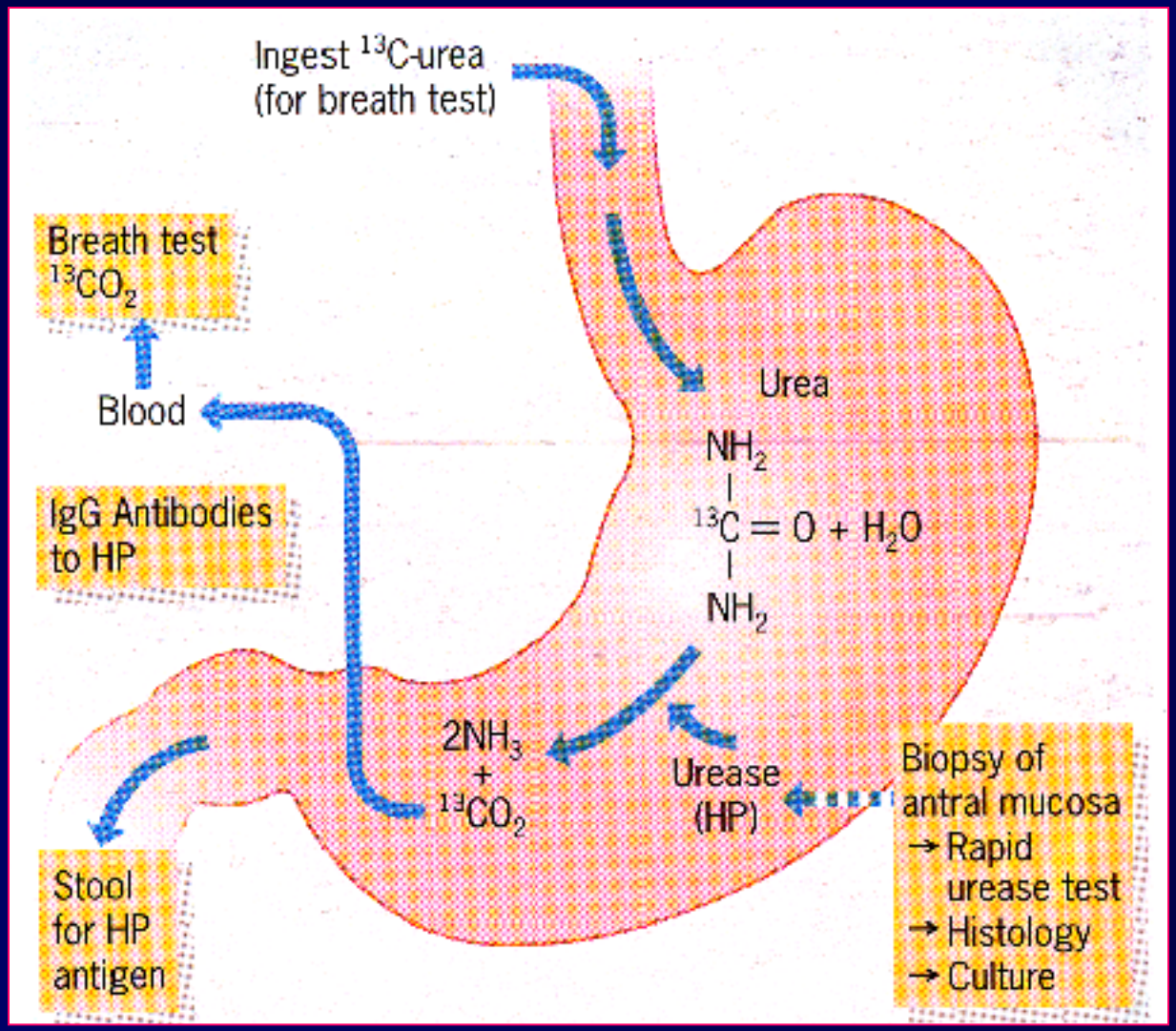
Investigations of suspected peptic ulcer disease

1. Endoscopy is required when:

- There is any of the alarm symptoms
- Old patients (above 50y)
- All gastric ulcers should be biopsied to exclude malignancy.

2. H pylori testing; Eradication therapy may be started without endoscopy in young patients with typical symptoms

Diagnosis of Hp infection



Diagnosis of Hp infection

Table 9.13 Methods for the diagnosis of *Helicobacter pylori* infection

Test	Advantages	Disadvantages
Non-invasive		
Serology	Rapid office kits available Good for population studies	Lacks sensitivity and specificity Cannot differentiate current from past infection
Urea breath tests	High sensitivity and specificity	^{14}C uses radioactivity ^{13}C requires expensive mass spectrometer
Hp stool antigen		
Invasive (antral biopsy)		
Histology	Sensitive and specific Cheap	False negatives occur Takes several days to process
Rapid urease tests, e.g. CLO, Pyloritek	Cheap, quick Specific	Lack sensitivity
Microbiological culture	'Gold standard', defines antibiotic sensitivity	Slow and laborious culture Lacks sensitivity

Treatment of peptic ulcers

- *Non-Surgical management:*
- Stop smoking.
- Avoid NSAIDS
- HP eradication
- Drugs that reduce acid secretion:

1. H_2-antagonists
2. H^+/K^+*ATpase (proton pump inhibitors).*

- Drugs that enhance mucosal defence:

1. Colloid bisthmus compounds
2. Sucrafate

- Prostaglandine analogues as Misoprostal

Hp Eradication Therapy

- *Combination therapy is essential.*
- *Good compliance is also essential.*
- *Pre-packed combination are available for 7 days but resistance is increasingly noticed*
- *During 2016, the rules have changed and 14 days regimens are now recommended.*
- *Clarithromycin's resistance is high in developed countries while resistance to metronidazole is extremely high in our country.*

- *Surgical management*:
- *Indicated in:*

Intractable heamorrhage or perforation.

- *Types of operation*:

1. Partial gastrectomy: remove the antral area that secrete gastrin
2. Vagotomy:

-Truncal -Selective -Highly selective

- *Complications of surgical resection:*

1. Recurrent ulcer
2. Dumping
3. Diarrhea
4. Nutritional deficiencies: anemia (iorn, folate or B12 deficiency)

Hp Eradication Therapy

- *Metronidazole, clarithromycin, amoxicillin, tetracycline and bismuth are the most widely used agents.*
- *Resistance to metronidazole and amoxicillin is common in our country.*
- *Quinolones such as ciprofloxacin and levofloxacin are also used when standard regimens have failed ('rescue therapy').*
- *Combination therapy is essential.*
- *Good compliance is also essential.*

Hp Eradication Therapy

- *Most common used triple therapy:*

1. PPI (omeprazole or Lansoprazole) 20-40 mg
   +Metronidazole 400 mg
   + clarithromycin 500 mg
   all twice daily for 14 days.
2. PPI (omeprazole or Lansoprazole) 20-40 mg
   + clarithromycin 500 mg
   + Amoxicillin I gm
   all twice daily for 14 days.

Patients with peptic ulcer disease usually require 3-4 weeks further treatment with PPI

Hp Eradication Therapy

When drug resistance is higher than 15% or when resistance is unknown: quadruple therapy is recommended for 14 days

- The bismuth-based

Bismuth subsalicylate or chelate + Metronidazole or Amoxicillin +Tetracycline + PPI

- Non-bisthmus-based

Amoxicillin + metronidazole + Tetracyclin + PPI

- **Follow up after eradication by stool antigen test or urea breath test.**

When there is failure of therapy; rescue regimen may include;

- Levofloxacin
- Amoxicillin
- PPI

Complications of peptic ulcers

1. Heamorrhage.
2. Perforation:

   Sudden severe abdominal pain followed by collapse and shock.
3. Pyloric stenosis or gastric outflow obstruction

   Due to: - Active ulcer with edema.

   - Healing and scarring.

   Symptoms:

   - Painless, Huge volume, projectile vomiting.
   - Metabolic alkalosis

Functional (non-ulcer) dyspepsia

- Common.
- H. pylori eradication (only after a +ve result) may help.
- Some evidence favours PPIS and psychotherapy.
- Antacids, antispasmodics, H2 blockers, misoprostol, prokinetic agents, bismuth, or sucralfate all have less evidence.

Autoimmune gastritis

- Affects the fundus and body of the stomach (pangastritis), leading to atrophic gastritis and loss of parietal cells *(achlorhydria)* and intrinsic factor deficiency *(pernicious anaemia)*.
- Pernicious anaemia is an autoimmune disorder ; commonly associated with other autoimmune diseases, particularly thyroid disease, Addison's disease and vitiligo.
- Serum autoantibodies to gastric parietal cells are common and nonspecific: antibodies to intrinsic factor are rarer and more significant

Gastric Tumors

- *Gastric polyps:*

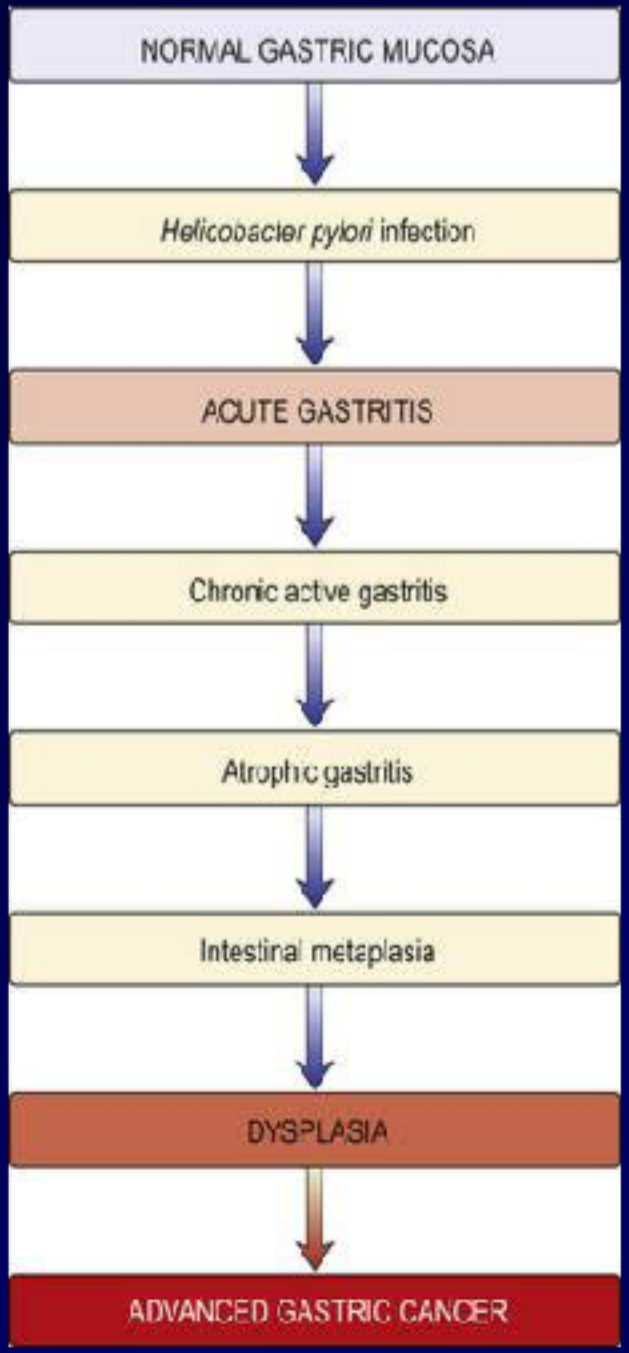
1. Hyperplastic or regenerative polyps
2. Adenomatous polyps

- *Stromal Tumors*
- Arising from the stroma.
- Usually there is a mutation in the proto-oncogene KIT.
- Rapid growth suggest malignancy and should be resected surgically.

Gastric carcinoma

- One of the most common malignant tumors of the GIT.
- Rare before 30 years, incidence increases with age, higher in males.
- *Epidemiology and pathogenesis*:

1. Strong link to HP infection (class I carcinogen).
2. Diet: Salted or smoked food, Rich in nitrates, lack of fresh fruits or vegetables
3. Smoking, Alcohol.
4. Higher incidence in blood group A
5. Increased risk after partial gastrectomy, in Ménétrier's disease and autoimmune gastritis



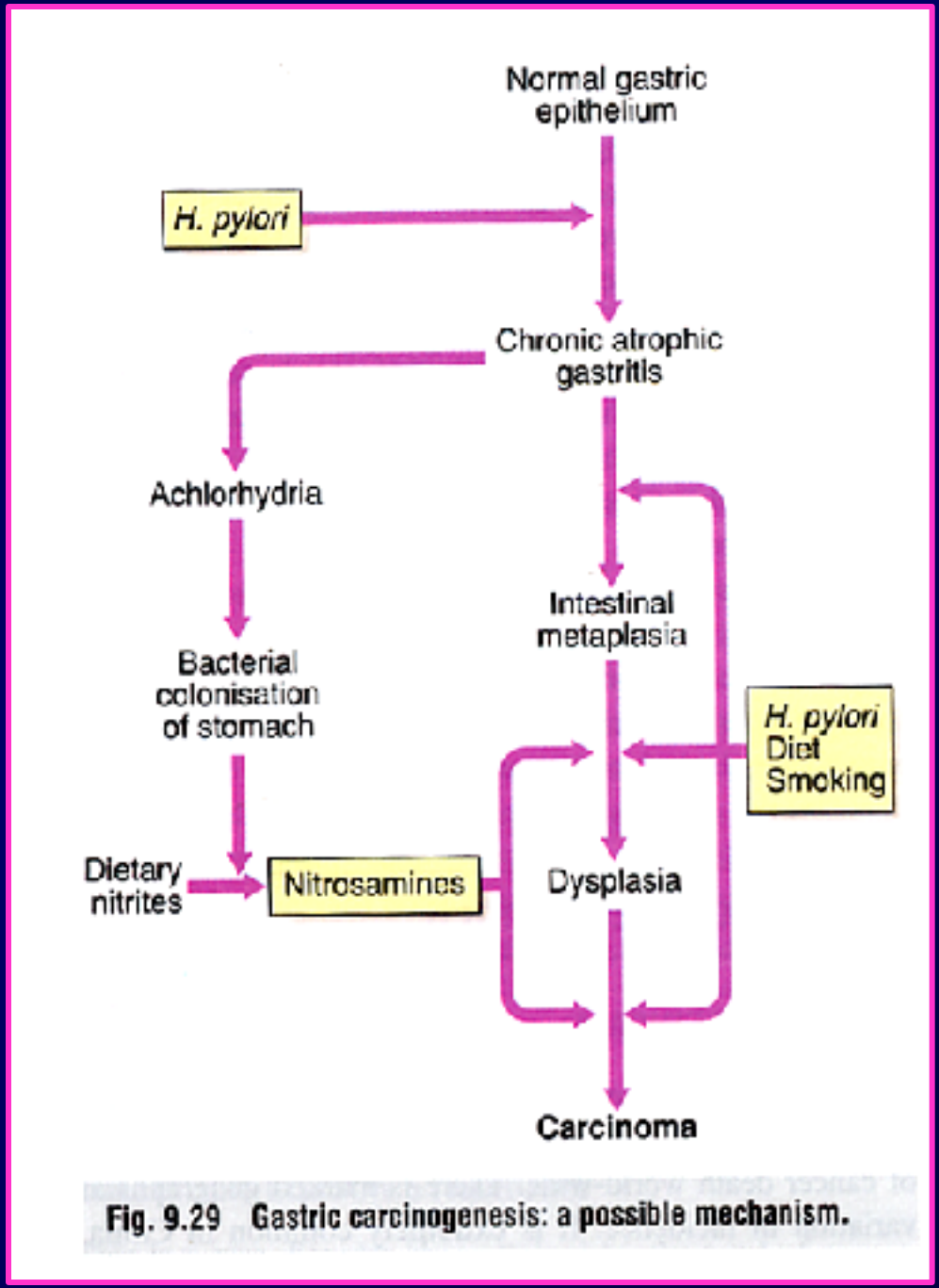
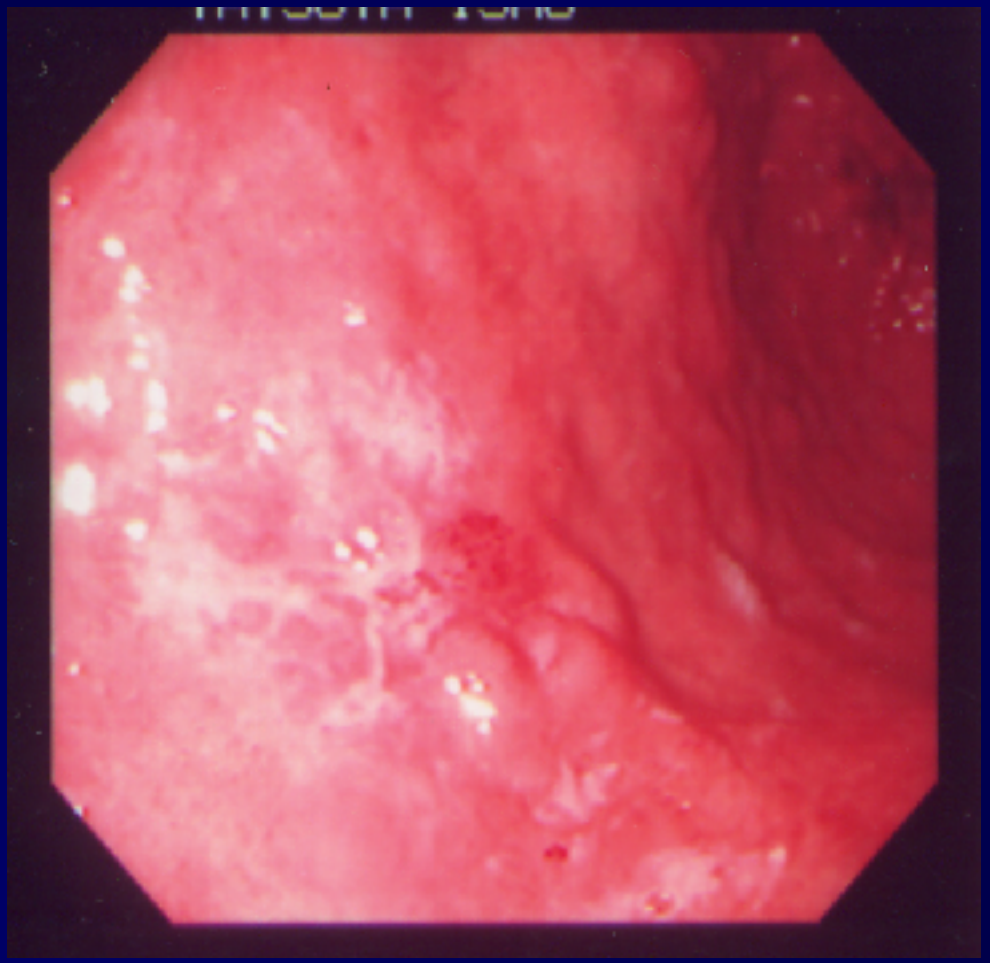


Fig. 9.29 Gastric carcinogenesis: a possible mechanism.

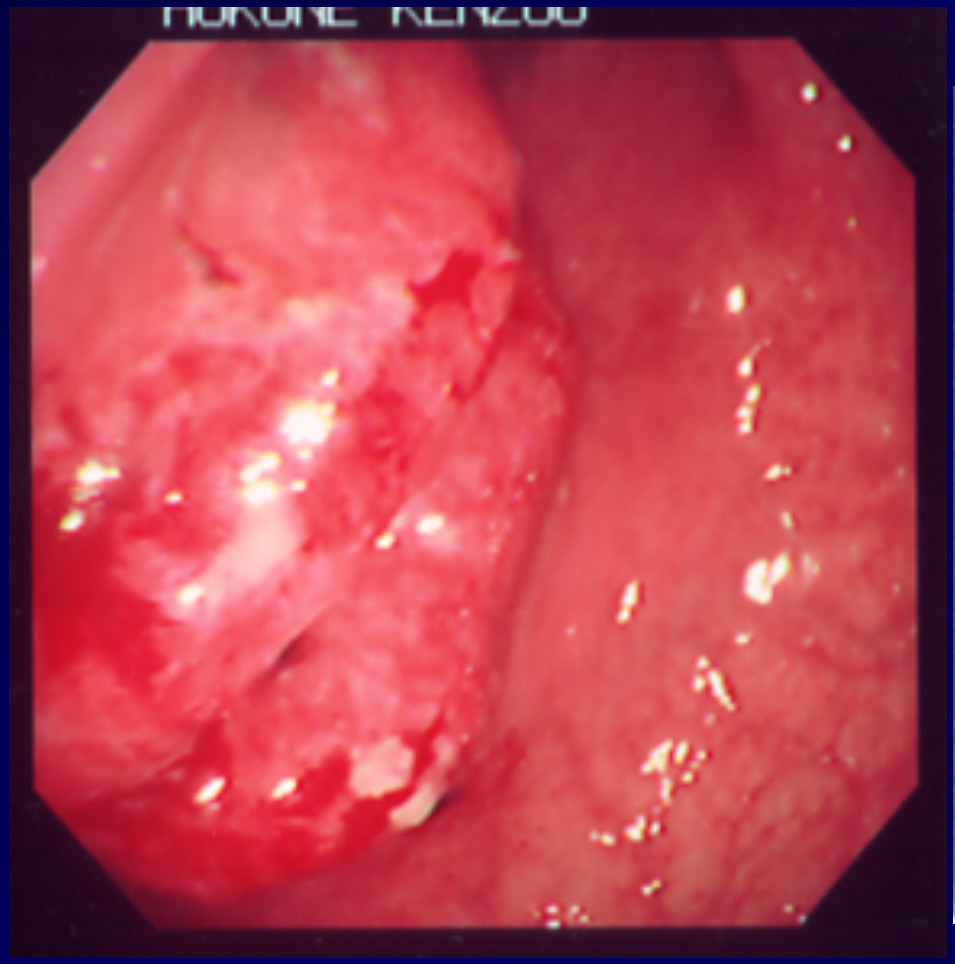
Pathology

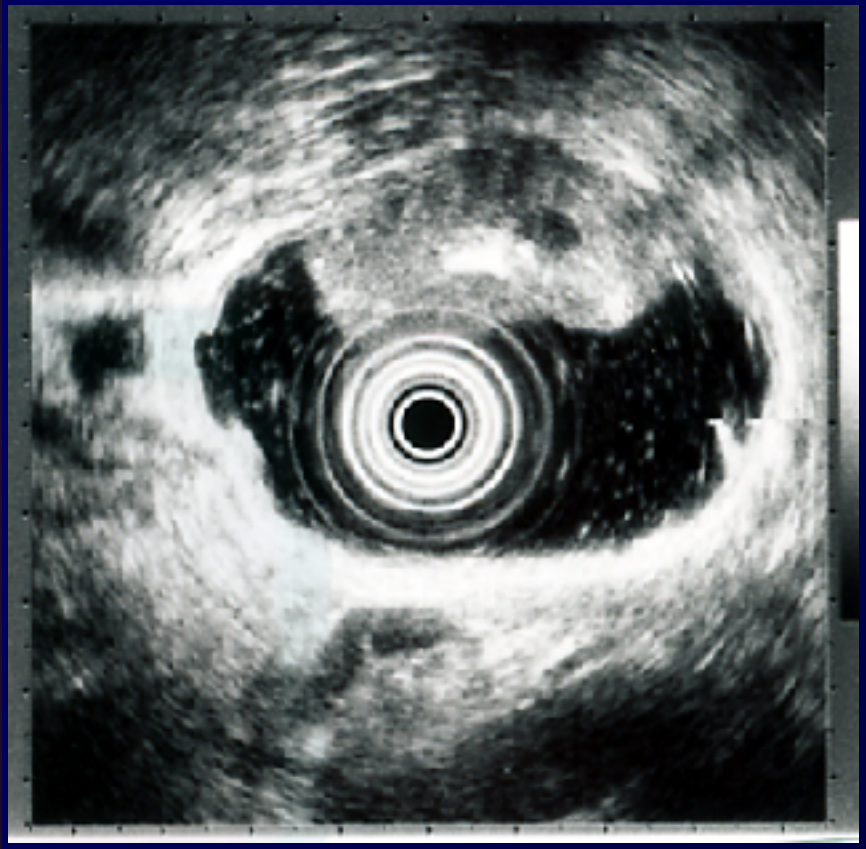
- Almost all cancers are adenocarcinoma arising from mucus-secreting cells.
- 50% at the antrum, 20-30% at the body, cancers in the proximal 1/3 are rare.
- Most of cancers occur on a background of chronic atrophic gastritis with intestinal metaplasia (intestinal type). . Diffuse type is less common and tend to be poorly differentiated.
- Early cancers: limited to the mucosa or submucosa.
- Advanced cancers: infiltrating to or beyond the muscularis propria

Early gastric cancer

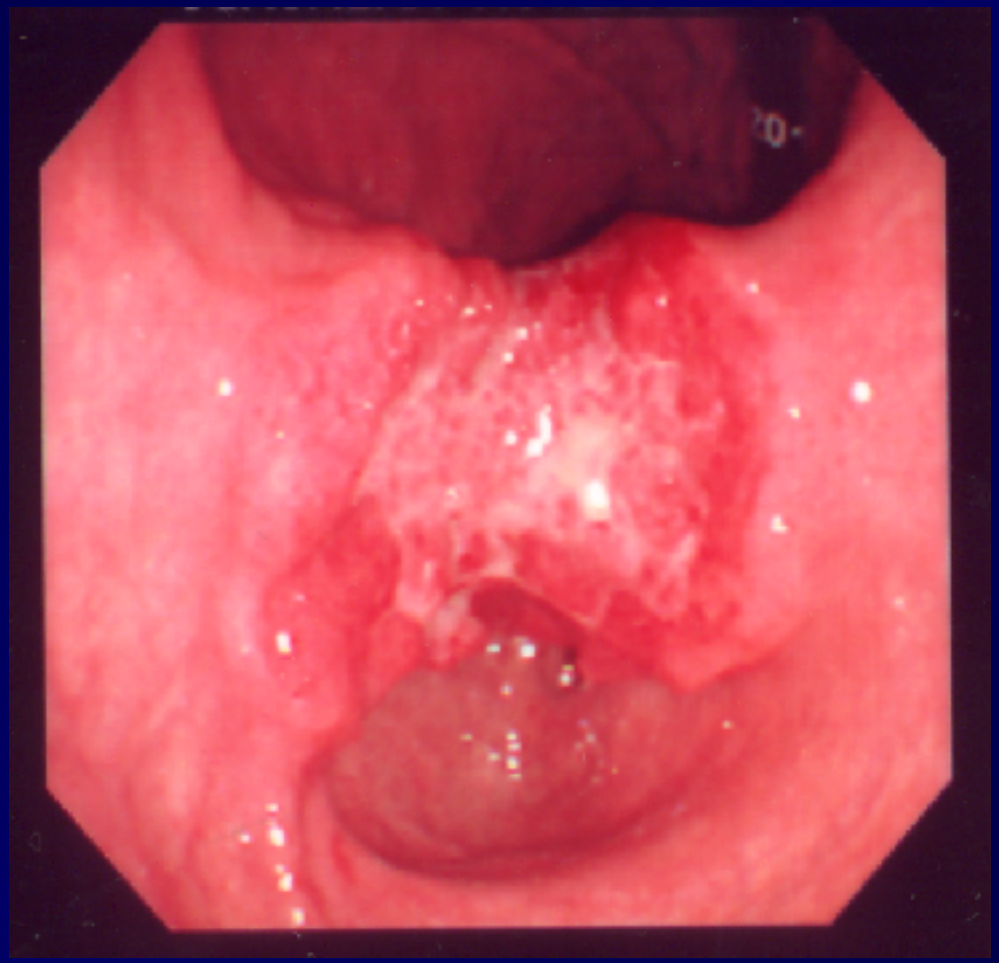


Advanced Gastric cancer: Borr-1

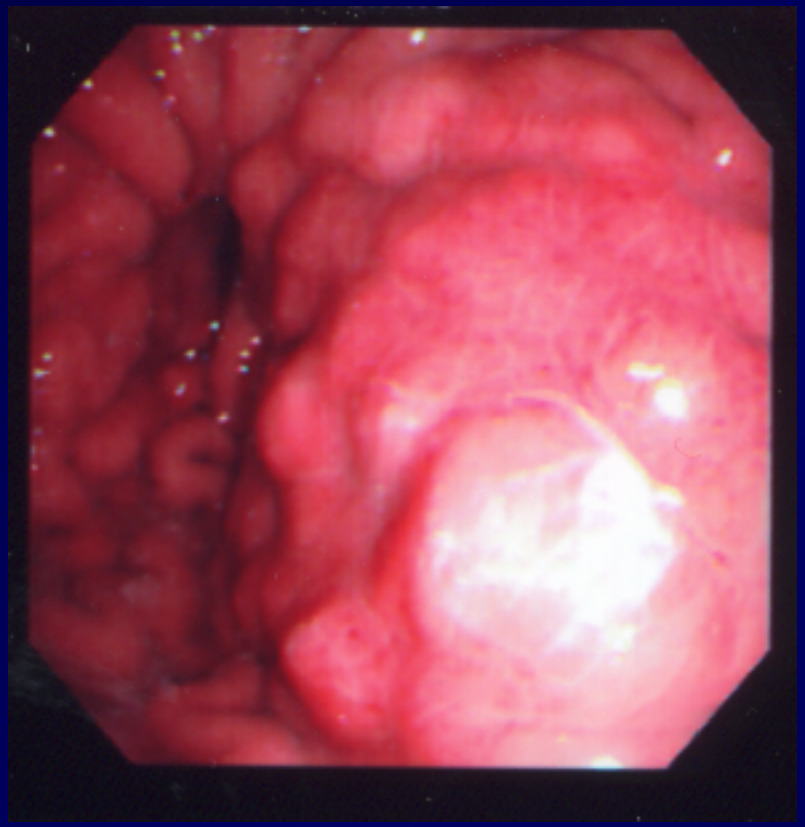


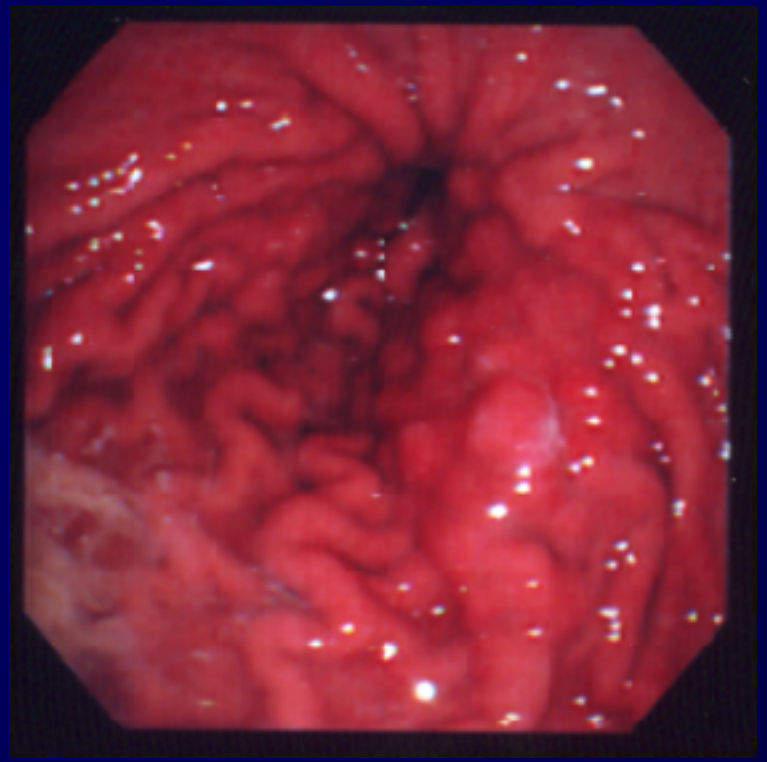


Advanced Gastric cancer: Borr-2



Advanced Gastric cancer: Borr-4





Clinical Features

- Early cancers: asymptomatic.
- Dyspepsia
- Ulcer-like symptoms
- Anorexia, early satiety or nausea.
- Weight loss
- Anemia
- Heamatemesis or melena
- Manifestations of metastasis: jaundice, ascites,..
- Paraneoplastic phenomenon: thrombophlebitis, dermatomyositis,..

Diagnosis

- Endoscopy and biopsy
- EUS
- Abdominal sonography
- CT and MRI

Treatment

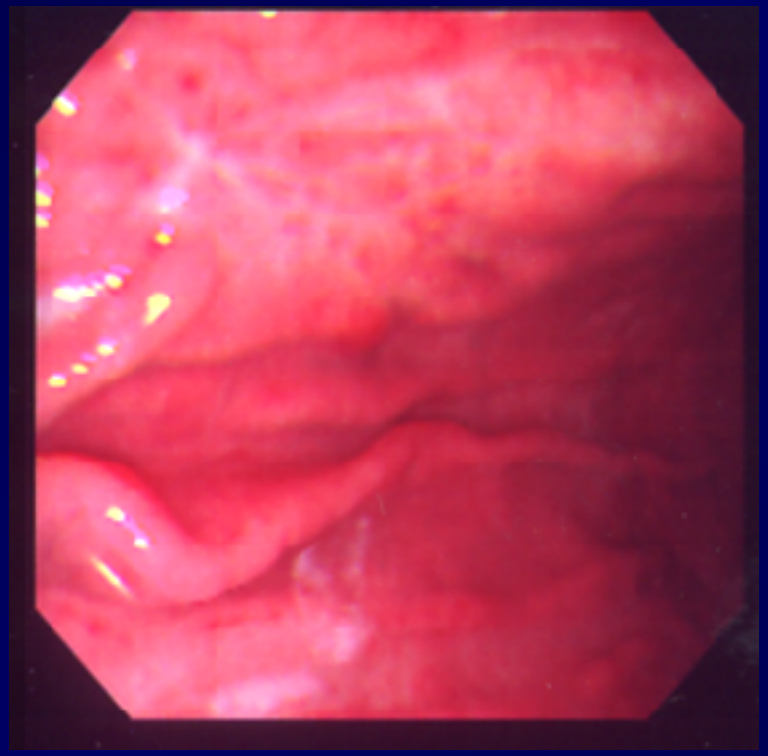
- Early: endoscopic resection, Laser therapy, APC.
- Advanved:

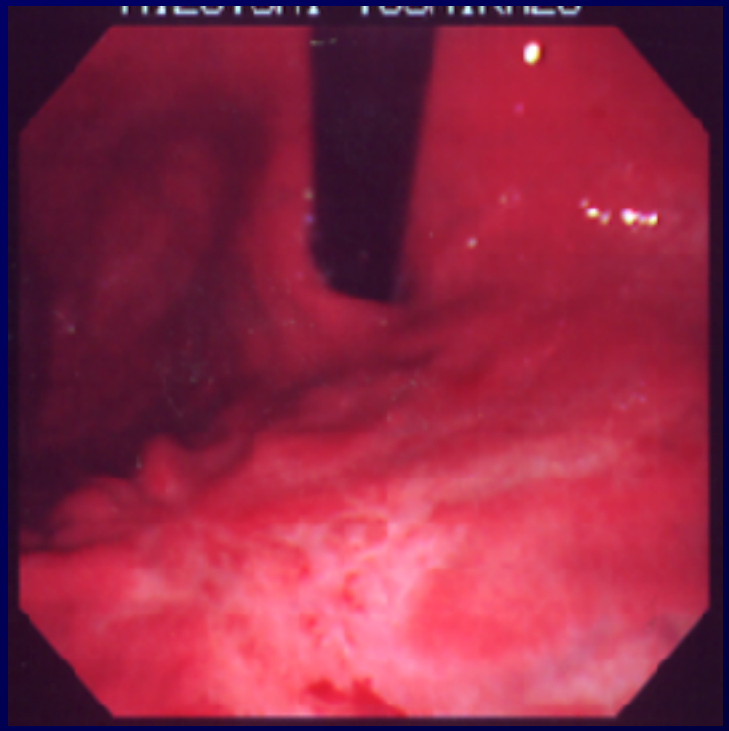
  Subtotal or total gastrectomy

  Palliative measures

Gastric lymphoma

Gastric B cell lymphoma. Over 70% of patients with gastric B cell lymphomas (mucosal-associated lymphoid tissue – MALT





Gastric lymphoma

- 90% of cases are associated with H. Pylori infection
- Early cases may resolve after H. pylori eradication.
- Stage III or IV disease is treated with surgery or chemotherapy with or without radiation.
- The prognosis is good, with an estimated 90% 5- year survival.

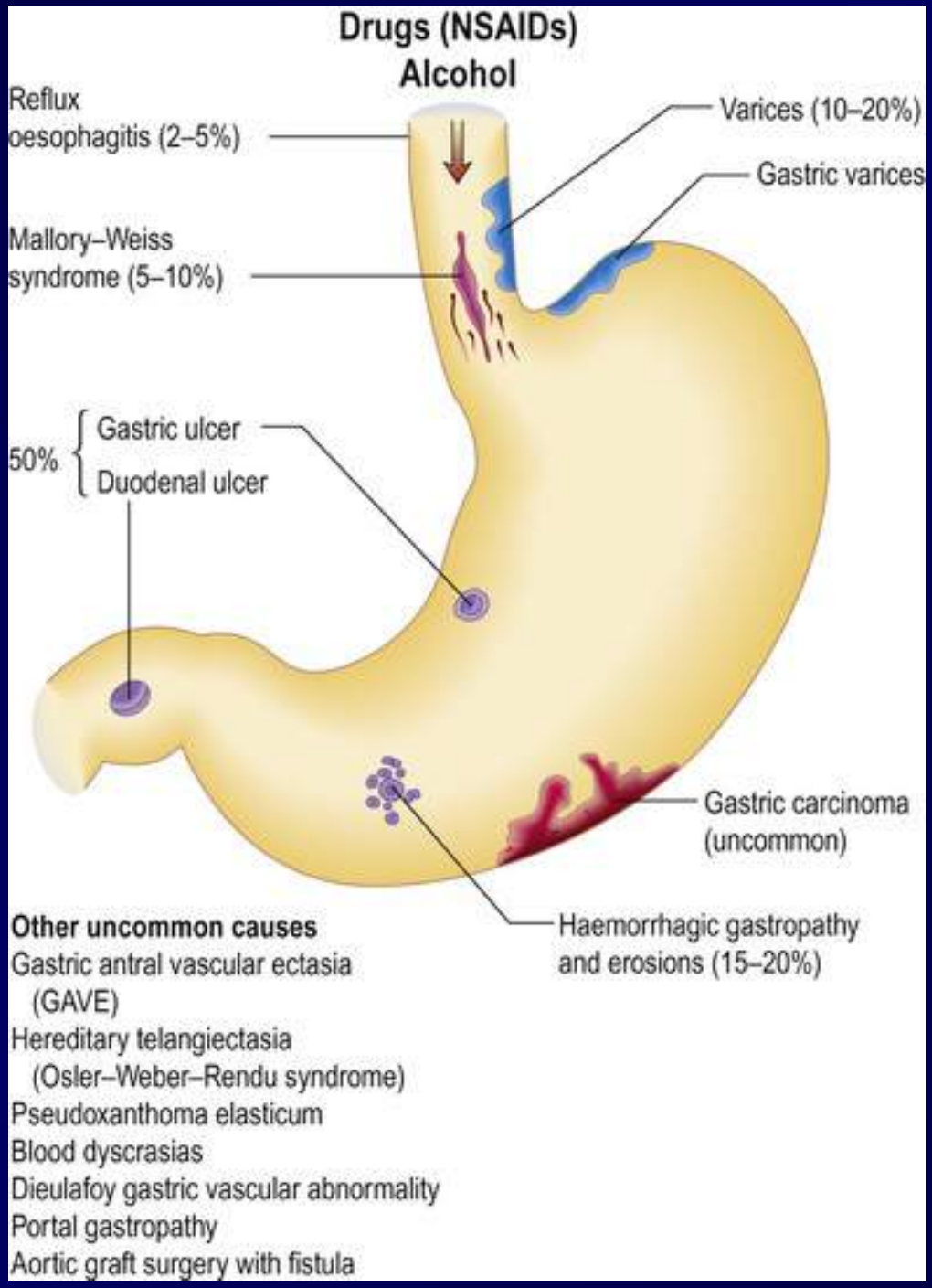
Acute upper gastrointestinal bleeding

The cardinal features are

Haematemesis ; vomiting of blood

Melena ; passage of black tarry stools, the black colour being due to blood altered by passage through the gut.

Melena can occur with bleeding from any lesion proximal to the right colon


Drugs (NSAIDs)
Alcohol
Reflux oesophagitis (2–5%)
Varices (10–20%)
Gastric varices
Mallory–Weiss syndrome (5–10%)
50%
Gastric ulcer
Duodenal ulcer
Gastric carcinoma (uncommon)
Haemorrhagic gastropathy and erosions (15–20%)
Other uncommon causes
Gastric antral vascular ectasia (GAVE)
Hereditary telangiectasia (Osler–Weber–Rendu syndrome)
Pseudoxanthoma elasticum
Blood dyscrasias
Dieulafoy gastric vascular abnormality
Portal gastropathy
Aortic graft surgery with fistula