Pathology of the stomach

Prof.Dr. Haider Abd Ul Ridha

M.B.ch.B. F.I.C.M.S. path.

Objectives:

1. Study the etiology, pathogenesis, pathological features & complication of acute & chronic gastritis.
2. Study the etiology, pathogenesis, pathological features & complication of peptic ulcer disease.
3. Study the etiology, pathogenesis, pathological features of gastric neoplasms.

Gastritis

Inflammation of the gastric mucosa occurs in many conditions, and is called acute gastritis when neutrophils are present and gastropathy when inflammatory cells are rare or absent. Irritants including non-steroidal anti-inflammatory drugs (NSAIDs), alcohol, and bile are the most common causes of gastropathy. Both gastropathy and gastritis may be asymptomatic or associated with epigastric pain, nausea, and vomiting. In more severe cases there may be mucosal erosion, ulceration, hemorrhage, hematemesis, melena, or, rarely, massive blood loss.

Gastritis

Nonspecific symptoms, abdominal pain

Acute

- Causes: infectious, chemical
- Histologically: Edema, hyperemia, mucosal erosions and hemorrhage.

Chronic

- Helicobacter pylori infection (type B, antral, chronic active with lymphoid follicles)
- Autoimmune (type A, body, atrophy, pernicious anemia)
- Chemical (induced by drugs, bile reflux, alcohol, regenerative mucosal changes)

The pathogenesis of acute ulceration

1. NSAID-induced ulcers are caused by

- Direct chemical irritation as well as cyclooxygenase inhibition, which prevents prostaglandin synthesis.
- This eliminates the protective effects of prostaglandins, which include enhanced bicarbonate secretion and increased vascular perfusion.

2. Lesions associated with intracranial injury are thought to be caused by direct stimulation of vagal nuclei, which causes gastric acid hypersecretion.

3. Systemic acidosis, a frequent finding in critically ill patients, also may contribute to mucosal injury by lowering the intracellular pH of mucosal cells.

4. Hypoxia and reduced blood flow caused by stress-induced splanchnic vasoconstriction also contribute to pathogenesis of acute ulcer.

Stress-related mucosal disease occurs in patients with severe trauma, extensive burns, intracranial disease, major surgery, serious medical disease, and other forms of severe physiologic stress.

In some cases, stress-related ulcers are given specific names based on location and clinical associations.

For example:

1. Stress ulcers are most common in the setting of shock sepsis, or severe trauma.
2. Curling ulcers refer to ulcers occurring in the proximal duodenum in the context of severe burns or trauma.
3. Cushing ulcers refer to gastric, duodenal, and esophageal ulcers arising in those with intracranial disease. They have an elevated risk of perforation.

Acute gastric ulcers

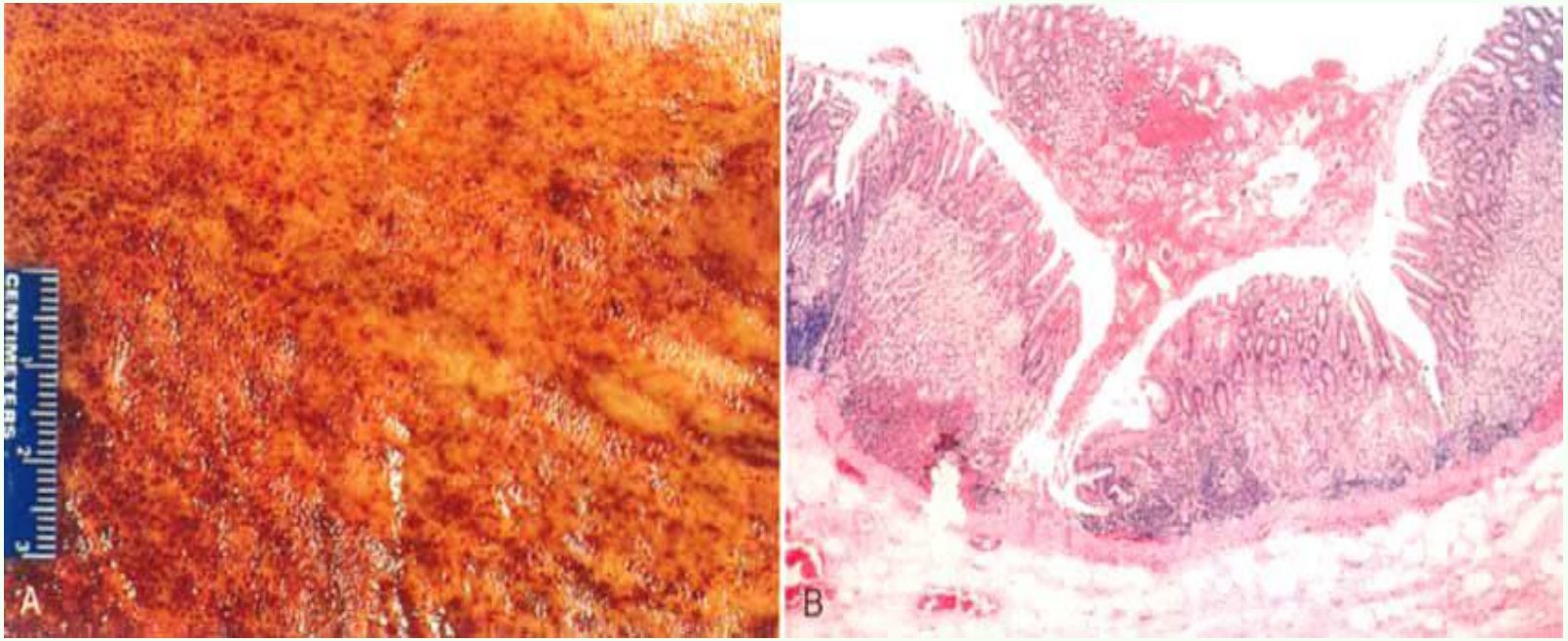
Morphology: gross (Macroscopic finding)

It range in depth from shallow erosions caused by superficial epithelial damage to deeper lesions that penetrate the mucosa.

Acute ulcers are rounded and typically are less than 1 cm in diameter.

The ulcer base frequently is stained brown to black by acid digested extravasated red cells, in some cases associated with transmural inflammation and local serositis. While these lesions may occur singly, more often multiple ulcers are present within the stomach and duodenum.

Acute stress ulcers are sharply demarcated, with essentially normal adjacent mucosa, although there may be suffusion of blood into the mucosa and submucosa and some inflammatory reaction.



Acute gastritis

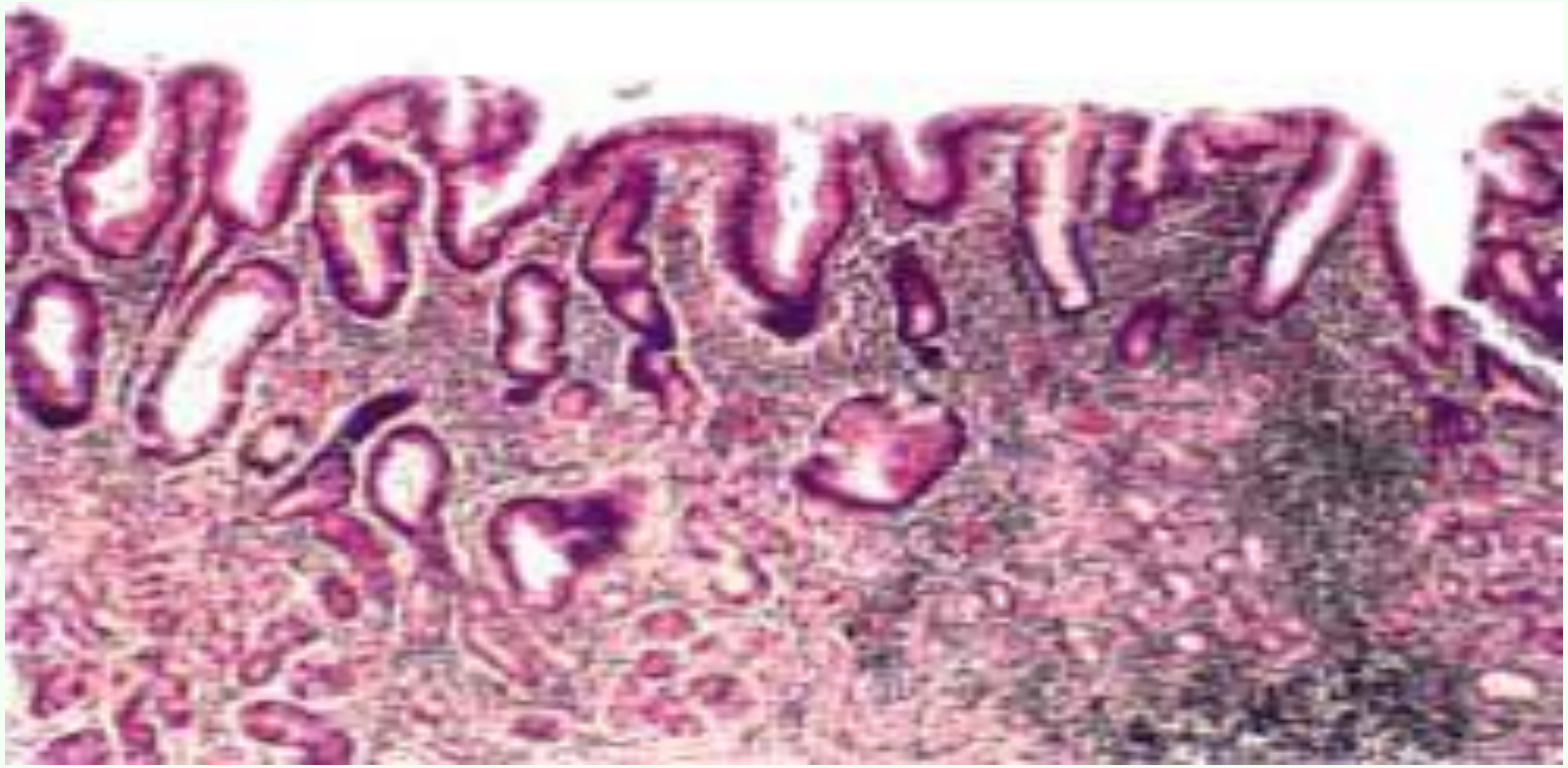
A. Gross view showing punctate erosions in an otherwise unremarkable mucosa; adherent blood is dark due to exposure to gastric acid.

B. Low-power microscopic view of focal mucosal disruption with hemorrhage; the adjacent mucosa is normal.

Chronic gastritis the symptoms associated with chronic gastritis are typically less severe relative to acute gastritis but more persistent. Nausea and upper abdominal pain are typical, sometimes with vomiting, but hematemesis is uncommon.

Chronic gastritis

- Epithelial damage: increase of nuclei, distorsion of foveolae and glands)
- Mucosal infiltrates of lymphocytes and plasma cells
- Active process: neutrophil granulocytes (acute damage of epithelial cell)
- Atrophy: chief and parietal cell loss and replacement by intestinal type epithelial cells.
- Intestinal metaplasia: acid mucin containing goblet cells, microvilli, Panneth cells
- Regenerative changes: foveolar hyperplasia, increase of myofibroblasts and capillaries.



Chronic gastritis

Partial replacement of the gastric mucosal epithelium by intestinal metaplasia (upper left) and inflammation of the lamina propria (right) containing lymphocytes and plasma cells.

Helicobacter associated chronic gastritis

H. pylori are spiral-shaped or curved bacilli present in gastric biopsy specimens of almost all patients with duodenal ulcers as well as most individuals with gastric ulcers or chronic gastritis.

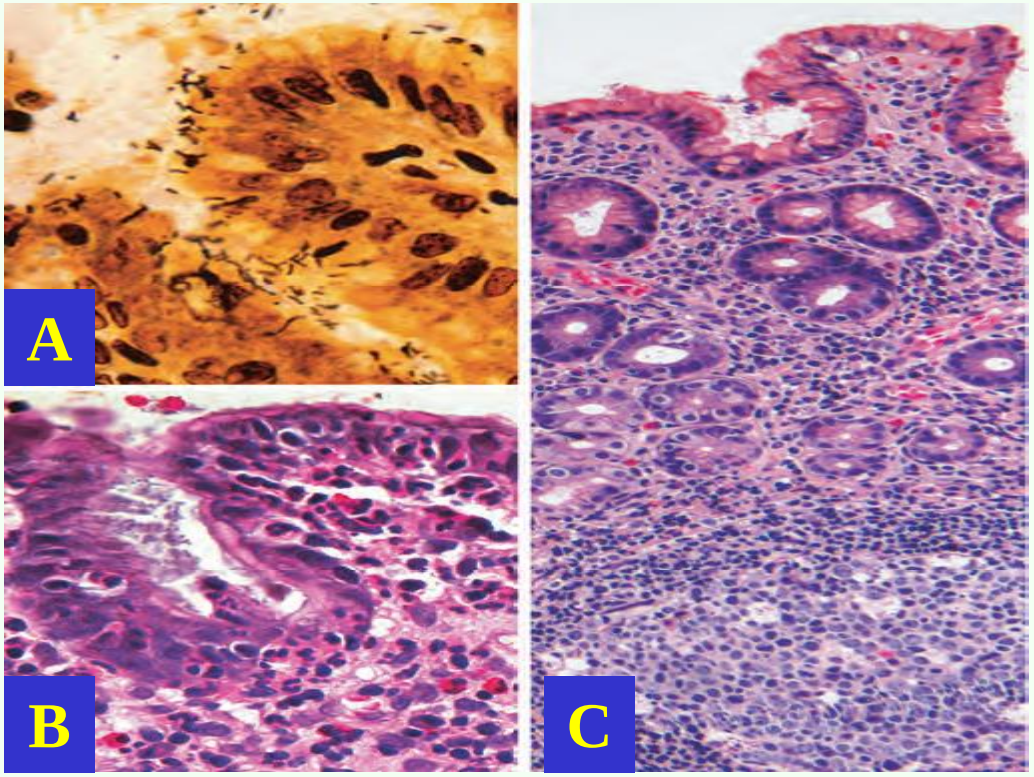
Acute H. pylori infection does not produce sufficient symptoms to come to medical attention in most cases; it is the chronic gastritis that ultimately causes the individual to seek treatment. H. pylori organisms are present in the majority of individuals with chronic antral gastritis.

Helicobacter associated chronic gastritis

Gross: red mucosa, coarser texture than normal, may have thickened rugal folds or thin/flat mucosa; with long term disease, mucosa may be thin/flat; usually affects antrum (particularly in children), and cardia .

Microscopical:

Bacteria is curved, spirochete-like, in superficial mucus layer and along microvilli of epithelial cells; are not invasive; are usually not seen in areas of intestinal metaplasia; associated with chronic inflammatory infiltrate with germinal centers (follicular gastritis) and plasma cells in lamina propria; active inflammation if neutrophils in glandular or surface epithelial layer.



Helicobacter pylori gastritis. (A) Spiral-shaped H. pylori are highlighted in this Warthin-Starry silver stain. Organisms are abundant within surface mucus. (B) Intraepithelial and lamina propria neutrophils are prominent. (C) Lymphoid aggregates with germinal centers and abundant subepithelial plasma cells within the superficial lamina propria are characteristic of H. pylori gastritis.

Helicobacter pylori.

Steiner silver stain demonstrates the numerous darkly stained *Helicobacter* organisms along the luminal surface of the gastric epithelial cells.

Note that there is no tissue invasion by bacteria.

Autoimmune atrophic gastritis

It typically spares the antrum and is **often associated with marked hypergastrinemia.**

It accounts for less than 10% of cases of chronic gastritis and has an estimated prevalence of 2% in those over 60 years of age.

Autoimmune atrophic gastritis is characterized by:

1. Antibodies to parietal cells and intrinsic factor that can be detected in serum and gastric secretions.
2. Reduced serum pepsinogen I concentration.
3. Endocrine cell hyperplasia.
4. Vitamin B12 deficiency.
5. Defective gastric acid secretion (achlorhydria).

Pathogenesis

Autoimmune atrophic gastritis is associated with

1. loss of parietal cells, which are responsible for secretion of gastric acid and intrinsic factor.
2. The absence of acid production stimulates gastrin release, resulting in hypergastrinemia and hyperplasia of antral gastrin-producing G cells.
3. Intrinsic factor loss results in defective ileal vitamin B12 absorption, which ultimately leads to vitamin B12 deficiency and pernicious anemia (a form of megaloblastic anemia).
4. CD4+ T cells directed against parietal cell components, including hydrogen potassium adenosine triphosphatase (H+,K+-ATPase), are considered to be the principal agents of injury in autoimmune atrophic gastritis.

   There is no evidence of an autoimmune reaction to chief cells, suggesting that these may be lost through gastric gland destruction

Features	H. pylori–Associated	Autoimmune
Location	Antrum	Body
Inflammatory infiltrate	Neutrophils, subepithelial plasma cells	Lymphocytes, macrophages
Acid production	Increased to slightly decreased	Decreased
Gastrin	Normal to markedly increased	Markedly increased
Other lesions	Hyperplastic/inflammatory polyps	Neuroendocrine hyperplasia
Serology	Antibodies to *H. pylori*	Antibodies to parietal cells (H_+,K_+-ATPase, intrinsic factor)
Sequelae	Peptic ulcer, adenocarcinoma, lymphoma	Atrophy, pernicious anemia, adenocarcinoma, carcinoid tumor
Associations	Low socioeconomic status, poverty, residence in rural areas	Autoimmune disease; thyroiditis, diabetes mellitus, Graves disease

PEPTIC ULCER DISEASE

- Ulcer: focal destruction of mucosa or deeper (necrosis)
- Erosion: less than full thickness focal loss of mucosa, can progress to ulcer or heal without scarring.
- Peptic : primary autodigestive lesion caused by the action of gastric juice.
- Sites: Esophagus, stomach, duodenum and ectopic mucosa

Hyperacidity.

Decreased mucosal protection.

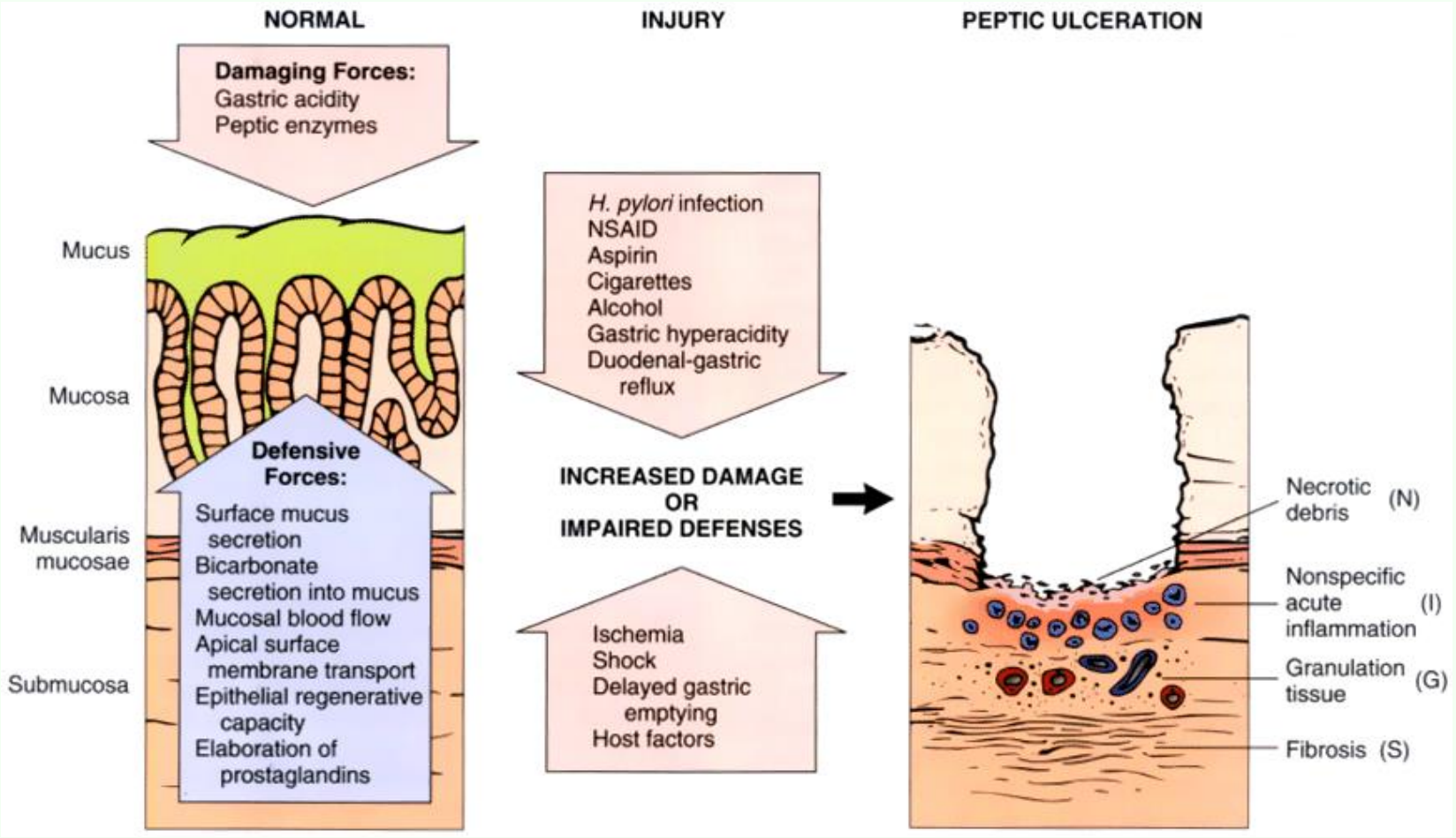


Diagram of causes of, and defense mechanisms against, peptic ulceration.

Diagram of the base of a non perforated peptic ulcer, demonstrating the layers of necrosis (N), inflammation (I), granulation tissue (G), and scar (S), moving from the luminal surface at the top to the muscle wall at the bottom.

Complications of ulcer

- Bleeding
- Perforation
- Obstruction
- Penetration
- Pain

Complications of gastric ulcer:

Bleeding

1. Occurs in 15% to 20 % of patients.
2. Most frequent complication.
3. May be life-threatening.
4. Accounts for 25% of ulcer deaths.
5. May be the first indication of an ulcer.

Perforation

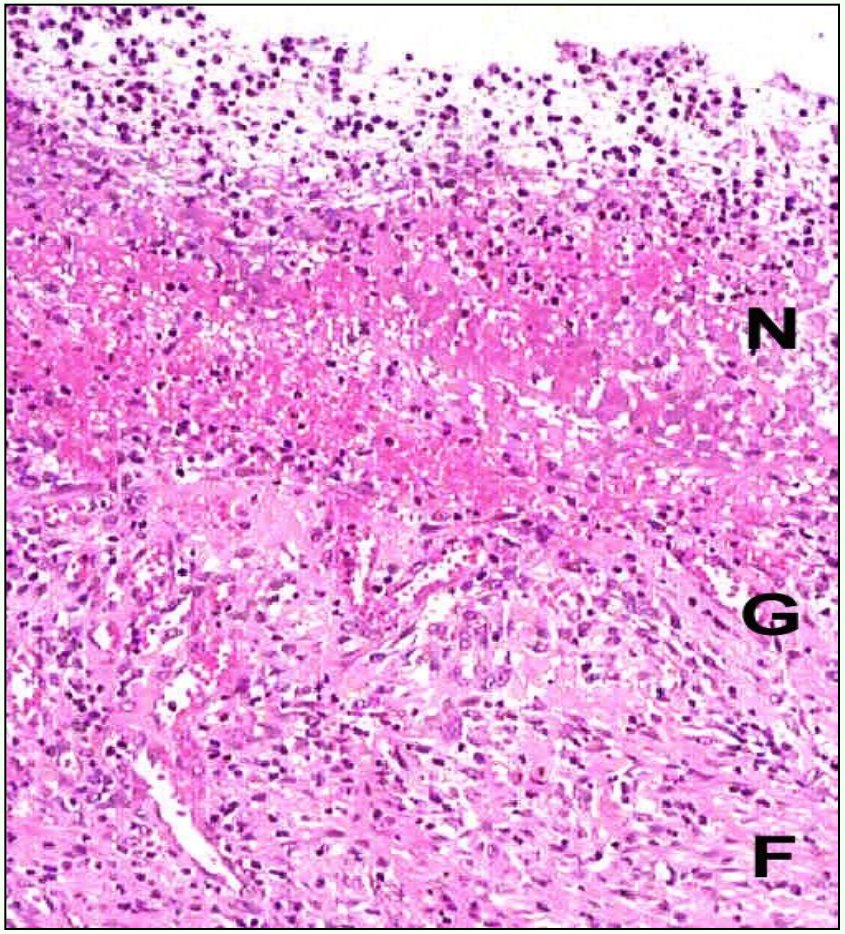
1. Occurs in up to 5% of patients.
2. Accounts for two thirds of ulcer deaths.
3. It is rarely the first indication of an ulcer.

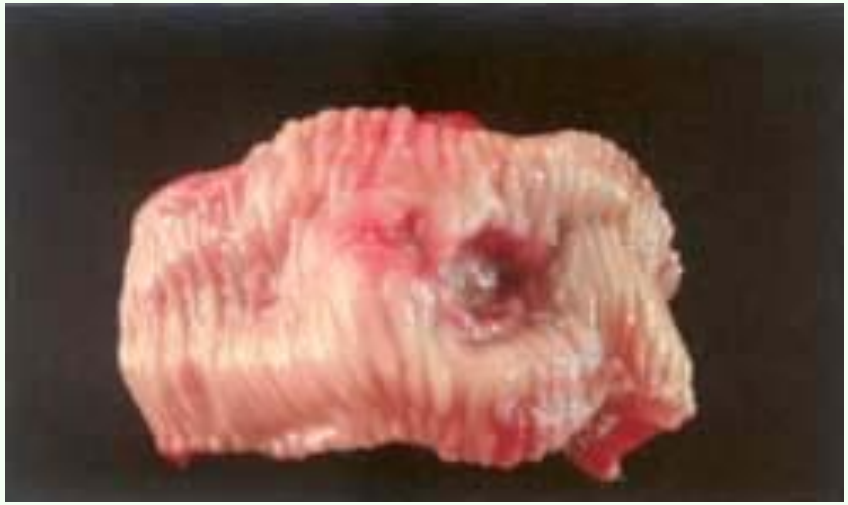
Obstruction

1. Mostly in chronic ulcers.
2. Secondary to edema or scarring.
3. Occurs in about 2% of patients.
4. Most often associated with pyloric channel ulcers.
5. May occur with duodenal ulcers.
6. Causes incapacitating crampy abdominal pain.
7. Can rarely cause total obstruction and intractable vomiting.

Predisposing factors for peptic ulcer of stomach and duodenum

- Helicobacter pyIori
  - direct mucosal injury
  - increased acid secretion
  - inflammatory reaction
- Trauma: burns, surgery, fractures (Curling ulcer)
- Stress.
- Cerebral Lesions.
  - Vagus nerve stimulation (hypothalamus)
- Smoking.
- Zollinger-Ellison syndrome.
  - gastrin overproduction, tumor (gastrinoma)
- Genetic Factors.
- Steroid hormons and Nonsteroidal anti-inflammatory drugs.
  - blocks prostaglandin synthesis.





Peptic ulcer of the duodenum.

Note that the ulcer is small (2 cm) with a sharply punched-out appearance. Unlike cancerous ulcers, the margins are not elevated. The ulcer base is clean.