GIT Pathology
LEC 3

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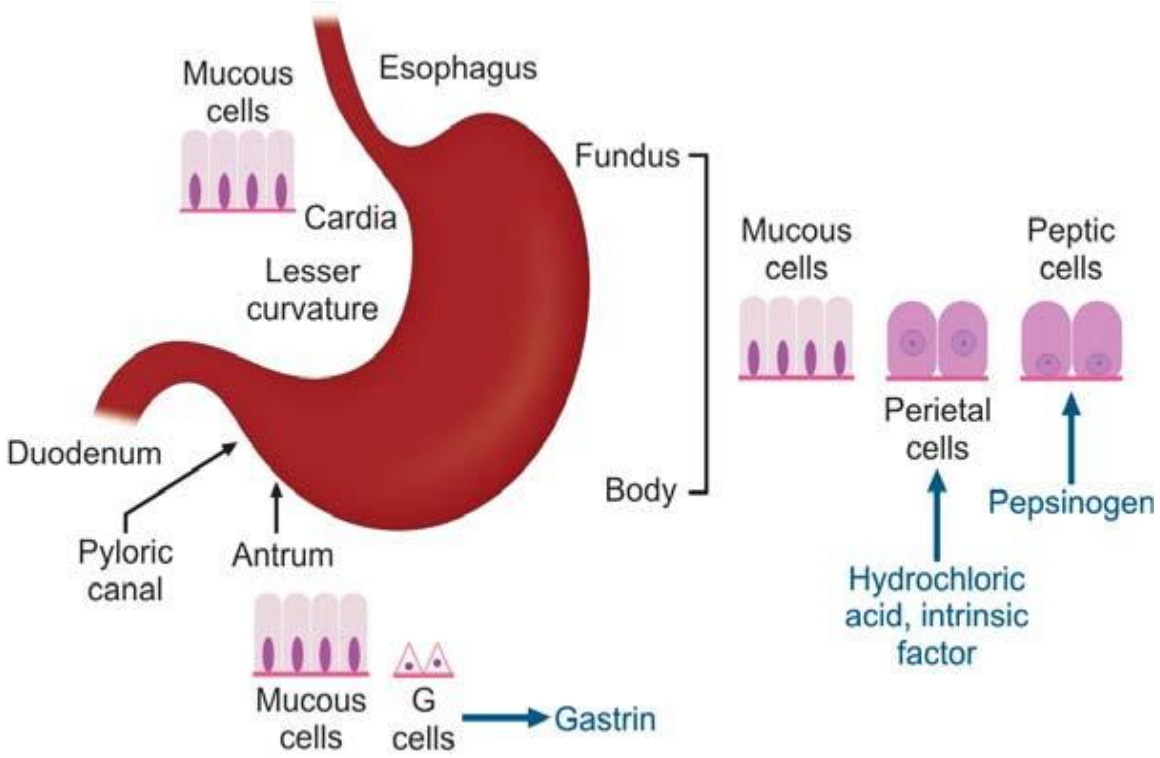
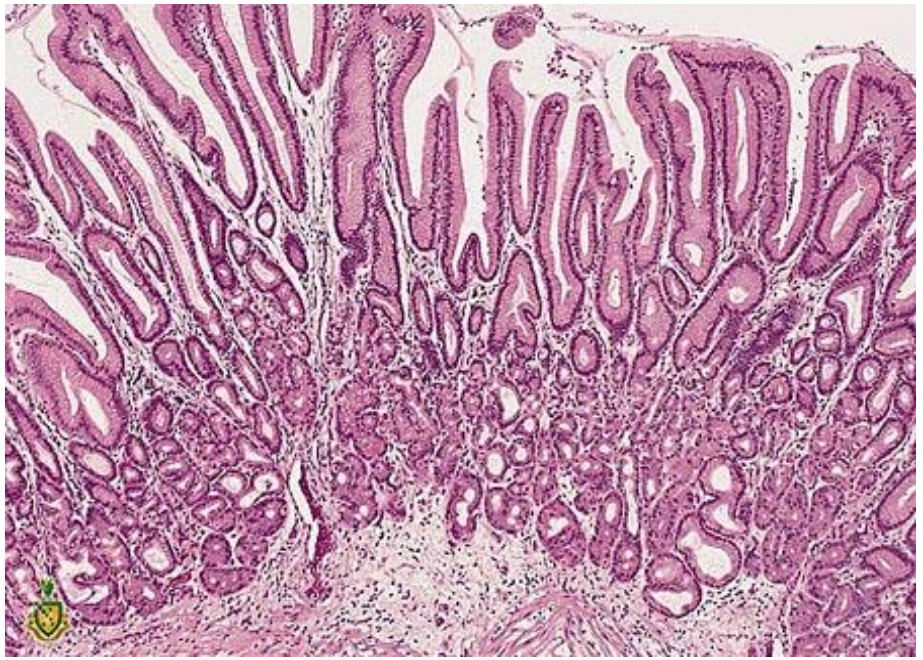
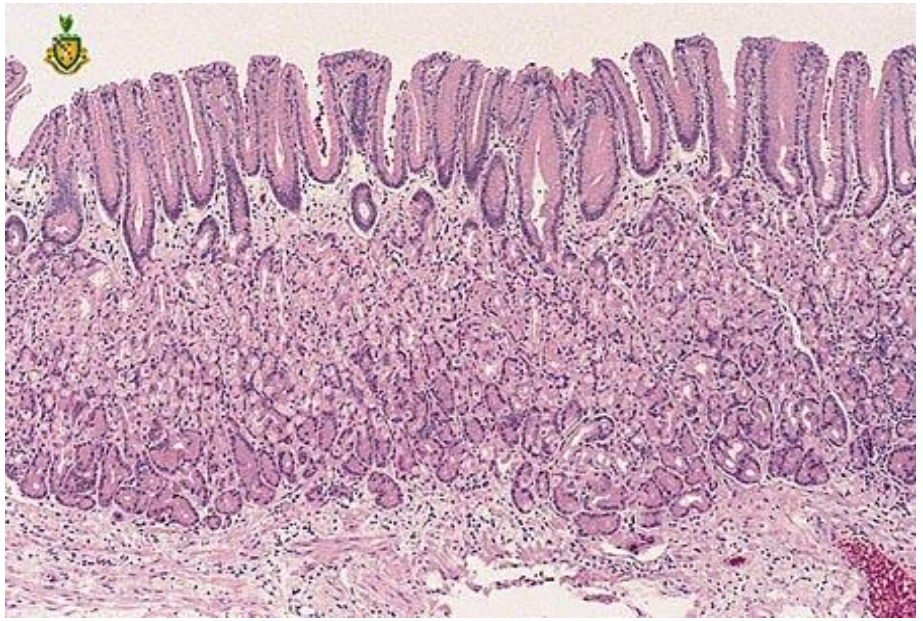
Gastric anatomy and histology







Gastritis

- It is defined as inflammation of the gastric mucosa.
- Acute gastritis with **neutrophilic** infiltration.
- Chronic gastritis with **lymphocytic** infiltration.

Acute gastritis

➢Is acute inflammation of the gastric mucosa.

➢**Etiology:**

- Heavy use of (non-steroidal anti-inflammatory drugs NSAID)
- Excessive alcohol intake
- Heavy smoking
- Uremia
- Severe stress (burn, trauma, surgery)
- Systemic infection (e.g. salmonellosis).
- Treatment with chemotherapeutic drugs.

➢Clinical features:

- Epigastric pain, nausea and vomiting, sometimes hematemesis

➢Grossly:

- Congested, edematous surface.

➢Microscopically:

- Neutrophils among the surface epithelial cells.
- Erosion (loss of superficial epithelial cells) resulting in a defective mucosa.
- Sometimes hemorrhage → acute hemorrhagic gastritis

Chronic gastritis

➢Defined as presence of mucosal inflammatory changes leading to:

- Mucosal **atrophy**
- H-pylori are found nestled within the mucus layer overlying the mucosal epithelium.
- Epithelial **metaplasia** (replacement of the gastric epithelium with columnar &goblet cells of the intestinal variety).
- Sometimes **dysplasia** which makes the background for carcinoma.
- H-pylori induced proliferation of lymphoid tissue within gastric mucosa is a precursor of gastric lymphoma.
- There is **No Erosion (**to differentiated from gastric ulceration)

Etiological factors:

1. Chronic inflammatory processes (helicobacter pylori H.P) which makes the most important factor and present in about 50% of cases.
2. Immunological (autoimmune) in association with pernicious anemia which makes about 10% of cases.
3. Toxic e.g. alcohol &cigarette smoking.
4. Post surgical e.g. reflux of biliary duodenal secretion
5. Motor and mechanical causes including: obstruction, bezoars.
6. Radiation
7. Granulomatous conditions
8. Miscellaneous e.g. amyloidosis.

Helicobacter pylori Gastritis (Type B)

* It is the most common cause of chronic gastritis.
* It can arise at any age.
* It involves the **antrum** of the stomach
* It is highly associated with:

1. Peptic ulcer disease
2. Gastric carcinoma
3. Gastric lymphoma

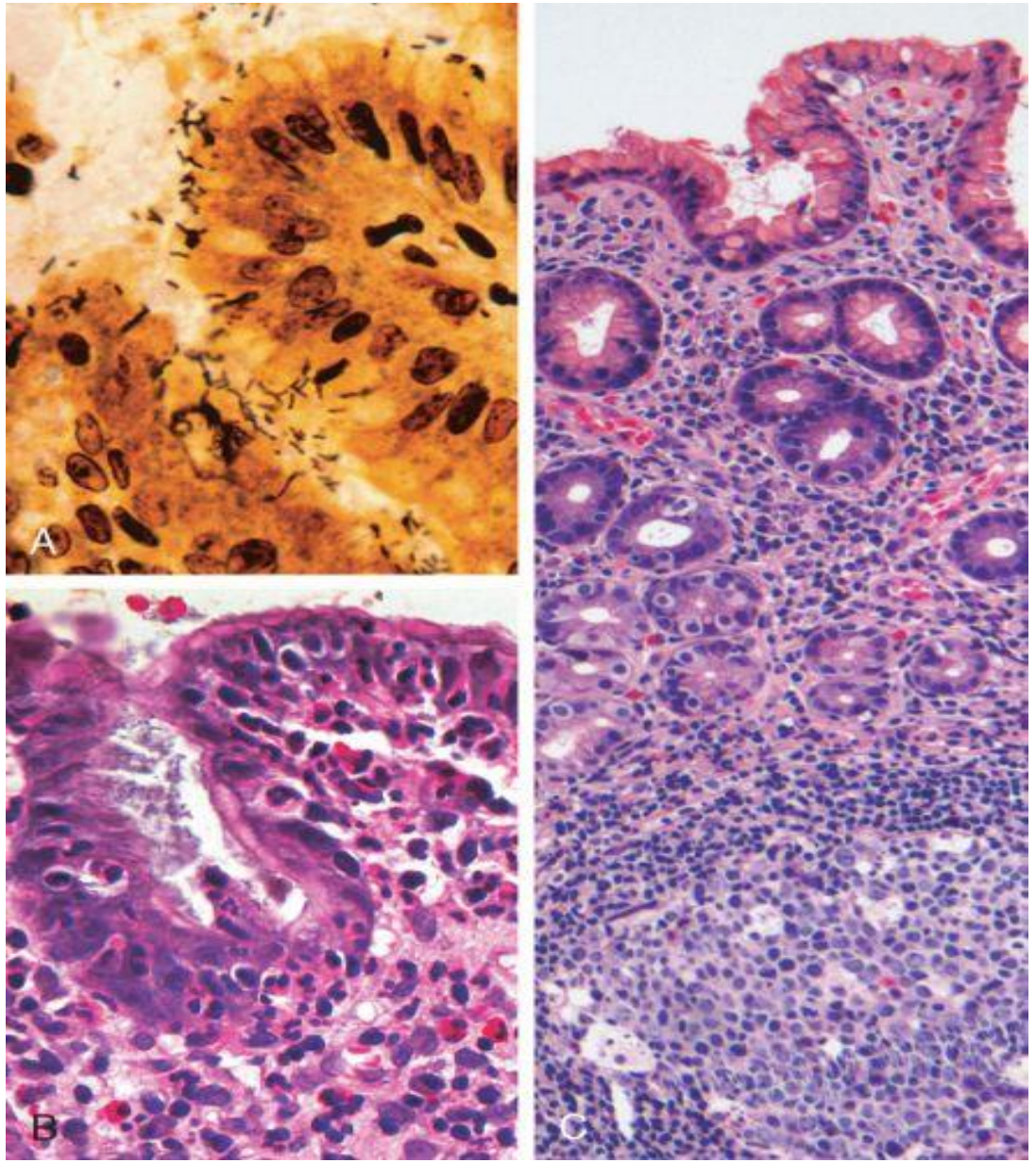
Mic.:

1. Organisms (Spiral-shaped H. pylori) are abundant within surface mucus, easily demonstrated with immunostains or histochemical stains.

2. The mucosa is infiltrated by chronic inflammatory cells (lymphocyte and plasma cells), and **neutrophils** in case of active inflammation.

* Lymphoid aggregates, some with germinal centers, are frequently present.

3. Mucosal atrophy and intestinal metaplasia are **sequelae** that can be the first step toward development of gastric adenocarcinoma.



Autoimmune Atrophic Gastritis (Type A)

*It accounts for less than 10% of cases of chronic gastritis

* Occur in late adult life.

* The **body and fundus** mucosa is mostly affected. typically **spares the antrum**

* There is a production of **antibodies against the parietal** cells which causes:

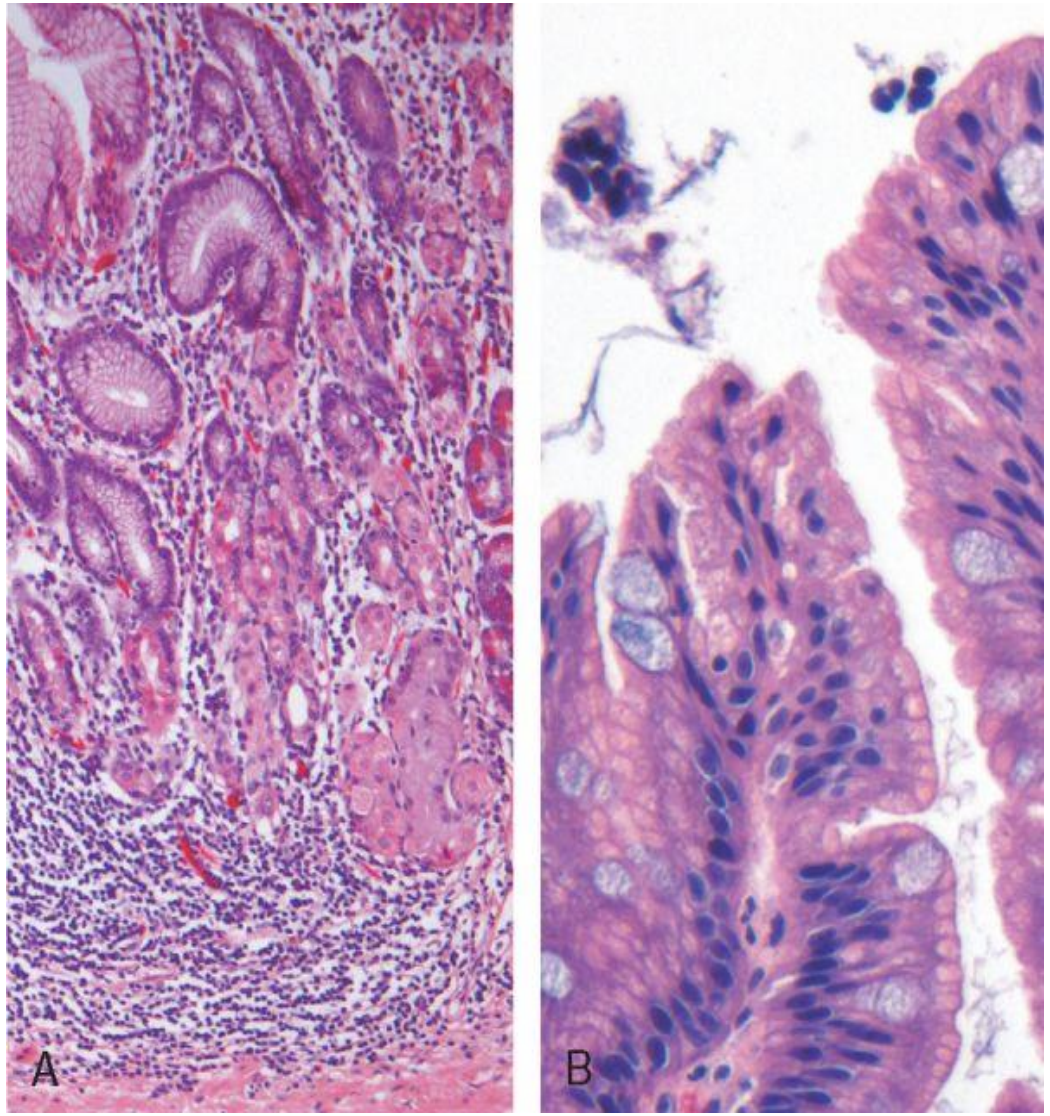
- Defective gastric acid secretion (hypo- or achlorhydria)
- Decrease in intrinsic factor secretion.
- Impaired Vit. B12 absorption and later on **pernicious anemia** as a result of the above cause.
- Often associated with marked **hypergastrinemia** (The absence of acid production stimulates gastrin release, resulting in hypergastrinemia and hyperplasia of antral gastrin-producing G cells.

*It can be associated with other autoimmune diseases e.g. diabetes, thyroiditis.

*There is high risk of developing **gastric carcinoma.**

Mic.:

1. The mucosa is infiltrated by lymphocytes & plasma cells, often in association with lymphoid aggregates and follicles.
2. Glandular atrophy.
3. Intestinal metaplasia, recognizable as the presence of goblet cells admixed with gastric foveolar epithelium



feature	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 decreased	Increased
Other lesions	Hyperplastic/inflammatory polyps	Neuroendocrine hyperplasia
Serology	Antibodies to H. pylori	Antibodies to parietal cells
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

Acute gastric ulcer:

➢It means the development of: **focal, acutely developing mucosal defects**.

➢**Causes:**

- Non-steroidal anti-inflammatory drugs (NSAID).
- May appear after severe physiological stress, whatever its nature;
- So it is called (STRESS ulcer) e.g.

-After severe burn (CURLING ulcer)

-After head or CNS injury (CUSHING ulcer)

- After severe trauma e.g. (sepsis and major surgery)

Pathogenesis:

- The development of acute mucosal defects in the above causes results from different settings:

1- In case of patient taking NSAID there will be a decrease in PG secretion which has an important protective effect on the mucosa.

2- Direct stimulation to the vagal nuclei (in head traumas) by increased intracranial pressure may cause hypersecretion of gastric acid.

Morphologically:

- Multiple, small, round-oval, superficial-deep, and may lead to perforation.

Clinical features:

- Either asymptomatic or bleeding.

Chronic peptic ulcer:

***An ulcer*:** is a defect in the mucosa causing a **discontinuity of the surface epithelium** which may extend into the **muscularis mucosae** into the **submucosa**, or **deeper.**

➢ ***Peptic* ulcer:** is an ulcer occurring in the areas of the GIT that are exposed to the acid –pepsin secretion as in:

- Stomach
- Duodenum
- Lower esophagus
- Margin of gastroenterostomy
- Meckel diverticulum that have an ectopic gastric mucosa

Pathogenesis:

Peptic ulcer appears to be produced by an **imbalance** between the gastroduodenal mucosal defense mechanisms and the damaging forces.

Defense forces:

1- Surface mucous layer secreted by the epithelial cells.

2- Bicarbonate secretion into the mucous.

3- Mucosal blood flow

4- Apical surface of the mucosal cells protect against back diffusion of H ion.

5- Epithelial regenerative capacity

6- Elaboration of prostaglandins from adequate blood flow

Aggressive forces:

1- Gastric acidity (Hcl) secretion.

2- Peptic enzymes.

3- Other induced cause:

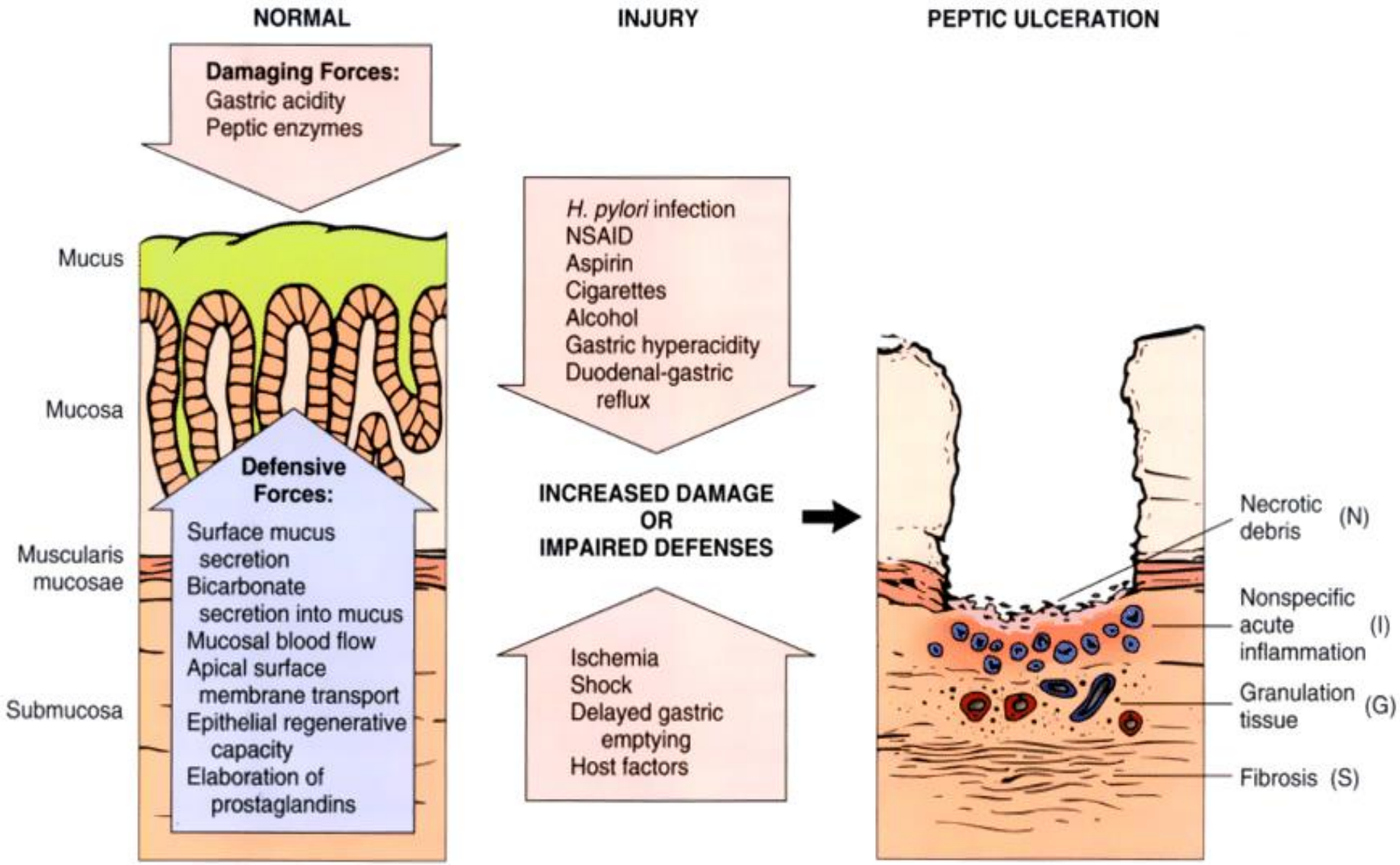
a- H. pylori infection.

b- Aspirin

c- NSAIDs

d- Cigarette

e- Alcohol


NORMAL
INJURY
PEPTIC ULCERATION
Damaging Forces:
Gastric acidity
Peptic enzymes
Mucus
Mucosa
Muscularis mucosae
Submucosa
Defensive Forces:
Surface mucus secretion
Bicarbonate secretion into mucus
Mucosal blood flow
Apical surface membrane transport
Epithelial regenerative capacity
Elaboration of prostaglandins
H. pylori infection
NSAID
Aspirin
Cigarettes
Alcohol
Gastric hyperacidity
Duodenal-gastric reflux
INCREASED DAMAGE OR IMPAIRED DEFENSES
Ischemia
Shock
Delayed gastric emptying
Host factors
Necrotic debris (N)
Nonspecific acute inflammation (I)
Granulation tissue (G)
Fibrosis (S)

Morphologically:

1-Site: *G.U usually located at the lesser curvature

*D.U at the first 2.5 cm of the duodenum

2- Size: 2-4 cm, sometimes larger

3- Number: usually solitary, sometimes two

4- Shape: round- oval, the margin of the crater are punched out, perpendicular unlike ulcerated cancers, there is No significant elevation or beading of the edges.

5-Floor: Clean

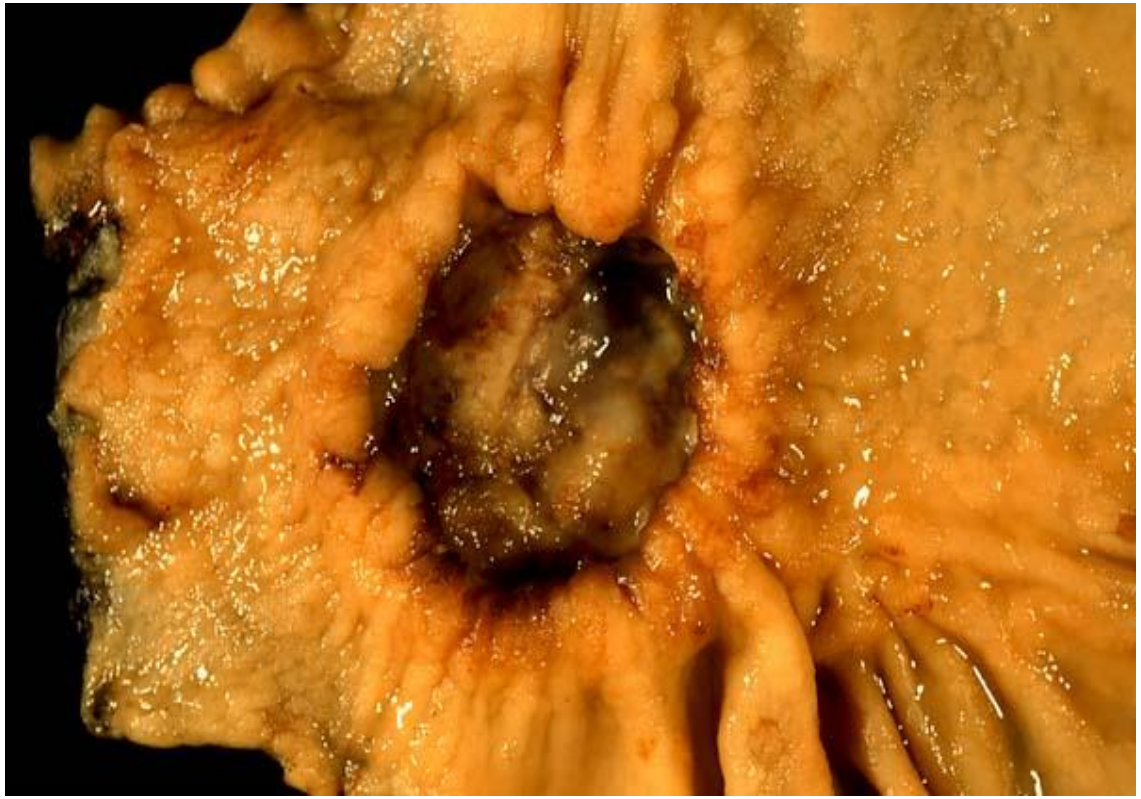
6-Base: Firm

7-Edge: Overhanging

8-Depth: may vary.

Feature	Benign ulcer	Malignant ulcer
Margins	Punched out, perpendicular	Elevated, beaded, sloping
Floor	Clean	Necrotic debris
Surrounding mucosa	Spoke wheel pattern	No spoke wheel Pattern

Chronic gastric ulcer



Malignant gastric ulcer

Microscopically:

- **Four zones** could be identified.
- Base &margin have a thin layer of necrotic fibrinoid debris
- Beneath is a layer of neutrophilic inflammatory cell infiltration
- In the deeper layers there is a granulation tissue formation.
- The granulation tissue rests on a fibrous tissues scarring.

Clinical features:

- **Epigastric pain**
- Might present with **complications.**

Complications:

1- Healing and scarring: which lead to contracture, caused by contraction of the fibrous scar→ *pyloric obstruction especially if the ulcer is located in the prepyloric area → vomiting, dehydration and hyperkalemic alkalosis.

* hour-glass deformity, if the ulcer is higher up in the stomach.

2- Bleeding: occur in 1/3 of patients &lead to:

- Hematemesis coffee ground appearance due to blood hemolysis by acid and melena
- Iron deficiency anemia due to *chronic* loss of small amounts of blood

3- Perforation:

4- Penetration: of the ulcer into the adjacent structures e.g. small intestine.

5- Malignant transformation: occur in less than 1% of G.U

NOTE: D.U *never* show a malignant transformation

TUMORS OF THE STOMACH

➢**Benign:**

- Polyps (hyperplastic or adenomatous), Leiomyomas and Lipomas.

➢**Malignant:**

- Adenocarcinoma and Lymphoma

➢**Others:**

- Gastro -Intestinal “Stromal” Tumor (GIST) and Carcinoid (neuroendocrine)

.

Benign tumors:

❖Gastric polyps

- **Polyp** is any nodule or mass that projects above the level of the surrounding mucosa. They are uncommon and classified as non-neoplastic or neoplastic.

➢**Hyperplastic polyps** (the most frequent; 90%) are small, sessile and multiple in about 25% of cases. There is hyperplasia of the surface epithelium and cystically dilated glandular tissue

➢**Adenomatous polyp (adenoma)**

- (10% of polypoid lesions): They contain proliferative dysplastic epithelium and hence **have malignant potential.** They are usually single, and may grow up to 4 cm in size before detection.

Gastric Adenocarcinoma

- It is the most common malignancy of the stomach, comprising more than 90% of all gastric cancers.
- Gastric cancer incidence varies markedly with geography. it is particularly high in countries such as Japan.
- It is more common in lower socioeconomic groups.
- There are mainly two subtypes of carcinoma**: intestinal and diffuse.** These sub-types appear to have different pathogenetic mechanisms of evolution.

Etiology &pathogenesis:

❖In intestinal type adenocarcinoma

1- Diet

* Nitrites and nitrates used for preservation of food .
* Smoked food &pickled vegetables
*Increased salt intake
* Lack of fresh fruit and vegetables (antioxidants present may inhibit nitrosation)
* Cigarette smoking.
* Low socioeconomic status

2- Host factors:

A. Chronic gastritis with intestinal metaplasia whether caused by *Helicobacter pylori Infection* **or** *Autoimmune gastritis*.

B. Adenomatous polyps

C. Genetic:

* Family history of gastric carcinoma

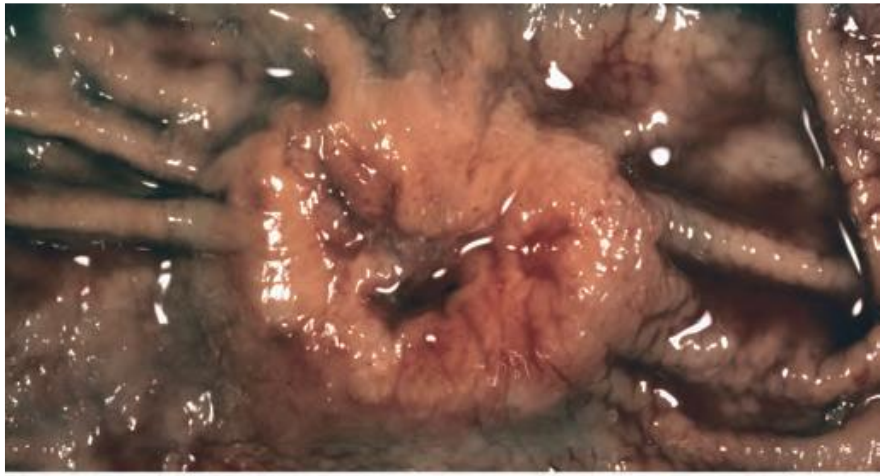
Grossly:

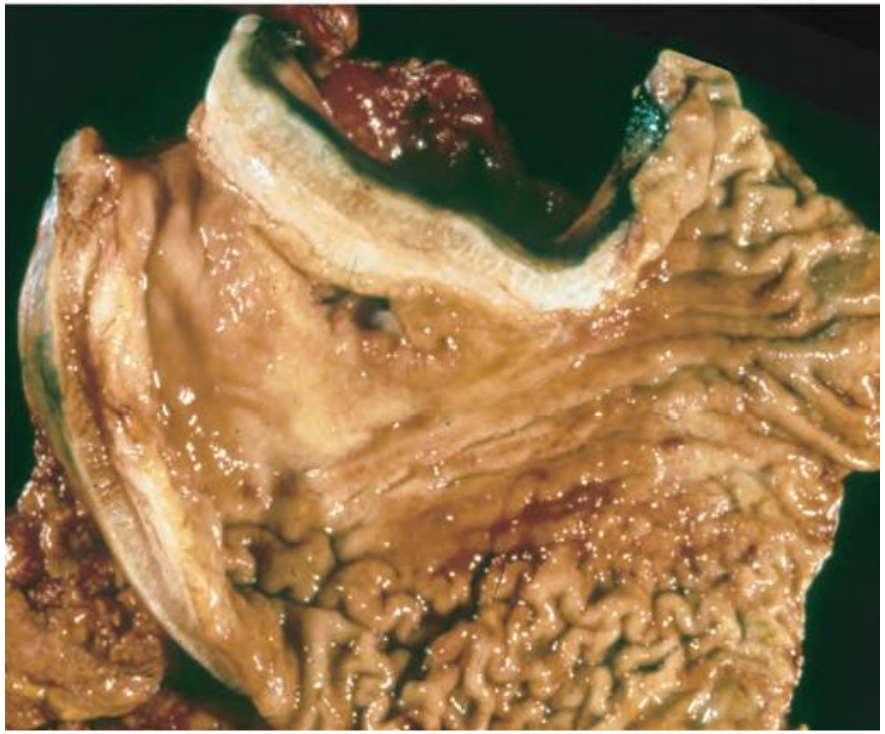
- Most of them located at the **antrum**

1- They are either exophytic (fungating) OR

2- Ulcerative (excavating) OR

3- Flat or depressed---diffuse thickening of the wall without obvious mass (linitis plastica and it look like leather bottle.

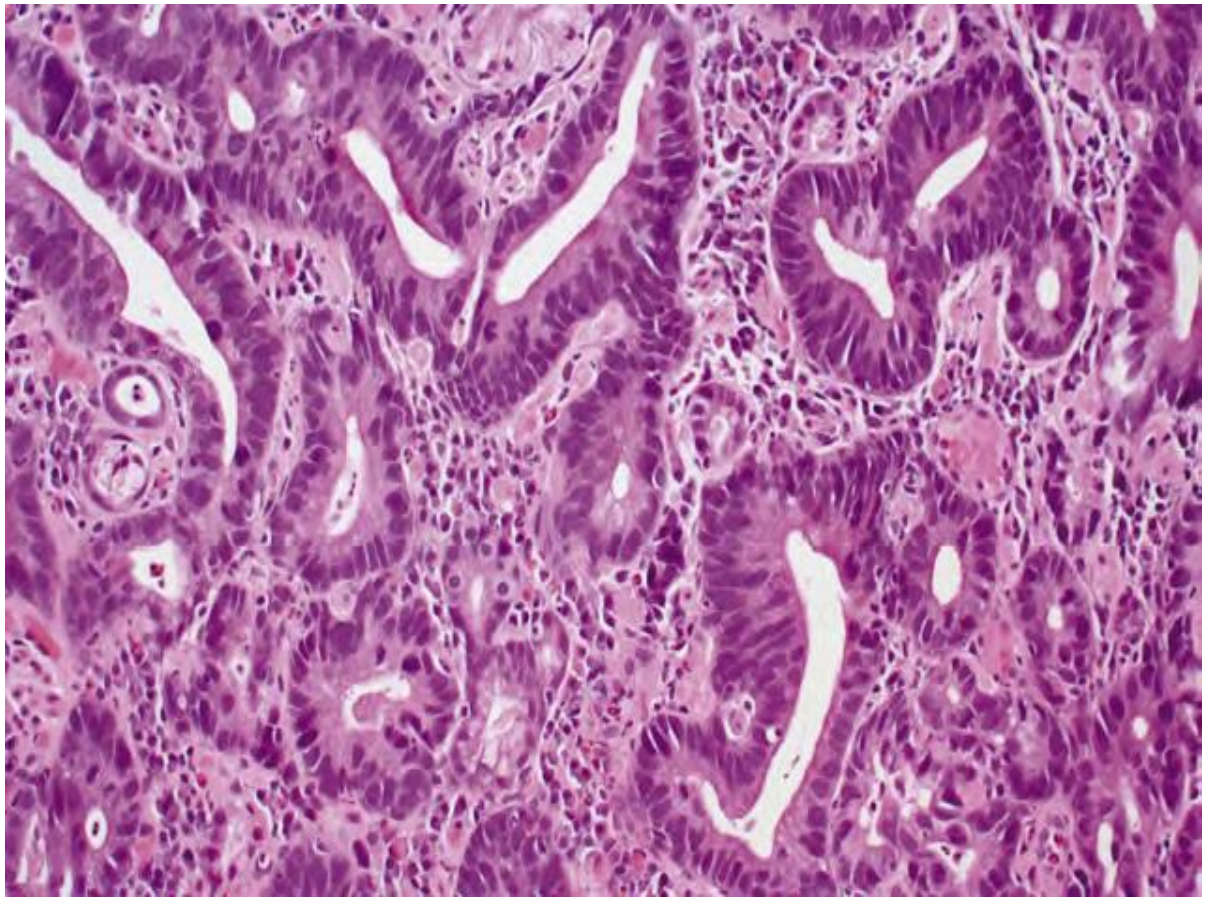




➢Microscopically:

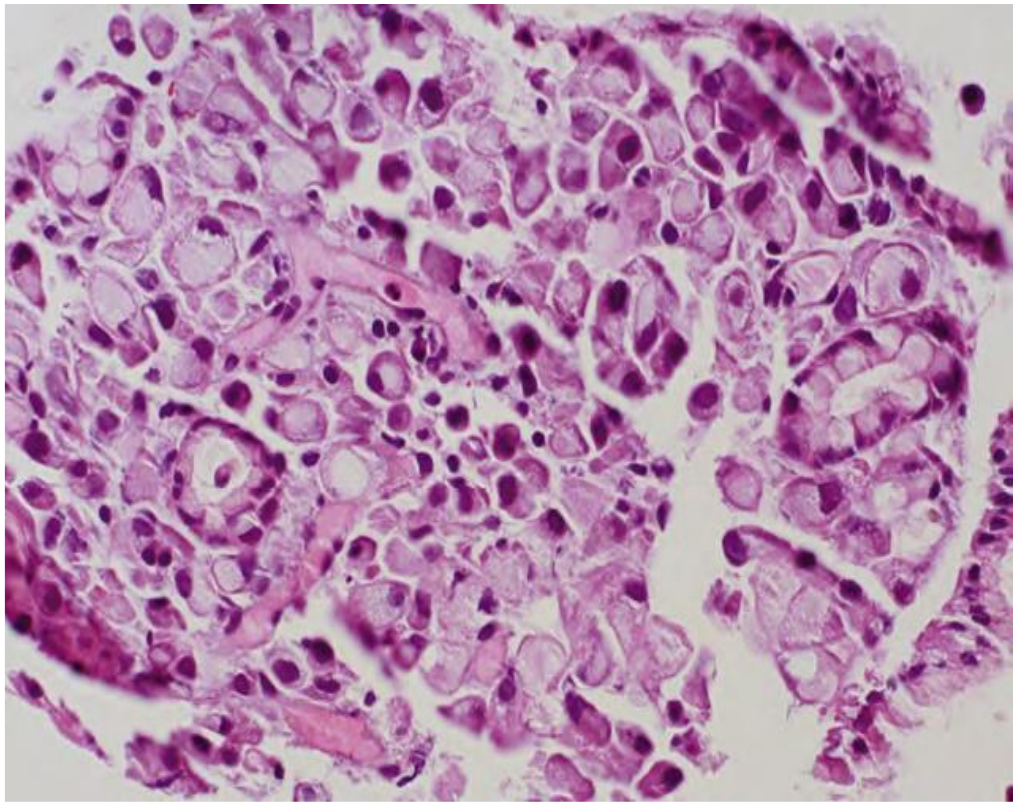
1- Intestinal type :

- Malignant cells forming neoplastic intestinal glands resembling those of colonic adenocarcinoma.
- Occur in old age group (55) years
- Better prognosis than other type



2- Diffuse type:

- The tumor is less differentiated
- The cells accumulate intracellular mucin forming a signet ring
- No glandular formation
- Occur in a slightly younger age group (48) years
- Worse prognosis



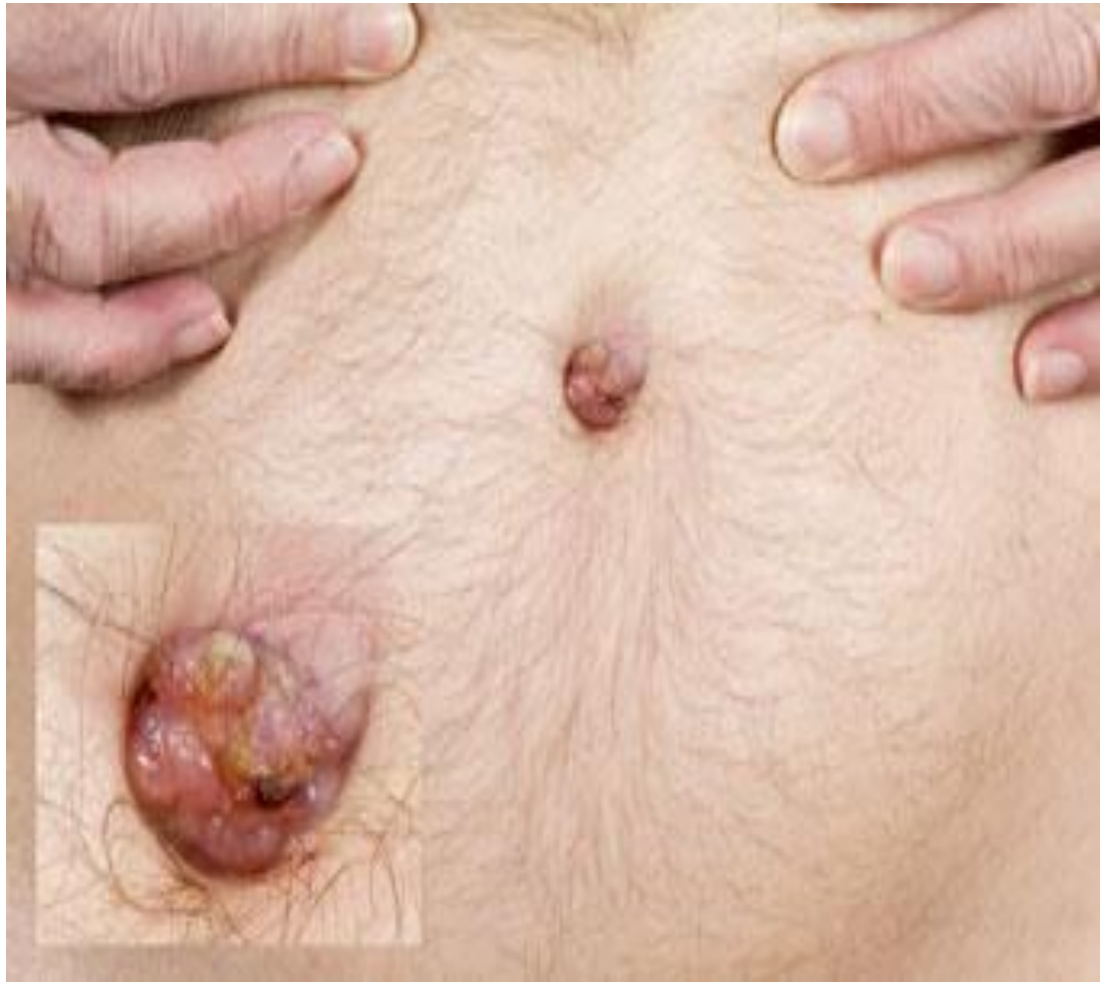
- Risk factors: undefined except rare inherited **mutation of E cadherin**
- Infection with H pylori and chronic gastritis often absent

Spread:

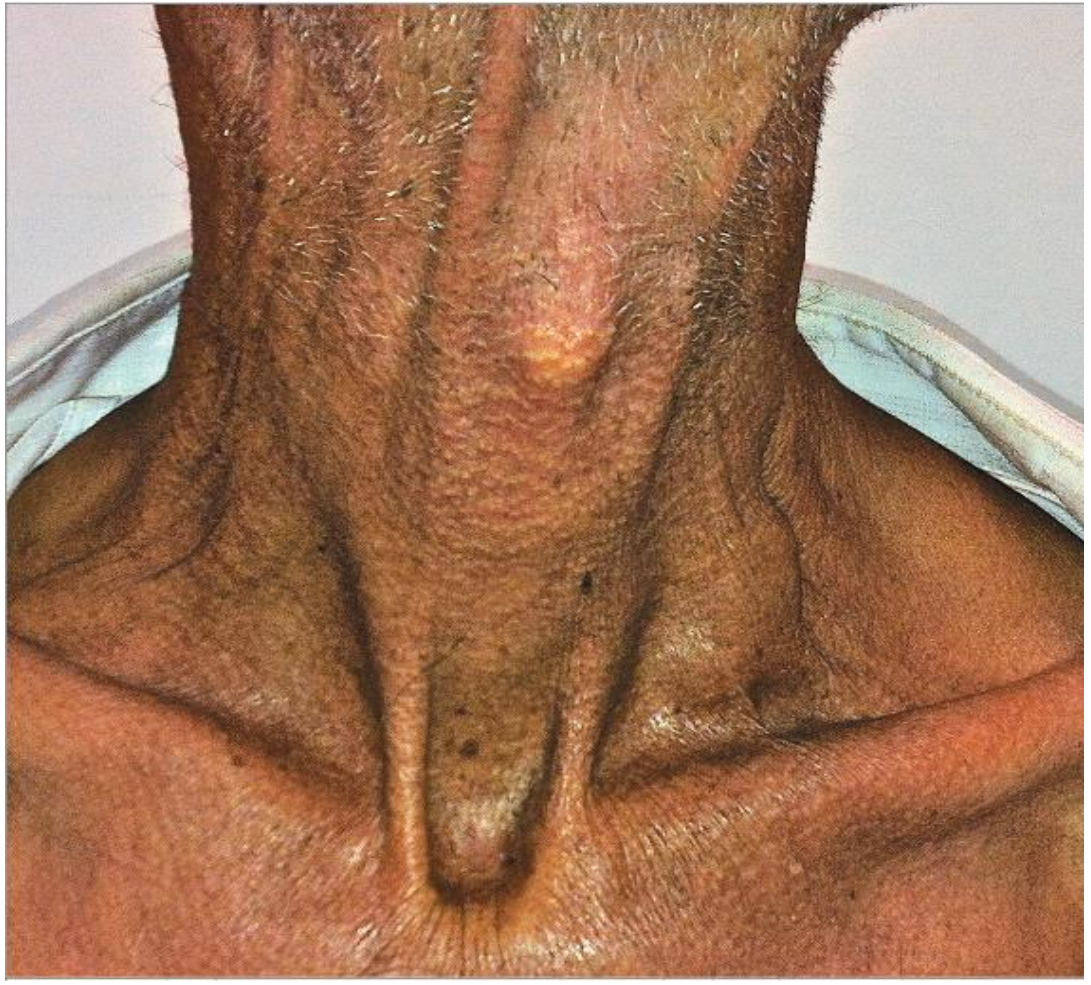
- Local spread: to adjacent organs: e.g. esophagus, duodenum.
- Lymphatic spread: to regional lymph nodes
  - For obscure reasons the earliest LN metastasis may sometimes involve a supraclavicular lymph node (Virchow's node)
- Transcoelomic spread: in which the tumor cells shed into the peritoneal cavity and if it get implanted on both ovaries it will form the interesting *KRUKENBERG TUMOR*
- Hematogenous spread: to the liver and lung.

Sister Mary Joseph’s nodule

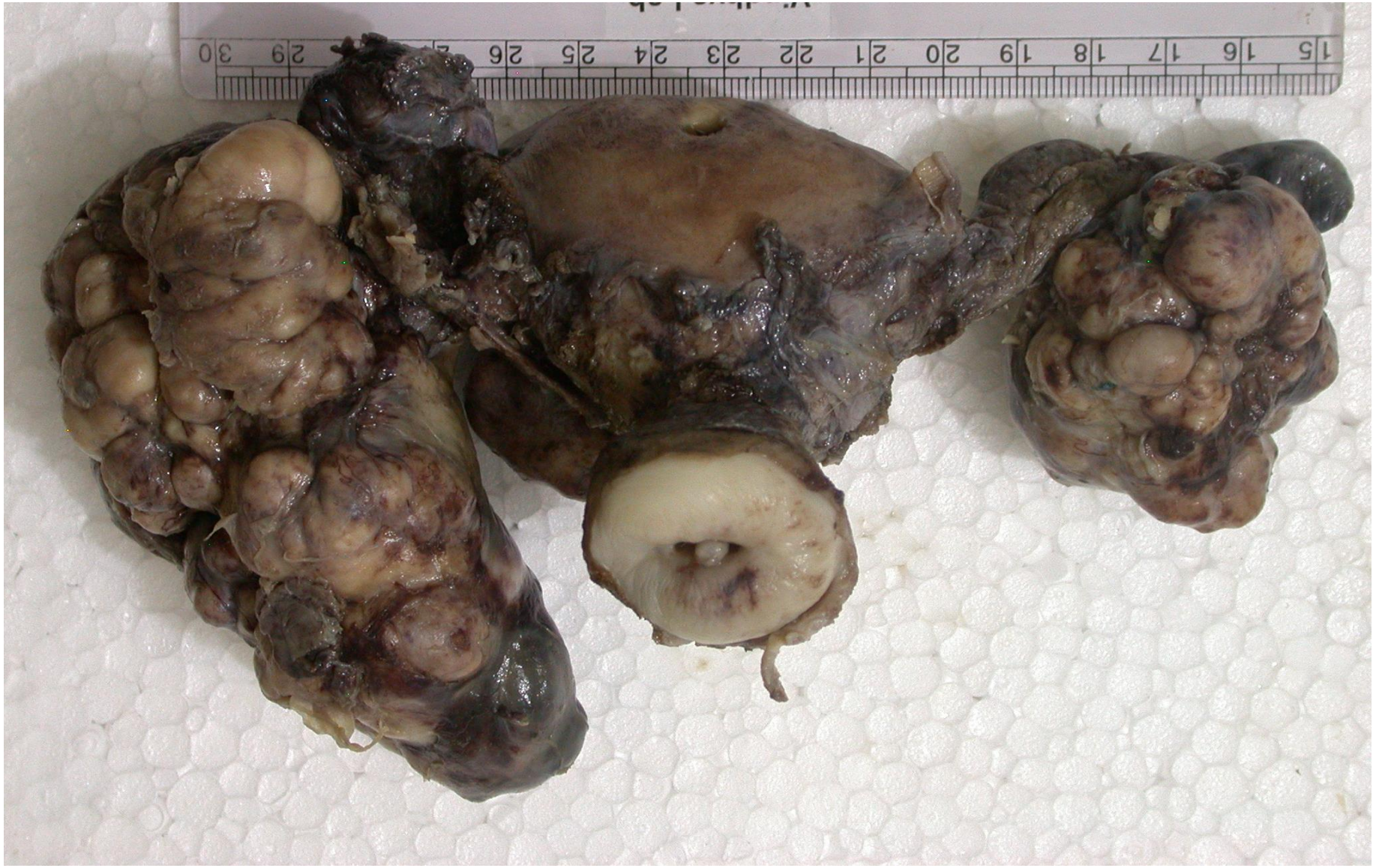
- 'nodule' in the umbilicus was often associated with advanced malignancy in the pelvis or abdomen half cases is associated with gastric, colonic or pancreatic cancers, other causes : ovarian and uterine cancers



Virchow's node



Krukenberg's tumor



Clinical features:

➢The most important are:

- Anorexia (loss of appetite)
- Severe weight loss with epigastric pain
- Anemia

Prognosis:

➢Prognostic indicators are;

1.The depth of invasion and

2.The extent of nodal and distant metastasis

Gastric Lymphoma

- 5% of all gastric malignancies.
- Nearly all primary gastric lymphomas are B-cell type and of mucosa-associated lymphoid tissue (MALT lymphomas).
- The majority of gastric lymphomas (>80%) are associated with chronic gastritis and H. pylori infection.
- Generally, the prognosis of gastric lymphoma is **better** than carcinoma.

Gastrointestinal Stromal Tumor

- Most common **mesenchymal tumor** of the abdomen, and more than half of these tumors occur in the stomach.

Epidemiology

- The peak incidence of gastric GIST is **around 60 years** of age, with less than 10% occurring in persons younger than 40 years of age.

Pathogenesis:

- GISTs appear to arise from the interstitial cells of Cajal, which express **c-KIT,** are located in the muscularis propria, and serve as pacemaker cells for gut peristalsis.
- Approximately **75% to 80%** of all GISTs have **mutations of c-KIT,**
- Another **8%** of GISTs have mutations platelet-derived growth factor receptor A **(PDGFRA)**

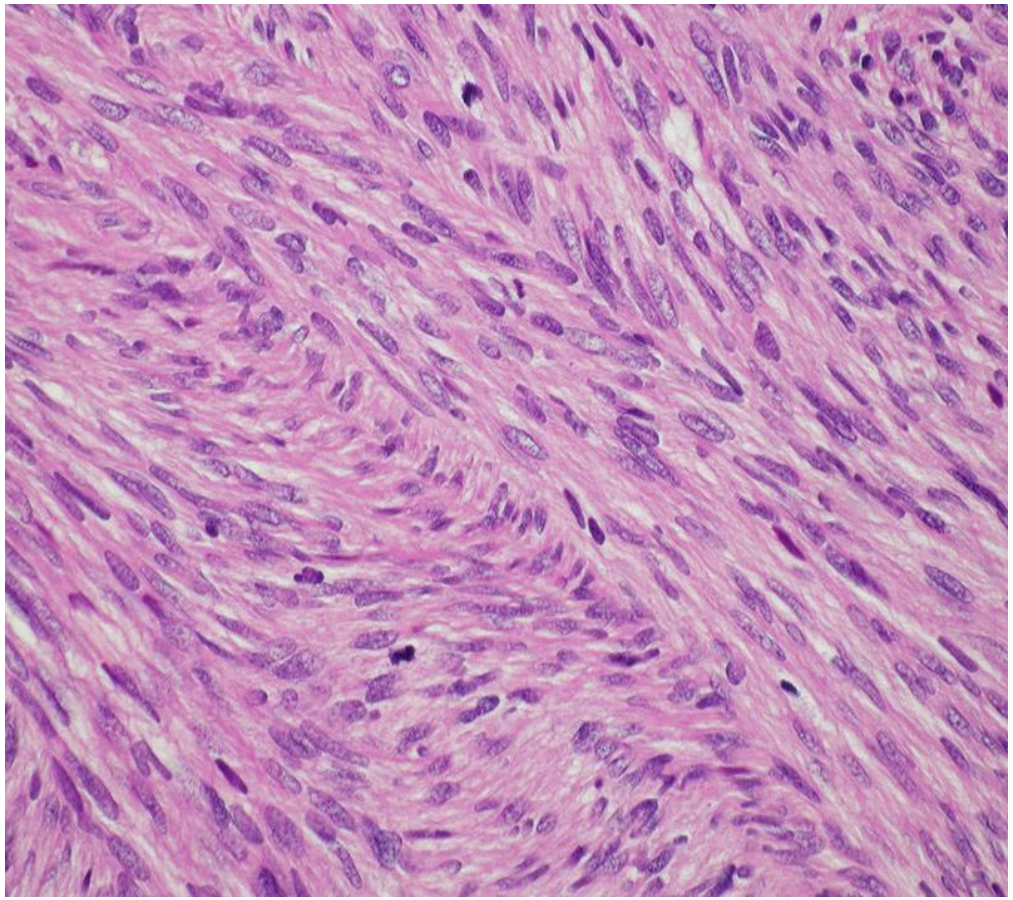
Morphology

Gross:

Solitary, well circumscribed, fleshy, submucosal mass.

Mic:

Composed of thin, elongated spindle cells or plumper epithelioid cells.



Clinical Features:

- Symptoms of GISTs at presentation may be related to mass effects or mucosal ulceration.
- Treatment: Complete surgical resection is the primary treatment for localized gastric GIST.
- **The prognosis** correlates with:

tumor size, mitotic index, and location, with gastric GISTs being somewhat less aggressive than those arising in the small intestine.

Recurrence or metastasis is rare for gastric GISTs less than 5 cm across but

common for mitotically active tumors larger than 10 cm.

➢Patients with unresectable, recurrent, or metastatic disease often respond to imatinib, an inhibitor of the tyrosine kinase activity of c-KIT and PDGFRA.

Metastases:

- May form multiple small serosal nodules or fewer large nodules in the liver
- spread outside of the abdomen is uncommon

Thank you