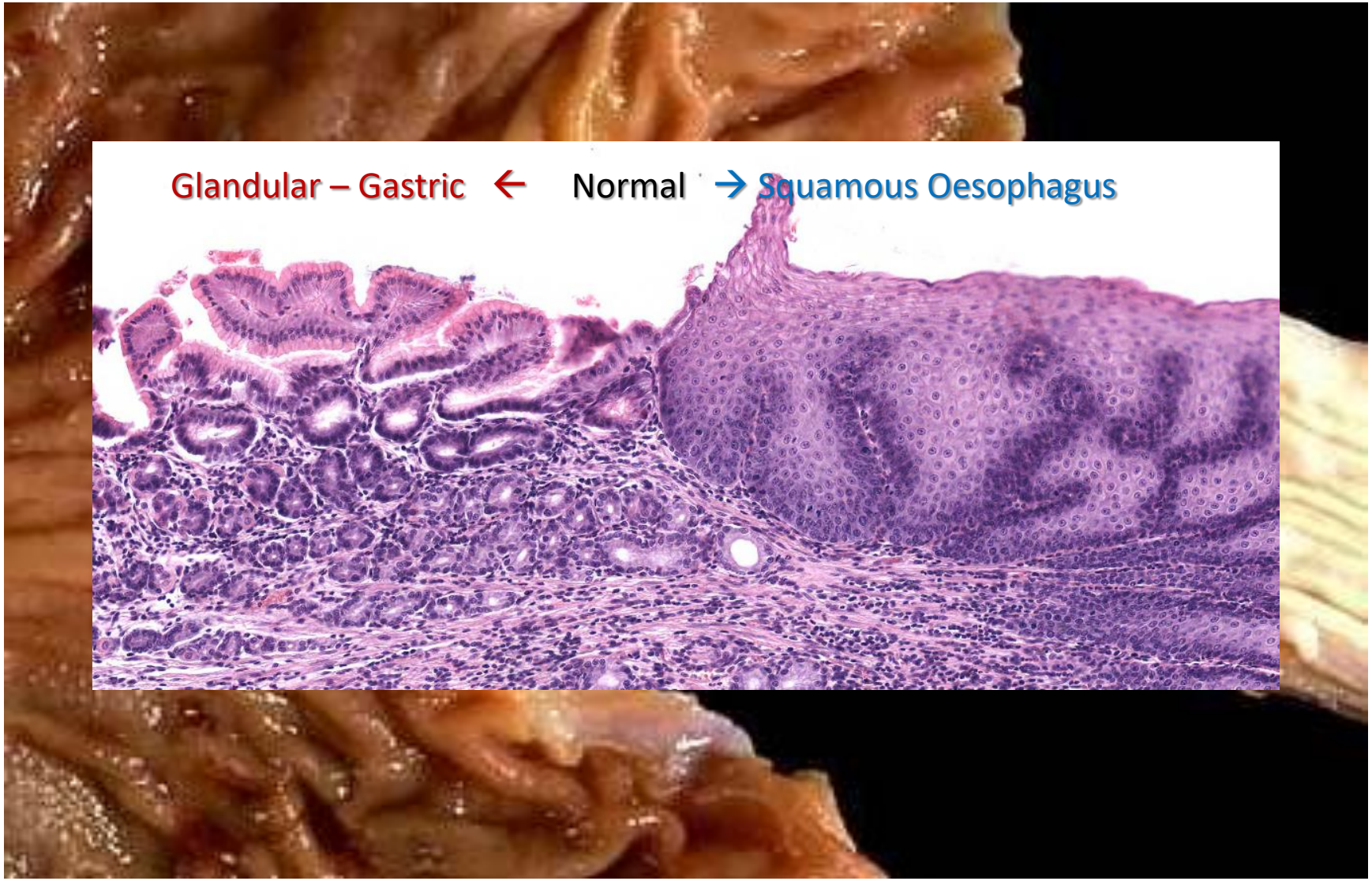
GIT pathology

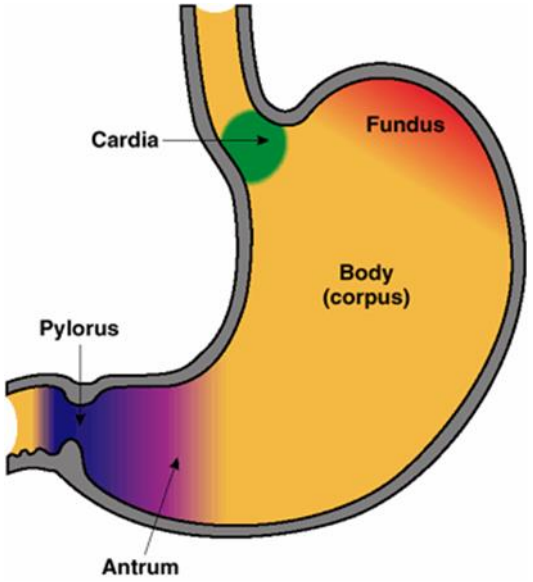
Dr. Methaq Mueen

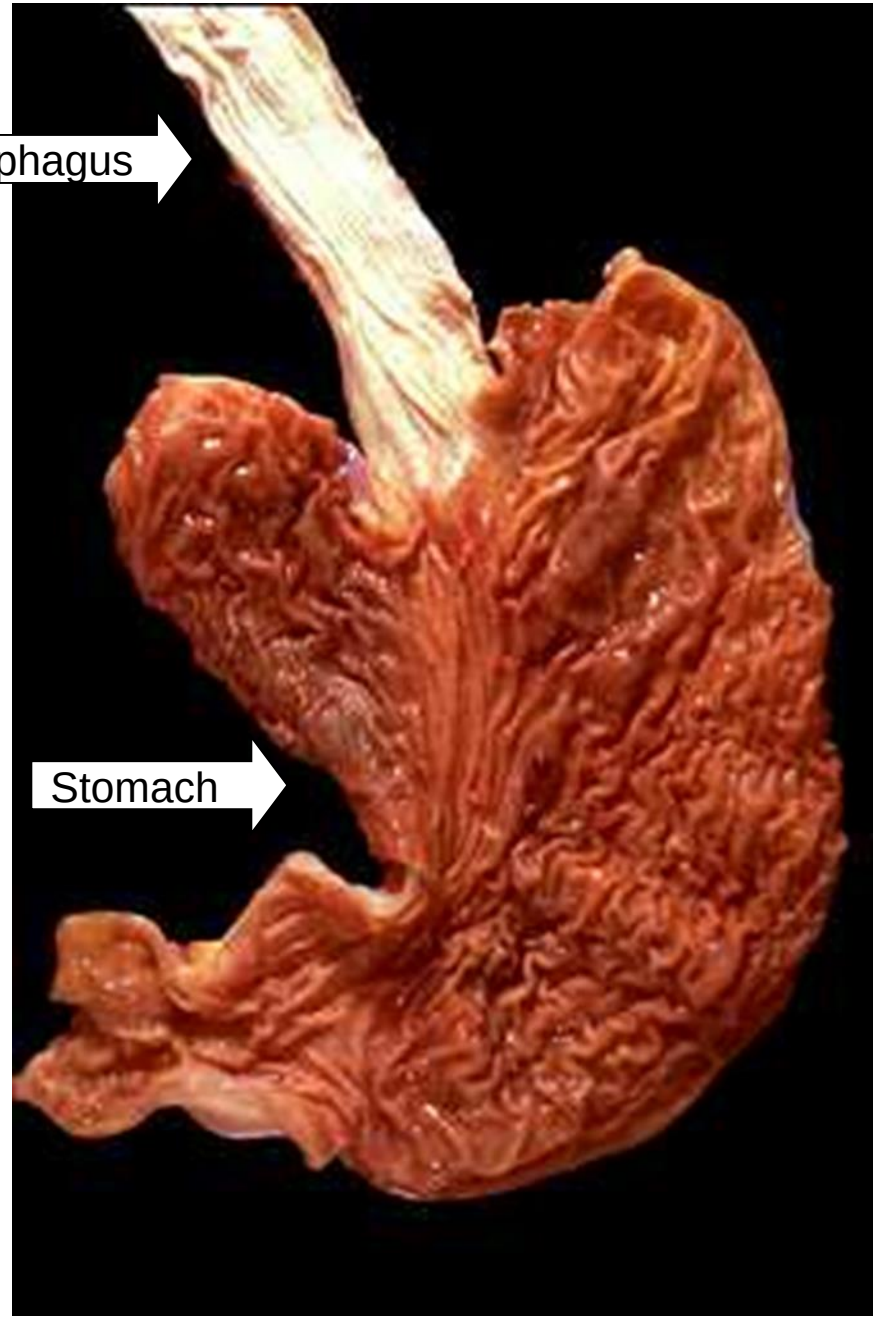
Lec 3: stomach

Esophagus & Stomach Normal



The stomach is divided into the following anatomic regions:
cardia,
fundus,
corpus or body,
antrum
and pylorus
The supermedial margin is termed lesser curvature and the inferolateral margin is termed greater curvature.
Internally, the mucosa is thrown into coarse folds **called rugae**





Normal histology

The normal gastric wall has the same layers as does the rest of the gut:

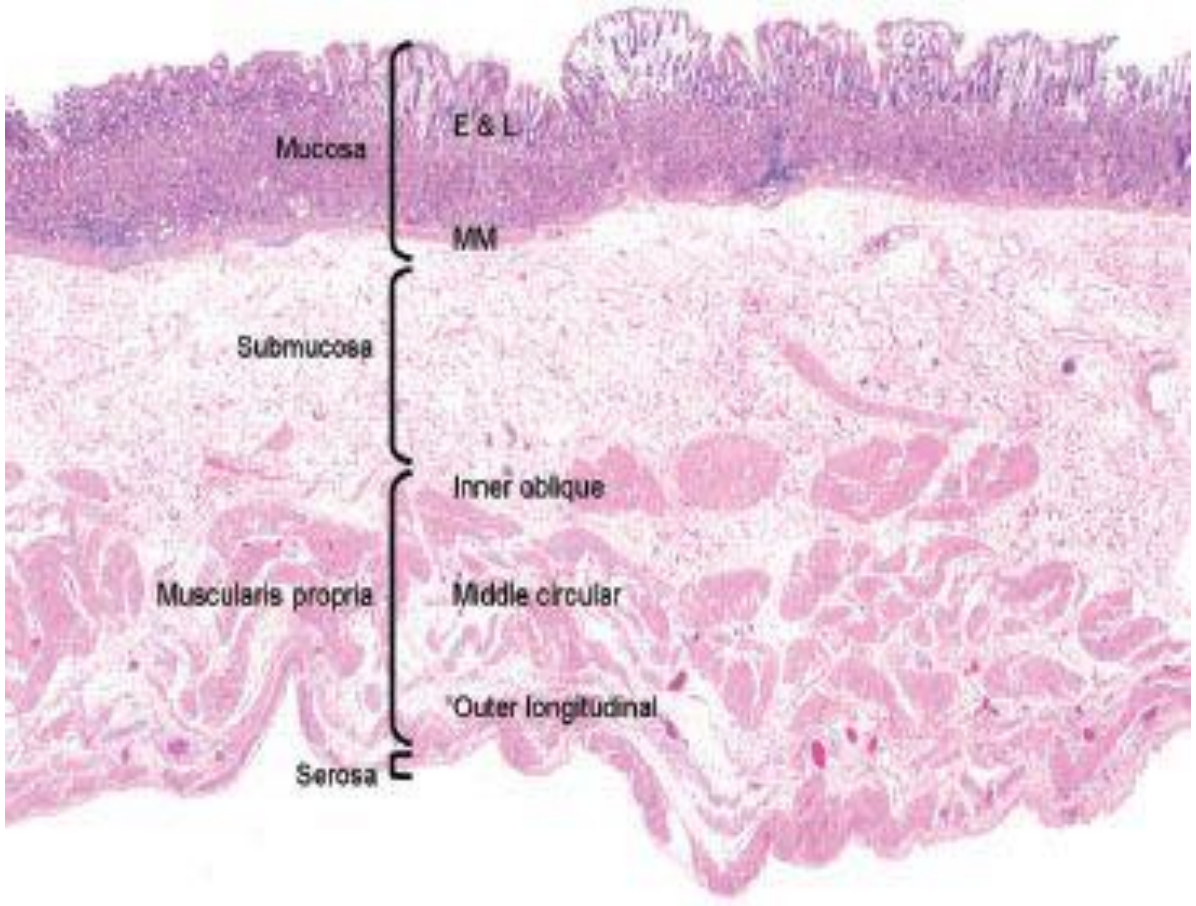
Mucosa:

- Epithelium and
- Lamina propria
- Muscularis mucosae at the base

Submucosa

Muscularis propria

Subserosa



- **Histology**:

A-The mucosa:

The entire stomach epithelium is composed of 2 major compartment:

1-the foveolar (surface epithelium and gastric pits(invagination from the surface), is columnar mucinous epithelium.

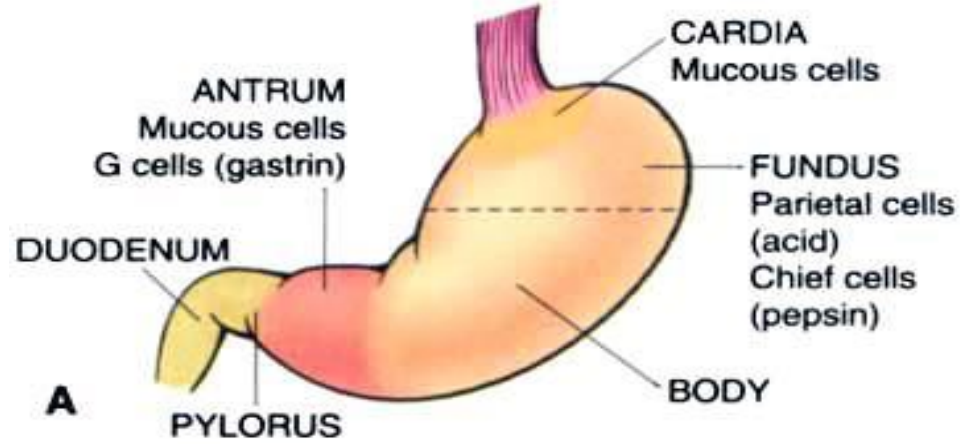
2- glandular component.differs according to the region:

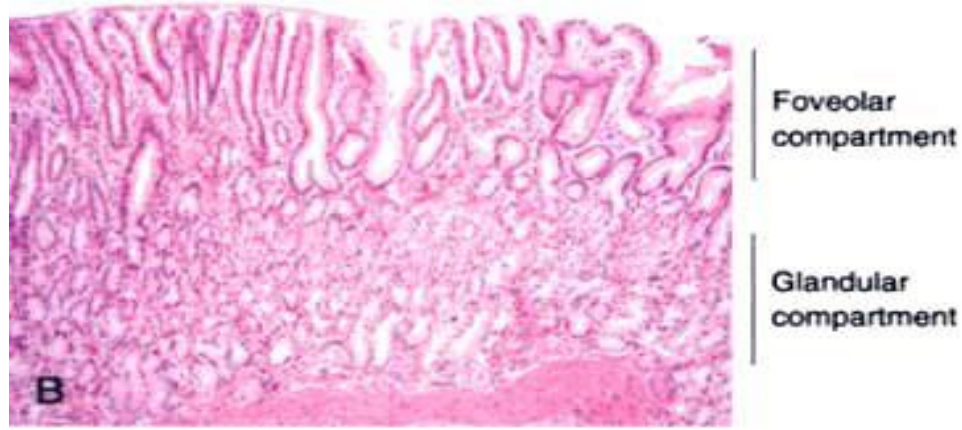
*

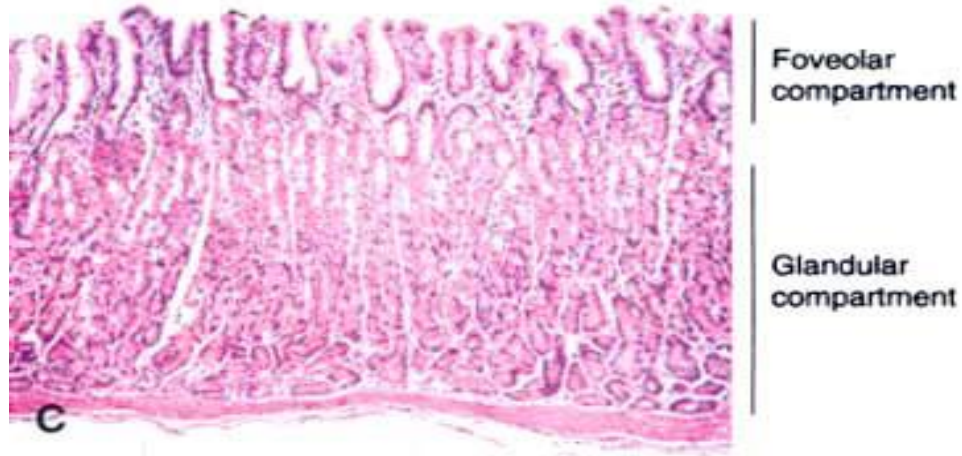
- The regions of the stomach are divided by the type of underlying glands:
- **Antral mucosa**: found in the borders of the stomach (cardia, antrum and pylorus) the glands loosely packed , mucinous and occupy about half of the epithelium.
- (foveolar :secretory gland 1:1)

- **Fundic (Oxyntic) mucosa**: found in the digestive regions of the stomach(fundus and body):the glands are tightly packed, composed of **chief cells (purple enzyme secreting)** that secrete pepsin, and **parietal cells** (pink acid secreting) that secrete acid (HCl) and intrinsic factor (IF), with some endocrine cells and mucous neck cells. The glandular portion occupy three fourths of the mucosal thickness.

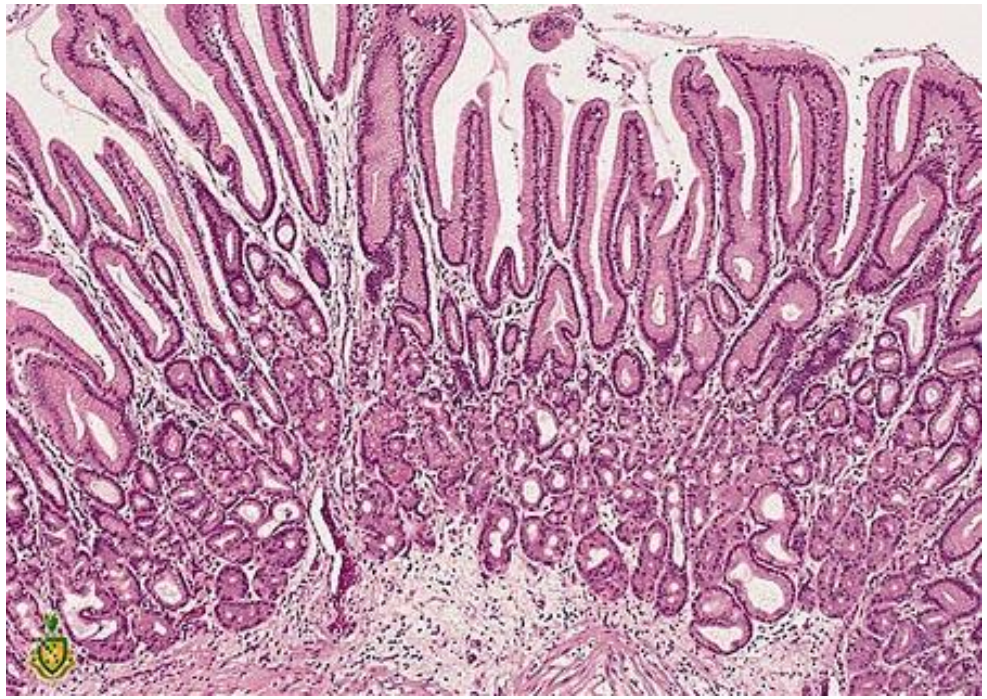
(foveolar :secretory gland 1:4)


CARDIA
Mucous cells
ANTRUM
Mucous cells
G cells (gastrin)
FUNDUS
Parietal cells
(acid)
Chief cells
(pepsin)
DUODENUM
BODY
A
PYLORUS

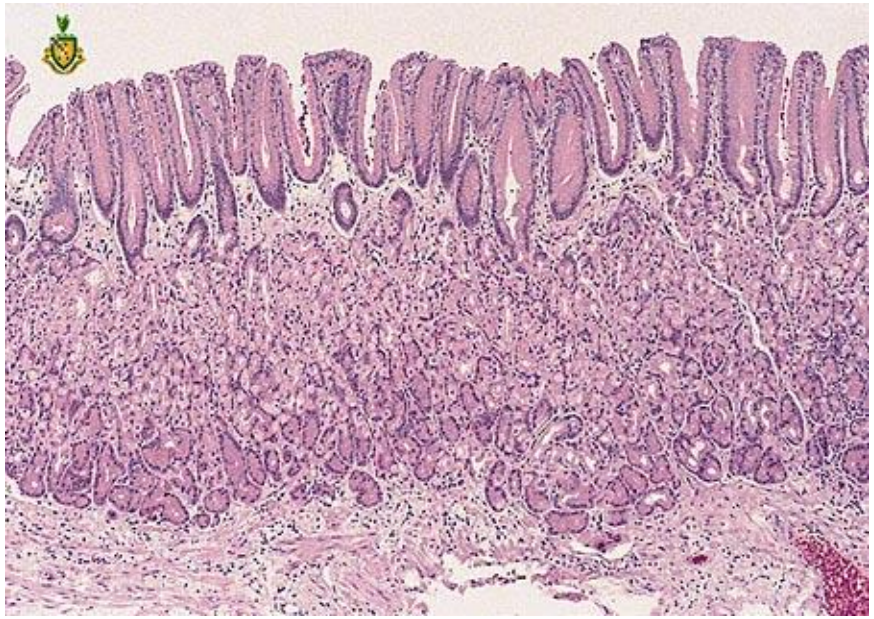

Foveolar
compartment
Glandular
compartment
B


Foveolar
compartment
Glandular
compartment
C

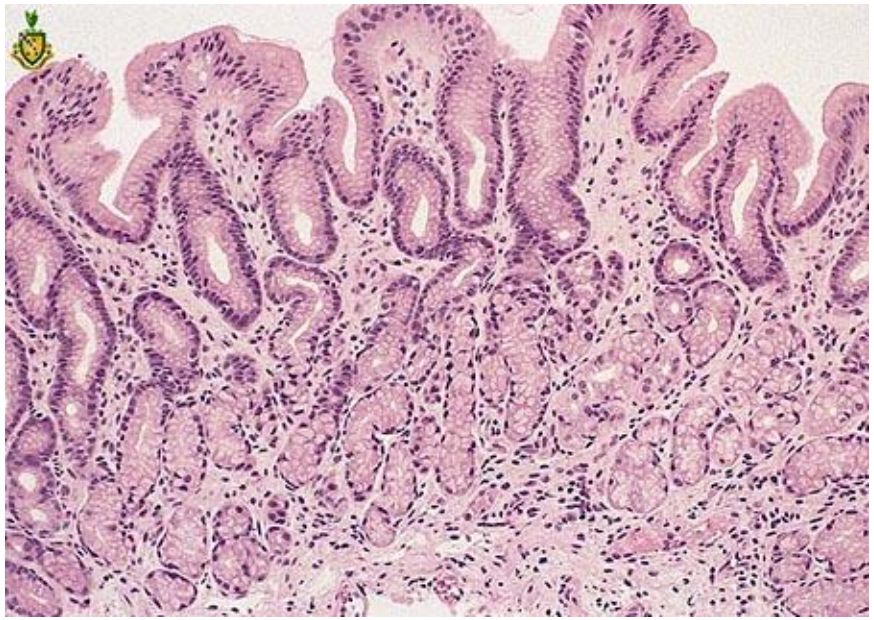
Mucosa has two compartments:
1-Superficial pit or foveolar compartment
2-Deep glandular compartment



NORMAL CARDIAC MUCOSA (1:1)

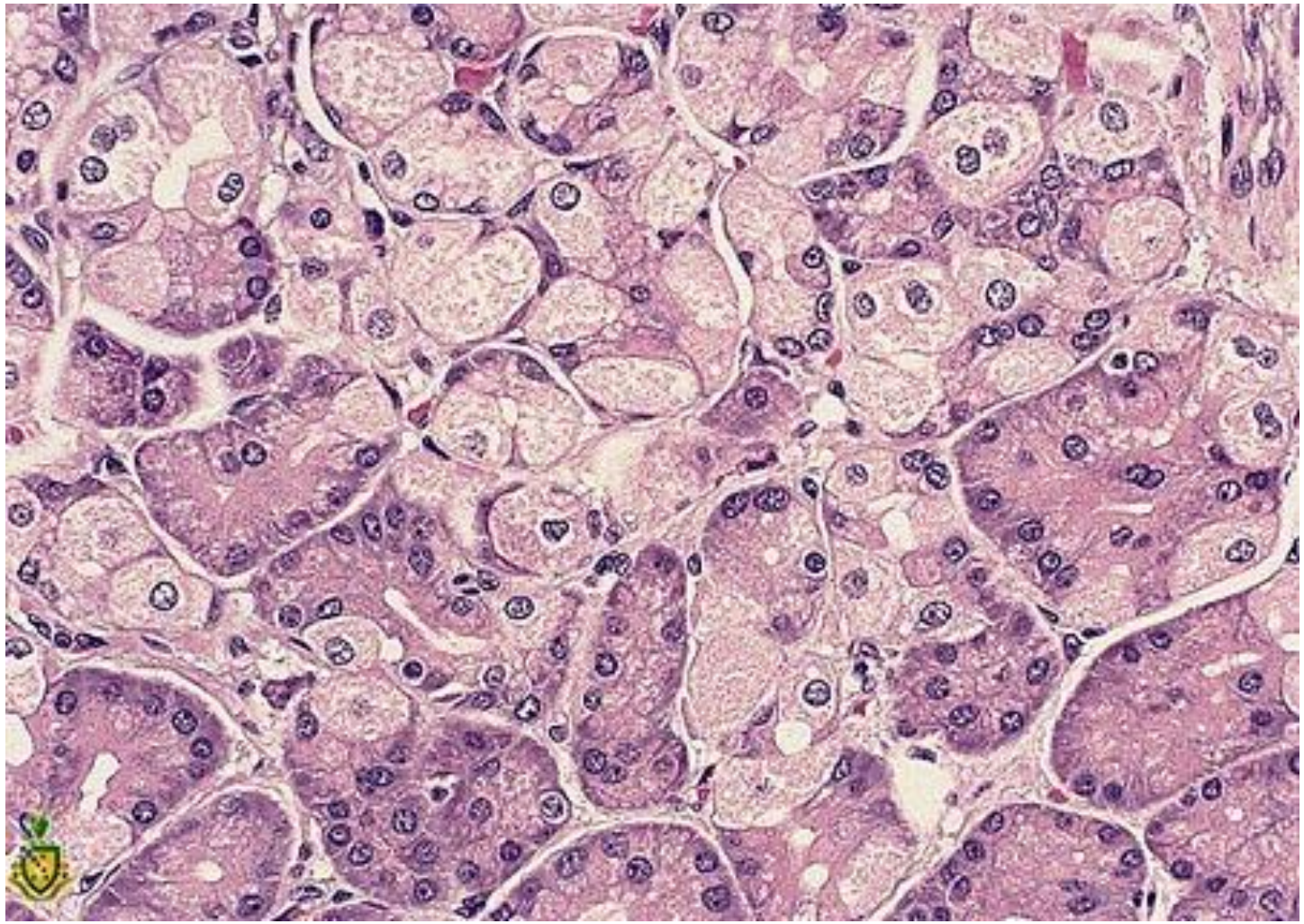


CORPUS, FUNDIC MUCOSA (1:4)



ANTRAL (PYLORIC) MUCOSA (1:1)

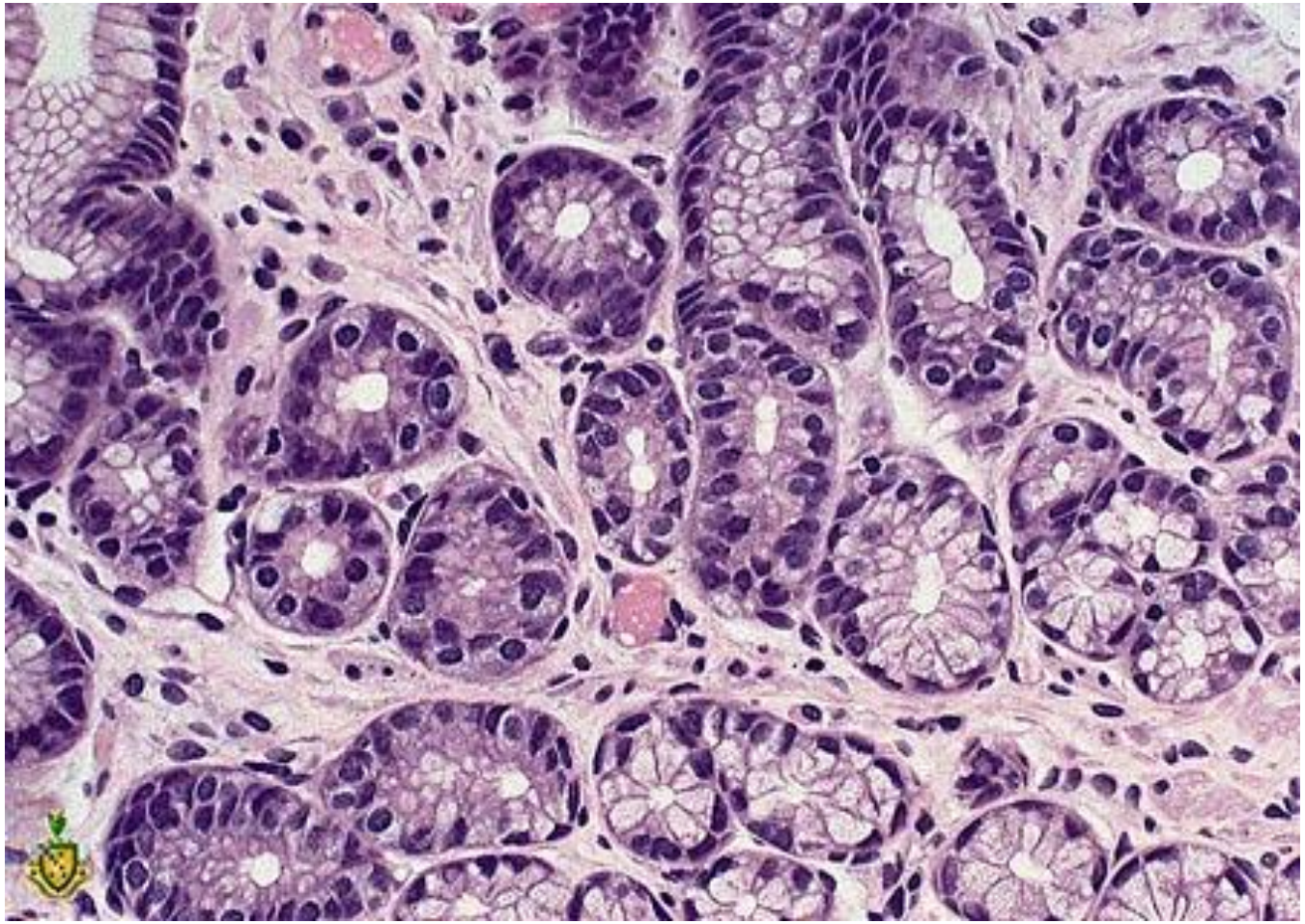
GLANDULAR COMPARTMENT OF THE BODY MUCOSA



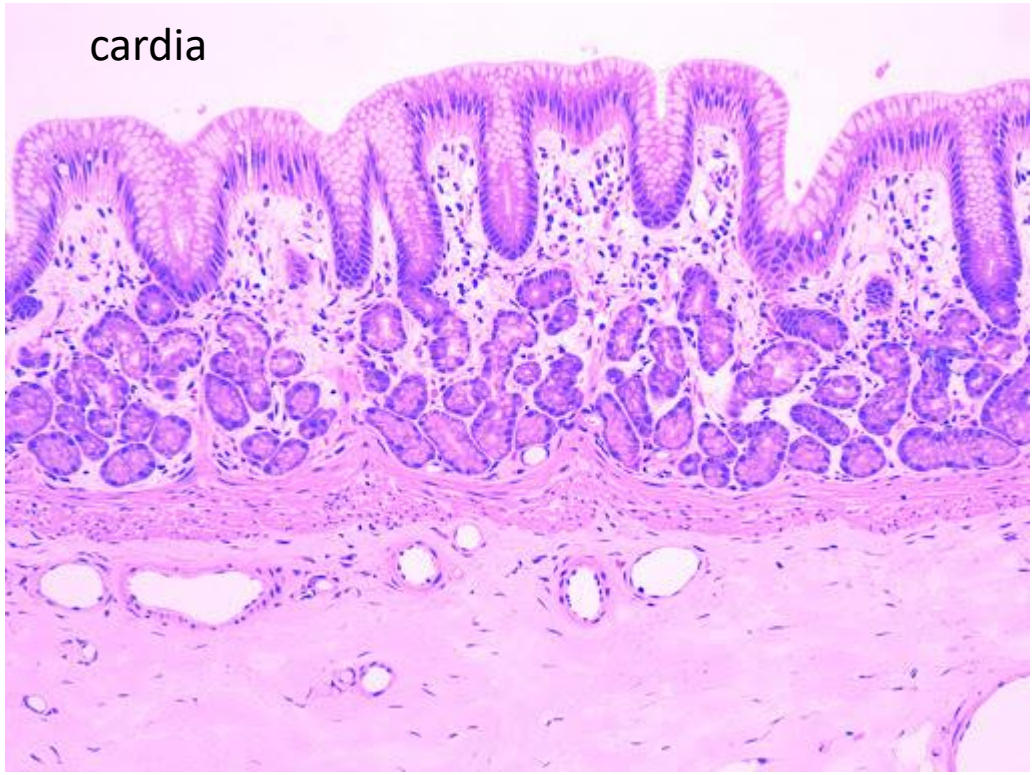
The pale cells: Parietal cells

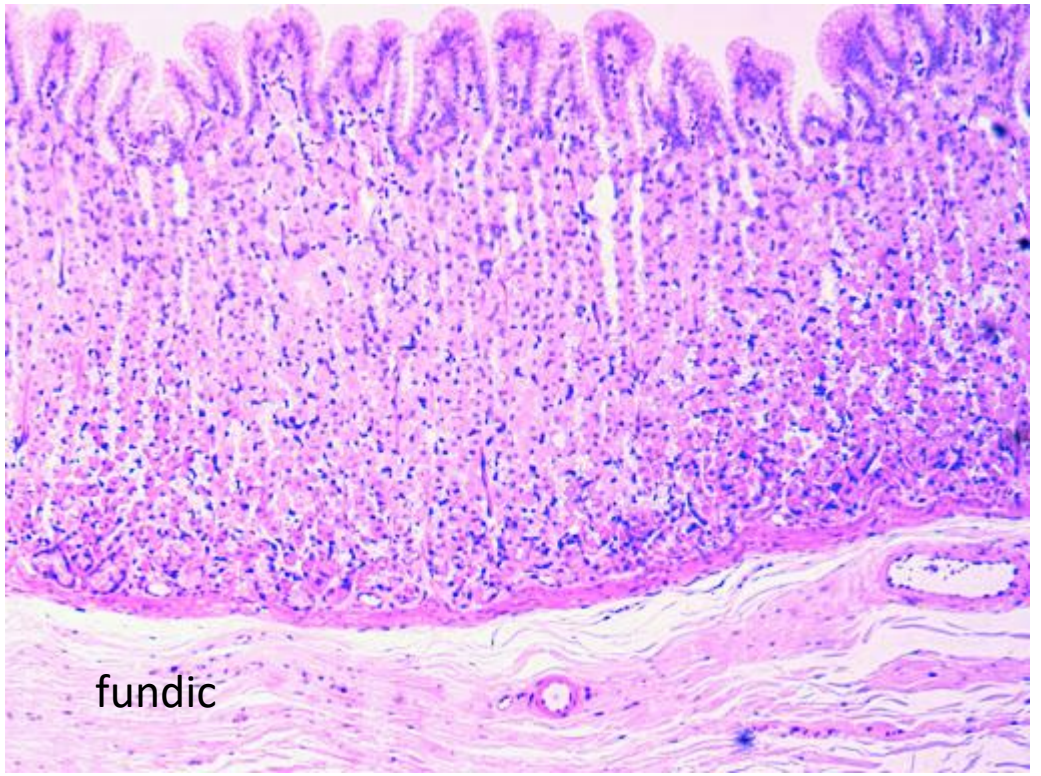
Darker cells: Chief cells

NECK REGION OF THE ANTRAL MUCOSA



The pits are at the top and the glands at the base. In between, the tubules are lined by a mucus-containing epithelium with nuclei that are slightly larger than in either the pits or the glands. This is the neck region, the proliferative zone for all gastric mucosae. The pale, pear-shaped cells with finely granular, gray cytoplasm at the base of the necks and glands are the gastrin-producing or G cells.


cardia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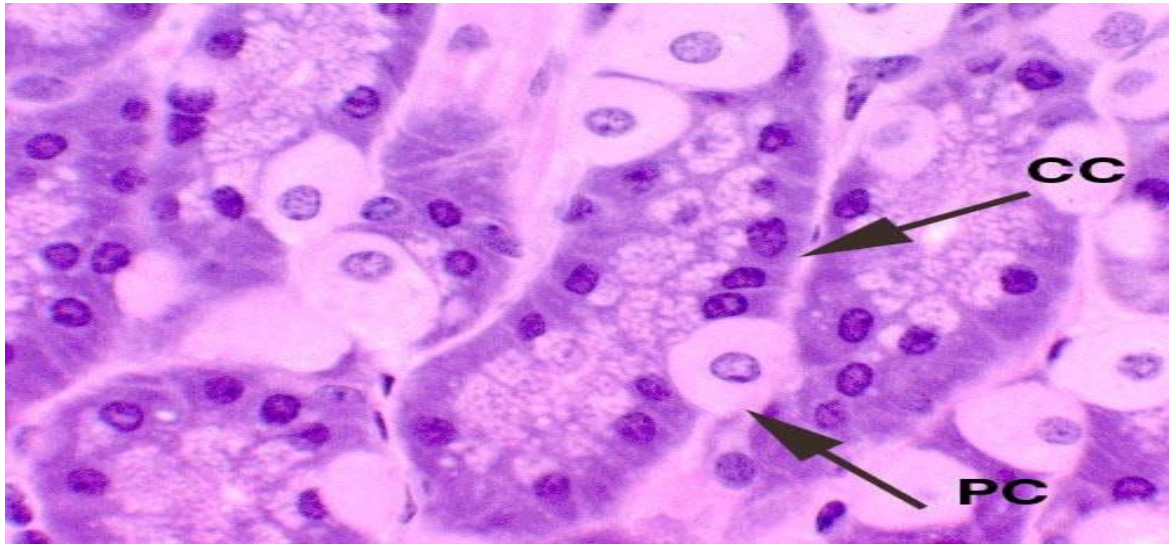

CC
PC

- **Gastritis:**

It is defined as inflammation of the gastric mucosa.

1- Acute gastritis with **neutrophilic** infiltration.

2- Chronic gastritis with **lymphocytic** infiltration.

1- Acute gastritis:

Is acute inflammation of the gastric mucosa

- **Etiology:**

1-Heavy use of(non steroidal anti-inflammatory drugs NSAID)

2-alcohol intake

3-Heavy smoking

4-Uremia

5-Severe stress (burn , trauma, surgery)

6-Systemic infection (e.g salmonellosis).

7-Treatment with chemotherapeutic drugs.

- **Clinical features:**

Epigastric pain, nausea and vomiting, sometimes hematamesis

- **Grossly:**

Congested, edematous surface .

- **Microscopically:**

1- Neutrophils among the surface epithelial cells.

2- Erosion (loss of superficial epithelial cells) resulting in a defective mucosa.

3- 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.

This is a trichobezoar that was removed from the stomach of a 12-year-old girl who ate her hair for six years. The hair took the shape of her stomach.

- **Classification of chronic gastritis:**

1- Type “A” chronic gastritis.

2- Type “B” chronic gastritis.

Type A:

*Is also called **Autoimmune** chronic gastritis.

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

* Occur in late adult life.

* The body (**fundus**) mucosa is mostly affected.

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

Decrease the HCL secretion.

Decrease in intrinsic factor secretion.

Impaired Vit B12 absorption and later on pernicious anemia as a result of the above cause.

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

- **Microscopically:**

The changes run in three stages:

1-Chronic superficial gastritis: there is infiltration of the foveolar part of the mucosa by chronic inflammatory cells (lymphocyte and plasma cells).

2-Chronic atrophic gastritis:

* The inflammatory infiltrate involve the foveola and deeper parts of the mucosa
* There is glandular destruction &loss
* Decrease in the mucosal thickness
* Epithelial metaplasia in the form of intestinal metaplasia (conversion of the gastric mucosa into intestinal type of mucosa, sometimes with villi or goblet cells).

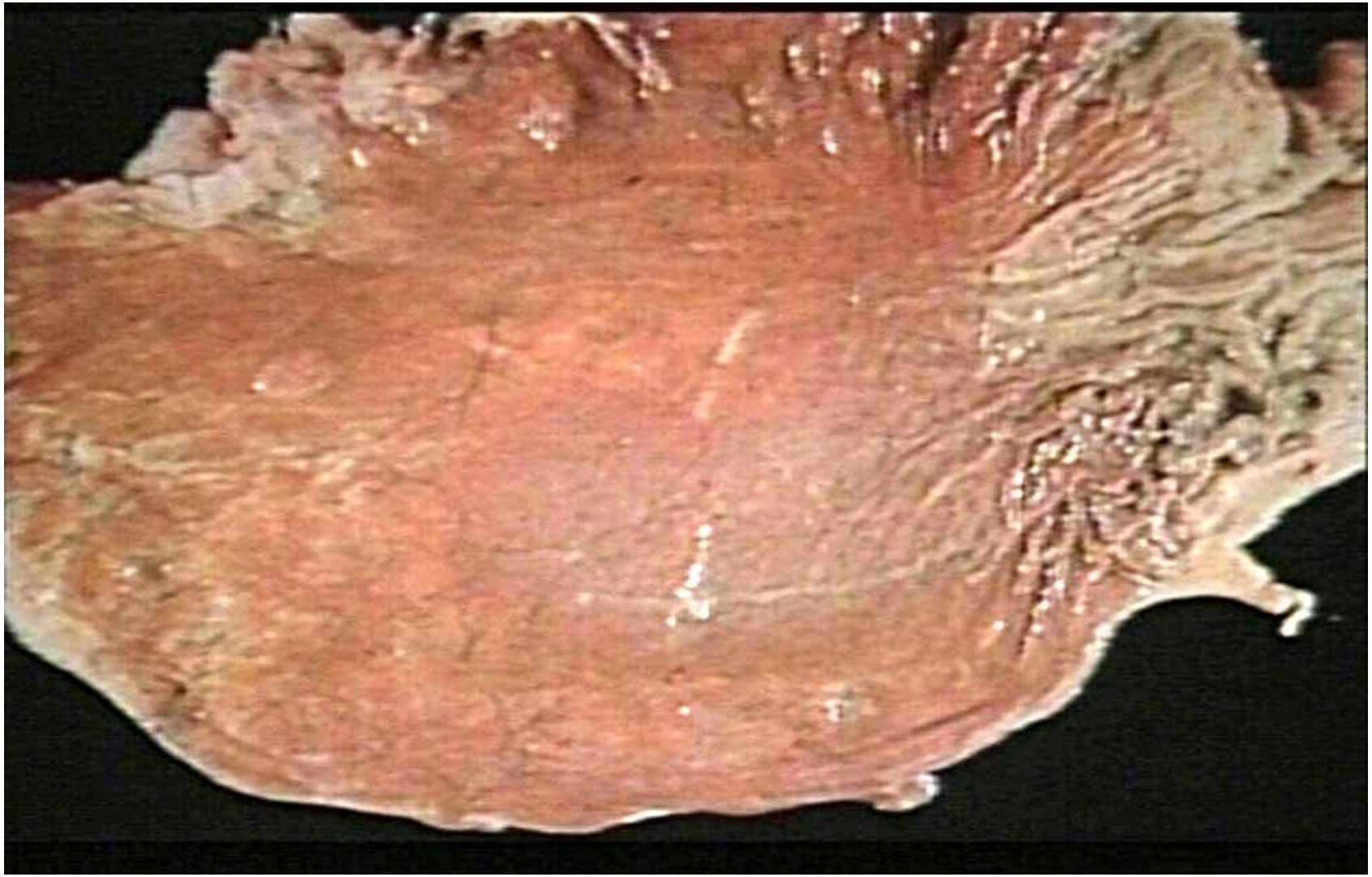
3- Gastric atrophy:

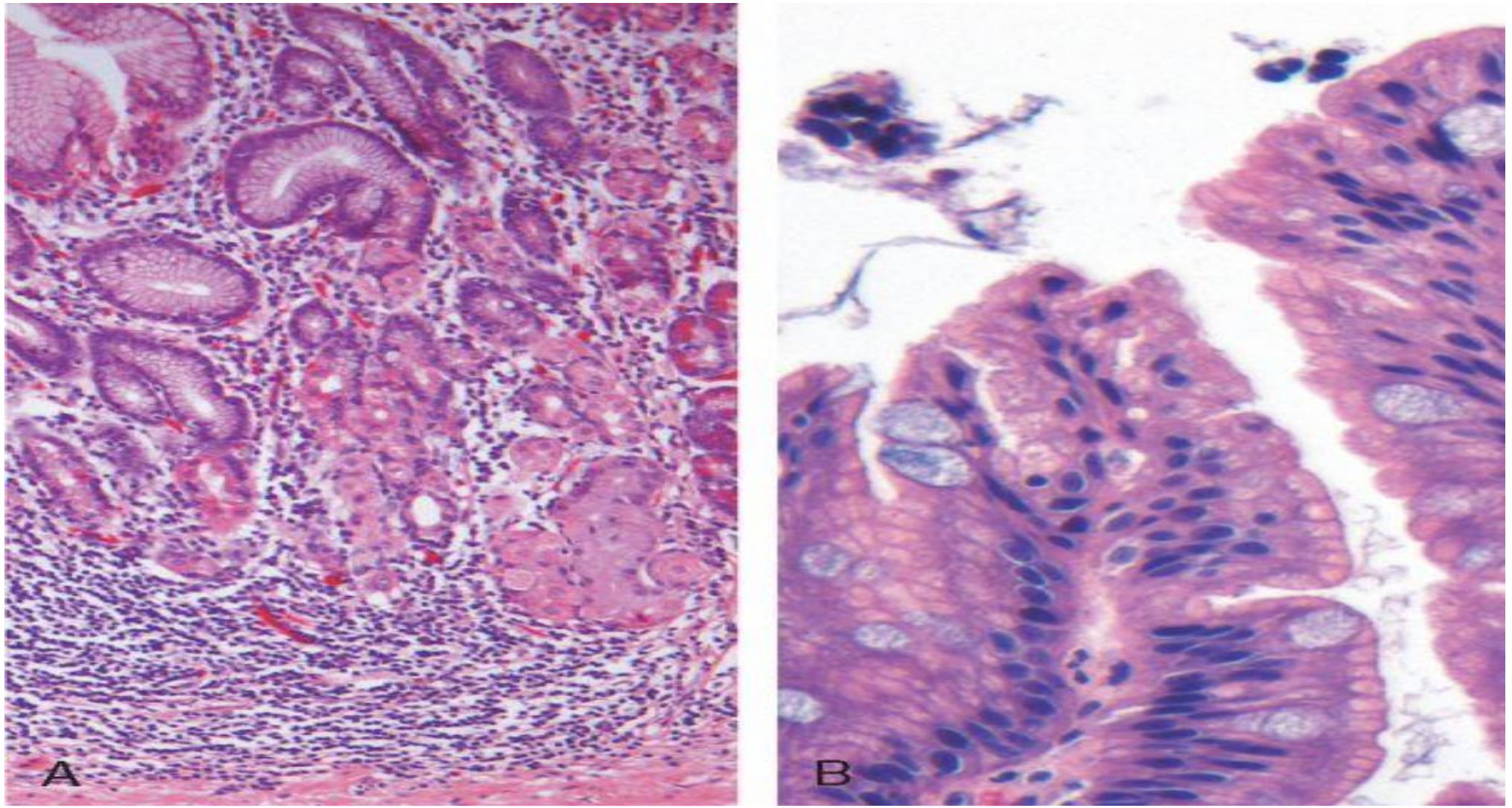
*there is thinning of the mucosa

* Minimal inflammatory infiltrate of the lamina propria.

- **Clinical picture:**
- Asymptomatic.
- Or with epigastric pain.
- Or pernicious anemia.

Gastric atrophy





Autoimmune gastritis:

A, Low-magnification image of gastric body demonstrating deep inflammatory infiltrates, primarily composed of lymphocytes, and glandular atrophy.

B, Intestinal metaplasia, recognizable as the presence of goblet cells admixed with gastric foveolar epithelium

- **Type “B”:**

*Is called **environmental** type.

* It is more common than type A

*It can arise at any age.

*It involves the **antrum** of the stomach

* The main causative agent is: helicobacter pylori infection, it is found in 80% of type B cases.

*Less common causes are:

chronic alcohol abuse,

cigarette smoking,

NSAID.

The importance of type B comes from:

1- It is highly associated with peptic ulcer

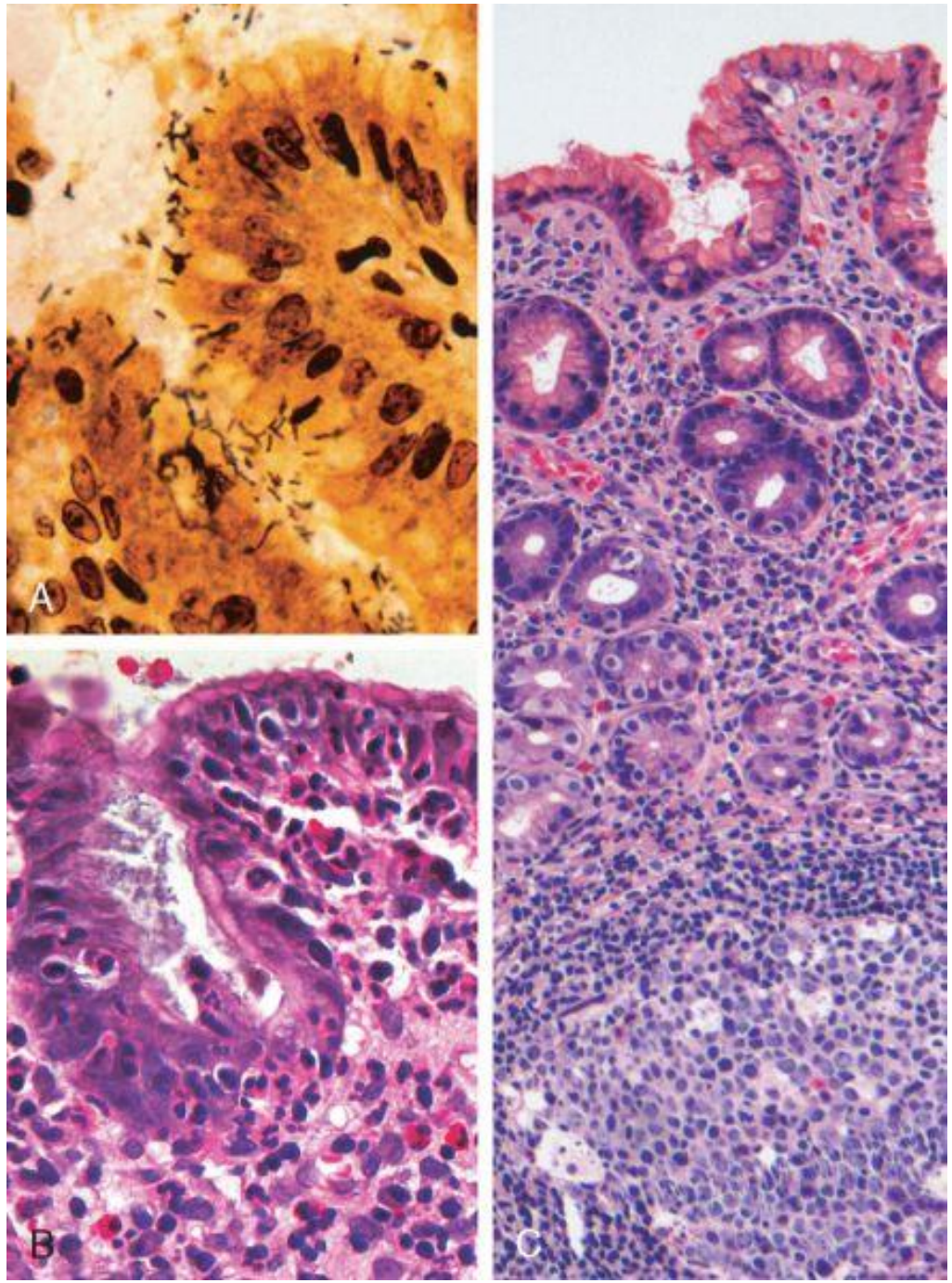
2- Associated with gastric carcinoma but less than type A.

- **Microscopically:**

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

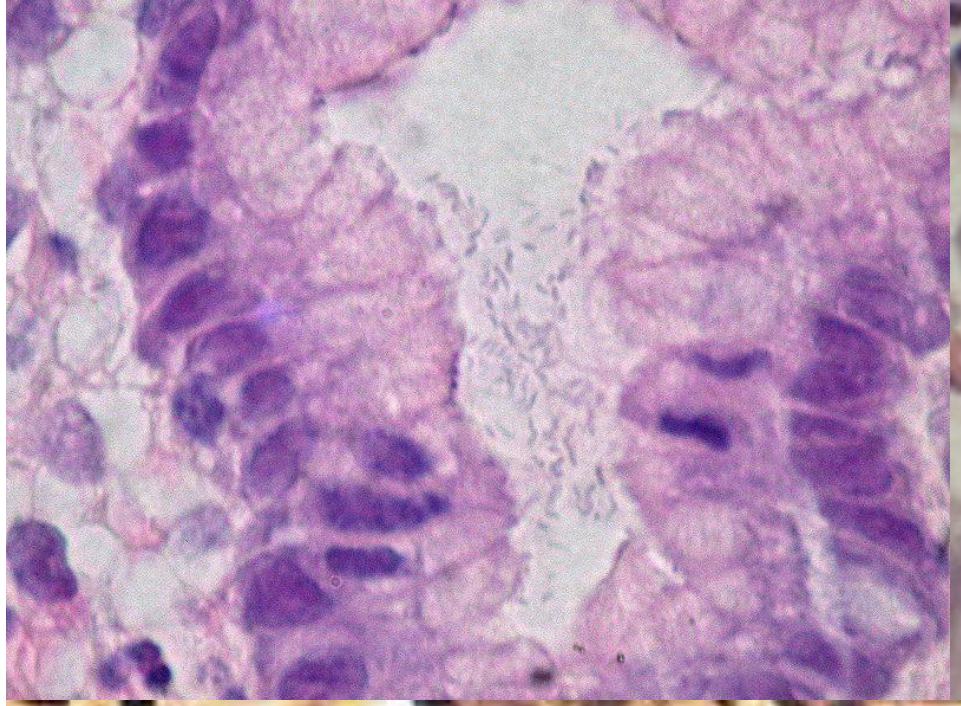
2- Some glandular atrophy.

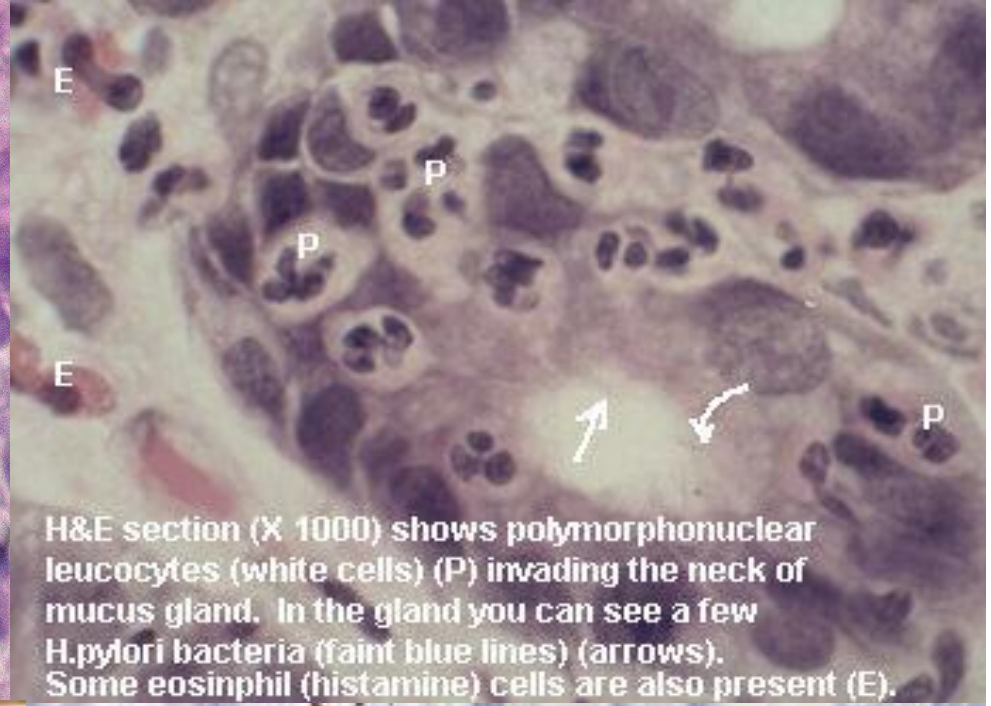
3- Intestinal metaplasia.



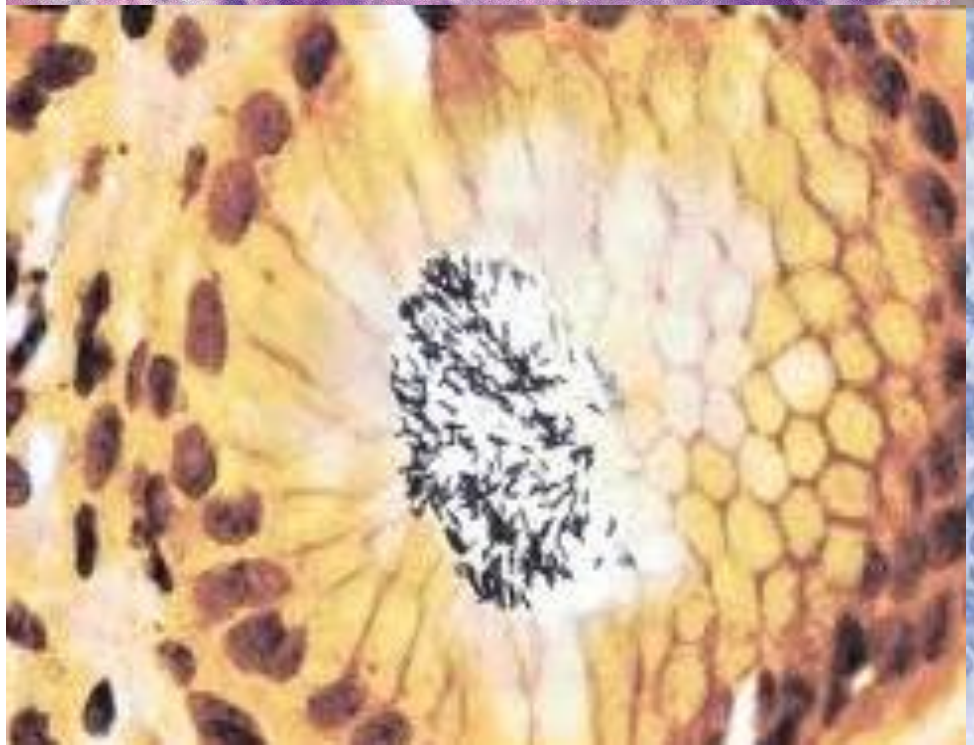
Helicobacter pylori gastritis:

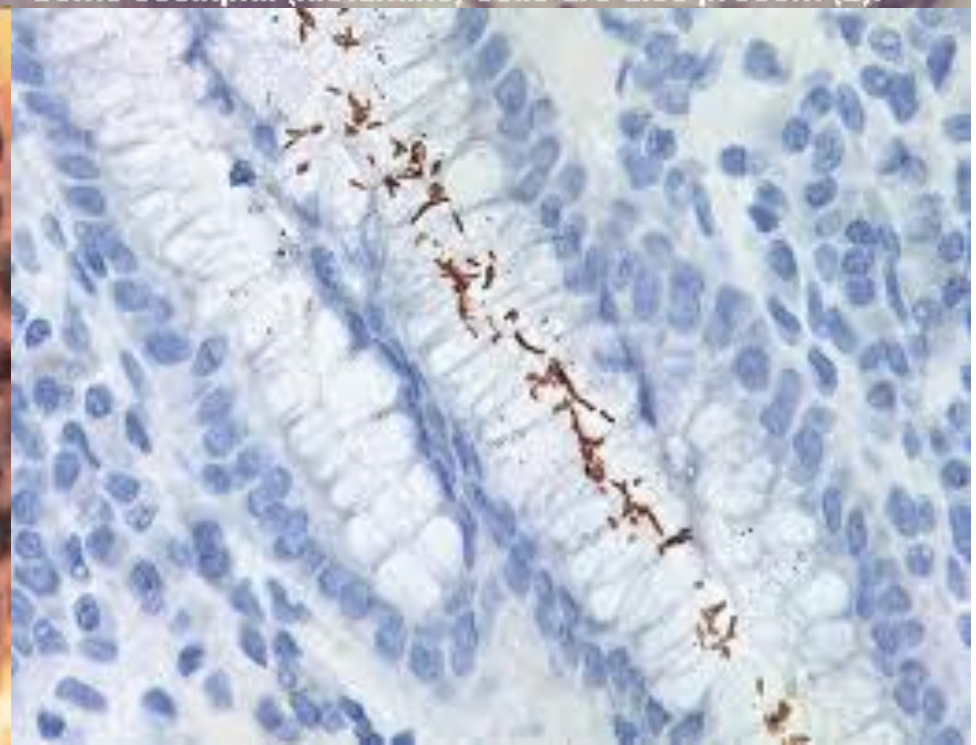
A, Spiral-shaped *H. pylori* are highlighted in this Warthin-Starry silver stain. Organisms are abundant within surface mucus.
B, Intraepithelial and lamina propria neutrophils are prominent.
C, Lymphoid aggregates with germinal centers and abundant subepithelial plasma cells within the superficial lamina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





H&E section (X 1000) shows polymorphonuclear leucocytes (white cells) (P) invading the neck of mucus gland. In the gland you can see a few H.pylori bacteria (faint blue lines) (arrows). Some eosinphil (histamine) cells are also present (E).





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(erosion):**

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

- **Causes:**

1- Non steroidal anti-inflammatory drugs (NSAID).

- 2- May appear after severe physiological stress, whatever it's 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- e.g 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 intracrainial pressure may cause hypersecretion of gastric acid.

3- In severe trauma &burns, systemic acidosis which lowers the mucosal cell PH which are already hypoxic by impaired mucosal blood flow.

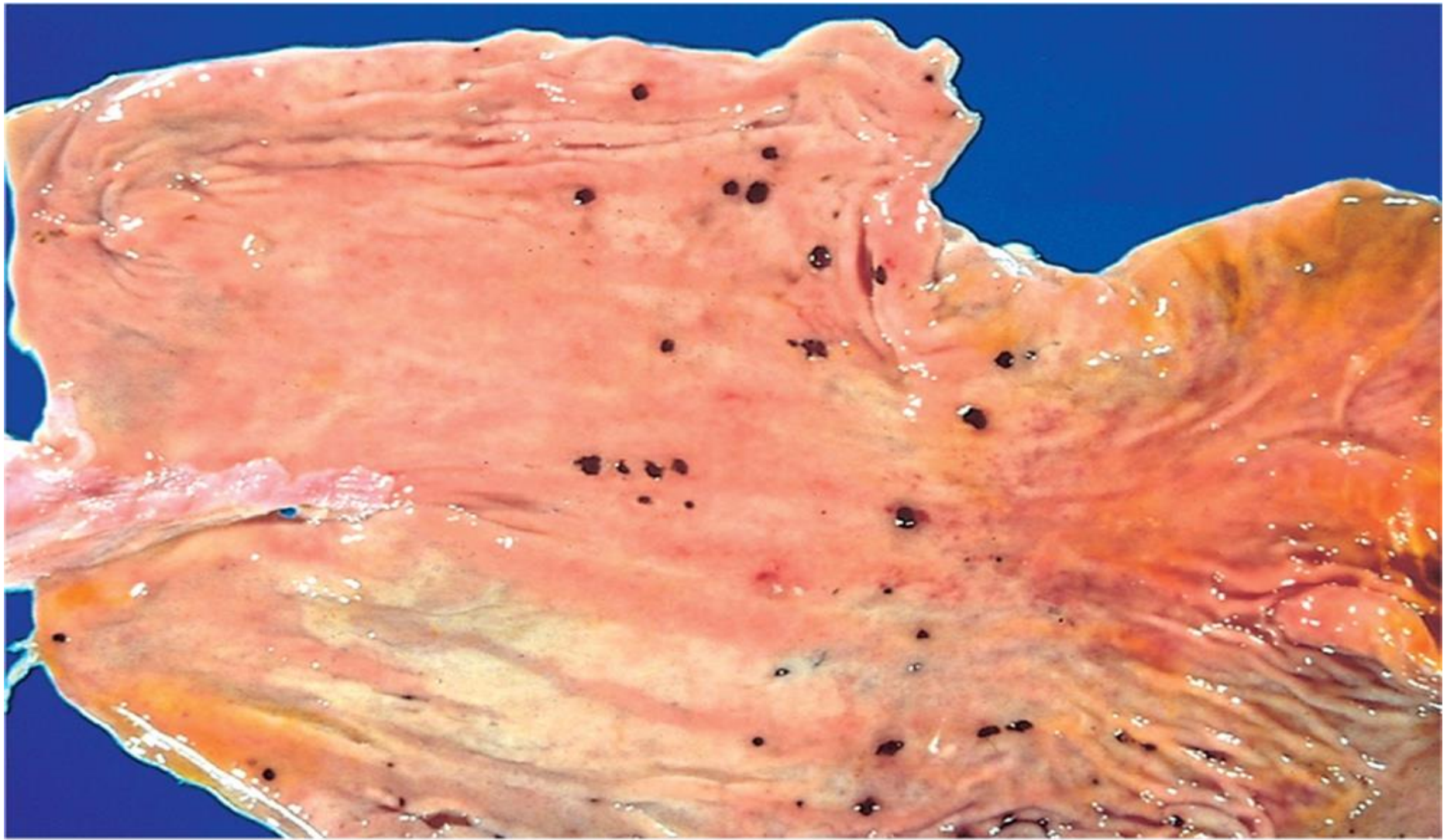
- **Morphologically:**

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

- **Clinical features:**

Either asymptomatic Or bleeding.

Acute gastric ulcer (erosion) :multiple,small round-oval, superficial hemorrhagic



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

- **Epidemiology**:

- The ratio of duodenal ulcer/ gastric ulcer = 4/1
- Male/female = 3/1 for duodenal ulcer, 2/1 for gastric ulcer
- There is no racial difference in the incidence
- It is characterized by remission and relapse

- **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:

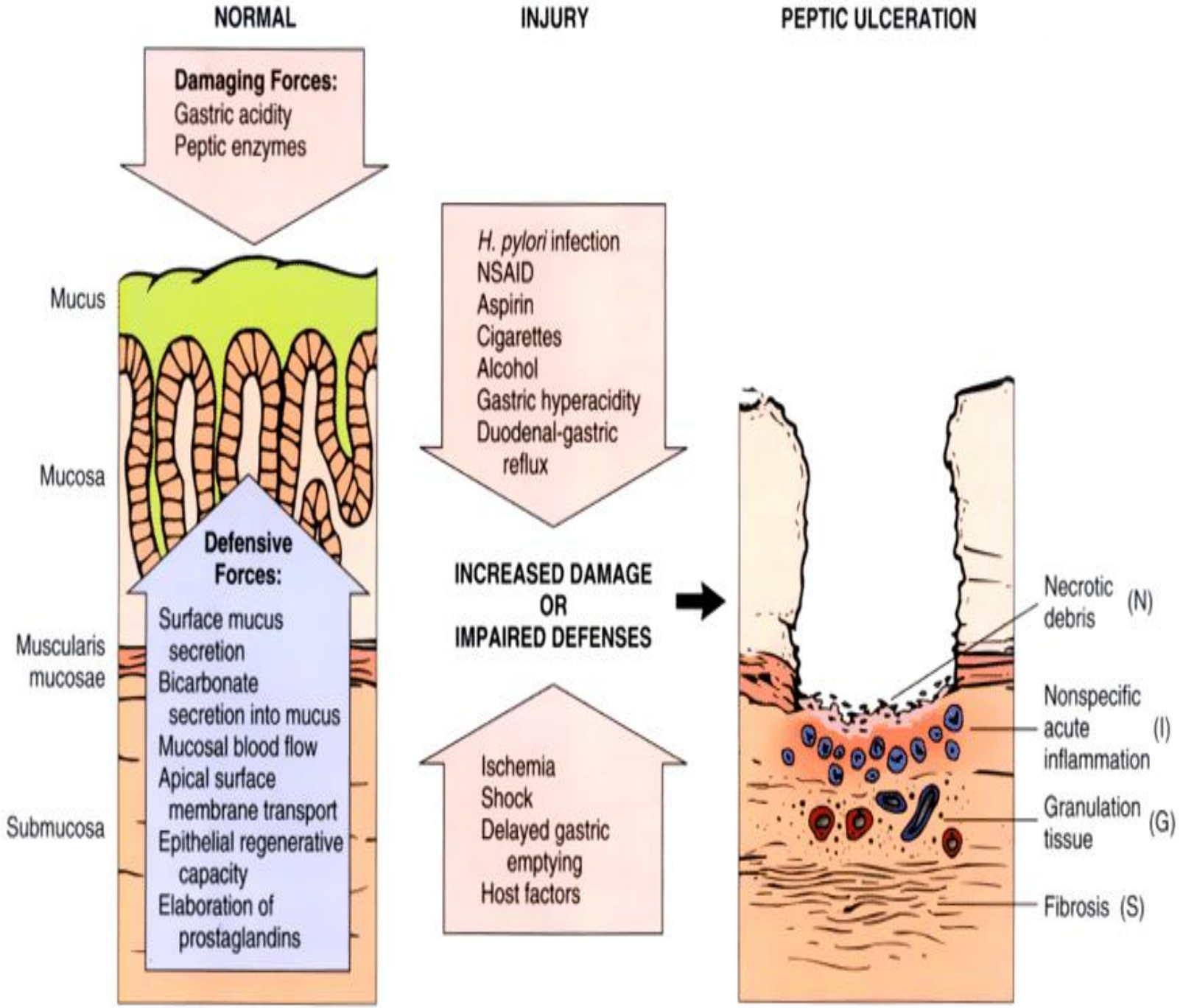
a- H.pylori infection.

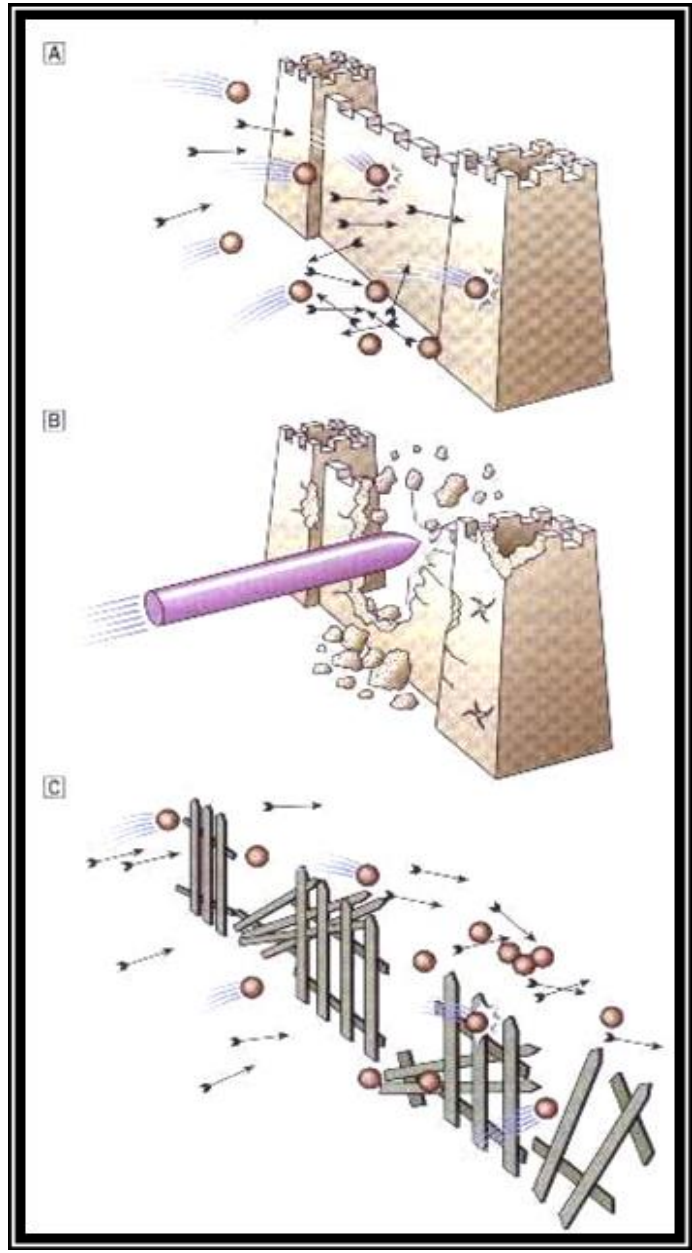
b- Aspirin

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)


A
B
C

*This concludes that HYPERACIDITY is **not** the actual cause because only few patients with D.U (duodenal ulcer) and less than few in G.U (gastric ulcer) have hyperacidity.

*The most important cause for developing ***GU*** found to be a decrease in the **defense** mechanism

H.pylori infection is the most important cause &present in 70% of GU.

*For ***D.U,*** **H. pylori** present in 70-90%

- **Genetic** susceptibility play role also that is 20-40% of D.U have a +ve family history.

H pylori bacteria

the organism acquired in childhood and persists for decades.

The mode of transmission of *H. pylori* has not been well defined, although oral-oral transmission, fecal-oral transmission, and environmental spread(using infected utensils) are among the possible routes.

H.pylori related disorders:

infected persons are at increased risk for the development of :

Chronic gastritis, 90%

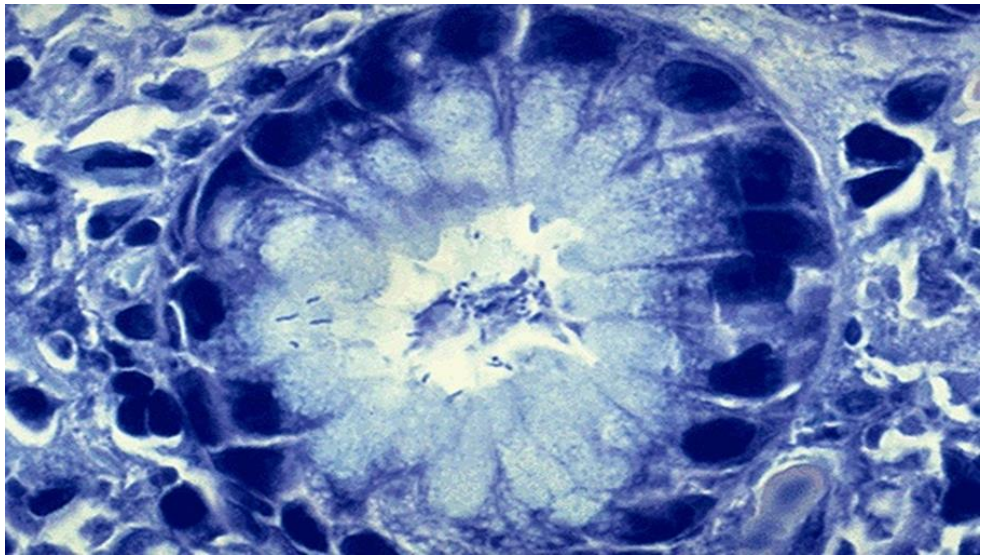
Peptic ulcer disease 95-100%

Gastric carcinoma 70%

and Gastric MALT lymphoma.

Reflux Oesophagitis.

Non ulcer dyspepsia



H. pylori is a nonsporing, curvilinear gram-negative rod

It is adapted to live in the gastric mucus, which is lethal to most bacteria.

The specialized traits that allow it to flourish include:

- Motility (via **flagella)**, allowing it to swim through viscous mucus
- Elaboration of a *urease,* which produces ammonia and carbon dioxide from endogenous urea, thereby buffering gastric acid in the immediate vicinity of the organism.

Bacterial **protease** and **phospholipase** break down the glycoprotein –lipid complex in the gastric mucoid , thus weakening the first line of mucosal defence.

- Expression of bacterial toxins, such as cytotoxin association gene A ***(CagA)*** and vacuolating cytotoxin gene A ***(VacA)*** ***which are responsible for the inflammatory response .***

10-20% of individual worldwide infected with H pylori actually develop peptic ulcer.

Studies shows that strains producing Vac A and Cag A causes more intense tissue inflammation and cytokins production

- **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.

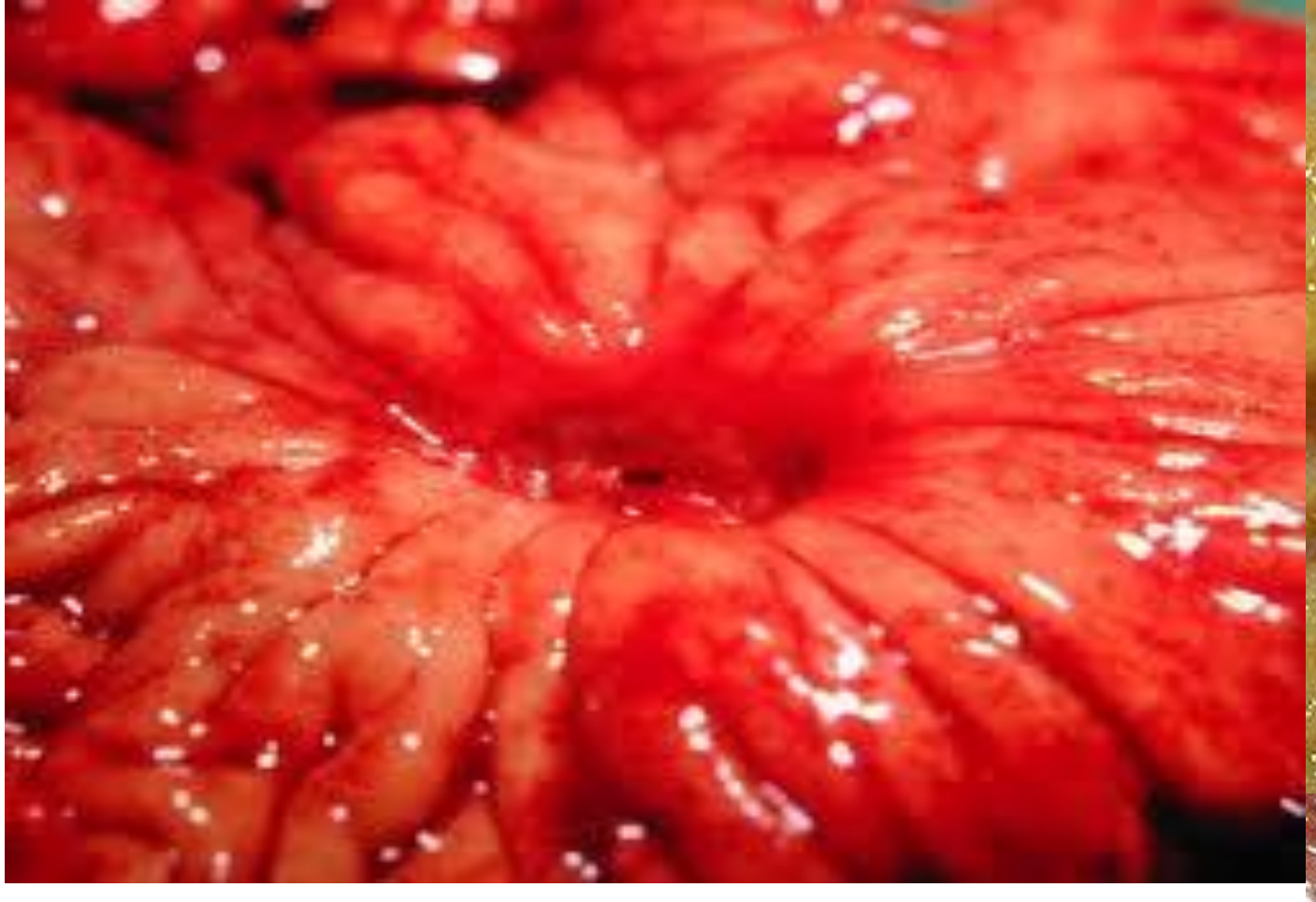
5-Floor: clean

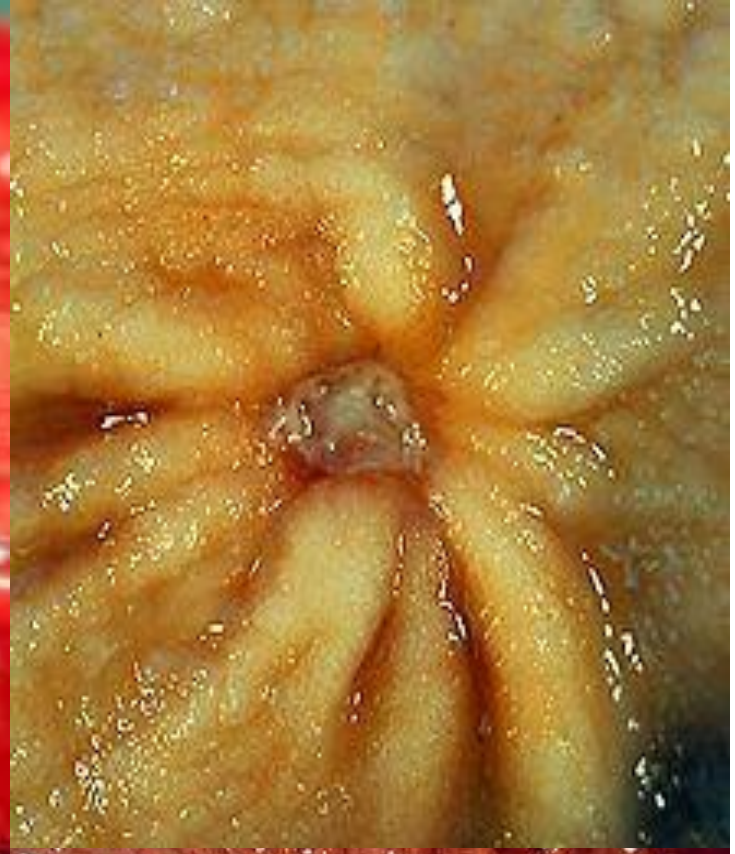
6-Base: Firm

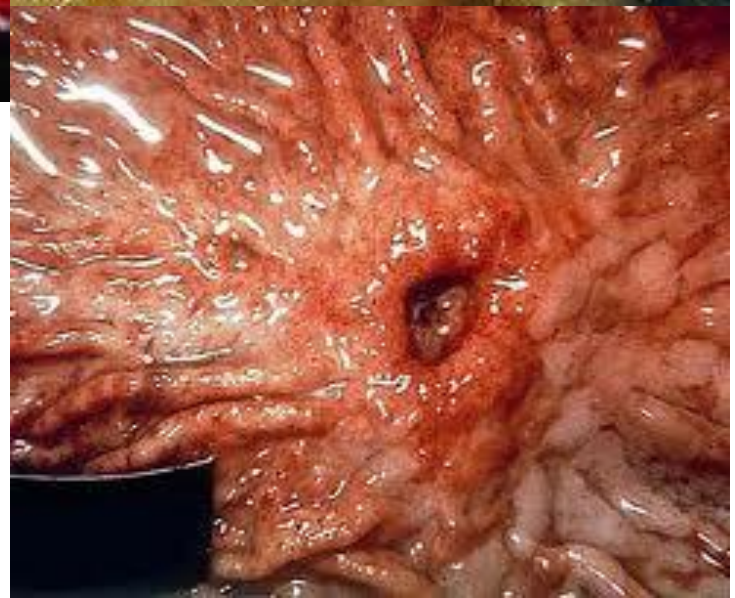
7-Edge: Overhanging

8-Depth may vary

Scarring -> puckering -> radiating mucosal folds (like spokes)







Gastric ulcer:

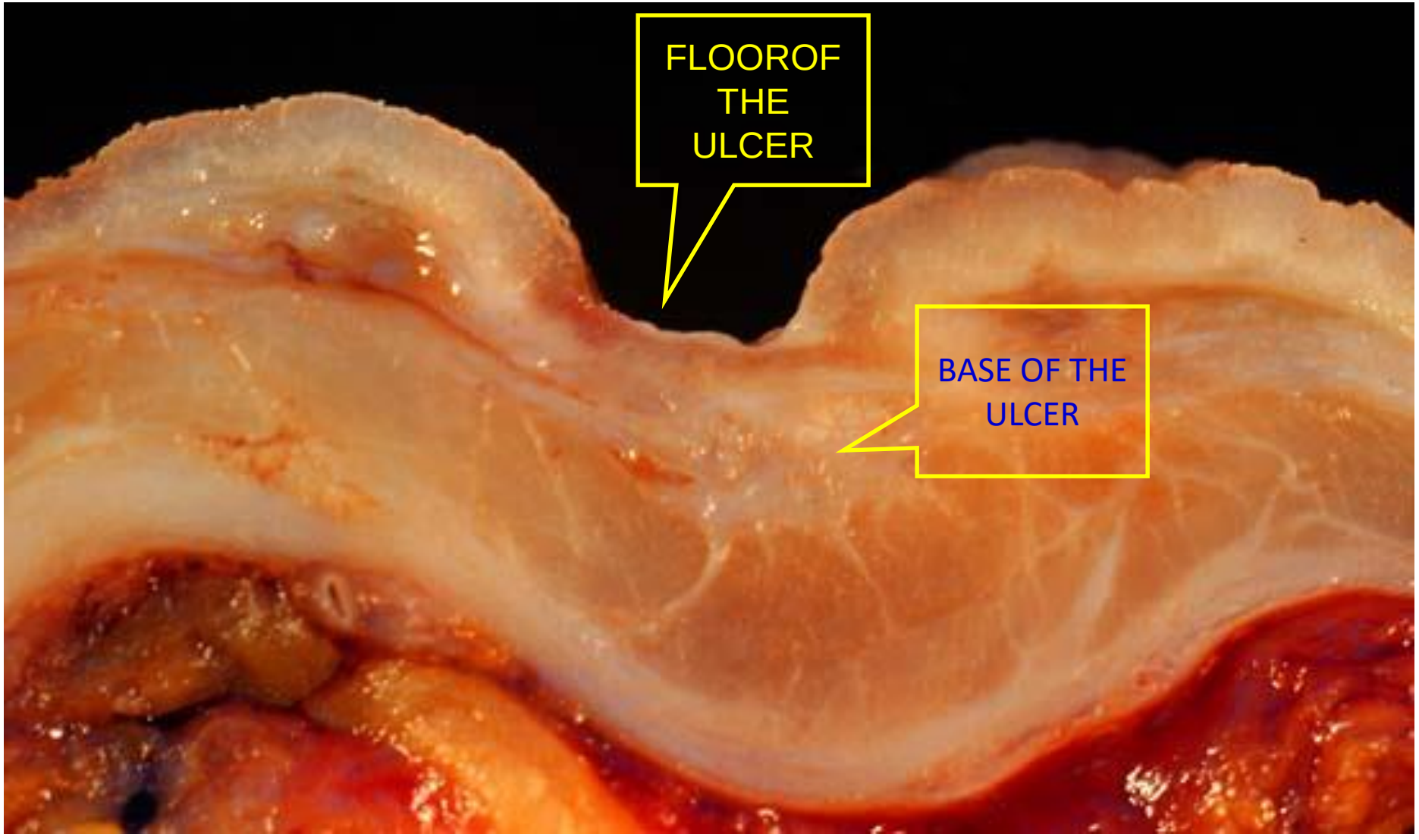
Rounded or oval shape

Radiating rugal folds (in spoke wheel pattern)

Clean floor

Punched out edges

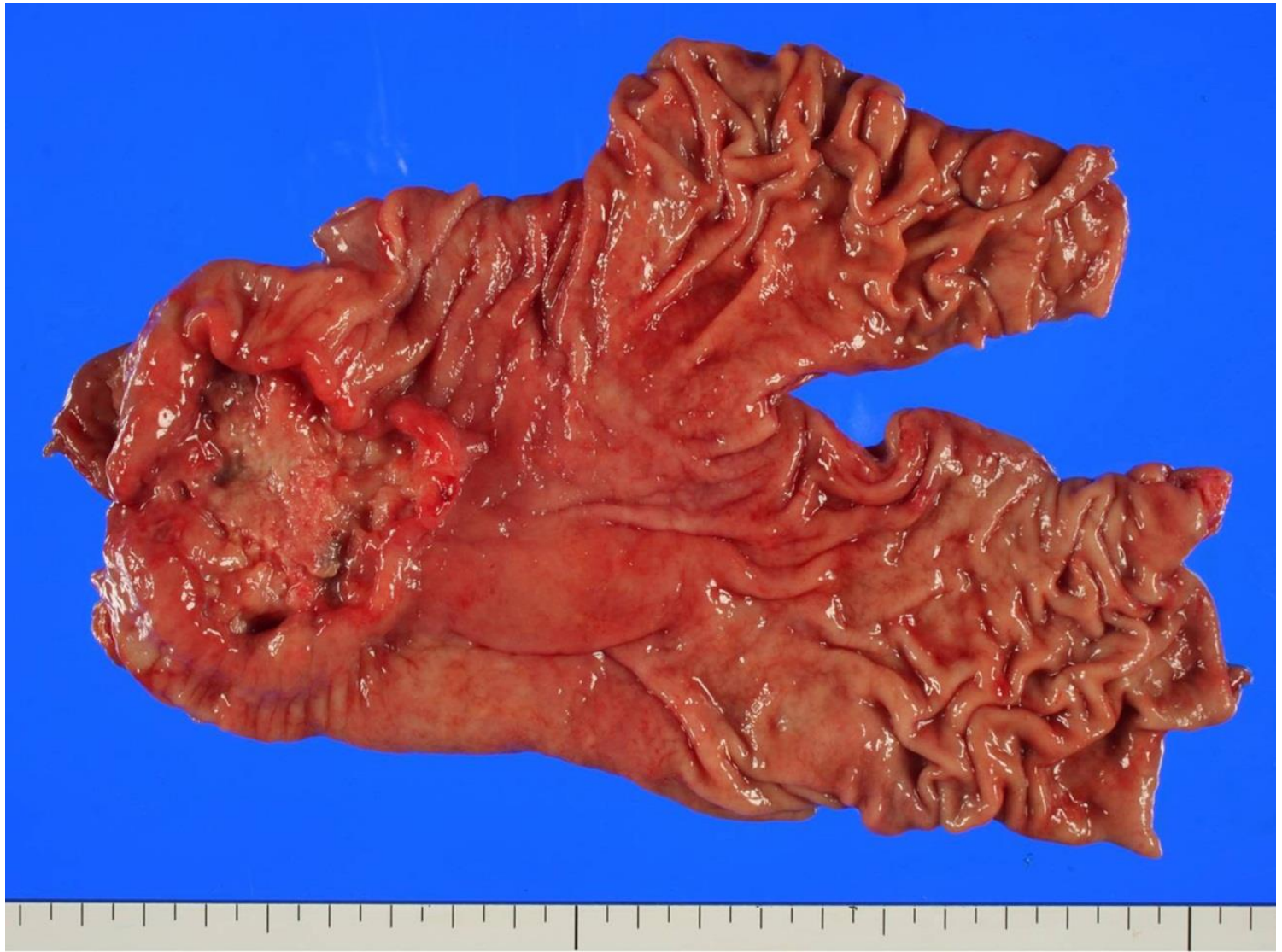
Cross section of ulcer



DDx Benign & malignant ulcers

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

Malignant ulcer

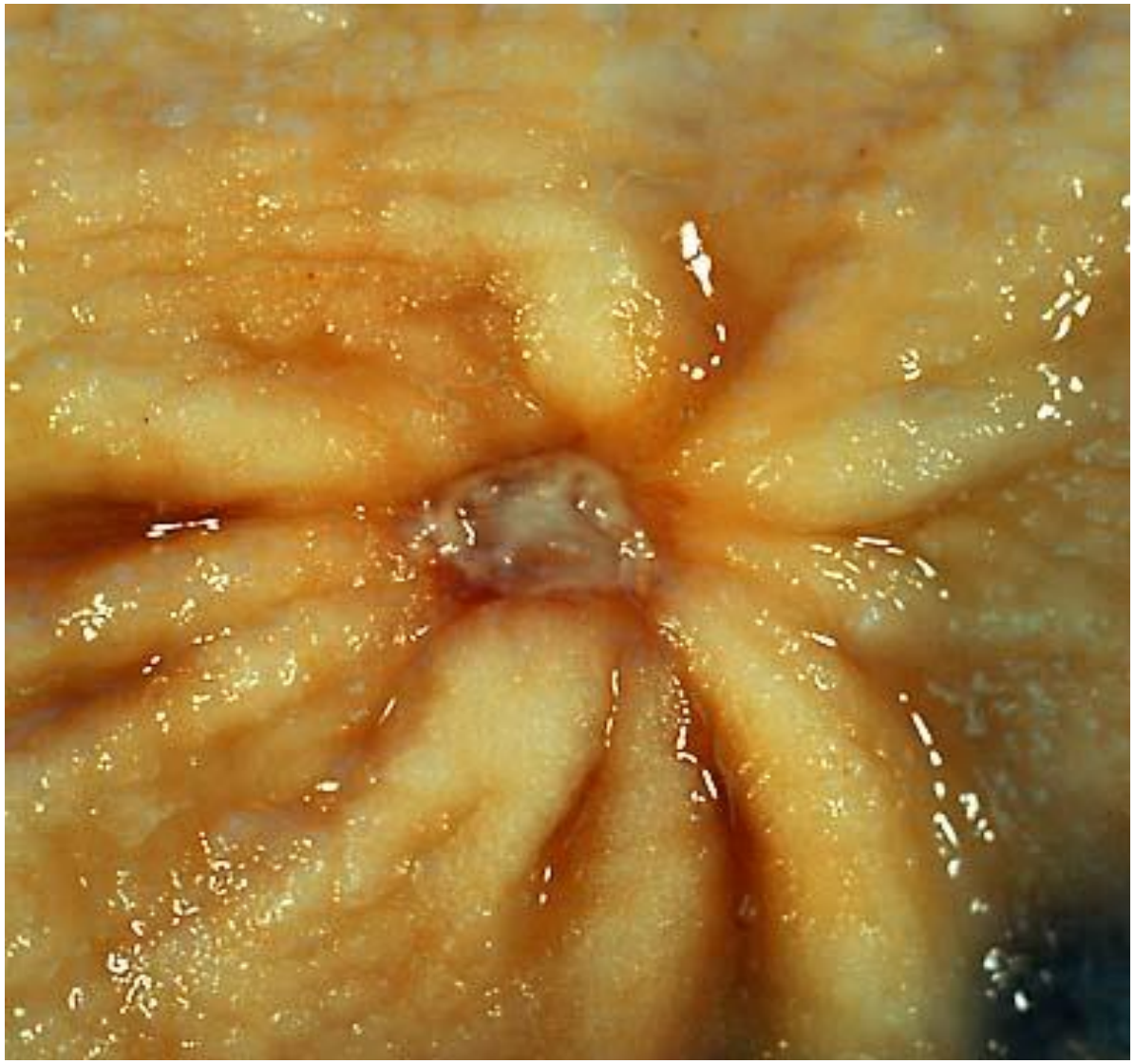


Gastric carcinoma:

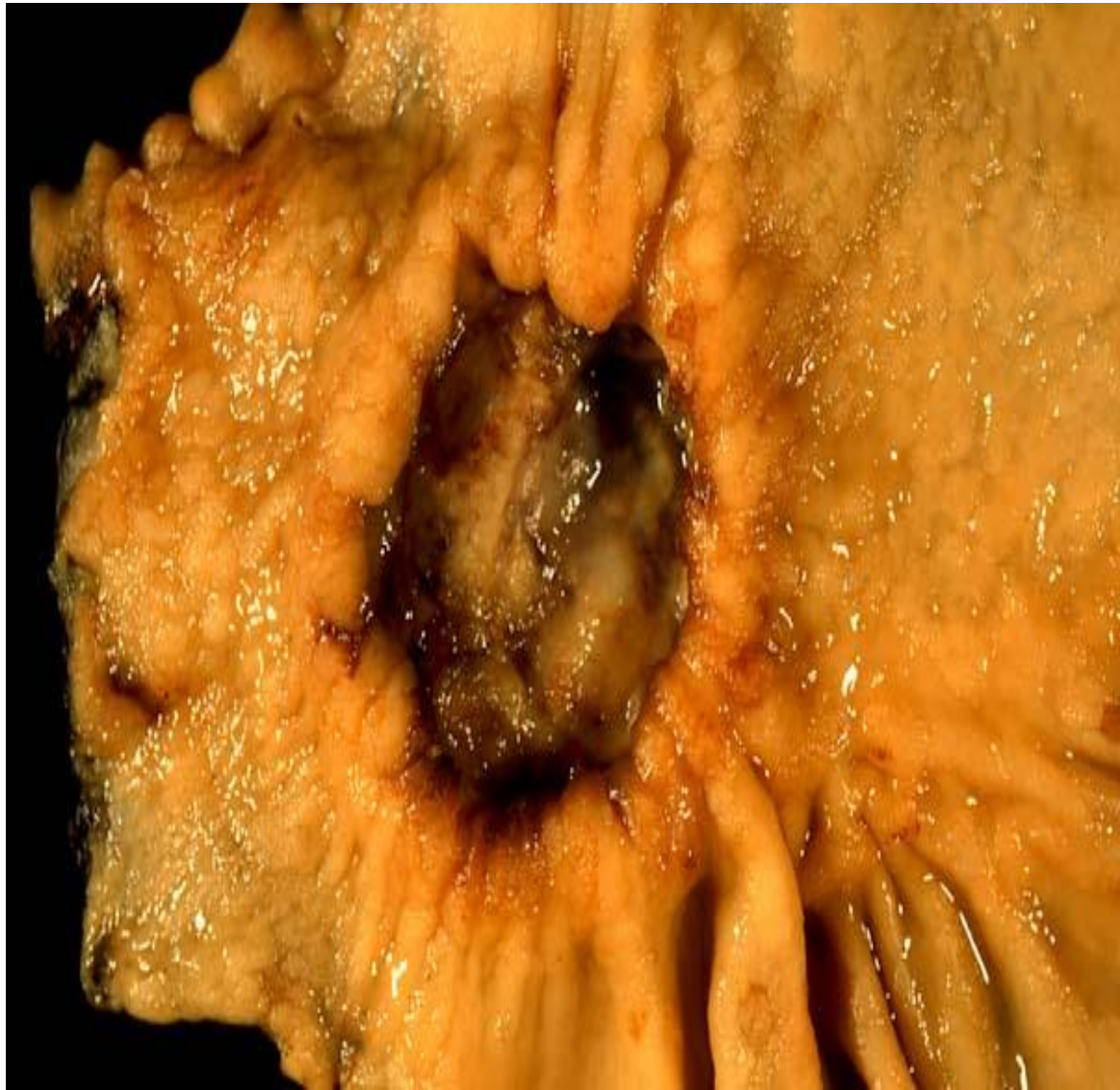
Heaped up(elevated ad beaded) and sloping margins

No spoke wheel pattern

Chronic gastric ulcer



Malignant gastric ulcer



- **5- 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

Peptic ulcers are chronic, recurring lesions.

occur most often in middle-aged to older adults.

A majority of patient complaints is epigastric burning or aching pain,

Other present with complications such as iron deficiency anemia, frank hemorrhage, or perforation.

The pain tends to occur 1 to 3 hours after meals during the day, is worse at night, and is relieved by alkali or food.

Nausea, vomiting, bloating, and belching may be present.

A variety of surgical approaches formerly were used to treat PUD, but current therapies are aimed at H. pylori eradication with antibiotics and neutralization of gastric acid, usually through use of proton pump inhibitors.

These efforts have markedly reduced the need for surgical management, which is reserved primarily for treatment of bleeding or perforated ulcers

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:

1- hematemesis coffee ground appearance due to blood hemolysis by acid) and malena

2- iron deficiency anemia due to *chronic* loss of small amounts of blood

3- Perforation: leading to escape of the gut content into the peritoneal cavity→ peritonitis presented with *acute* abdominal pain &is the major cause of death.

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

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

N.B: D.U ***never*** show a malignant transformation

•Gastric carcinoma:

It is one of the most important causes of death from malignant tumors.

Geographically:

Common in Japan, china, Chile, Portugal.

Uncommon in USA, U.K, Australia .

Gender : Common in male, male /female =2/1.

Age: Common in old age and later life (5th and 6th decades)

- **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:

1-chronic gastritis with intestinal metaplasia

2- Partial gastrectomy favors reflux of bilious alkaline intestinal food.

3- Gastric adenoma.

4- Genetic

* Family history of gastric carcinoma

•

- **Question ???**

What is the relation between chronic atrophic gastritis and gastric carcinoma??

- **Answer:**

1- In chronic gastritis the chronic inflammatory process may lead to metaplasia, then dysplasia followed by anaplasia or tumor formation .

2- In chronic gastritis, there is decrease in HCL secretion which promotes the growth of abnormal intragastric bacteria which act on dietary nitrate and convert them into nitrite which assist in further conversion of dietary amines into N- nitrosocompounds which is an important carcinogen.

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:**

The type is adenocarcinoma, classified into two types:

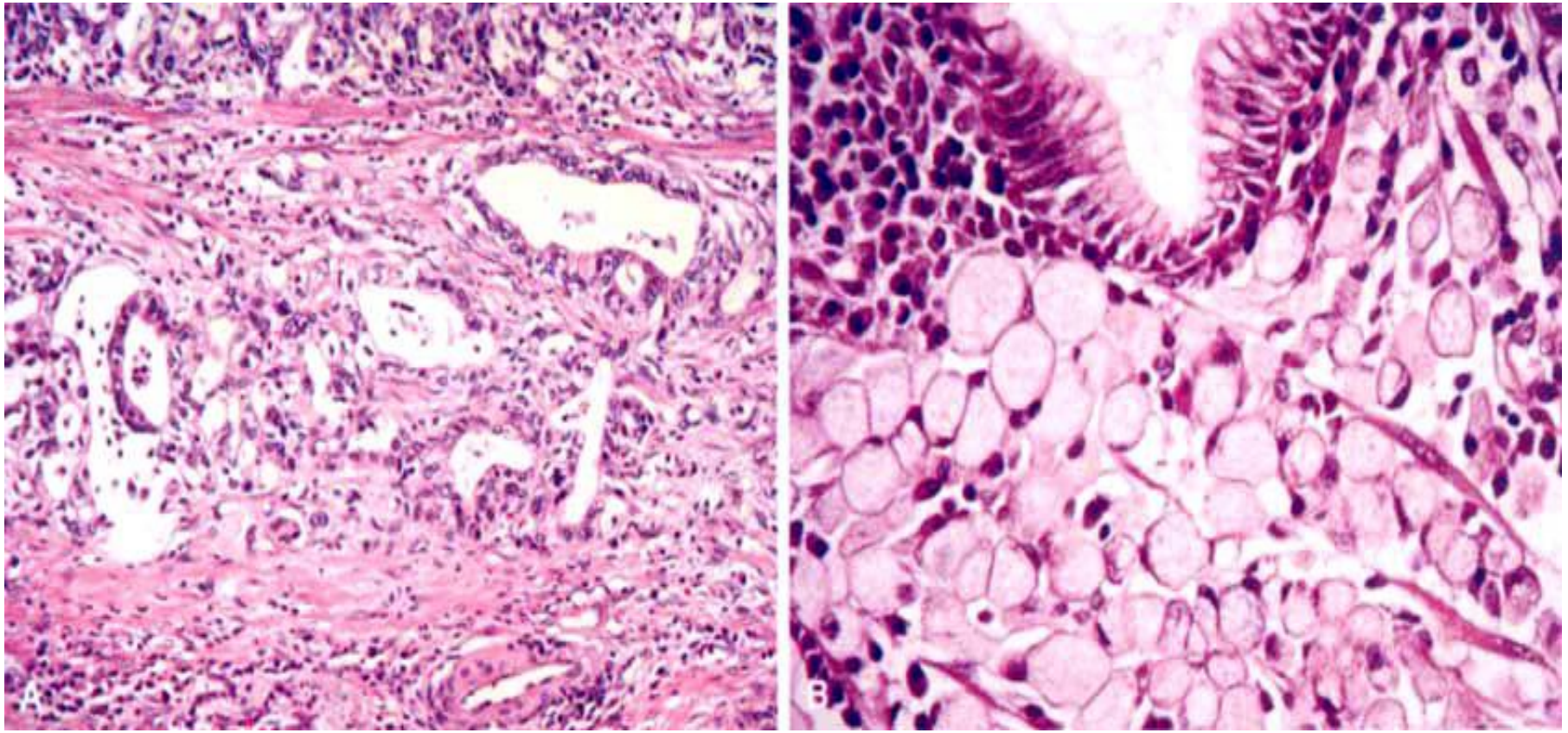
1- Intestinal type :

-Malignant cells forming neoplastic intestinal glands resembling those of colonic adenocarcinoma.

- It is the predominant type in high risk areas
- Occur in old age group (55) years
- Better prognosis than other type

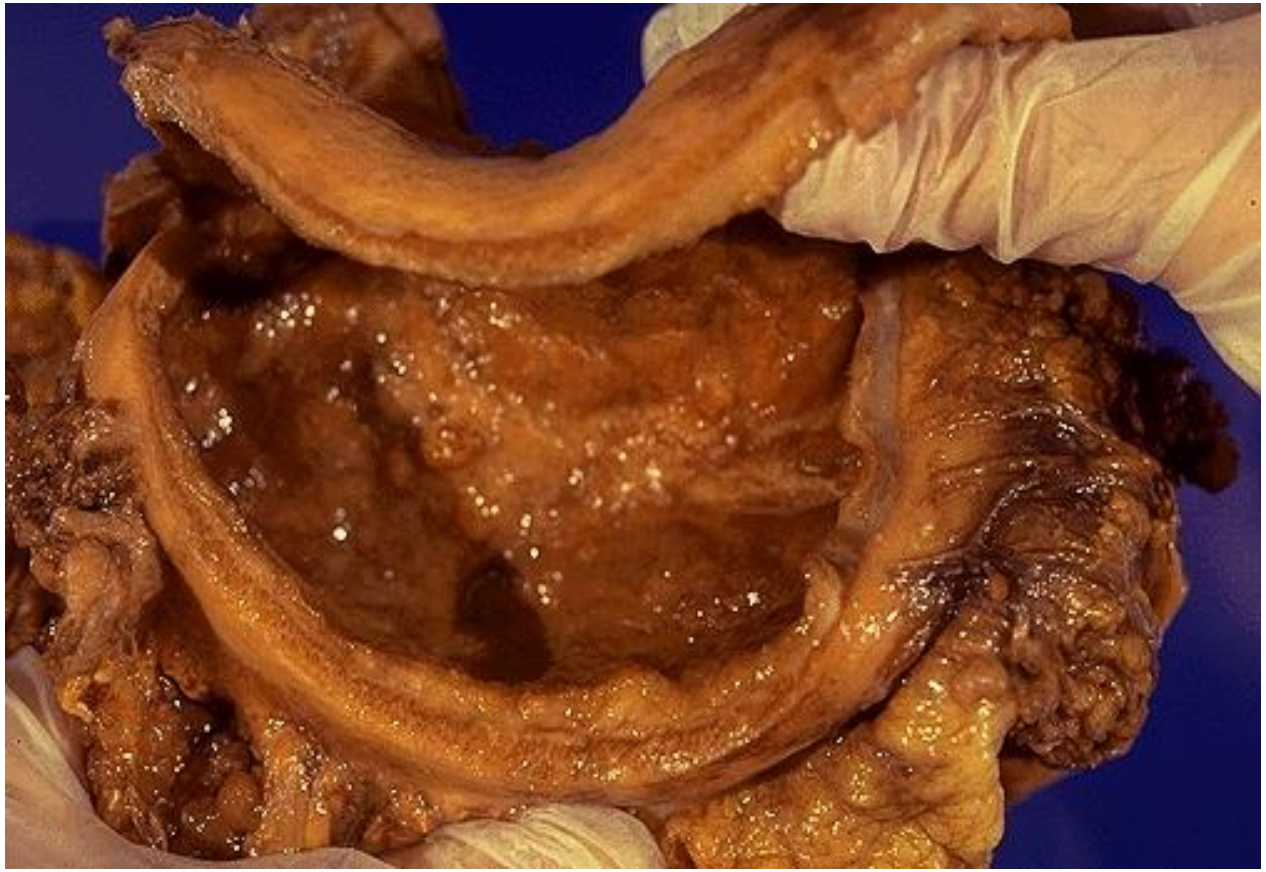
2- Diffuse type:

- 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


A
B

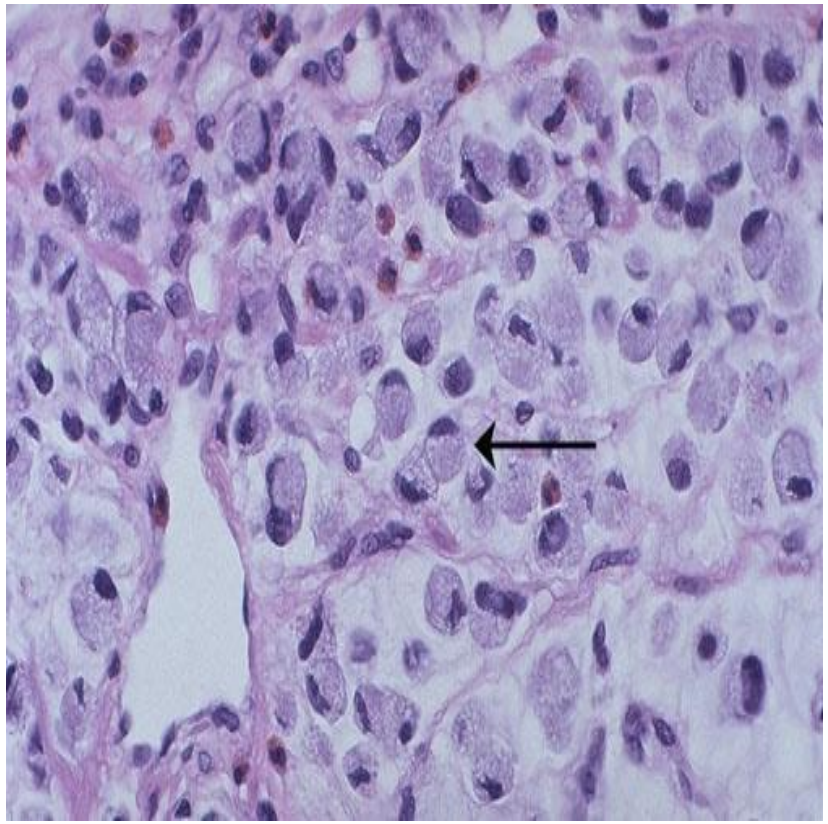
Infiltrating carcinoma (linitis plastica).
The stomach with stiff rigid walls caused by infiltrating tumor cells and extensive fibrosis has been referred to as a "leather-bottle stomach."

Linitis plastica

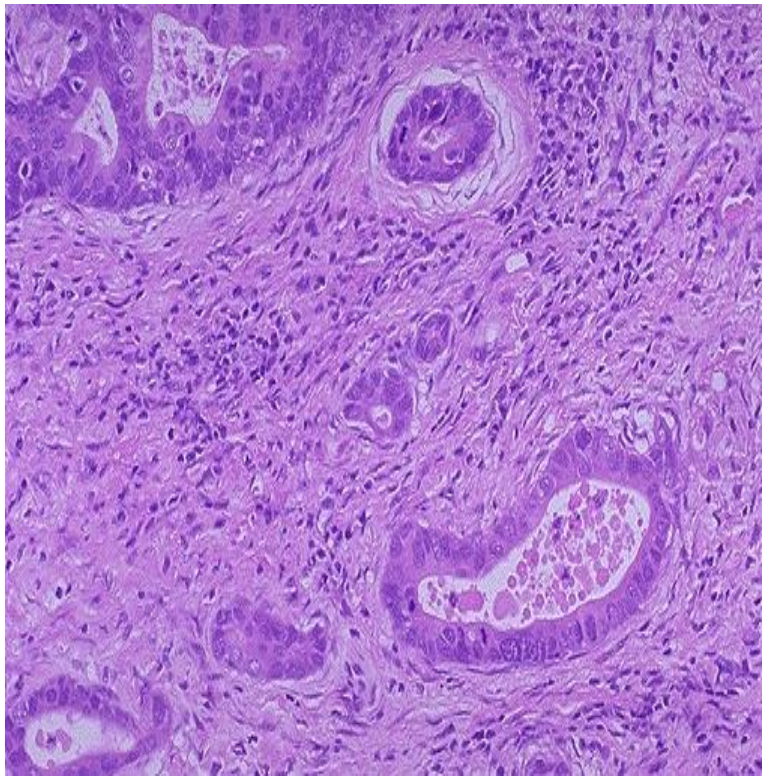


Adenoca , signet ring

- Diffuse signet ring



- Intestinal or glandular



- **Spread:**

2- Local spread: to adjacent organs: e.g esophagus, duodenum.

2- Lymphatic spread: to regional lymph nodes

For obscure reasons the earliest LN metastasis may sometimes involve a supraclavicular lymph node (Virchows node)

3- 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*

4- Hematogenous spread: to the liver and lung.

Gastric carcinoma

Prognostic indicators:

The depth of invasion and

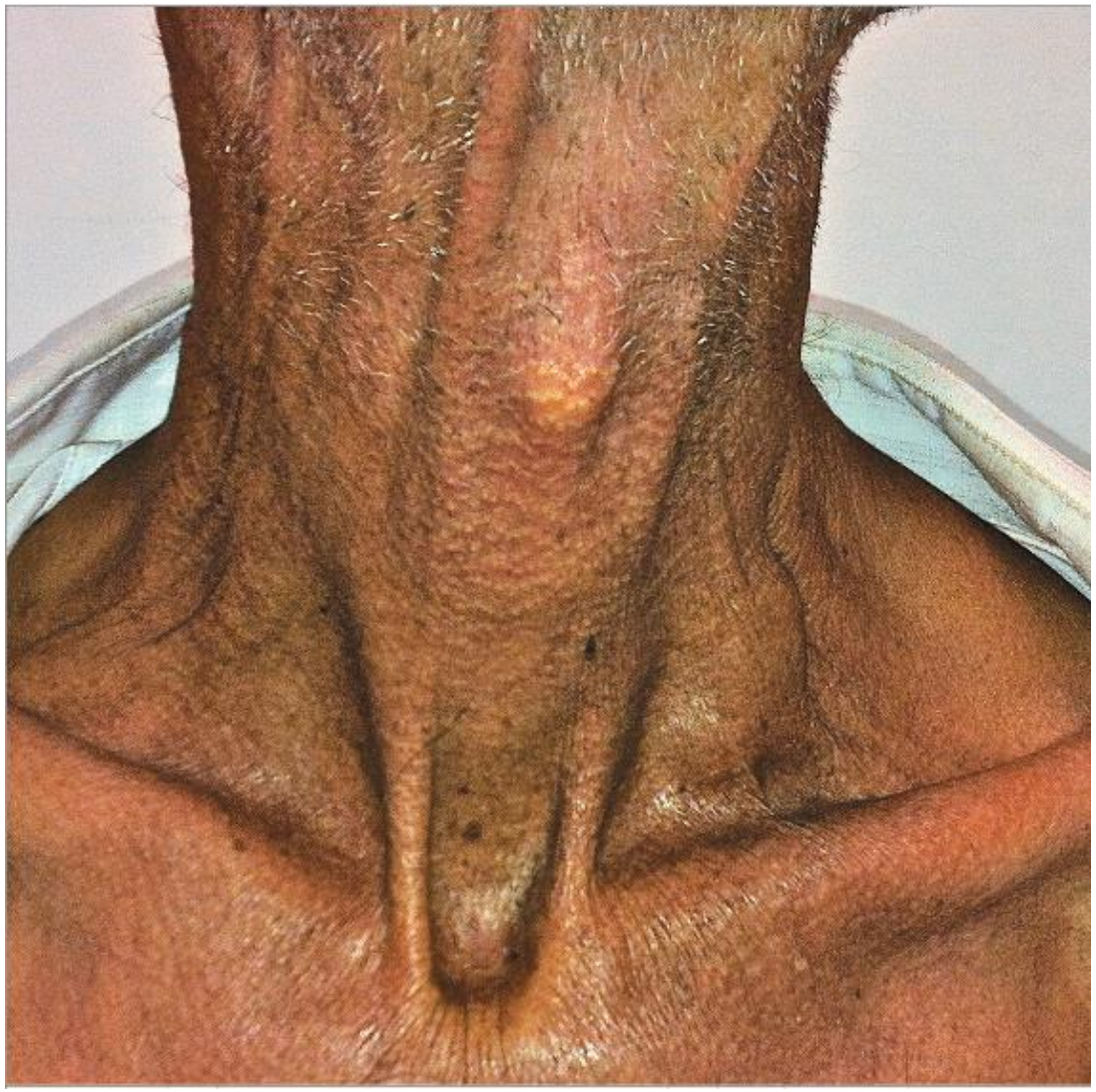
The extent of nodal and distant metastasis

Virchow's node (supraclavicular)

Sister Mary Joseph's nodule

Krukenberg's tumor

Virchow's node



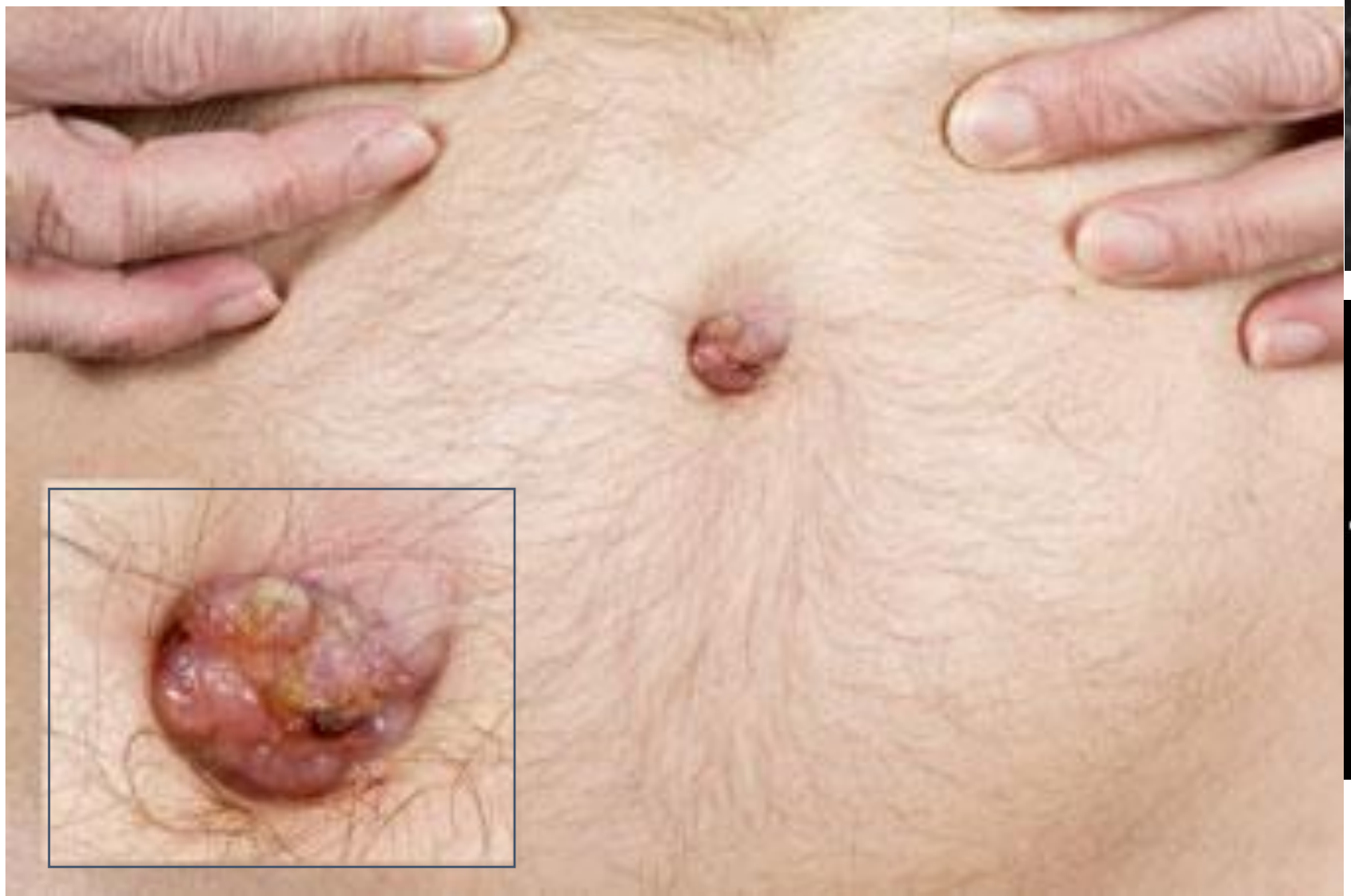
The NEW ENGLAND JOURNAL of MEDICINE

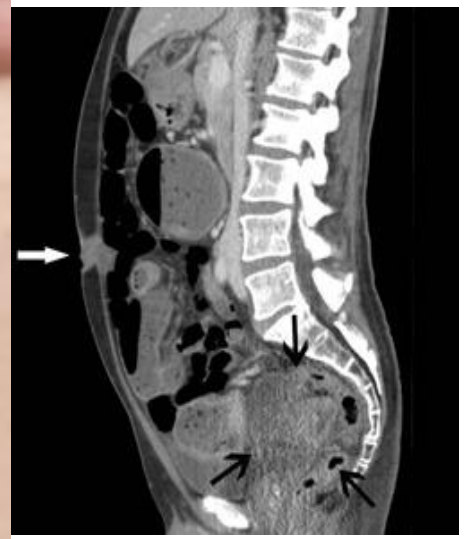
Marcos Duarte Siosaki, M.D., and Ana Tarsila Souza, M.D.
N Engl J Med 2013; 368:e7February 7, 2013
DOI: 10.1056/NEJMicm1204740

Sister Mary Joseph's nodule

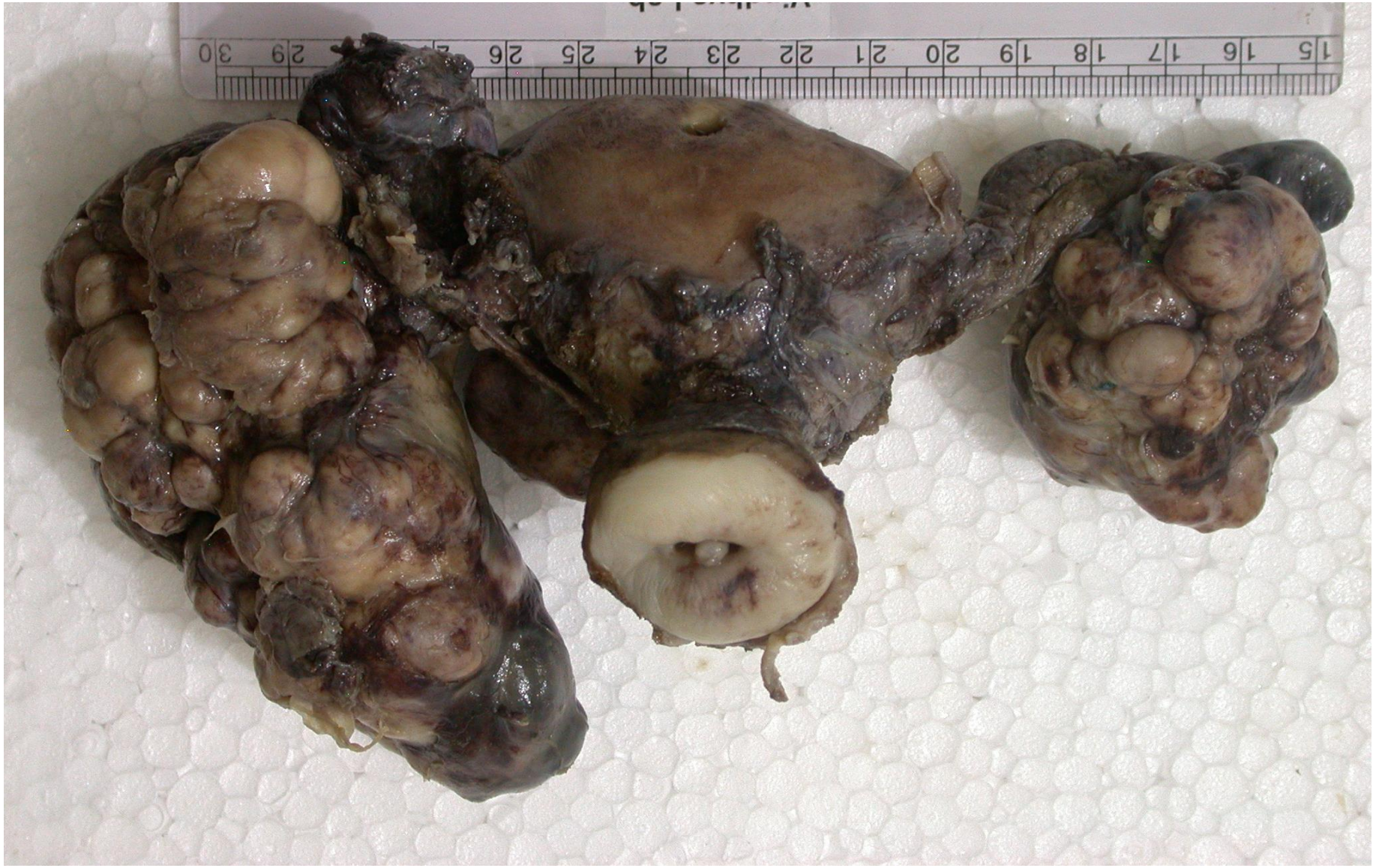
Sister Mary Joseph first noticed that a 'nodule' in the umbilicus was often associated with advanced malignancy in the pelvis or abdomen

half cases is associated with gastric,colonic or pancreatic cancers, other causes : ovarian and uterine cancers

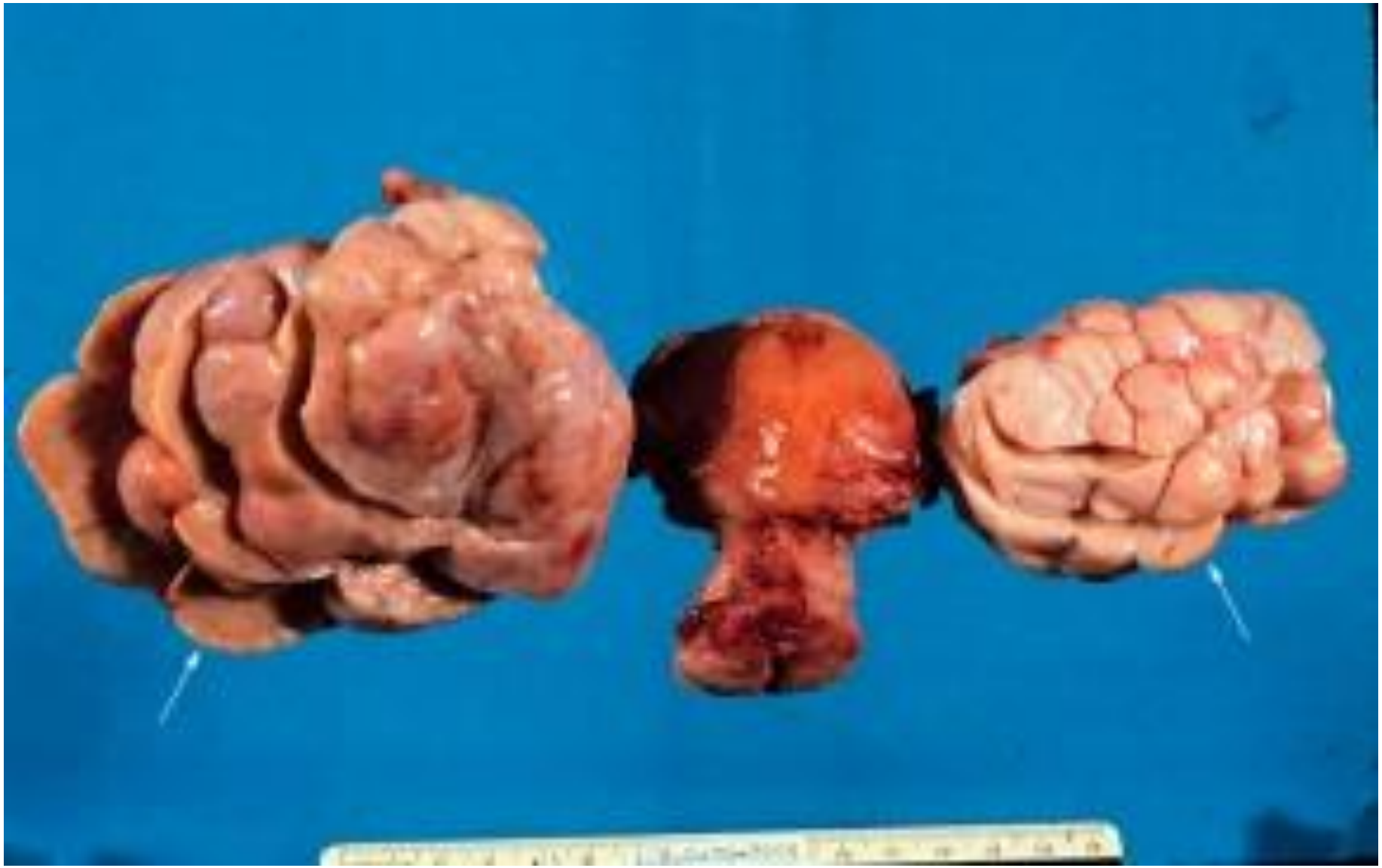




Krukenberg’s tumor



Krukenberg's tumor



- **Clinical features:**
- The most important are:
- Anorexia (loss of appetite)
- Severe weight loss
  with epigastric pain
- Anemia

- **Early gastric carcinoma:**
- Is the carcinoma which is limited to the mucosa or submucosa, and it is of good prognosis.

Prognosis:

- For early gastric ca. the 5-years survival rate is 90-95%
- For advanced gastric ca. the 5-years survival rate is 15%.

Gastrointestinal Stromal Tumor

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

Epidemiology

GISTs are slightly more common in males.

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.

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.

Pathogenesis:

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.

The most useful diagnostic marker is c-KIT, consistent with the relationship between GISTs and interstitial cells of Cajal, which is immunohistochemically detectable in 95% of these tumors.

Other marker is CD34, DOG1

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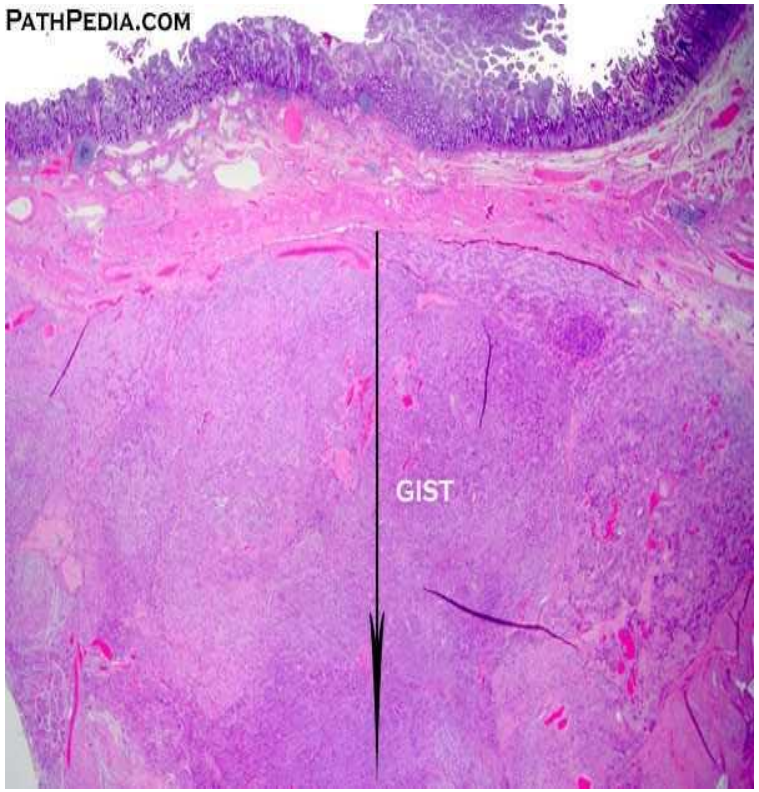
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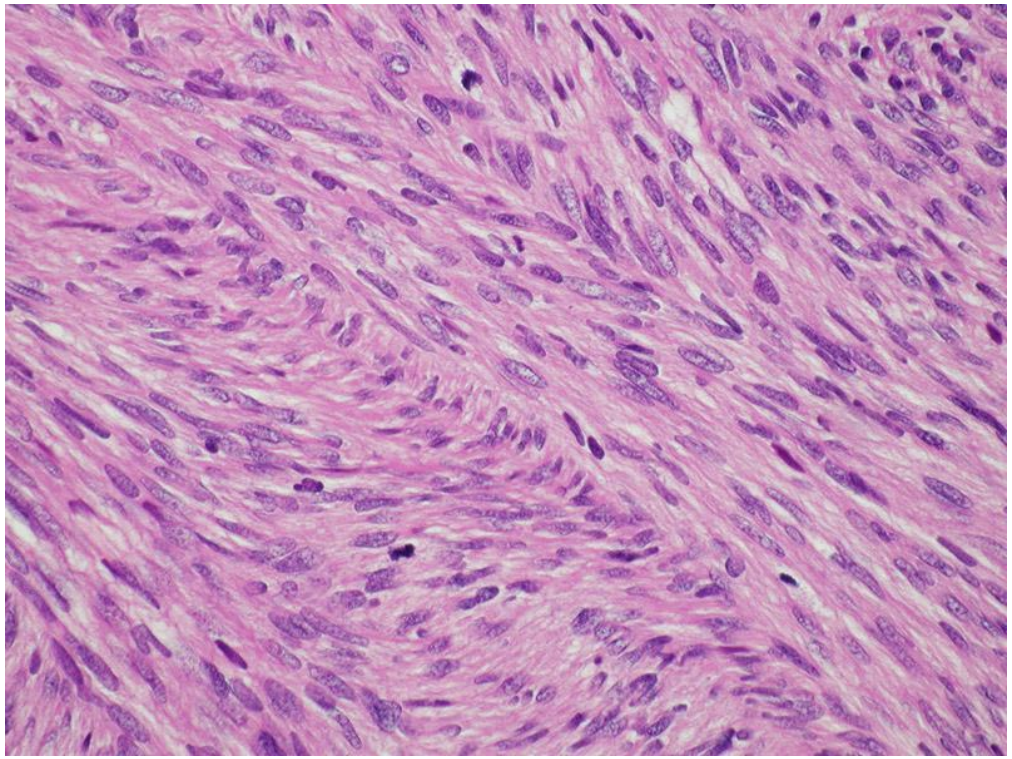
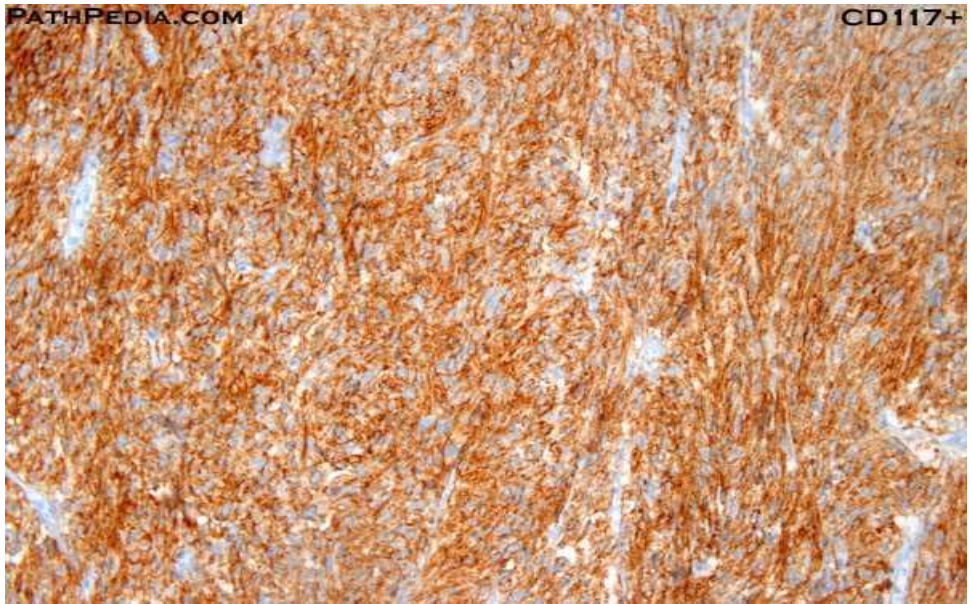
GIST

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CD117+

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