GI

PATHOLOGY

2

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Barrett Esophagus

One of the complications of reflux esophagitis is barrett esophagus, it's a metaplasia (from squamous to another type of epithelium which is more resistant to acids, **usually intestinal type**, might be glandular gastric type).

The definite diagnosis of barrett esophagus is intestinal type epithelium in esophagus (which can be seen in **biopsy** (the gold standard))

- Complication of chronic GERD
- Intestinal metaplasia within the esophageal squamous mucosa.
- 10% of individuals with symptomatic (Long lasting) GERD (Gastro esophageal reflux disease)
- Males>>females, 40-60 yrs
- **Direct precursor of esophageal adenocarcinoma**
- **Metaplasia >> 0.2-1% /year >>dysplasia>> adenocarcinoma**.

Metaplasia is Reversible, since it's an adaptive mechanism

at some point of metaplasia aposition of many mutations will happen producing dysplasia

MORPHOLOGY

- Endoscopy:
- Red tongues extending upward from the GEJ. (Gastro esophageal sphincter)

Contains reddish mucosa which is also present in reflux BUT it have certain changes that allow endoscopists to expect that this is metaplasia(barrett esophagus).

- Histology:
- Gastric or **intestinal metaplasia** (The gold standard for the diagnosis)
- Presence of goblet cells

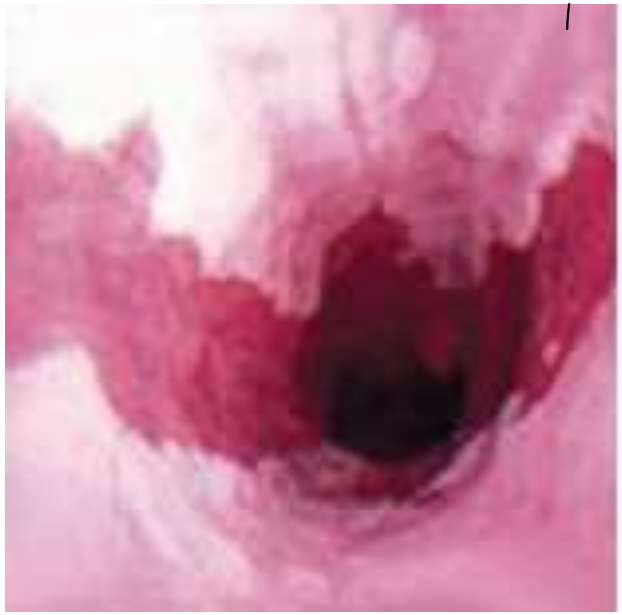
To tell that this is an intestinal epithelium, which type of cells should be seen? Goblet cells

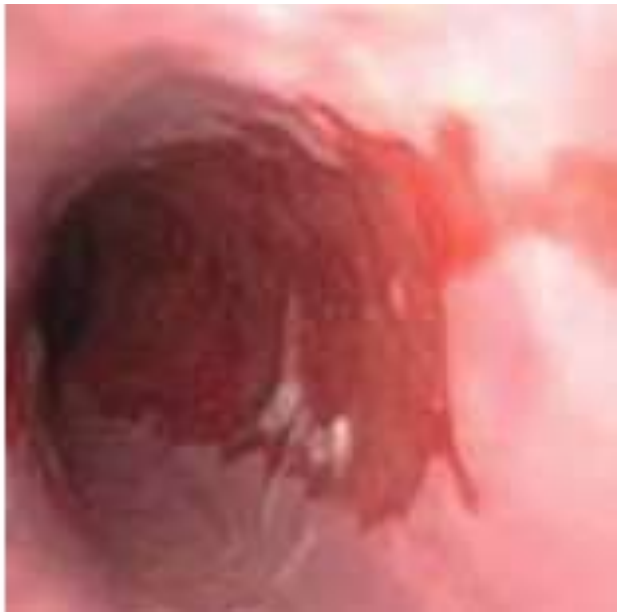
ممكن الوضع يتطور لdysplasia وممكن لا

- +-Dysplasia : low-grade or high-grade
- Intramucosal carcinoma: invasion into the lamina propria.

Low grades can regress while in high grade there is a high incidence to become an invasive carcinoma

These are the tongues of red mucosa which ascend from the gastro esophageal sphincter upward in the esophagus





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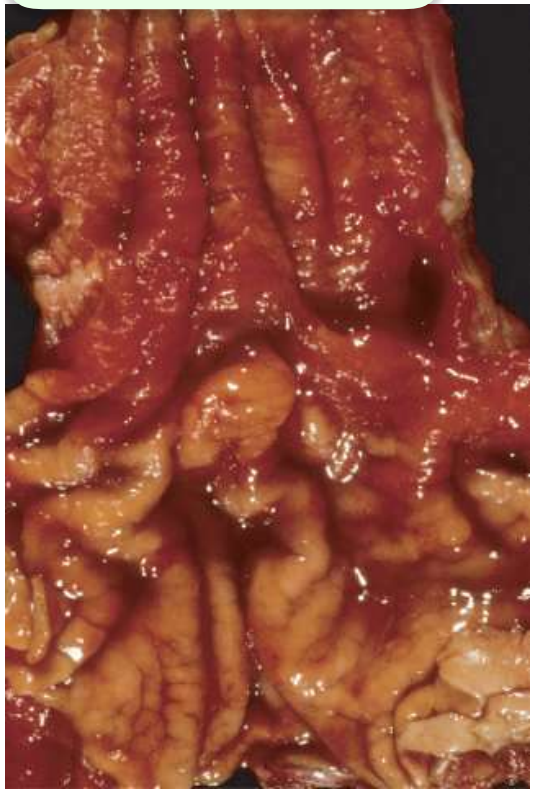
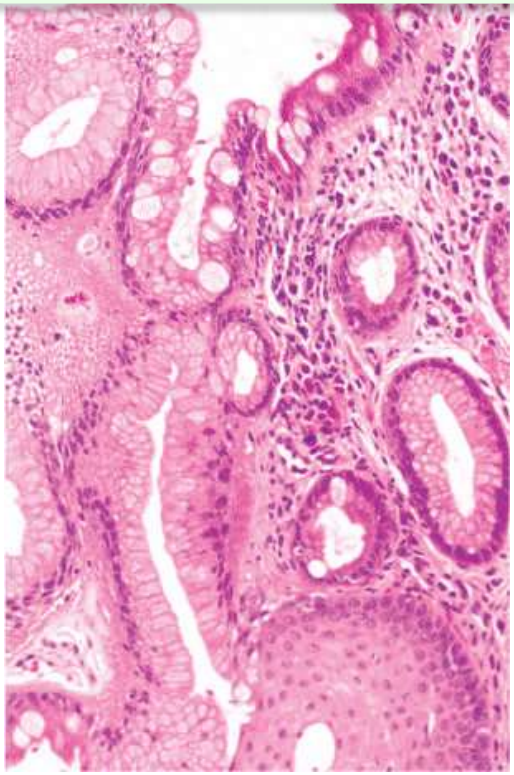
The pink nice color of esophagus is lost



Notice that here we have many glands, containing goblet cells instead of sequamus epithelium



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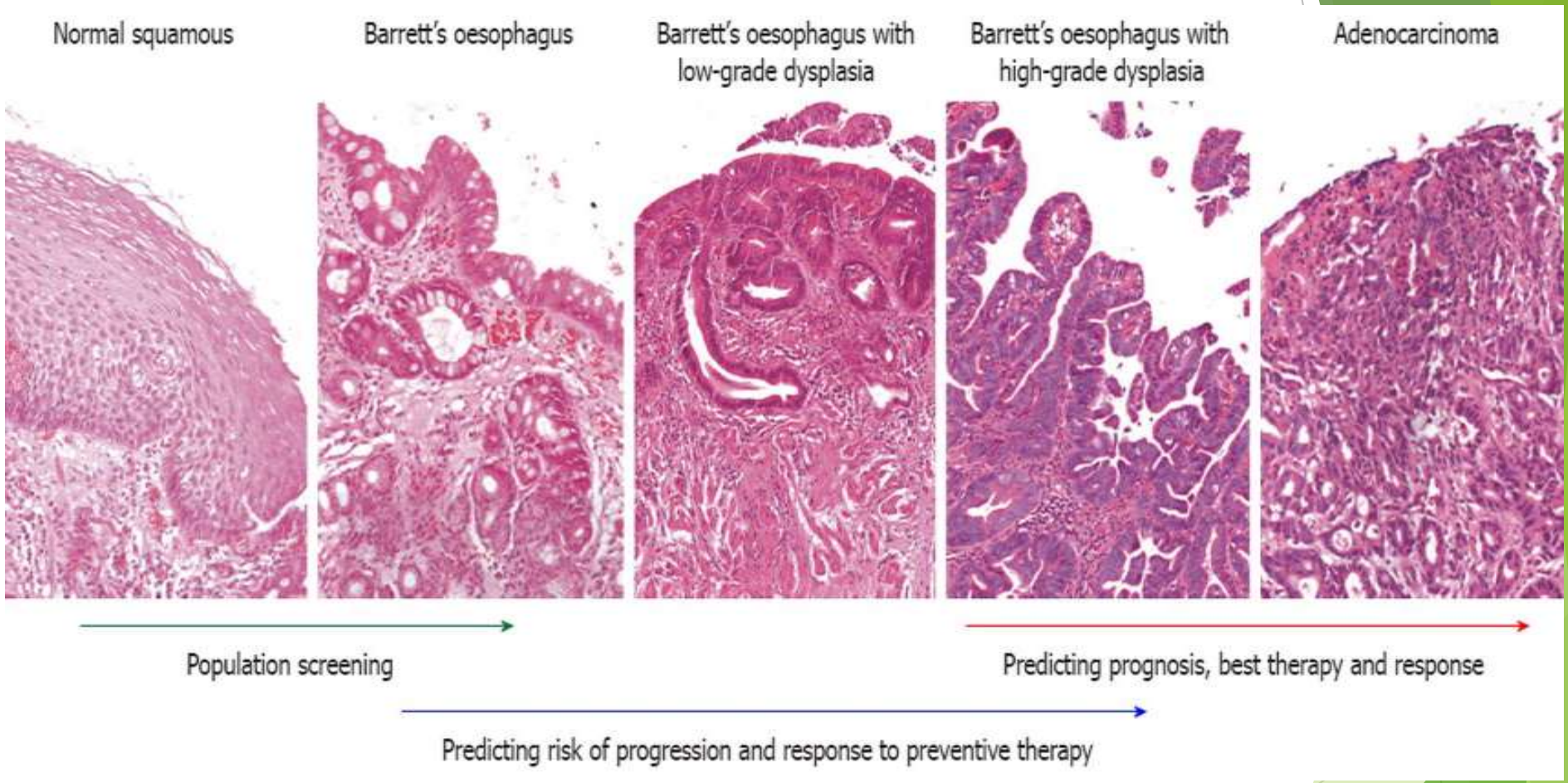


Management of Barrett

If there is no dysplasia (dysplasia عندهم يصير ما قبل).

- Periodic surveillance endoscopy with biopsy to screen for dysplasia (Follow up) + **proton pump inhibitors**.
- High grade dysplasia & intramucosal carcinoma needs Surgical interventions.

ESOPHAGEAL TUMORS

There are many esophageal tumors ,but the most important that you should know these two epithelial tumors :-

- Squamous cell carcinoma (most common worldwide)
- Adenocarcinoma (on the rise, half of cases)

Because of the development of Barrett esophagus

In the past, squamous cell carcinoma was more common than adenocarcinoma but nowadays they are comparable (because adenocarcinoma is on the raise).

Adenocarcinoma

- Background of Barrett esophagus and long-standing GERD.
- Risk factors: dysplasia associated Barrett, smoking, obesity, radioTx.
- Male : female (7:1)
- Geographic & racial variation (developed countries)

Pathogenesis

- From Barrett>>dysplasia>>adenocarcinoma
- Acquisition of genetic and epigenetic changes. (Mutations)
- Chromosomal abnormalities and TP53 mutation.

MORPHOLOGY

- Distal third.
- Early: flat or raised patches
- Later: exophytic infiltrative masses

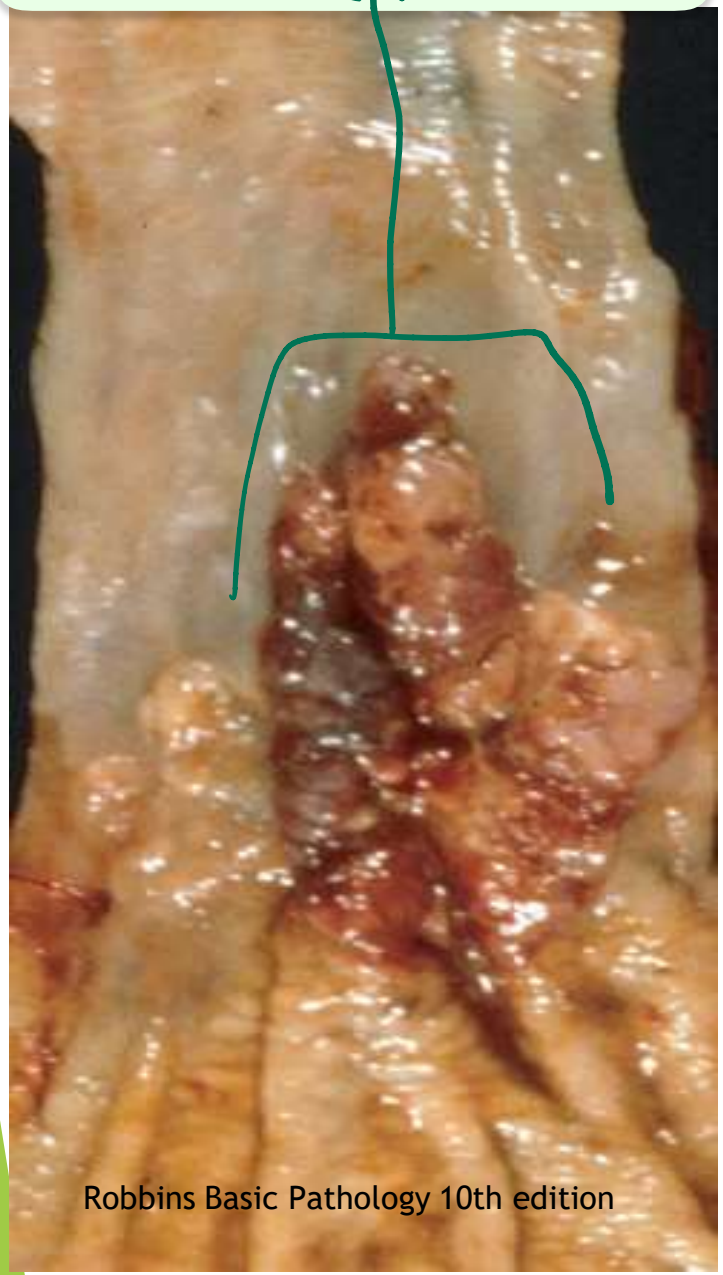
We usually say tumor means mass, but it is not necessary, sometimes it's an ulceration.
So it can be flat or raised tumor polypoid lesion.

- Microscopy:
- Forms glands and mucin.

→ "Adenocarcinoma"

From google :Ulcerating cancers are sometimes called fungating cancers (tumours) or wounds.

Fungating mass with adjacent ulcer at the junction between the stomach & the esophagus



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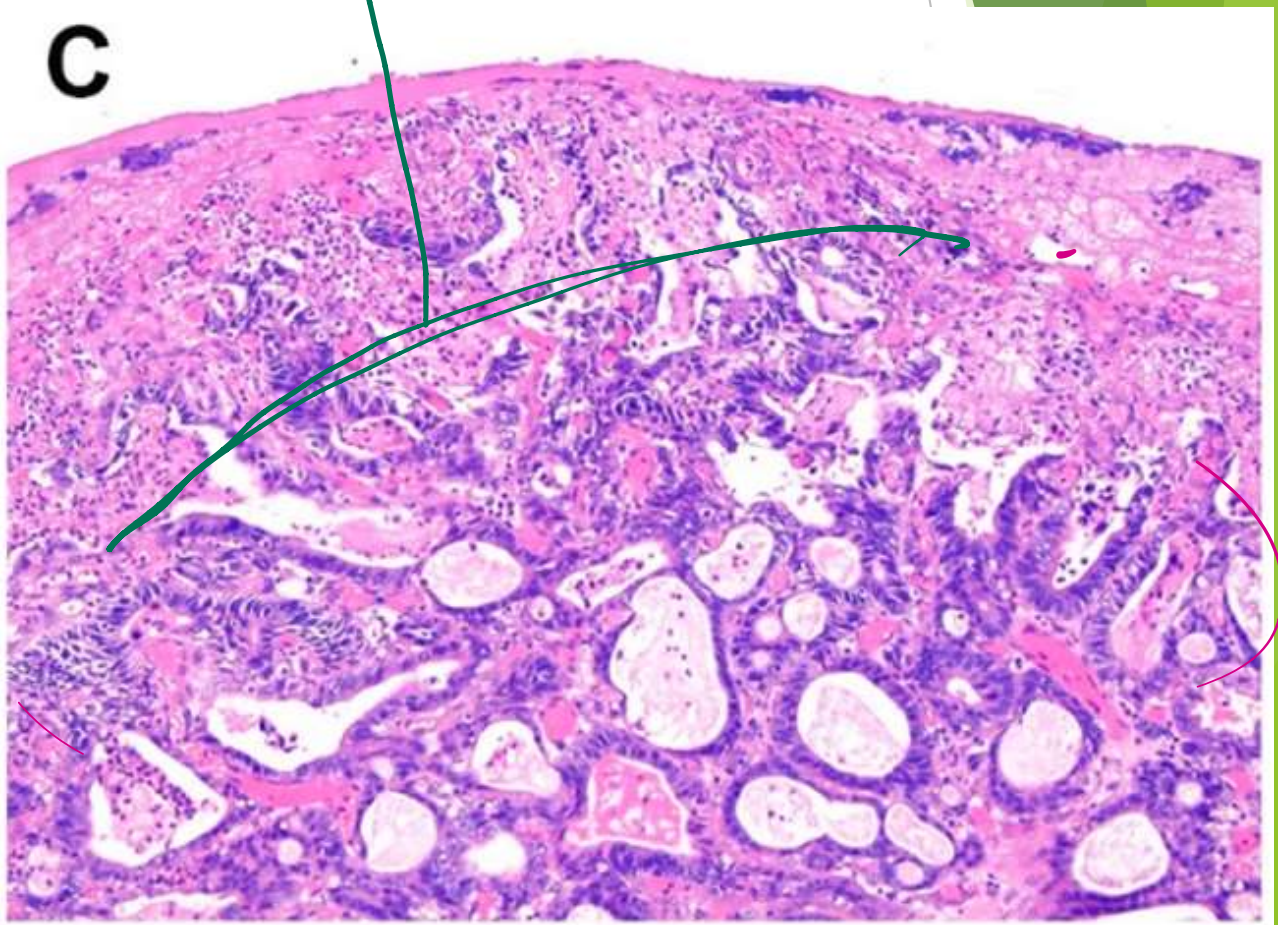
Here we can see the infiltrative glands that are invading the stroma, without invasion we can't call it cancer (dysplasiaبضل اسمها).



Clinical Features

Patients with cancer & barrett esophagus are more likely to have symptoms of reflux with the symptoms of barrette (heartburn + dysphagia) , then they develop :-

حرقة المعدة عسر البلع

- Pain or difficulty swallowing worsening of dysphagia
- Progressive weight loss
- Chest pain
- Vomiting.
- Advanced stage at diagnosis: 5-year survival <25%.
- Early stage: 5-year survival 80%

Sometimes tumor can make a fistula, especially in squamous cell carcinoma—> connection with trachea—>aspiration pneumonia

What is really bad about adenocarcinoma that when they present, they present in a late stages ,,,meaning that (at the time of diagnosis they already have metastasis)

فقط المرضى المحظوظين(وهم نسبة قليلة من المرضى) هم اللي بكون عندهم reflux واكتشفنا انه عندهم barrett بنخليهم تحت المراقبة (Periodic surveillance) عشان اذا صار في سرطان نكتشفه بمرحلة مبكرة.

Squamous Cell Carcinoma

- Male : female (4:1)
- Underdeveloped countries. At higher risk

- **Risk factors:**
- Alcohol
- Tobacco use

most important

- Poverty
- Caustic injury
- Achalasia .
- Plummer-Vinson syndrome
- Frequent consumption of very hot beverages
- Previous radiation Tx .

Females with iron deficiency anemia,esophageal webs/pathology

From google:A disorder marked by anemia caused by iron deficiency, and a web-like growth of membranes in the throat that makes swallowing difficult

barrett esophagus الدكتورة ركزت على انه هون ما في

Pathogenesis

- In western : alcohol and tobacco use.
- Other areas: polycyclic hydrocarbons, nitrosamines, fungus-contaminated foods
- HPV infection implemented in high risk regions.
  - Not very common

In all upper aerodigestive tract squamous cell carcinoma there is a role of HPV

MORPHOLOGY

Mass
One ulcer
One site of squamous cell carcinoma

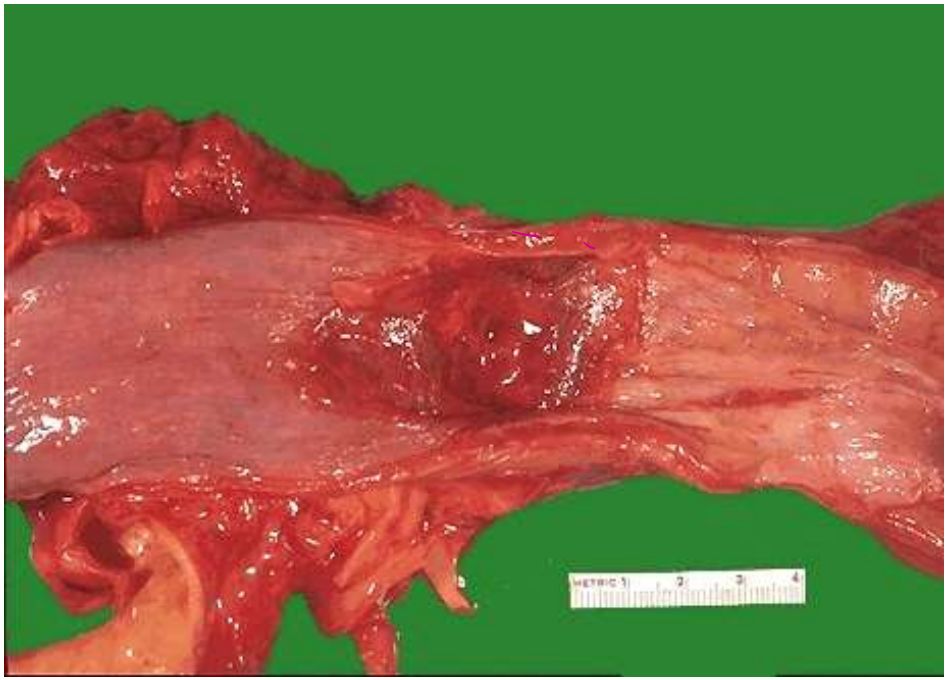
- Middle third (50% of cases)
- Polypoid, ulcerated, or infiltrative.
- Wall thickening, lumen narrowing
- Invade surrounding structures (bronchi, mediastinum, pericardium, aorta).

Or other areas like lower esophagus, in this case we have to take a biopsy for diagnosis (endoscopy isn't enough)

Gold standard

Mid esophagus

Polypoid red mass in the mid esophagus



Microscopy:

Infiltrative squamous cell carcinoma

- Pre-invasive: Squamous dysplasia & CIS. → Carcinoma in situ
- Well to moderately differentiated invasive SCC.
- Intramural tumor nodules → مثلا بتلاقي وحدة بال upper ووحدة بال middle ووحدة بال lower
- Lymph node metastases : → This is peculiar (غير مألوف) for squamous cell carcinoma
- Upper 1/3: cervical LNs
- Middle 1/3: mediastinalparatracheal, and tracheobronchial LNs.
- Lower 1/3: gastric and celiac LNs.

Clinical Features

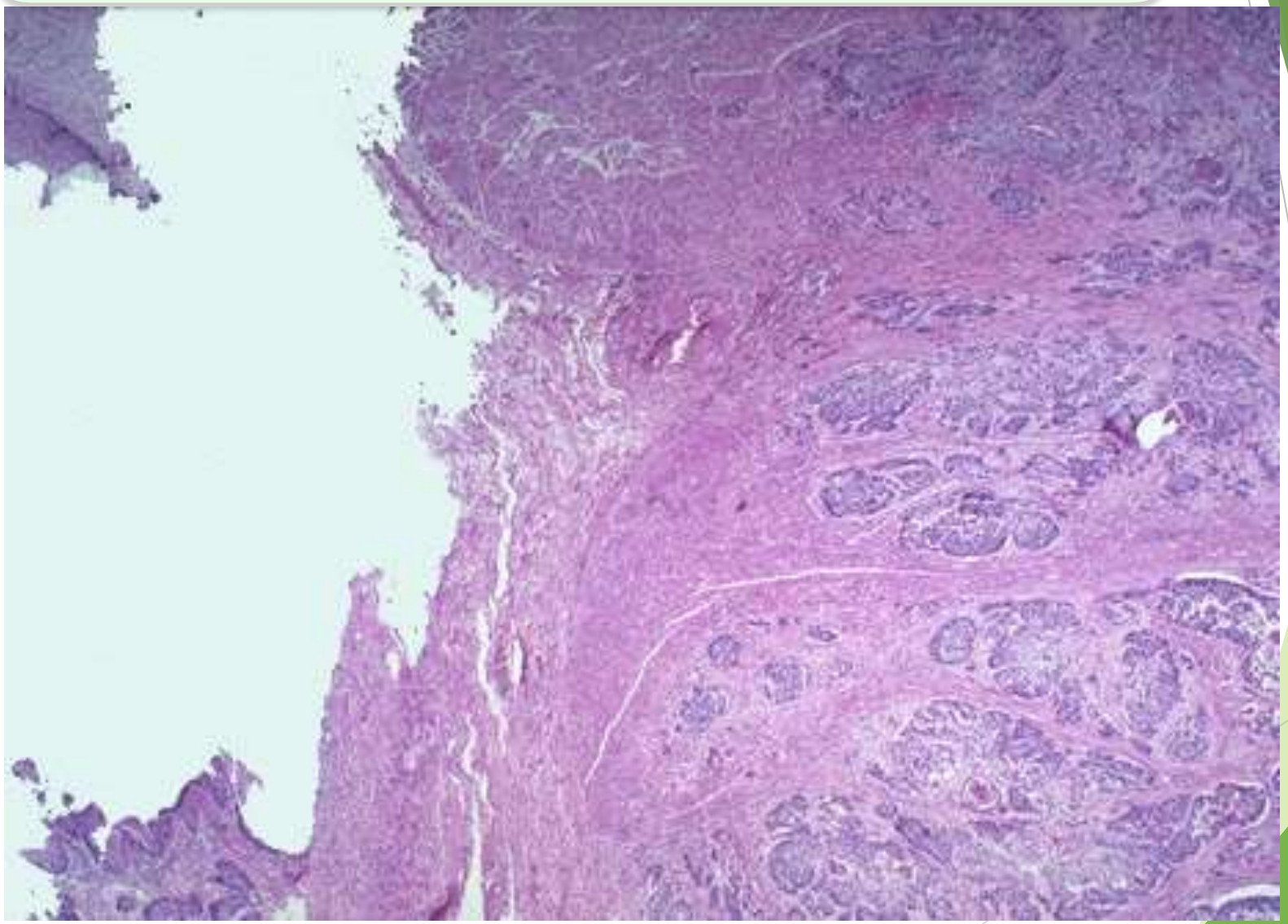
- Chest pain
- Dysphagia
- Odynophagia
- Obstruction
- Weight loss and debilitation
- Impaired nutrition & tumor associated cachexia
- Hemorrhage and sepsis if ulcerated.
- Aspiration via a tracheoesophageal fistula
- Dismal Px: 5 year survival <9%

Weight loss is the alarming sign for any malignancy

"Aspiration pneumonia"

Invasive SCC

Infiltrative,ugly squamous epithelial cells ➡ invasion to the underling mucosa



Carcinoma in situ limited by the basement membrane → invasion to the wall

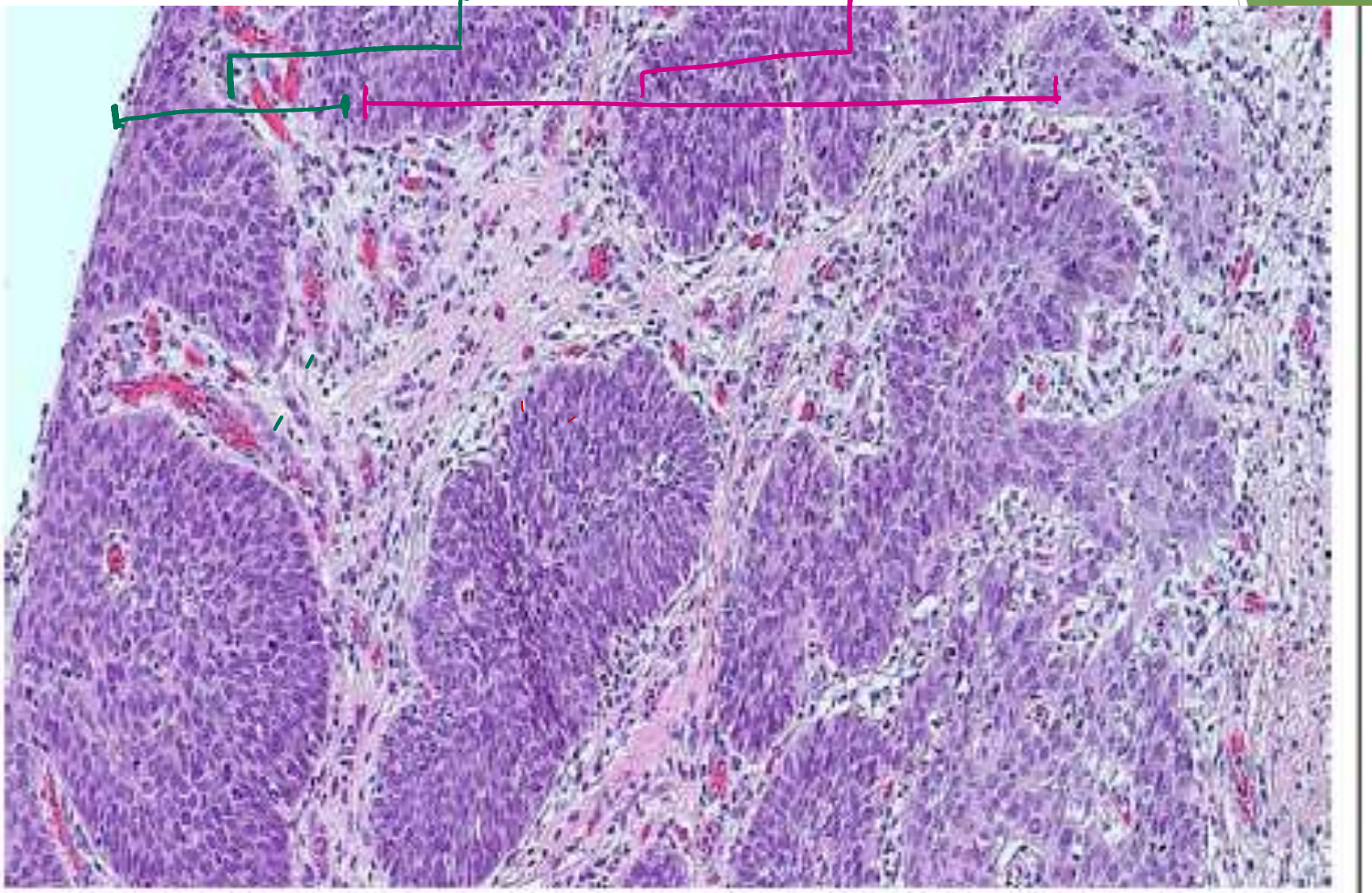


Figure 4: Squamous cell carcinoma of the esophagus with focal invasion into the muscularis mucosa and associated desmoplastic response.

Pathology of the stomach-part 1

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overview

- Gastric diseases:
- 1-Inflammatory.
- 2-Neoplastic.

The middle part of stomach

- Stomach parts: cardia, fundus, body, antrum, pylorus.

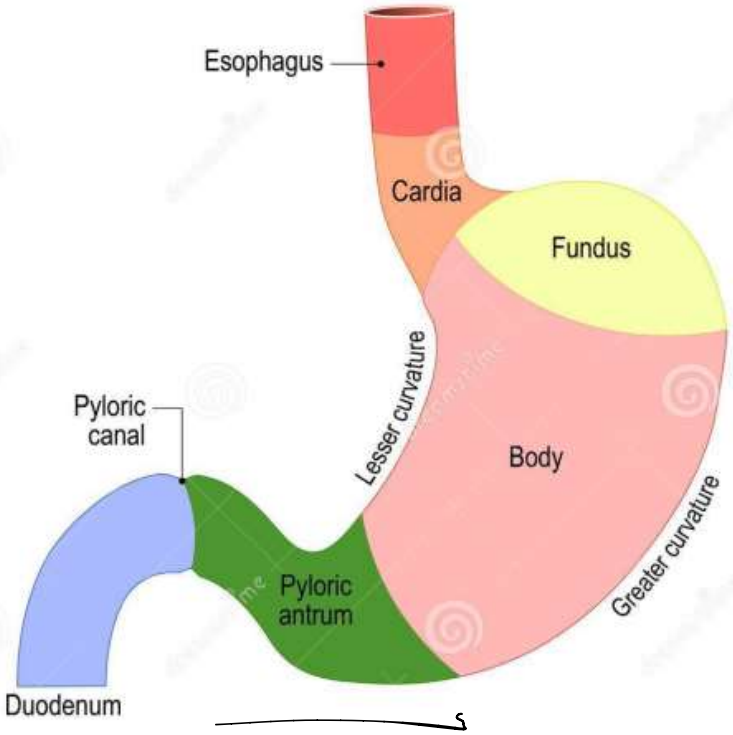
Cardia is located immediately under gastroesophageal sphincter

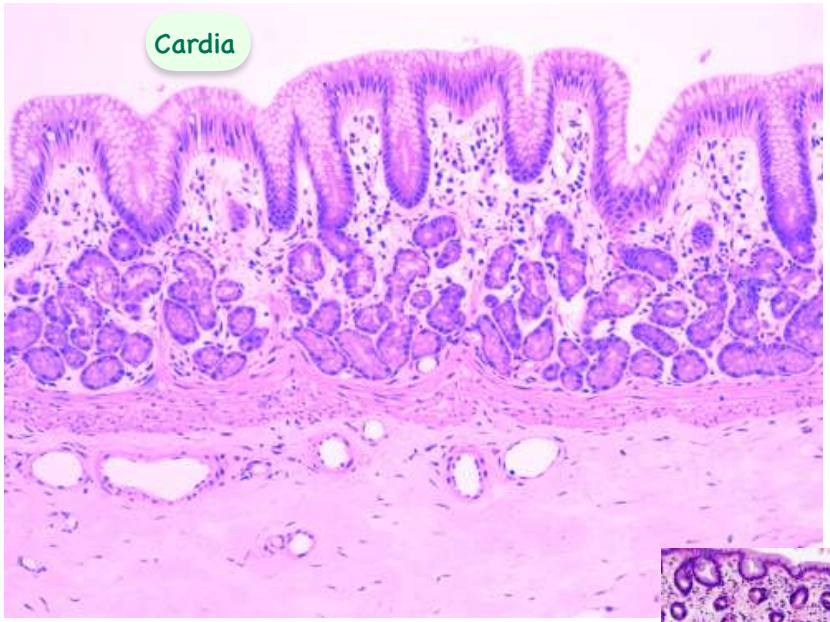
But why should we know about these regions of stomach ,,,,,
The cellular component & the distribution of cells are different among these parts ,hence the pathology will be different

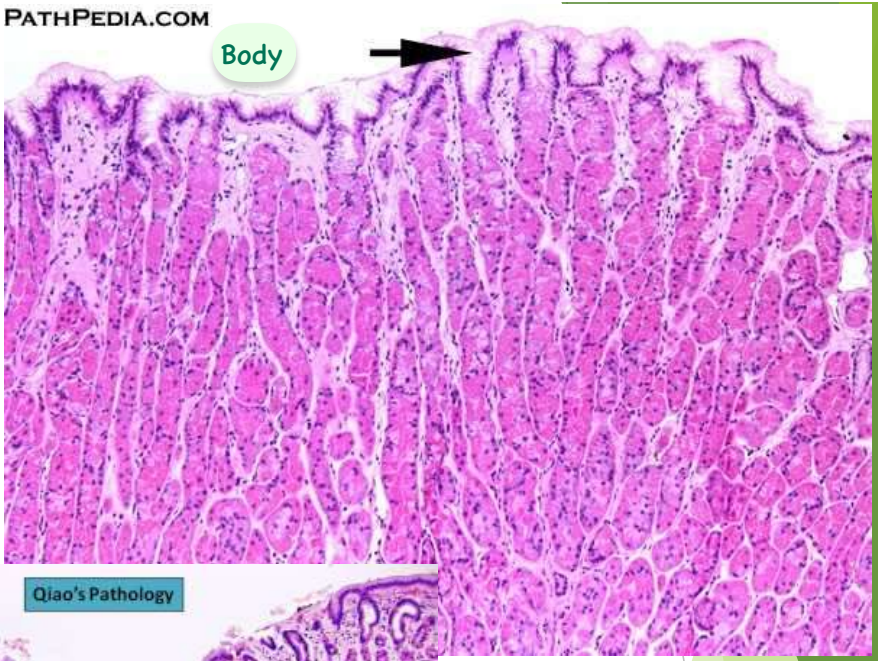
- Cardia: mucin secreting foveolar cells.
- Body and fundus: parietal cells (HCL) and chief cells (pepsin).
- Antrum: neuroendocrine G cells (gastrin)

#Ponder the histological sections below

Sections of human the stomach







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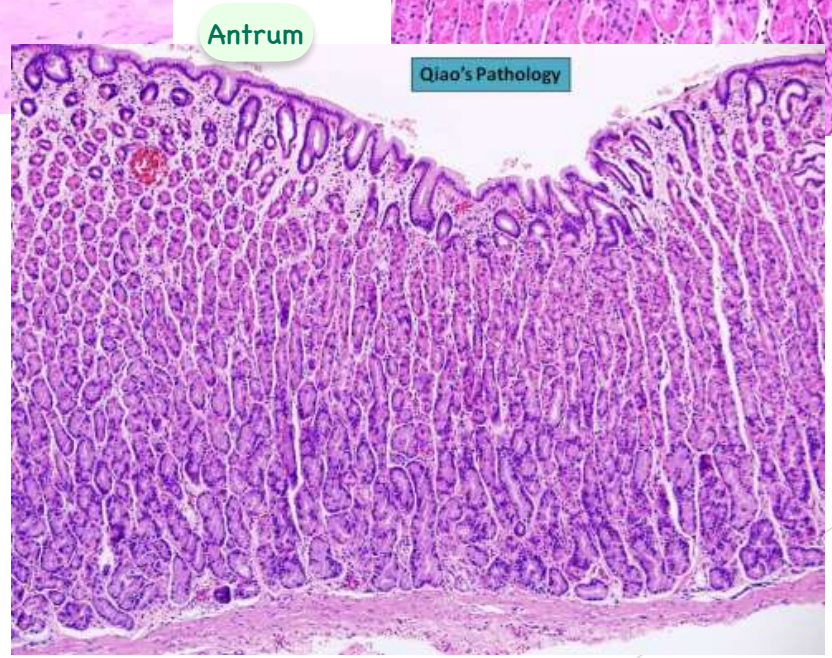


Inflammatory conditions

- Acute gastritis.
- Chronic gastritis.
- Acute gastric ulcer.
- Chronic peptic ulcer.

ACUTE GASTRITIS and gastropathy

- **Acute gastritis**: Mucosal injury, neutrophils present. ITIS ⟶ obvious inflammation & inflammatory cells
- **Gastropathy**: regenerative, no inflammation. no ITIS ⟶ not obvious inflammation

- **Causes:**
- NSAIDs, alcohol, bile, and stress-induced

So we say don't take them on empty stomach

- **Clinical features:**
- Asymptomatic; epigastric pain, nausea, vomiting.

Can be

Or symptomatic, M.C symptoms :-

Acute gastritis vs chronic gastritis

Sudden , for short period of time

Most commonly caused by NSAIDs

Gradual , for long period of time

Most commonly caused by H.pylori infection

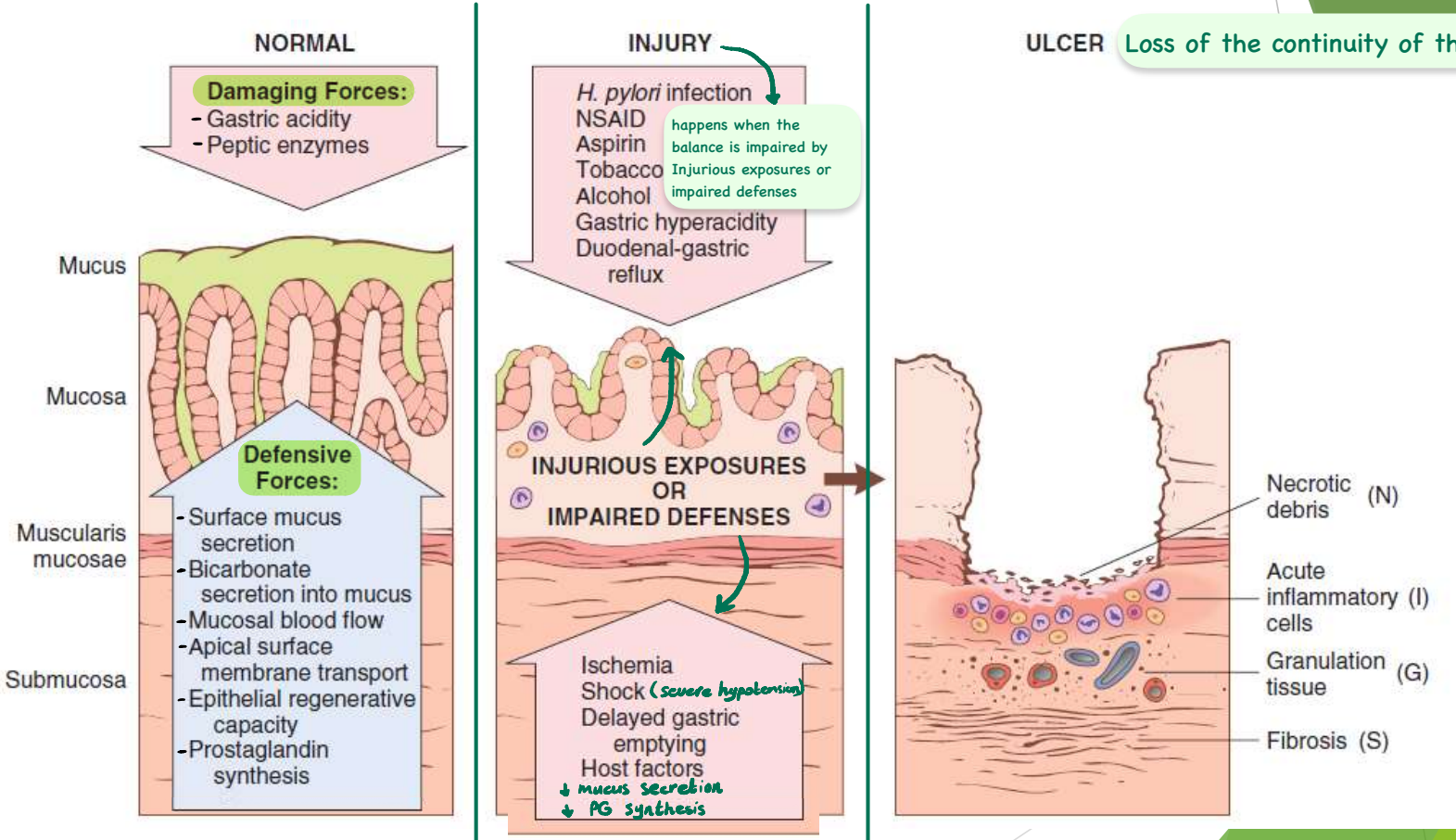
Notes :

1- Pylori gastritis is the most common type of gastritis

2- The acute gastritis which caused by H.pylori is usually asymptomatic

Pathogenesis

for all types of gastritis & gastric ulcers is the same (imbalance between gastric protective forces & gastric damaging forces)



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Pathogenesis

- Imbalance between protective and damaging forces

- **Main causes:**
- **NSAIDs (COX1 and COX2 inhibitors)** → inhibit PG synthesis (PGs stimulate almost all of the protective factors in stomach) ,next slide
- **Uremic patients (ammonia inhibit bicarbonate transport)** → ↑levels of ammonia
- **H pylori (urease produces ammonia)**
- **Old age (reduced mucin and bicarbonate secretion)**
- **Hypoxia**
- **Harsh chemicals**, (acids or bases) (direct epithelial injury)
- **Alcohol, NSAIDs, radiation therapy (direct mucosal damage)** → Note that NSAIDs have direct & indirect (via PG syn. Inhibition) effects
- **Chemotherapy (inhibit DNA synthesis and cellular renewal)**

prostaglandins E2 and I2:

- Stimulate nearly all of the defense mechanisms including
- Mucus and bicarbonate secretion,
- mucosal blood flow
- Epithelial restitution.
- Risk for development of NSAID- induced gastric injury is greatest with nonselective inhibitors, but selective COX2 inhibition, can also result in gastropathy or gastritis.

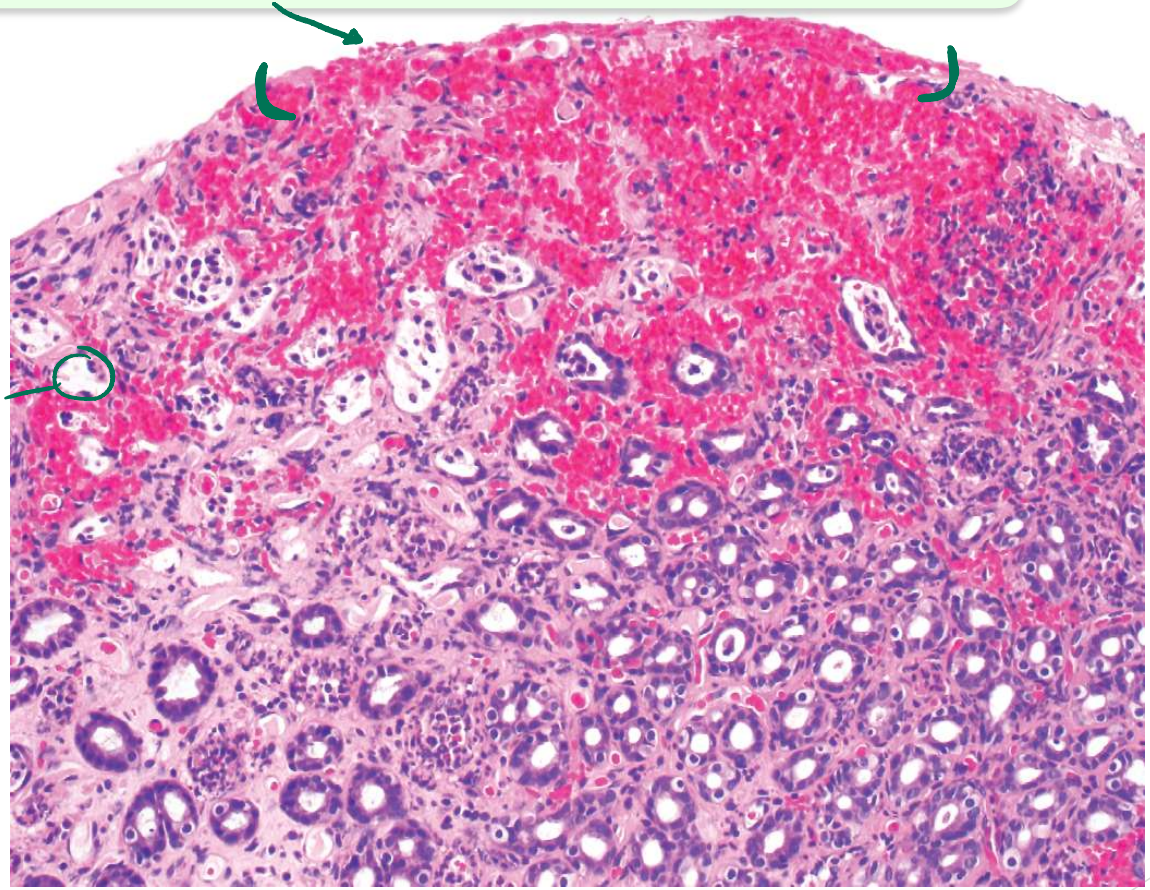
MORPHOLOGY

- Hyperemia (redness). Ponder the image in the next slide
- Edema and slight vascular congestion
- Neutrophils, lymphocytes, and plasma cells are not prominent.
- Intact surface epithelium. if the surface epi. damaged ➡ erosions , but if it severely damaged ➡ ulcers
- Advanced: Erosions and hemorrhage, acute erosive hemorrhagic gastritis.
  Only erosion —> erosive gastritis , erosion with bleeding —> erosive hemorrhagic gastritis
- Active inflammation (neutrophils) is not necessary.

ACUTE GASTRITIS

Usually we don't need biopsy ,but if we take :-

You will see :- Edema (whitish regions are edema fluid collection) , congestion of B.V , bleeding (reddish areas) , loss of surface (erosions) , not obvious inflammatory component (not chronic)



Stress-Related Mucosal Disease acute gastric ulcers

- Severe physiologic stress:

The stress in these conditions causes increased production of CORTICOSTEROIDS which cause imbalance .

- Trauma
- Extensive burns
- Intracranial disease , ex:- intracranial tumors , increased intracranial pressure
- Major surgery
- Serious medical disease
- Critically ill patients

Acute gastric ulcers:

- ***Stress ulcers**:* critically ill patients with shock, sepsis, or severe trauma.

2 types of stress ulcers :-

- ***Curling ulcers**:* proximal duodenum , severe burns or trauma.

- ***Cushing ulcers**:* stomach, duodenum, or esophagus, intracranial disease, high risk of perforation.

names/associations only , for example:- patient has gastric ulcer with high intracranial pressure –> this ulcer called Cushing ulcer

Pathogenesis

As we say most of ulcers have the same pathogenesis, here we lost the balance mainly due to ischemia (decrease in defense mechanisms of stomach)

- **Stress ulcers:**
- Mostly due to Local ischemia caused by.
- Systemic hypotension.
- Splanchnic vasoconstriction (stress induced).
- Systemic acidosis (lower intracellular PH).
- COX2 expression is protective.

V.C of the blood vessels that supply GIT

- **Cushing ulcers:**
- Direct vagal stimulation, acid hypersecretion.

MORPHOLOGY

- Acute ulcers are rounded and typically less than 1 cm in diameter
- Shallow to deep.
- Ulcer base brown to black
- Anywhere in stomach
- Usually, multiple.
- Normal adjacent mucosa
- No scarring
- Healing with complete epithelialization occurs days or weeks after removal of injurious factors

#Small ,rounded ,multiple and black in color due to the presence of blood & note that the adjacent gastric mucosa is normal (no chronic gastritis)

Clinical features

- Nausea, vomiting,
- Melena black stools that occur as a result of gastrointestinal bleeding ~Osmosis.
- Coffee -ground hematemesis (Blood / vomiting)
- Perforation complication.

- Prophylaxis with proton pump inhibitors
- Outcome depends on severity of underlying cause.

No One Can Survive Here ✓
Good luck 💚