GI

Pathology

LEC no.2

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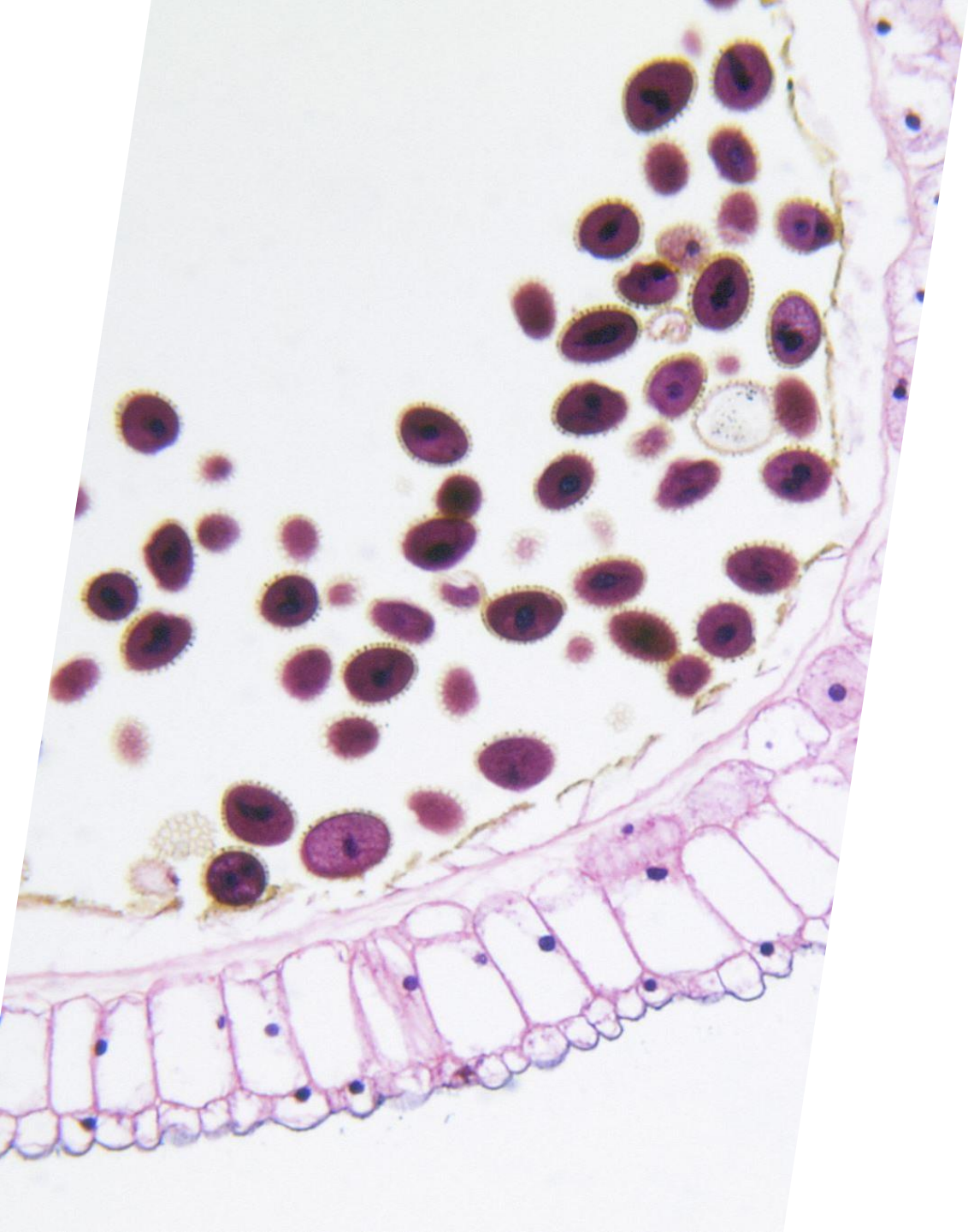

Pathology of the stomach- 1

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Overview

Gastric diseases:

1-Inflammatory.

Broad category

2-Neoplastic.

Polyps and cancers

Normal anatomy & histology:

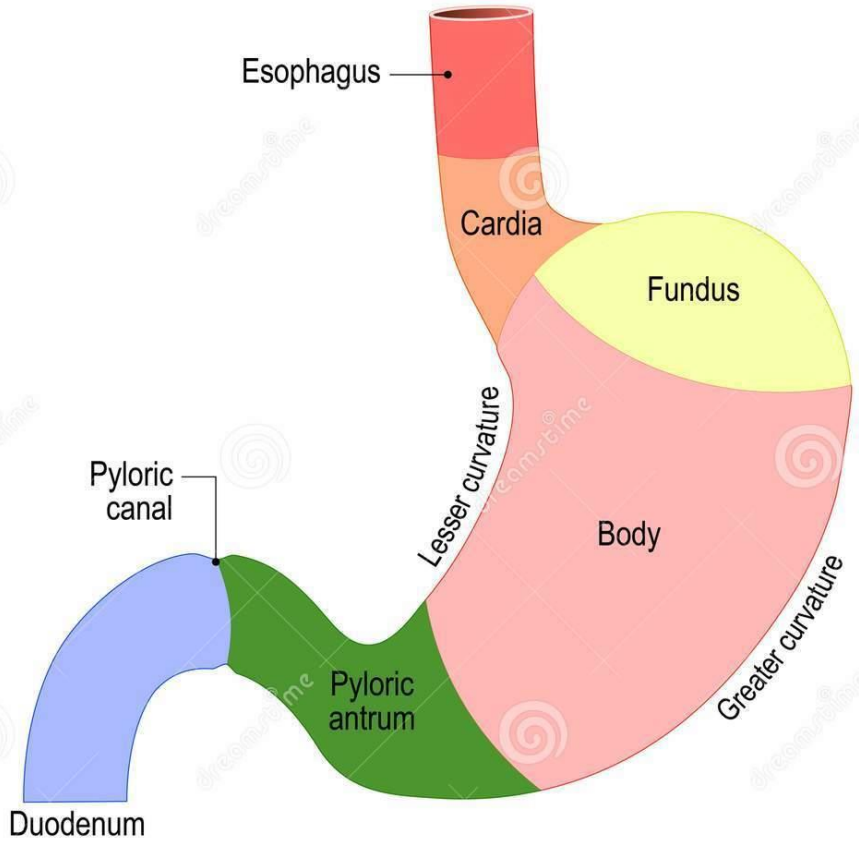
The stomach is subdivided into 4 parts

- 4 mains parts: cardia, fundus, body, antrum (pylorus).

We also have different anatomical landmarks with different histology, which is important for understanding the pathology. We, as pathologists, have to know the difference between a normal and an abnormal biopsy in order to diagnose correctly.

- Cardia: mucin-secreting foveolar cells. (produces mucin that lines the stomach from the inside)
- Body and fundus: characterized by the presence of two specialized cells: parietal cells (HCL) and chief cells (pepsin).
- Antrum: neuroendocrine G cells (produce gastrin, which in turn stimulates acid production) and there are foveolar cells as well.

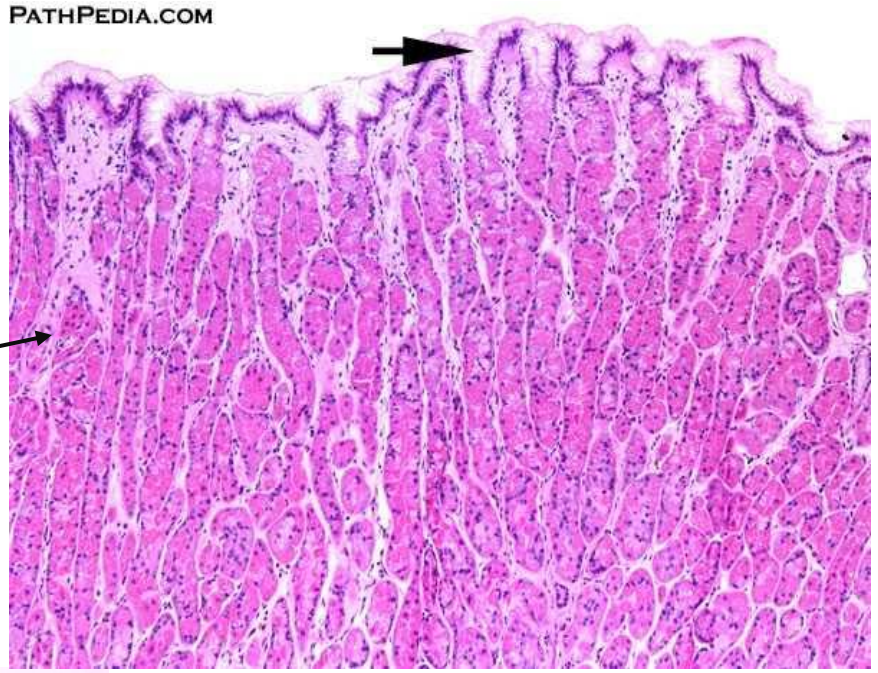
Sections of human the stomach

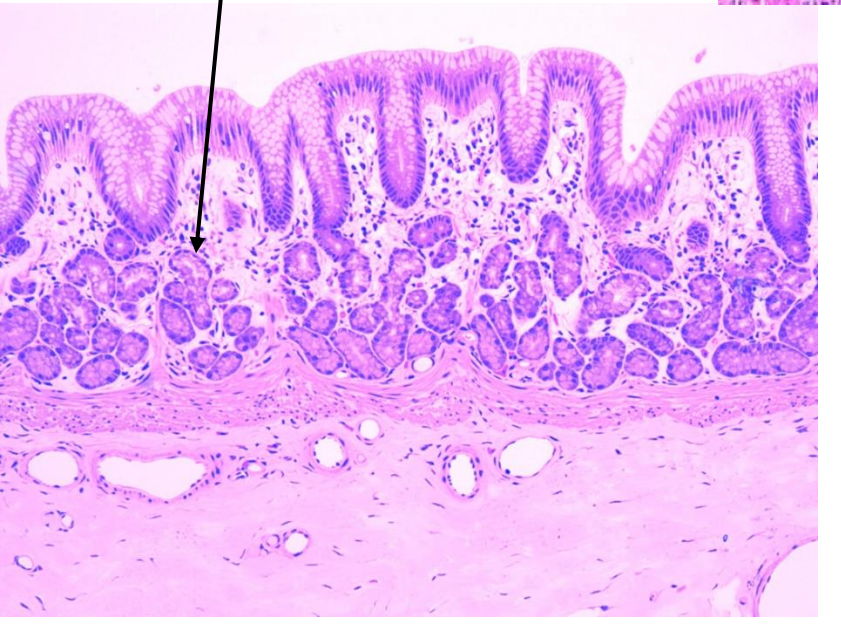


The esophagus ends in the gastroesophageal junction, then we have cardia, then the fundus, then the body (LARGEST AREA), then antrum, and finally duodenum.

On the right, histologically, this is the body and funds it has a thick mucosa (oxyntic mucosa), the pinkish cells are the parietal cells.

Below, this is the cardia it has a thin mucosa and it has a foveoler cells





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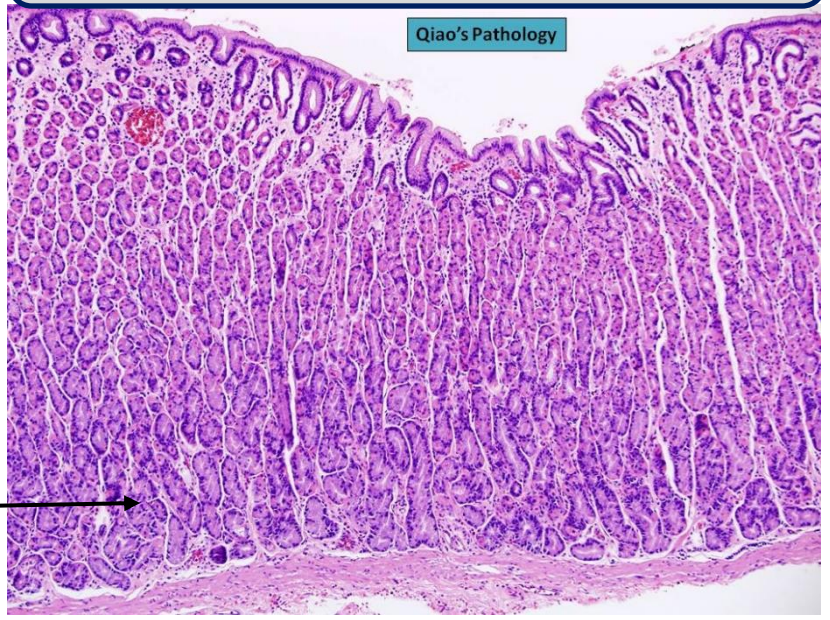
Pyrolic antrum, more blue-ish



Antral glands

Inflammatory conditions

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

ACUTE GASTRITIS and gastropathy

- **Acute gastritis**: Mucosal injury, neutrophils present.
- **Gastropathy**: regenerative, no/rare inflammation.

- **Causes of gastropathy (and acute gastritis to a certain extent):**

NSAIDs (mainly), alcohol, bile,

and stress-induced

Here we are talking about physiological stress (patient had trauma, patient in ICU, major surgery)

- **Clinical features (of both: acute gastritis and gastropathy):**

- Asymptomatic.

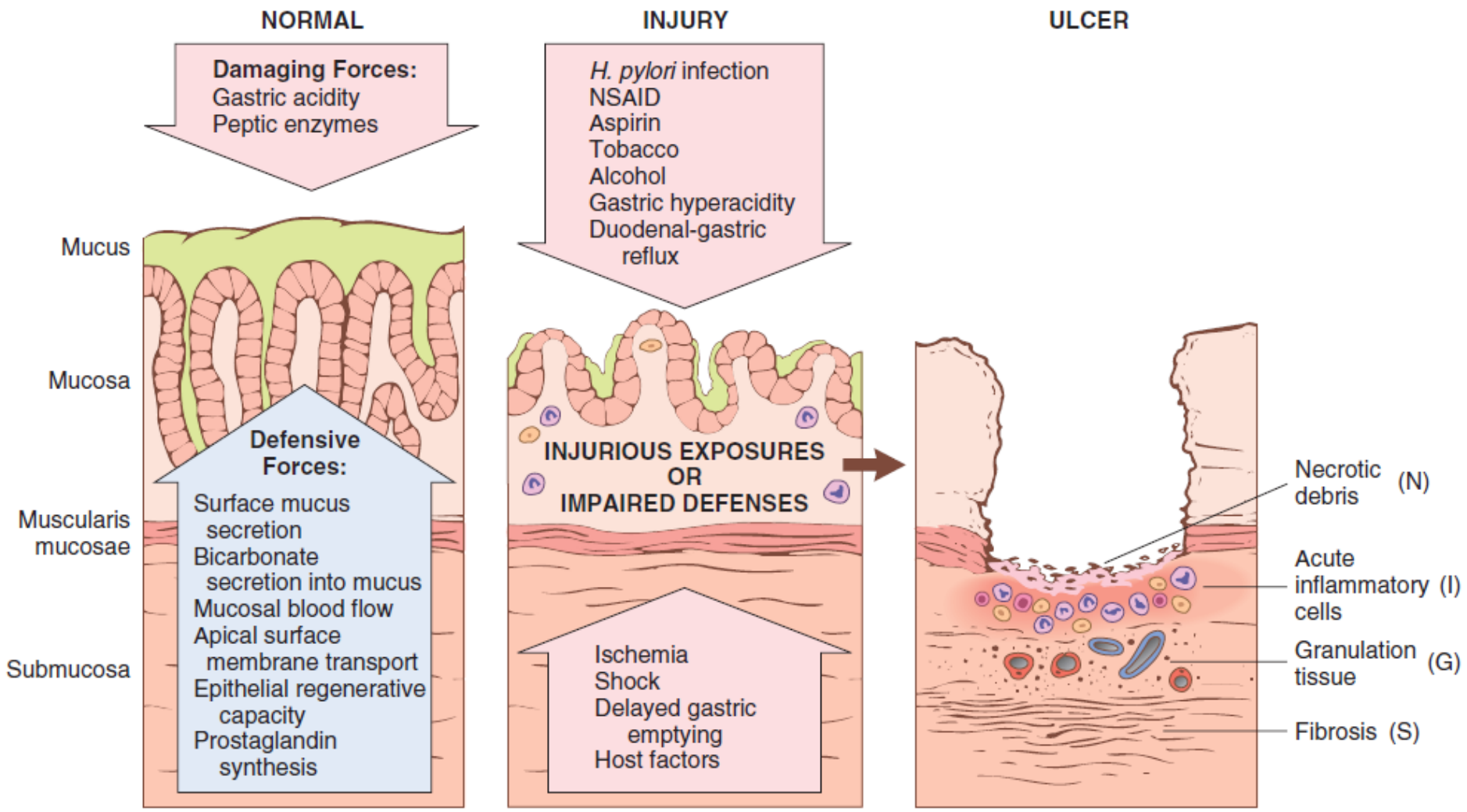
- Epigastric pain, nausea, vomiting (in milder forms, these are typical characteristics of all gastric diseases)

- Severe (acute gastric injury): erosions, ulcers, sometimes hemorrhage in the stomach which causes hematemesis and/or melena.

Acute gastritis are so similar. The difference between them is in the presence of inflammatory cells.
Acute gastritis → present
Gastropathy → absent

✦ **Hematemesis: vomiting of blood.**
✦ **Melena: black-colored stool**
Both are indications of upper GI bleeding.

Pathogenesis



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▷ Acute gastritis, acute ulcers, chronic peptic ulcer ALL have the same pathogenesis

▷ The stomach carries normal damaging forces, which are:

- The acid produced by parietal cells.
- Peptic enzymes.

If these two came into contact along with the gastric lining, they'll cause digestion. And for this purpose, we have defensive forces normally present which are :

- Surface mucus secretion, by foveolar cells. Lining the stomach interiorly, acting as a barrier so that the acid and pepsin don't come in direct contact with the lining cells
- Bicarbonate secretions, which needs continuous blood flow. They buffer the acidity. Present in mucus, protects the lining from damage.
- Mucosal blood flow also buffers the acidity, it's also important for the regeneration of the gastric lining. GIT lining is of a high regenerative capacity because of the blood flow to these organs.
- Apical surface membrane transport, epithelial regenerative capacity, PG synthesis. That's why a medication that interferes with the PG synthesis, like NSAID's, exposes the stomach to damage.

▷ Any imbalance that causes injury (like NSAID's, smoking, aspirin, alcohol, bile reflux from duodenum to stomach, H. pylori infection) OR decrease in defense mechanisms (impaired defense mechanism) exposes the patient to acute/chronic gastritis, ulcer.

Always remember the imbalance between the damaging forces and the protective ones.

One of the things that impair the defense mechanisms is ischemia/shock state, when someone undergoes severe bleeding. The blood flow to the GI system will decrease dramatically, which increase the chance of acute stress ulcers

Pathogenesis of gastropathy, acute and chronic gastritis:

* **Imbalance between protective and damaging forces**

Main causes:

- **NSAIDs (COX1 and COX2 inhibitors)**
- **Uremic patients (ammonia inhibit bicarbonate transport)**
- **H pylori (urease produces ammonia)**
- **Aging (reduced mucin and bicarbonate secretion)**
- **Hypoxia (high altitudes)**
- **Harsh chemicals, (acids or bases) (direct epithelial injury)**
- **Alcohol, NSAIDs, radiation therapy (direct mucosal damage)**
- **Chemotherapy (inhibit DNA synthesis and cellular renewal)**

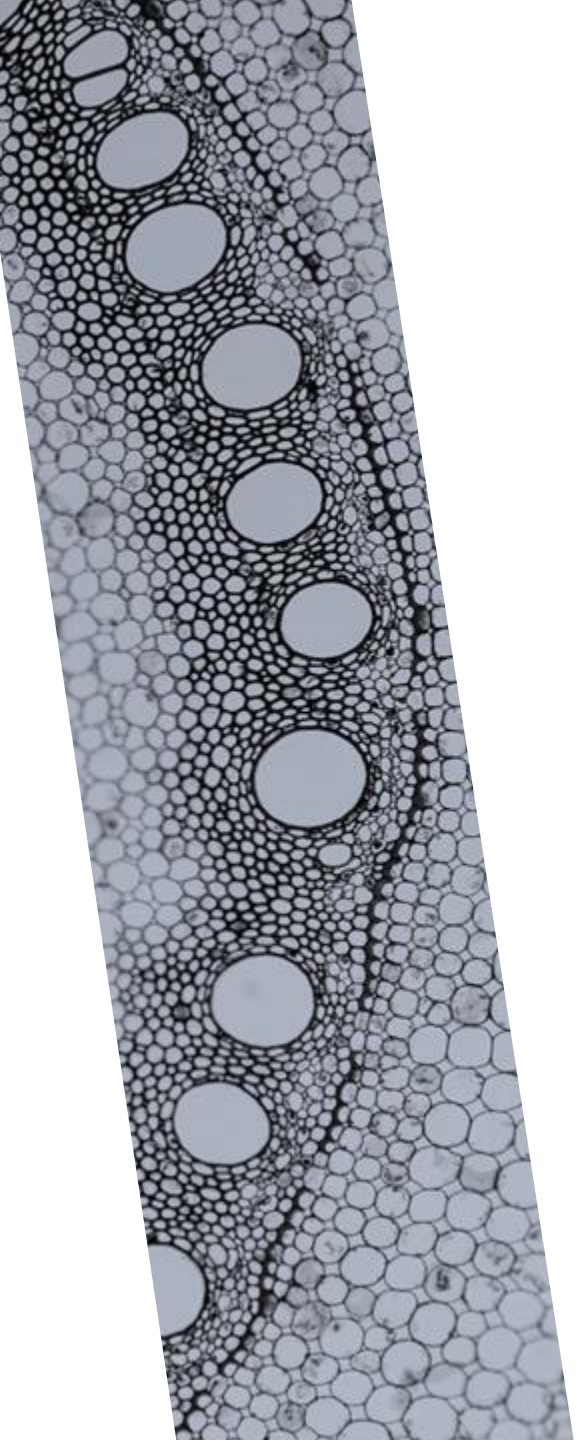
- **NSAIDs Inhibit PG synthesis.**
- **Uremia is present in patients with chronic renal failure, as they have high ammonia levels in blood.**
- **H. pylori possesses an enzyme called urease which converts urea to ammonia —> inhibiting bicarbonate secretion.**
- **Aging is associated with less efficiency of cellular properties. Old people have a higher chance of developing ulcers, gastritis.**
- **Harsh chemicals whether drunken accidentally or in suicidal attempts. Direct injury to epithelial cells, ulcers.**

prostaglandins **E2** and **I2**:

Anything that interferes with their production exposes the stomach to damage

- **Stimulate** nearly all the defense mechanisms including

1. Mucus and bicarbonate secretion,
2. mucosal blood flow
3. Epithelial restitution.



MORPHOLOGY

Either microscopic or macroscopic. Macroscopic tests are done by an internist through endoscopy or colonoscopy, which is essential before diagnosis.

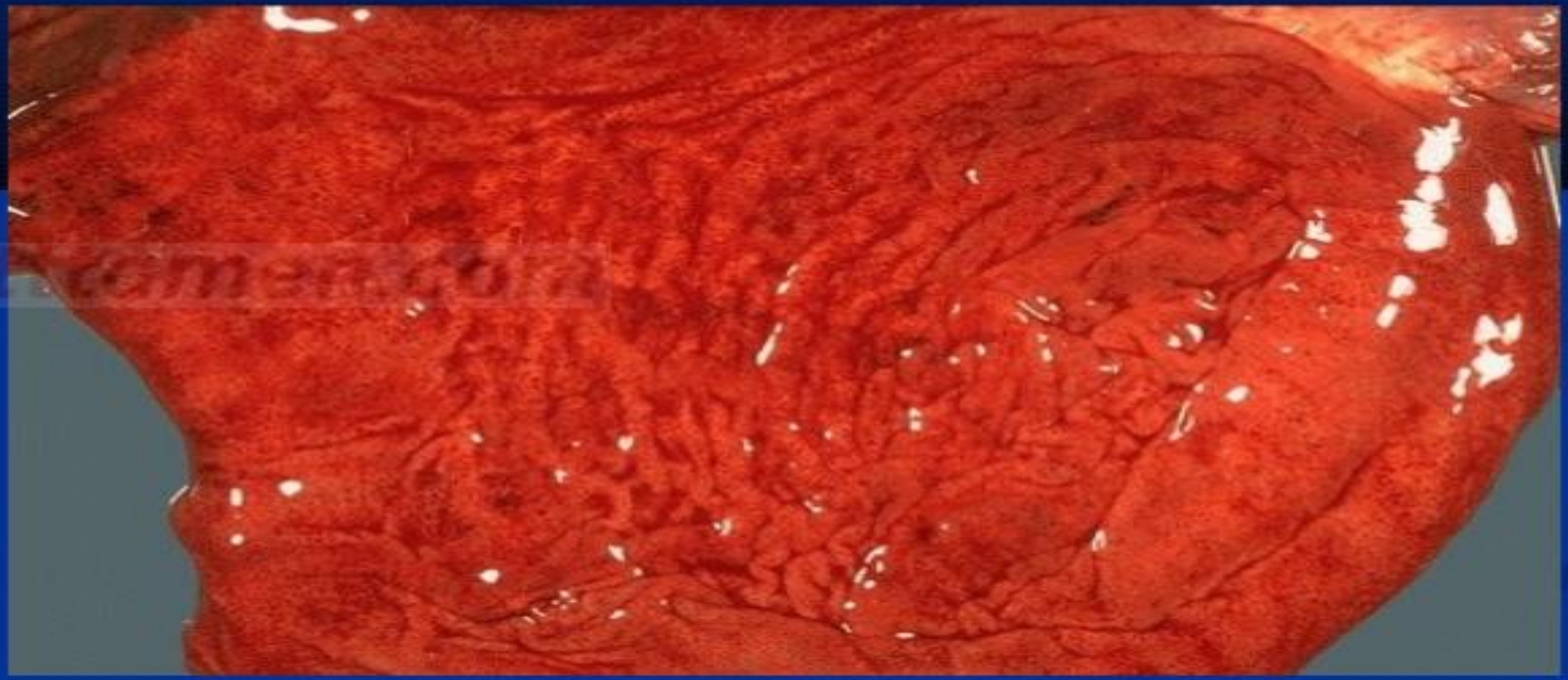
- Hyperemia (redness). The most common. We notice the red color of stomach mucosa instead of the normal light brown
- Edema and slight vascular congestion. And if we're talking about acute gastritis, we'll see neutrophils too.
- Neutrophils, lymphocytes, and plasma cells are not prominent.
- Neutrophils : Active inflammation (gastritis) .
- Intact surface epithelium if mild, or associated with ulcers and erosions. In this case we call it:
- **Acute erosive hemorrhagic gastritis (Advanced)**

Remember:
Treatment of gastritis & gastropathy is the same.

*** Erosions and ulcerations always lead to bleeding.**

ACUTE GASTRITIS

Hyperemia, under the microscope we see neutrophils.



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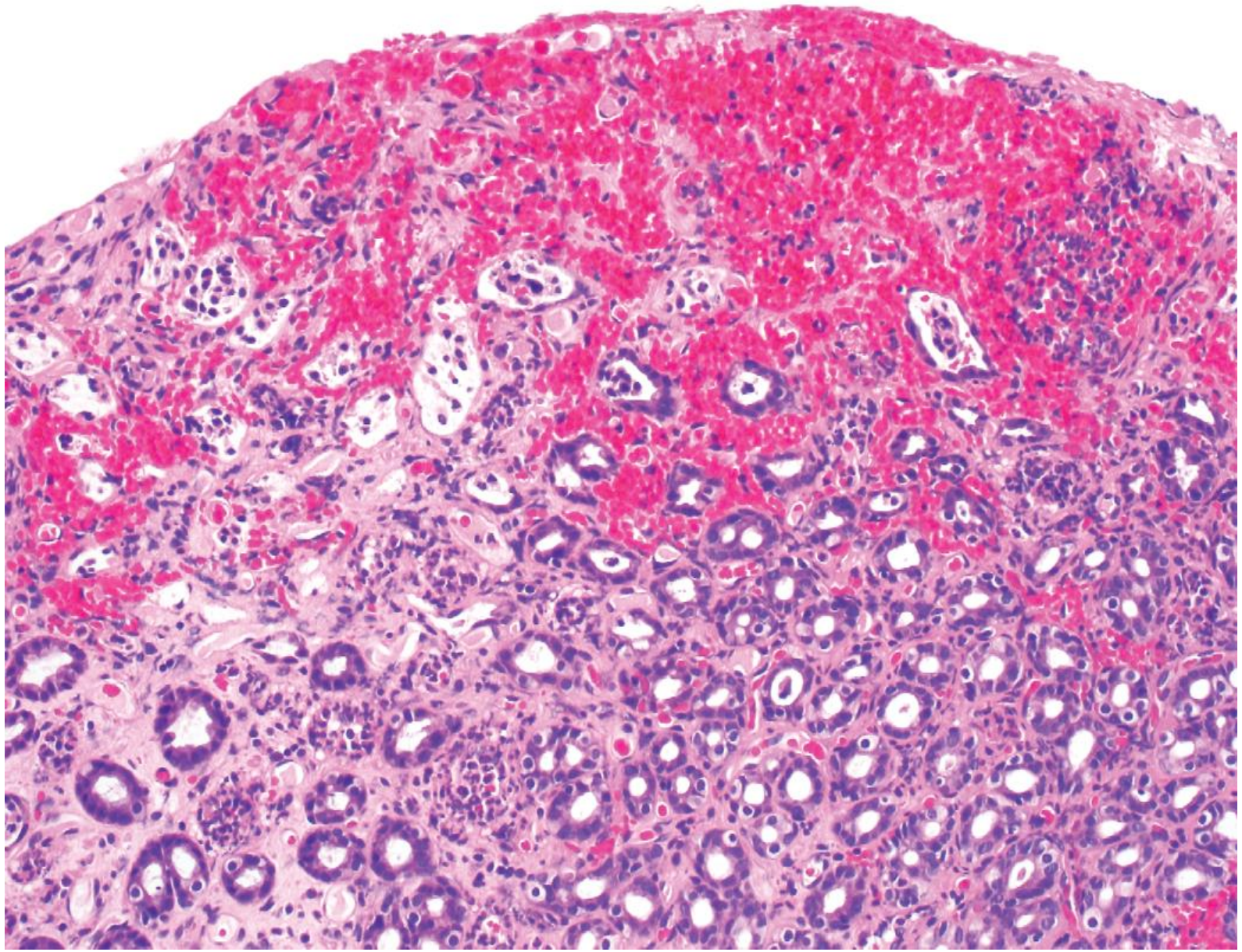

Edema and hemorrhage. The red coloration is due to RBCs outside of blood vessels. Notice the erosion of the surface (erosive hemorrhagic gastritis)

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Stress-Related Mucosal Disease

synonym for acute ulcers

- Severe physiologic stress, like:

- Trauma
- Extensive burns
- Intracranial disease (tumors, stroke)
- Major surgery
- Serious medical disease (diabetic, ICU)
- Critically ill patients

They usually follow a preventive healthcare measure or prophylaxis (proton pump inhibitors) to decrease acid secretion and prevent acute gastritis.

Stress-Related Mucosal Disease

They are named in different types according to location and associated features. However, under the microscope, they are the same.

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

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

- **Cushing ulcers**: stomach, duodenum, or esophagus, CNS injury as stroke, high risk of perforation.

Always associated with intracranial diseases (stroke, tumor), raising intracranial pressure, causing ulcers.

Ulcers in GI tract can occur in any site that gets exposed to acid and pepsin, not just in stomach. So, when we say "peptic ulcer", it's not just in the stomach, meanwhile a "gastric ulcer" is.

Pathogenesis

Diversion of blood in the case of surgery causing the blood to go to more vital organs like heart, kidneys. Which overall decreases the blood flow to GIT.

◑ **Stress related injury:**

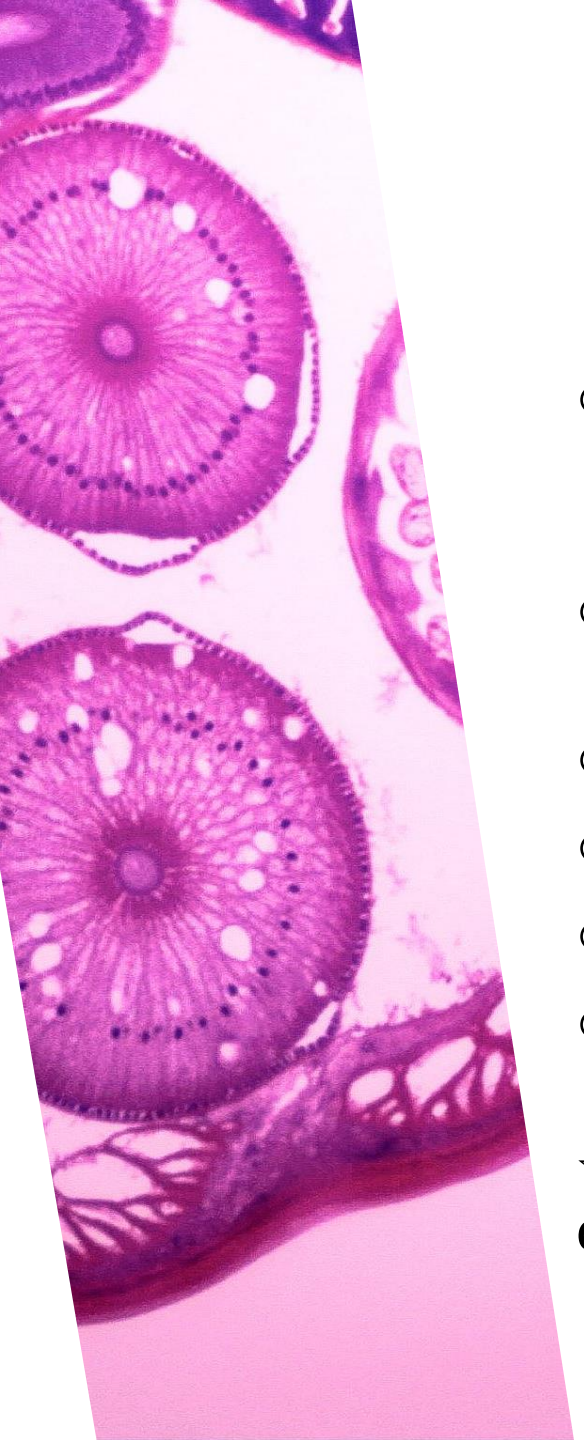
Mostly due to local ischemia caused by:

- Systemic hypotension.
- Decreased blood flow (Splanchnic vasoconstriction).
- Systemic acidosis (lower intracellular PH).
- COX2 expression is protective.

(vagus nerve innervates the stomach, and it's the parasympathetic pathway to promote acid secretion)

◐ **CNS injury and Cushing ulcers:**

Direct vagal stimulation leading to acid hypersecretion.

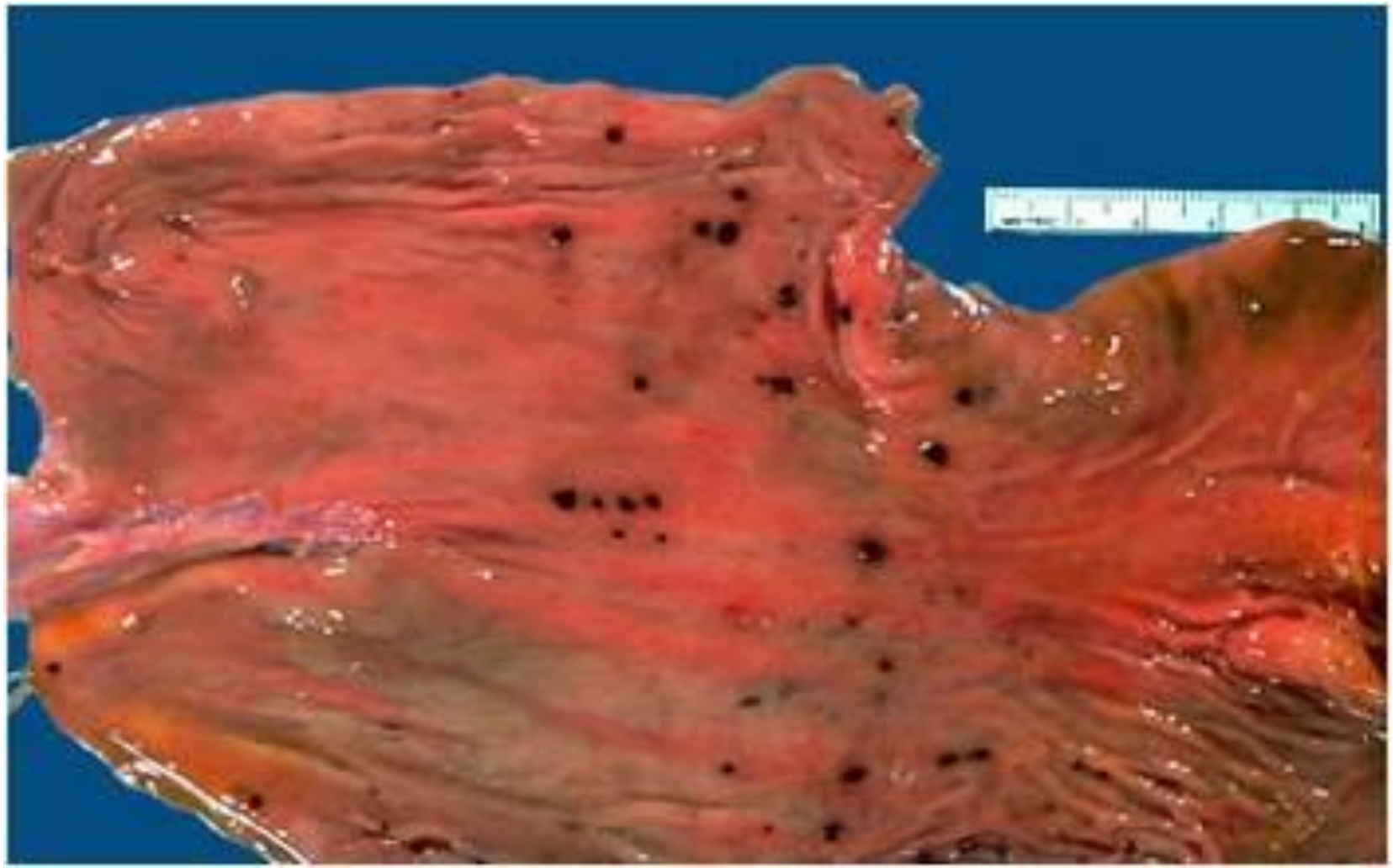


MORPHOLOGY

- Spectrum (ulcers vary from shallow to deep, deep ones may cause perforation and catastrophic ulcers).
- Acute ulcers are rounded and typically < 1 cm. (blood-stained)
- Ulcer base brown to black.
- Multiple, anywhere in stomach
- Normal adjacent mucosa
- No scarring because it's acute. Scarring occurs in chronic ulcers.

✯ Healing with complete epithelialization occurs days or weeks after removal of injurious factors

Stress ulcers



Distributed blood stains on the base due to bleeding caused by acidity of the stomach.

Clinical features

Usually hospitalized patients, after surgery.

- Nausea, vomiting,
- Melena, which indicates upper GI bleeding. But the alterations that happen to the blood during passage makes the color turn to black.
- Coffee -ground hematemesis
- Perforation complication.

❀ **Prophylaxis with proton pump inhibitors (most important)**

↳ Outcome depends on severity of underlying cause.

The previous slides were talking about the acute scenario, what about the chronic?
Same symptoms of acute but less severity and more prolonged period.

CHRONIC GASTRITIS

Causes (mainly):

1. ***Helicobacter pylori*** *associated gastritis: most common.* Especially in underdeveloped countries, crowded, poor sanitation.
2. ***Autoimmune atrophic*** *gastritis: less than 10% of cases.*

Less common causes:

- Chronic NSAID most commonly in western countries.
- Radiation injury
- Chronic bile reflux.

Clinical features

- Nausea and upper-abdominal discomfort
- Vomiting
- Hematemesis uncommon, **UNLIKE acute ulcers**
- Less severe but more prolonged symptoms.

Helicobacter pylori Gastritis

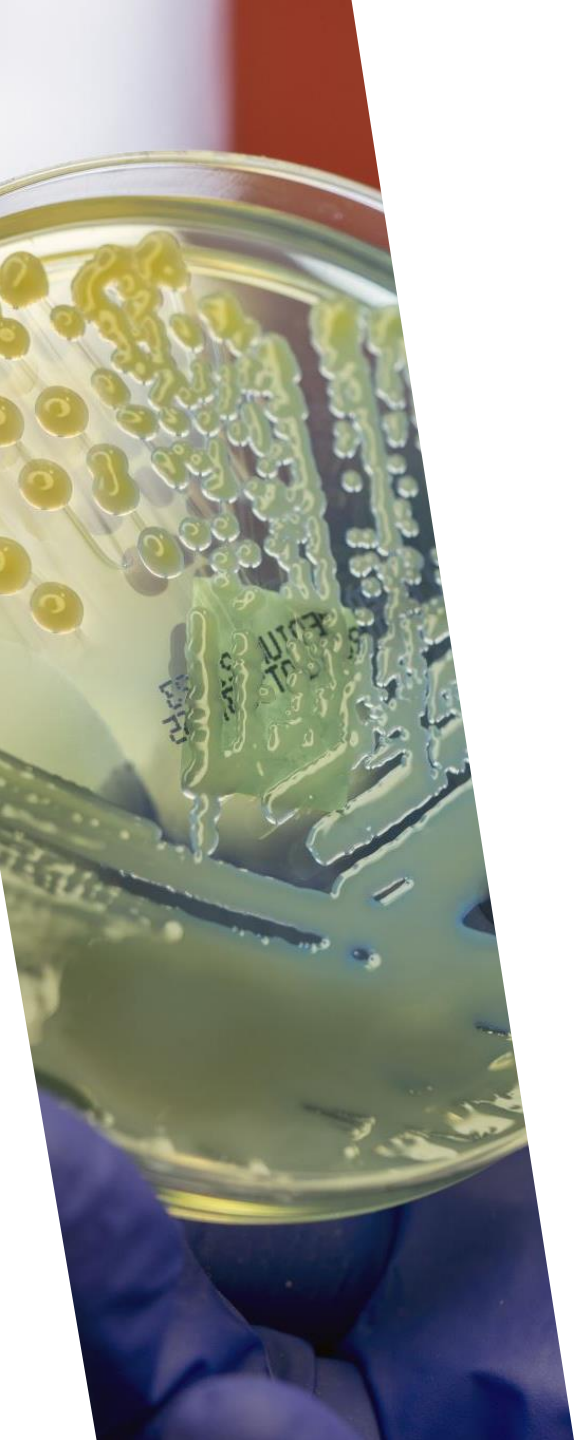
- Discovery of the association of ***H.pylori*** with peptic ulcer disease was a revolution in medicine!! Before that, it was only associated with skin and upper respiratory tract infections.
- Spiral or curved, G-ve bacilli.
- In almost all **duodenal** ulcers and majority of gastric ulcers or chronic gastritis.

But in stomach ulcers we may have other causes as mentioned earlier (NSAIDs, autoimmune…Etc).

🔑 ˚⊹ When we see a duodenal ulcer, it HAS TO be by H. pylori

- **Epidemiology:**
- Poverty, poor sanitation. Acquired in childhood (usually asymptomatic) and persists to adult-life (when symptoms usually appear).
- Acute infection is subclinical.

Symptoms always appear with chronic infection.
Always remember, chronic gastritis ➞ H. pylori, until proven otherwise.☝🤓



Pathogenesis

- Non-invasive, doesn't enter cells, adapted to live in the mucus layer and it protects itself from the acidity by certain virulent factors:

◈ **Flagella**: allow motility.

◈ **Urease**: split urea to ammonia, surrounding the bacteria, protecting it from acidic pH.

◈ **Adhesins**: bacterial adherence to foveolar cells

◈ **Toxins**: (CagA) is associated wih mucosal damage.

Pathogenesis:

Starts as Antral gastritis >>stimulate G cells >> increased acid production >> peptic ulcer

If severe: spread to body with atrophy (damage Parietal cells).

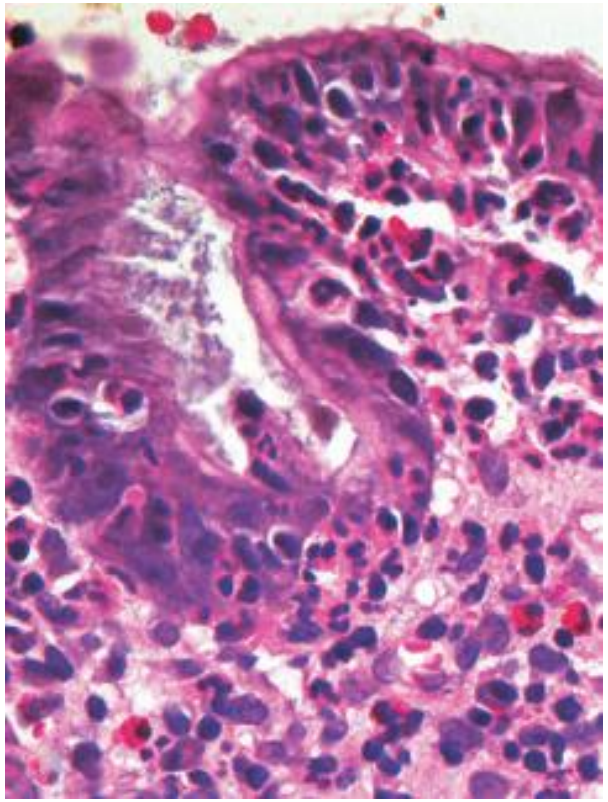
Intestinal metaplasia and increased risk of gastric cancer.

H. pylori loves going to the ❤antrum❤ (we don't know why 😳), causing antral gastritis. It stimulates G cells to produce gastrin, and gastrin promotes parietal cells to produce acid, increasing acidity while protecting itself. So, the best place to look for this bacteria is the antrum. But if we don't see H. pylori in the biopsy, that doesn't mean it's not there.
On the long run, it causes intestinal metaplasia, which is the first change in the process of carcinogenesis.

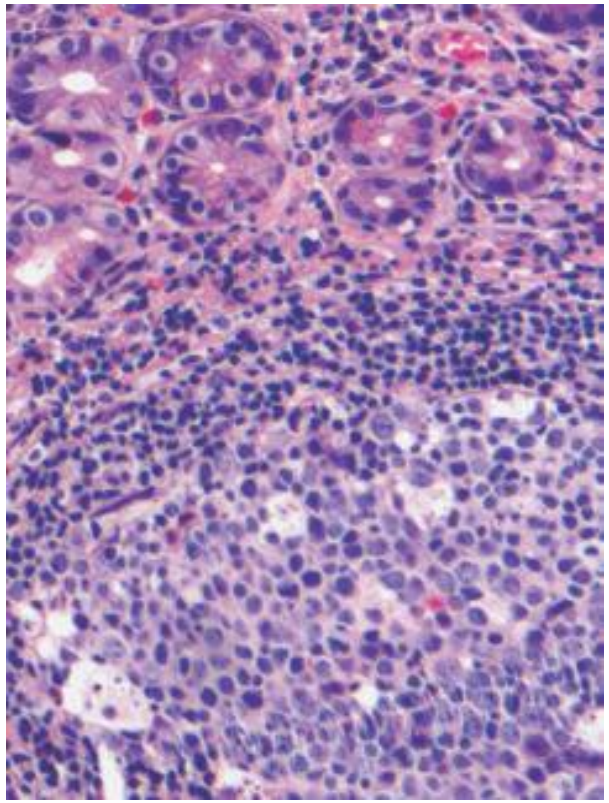
MORPHOLOGY

- **Gastric antral biopsy**: H. pylori in mucus layer.
- Regenerative changes (hyperplastic polyps)
- Neutrophils: in active inflammation
- Plasma cells, lymphocytes & macrophages: in chronic inflammation.
- **Lymphoid aggregates>>> increased risk of MALT lymphoma.**
- **Intestinal metaplasia (goblet cells)>>> dysplasia >> increased risk of adenocarcinoma**

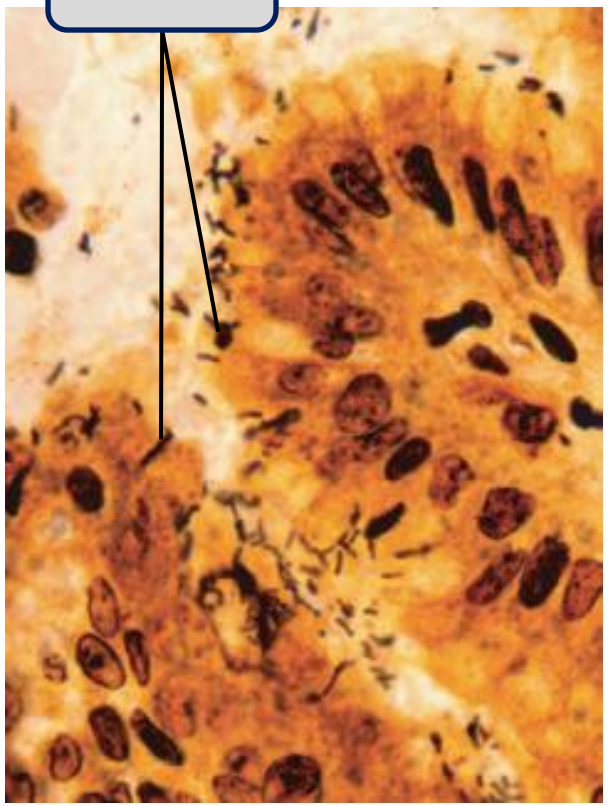
So, H. pylori causes TWO types of cancers:
1- Gastric cancer due to intestinal metaplasia
2- MALT lymphoma



Neutrophils attacking epithelial cells



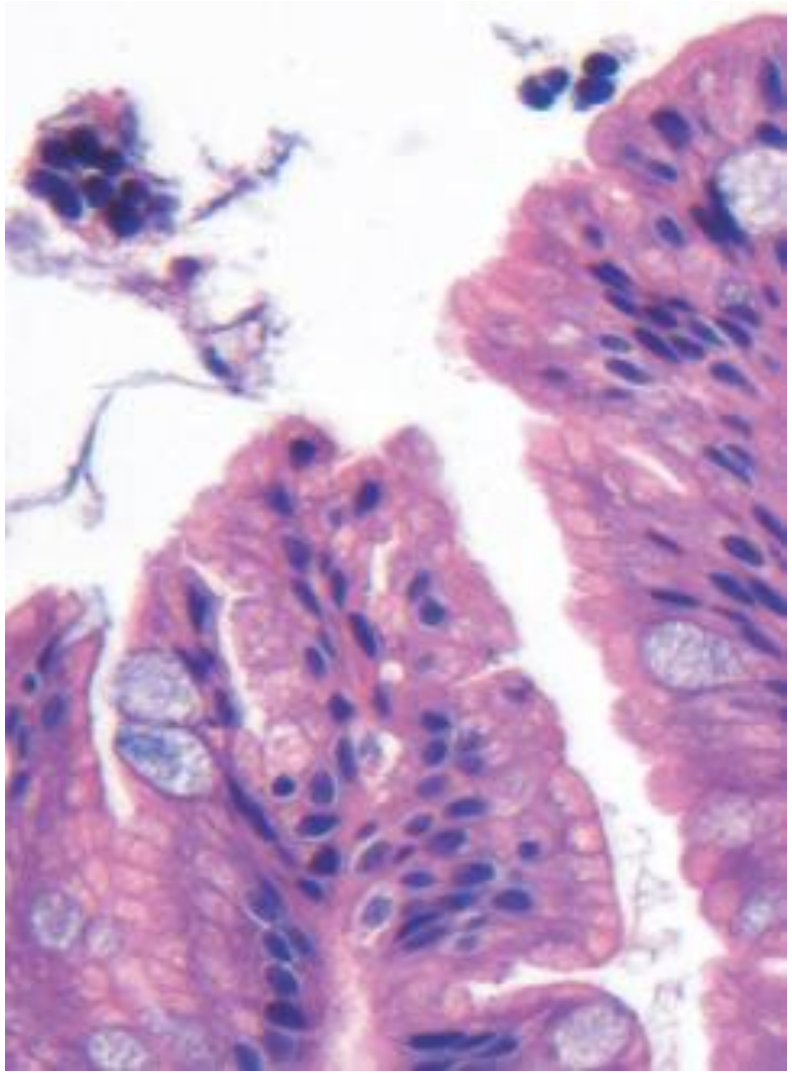
Aggregates of lymphocytes



H. pylori
We can see it using H&E stain or using certain types of stains, like giemsa stain and the one in the picture which is ✳silver✦ stain

Intestinal metaplasia

This is intestinal metaplasia which is defined as the presence of goblet cells in the stomach.
We normally see goblet cells in the intestine, so seeing it in the stomach is an alarm for intestinal metaplasia!! 🚨
So, this patient is at risk of gastric cancer.



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Diagnosis and treatment

We do some investigations, like:

- Serologic test: anti-H. pylori antibodies.
- Stool test for H. pylori antigens.
- Urea breath test.
- Gastric antral biopsy (rapid urease test during endoscopy)
- Bacterial culture.
- PCR test for bacterial DNA.

The usual mechanism is: Endoscopy → biopsy → H&E stain.
OR before endoscopy, we can use stool sample or serologic test (antibodies). But remember, we can find antibodies when the infection has already healed.
So, the ✨ gold standard ✨ is to see it in the biopsy, to see the inflammation. And here we start treatment.

❇ Treatment: combinations of <u>two antibiotics</u> with <u>PPI</u> (triple therapy).

Has to be eradicated or else it will infect the patient again, it'll relapse.

V2 ; slide 6 “In yellow”

اللـهم إنـا أستودعك أهل غزة ، اللَّـهُم كُن لـهم عونًـا،
اللـهم إنـا لا نملك لغزة إلا الدعاء فيارب لا ترد لنـا
دعاء ولا تخيب لنا رجاء وأنت أرحم الراحمين