بسم الله الرحمن الرحيم

PATHOLOGY

MID | Lecture 3

# Stomach (Pt.1)


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﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

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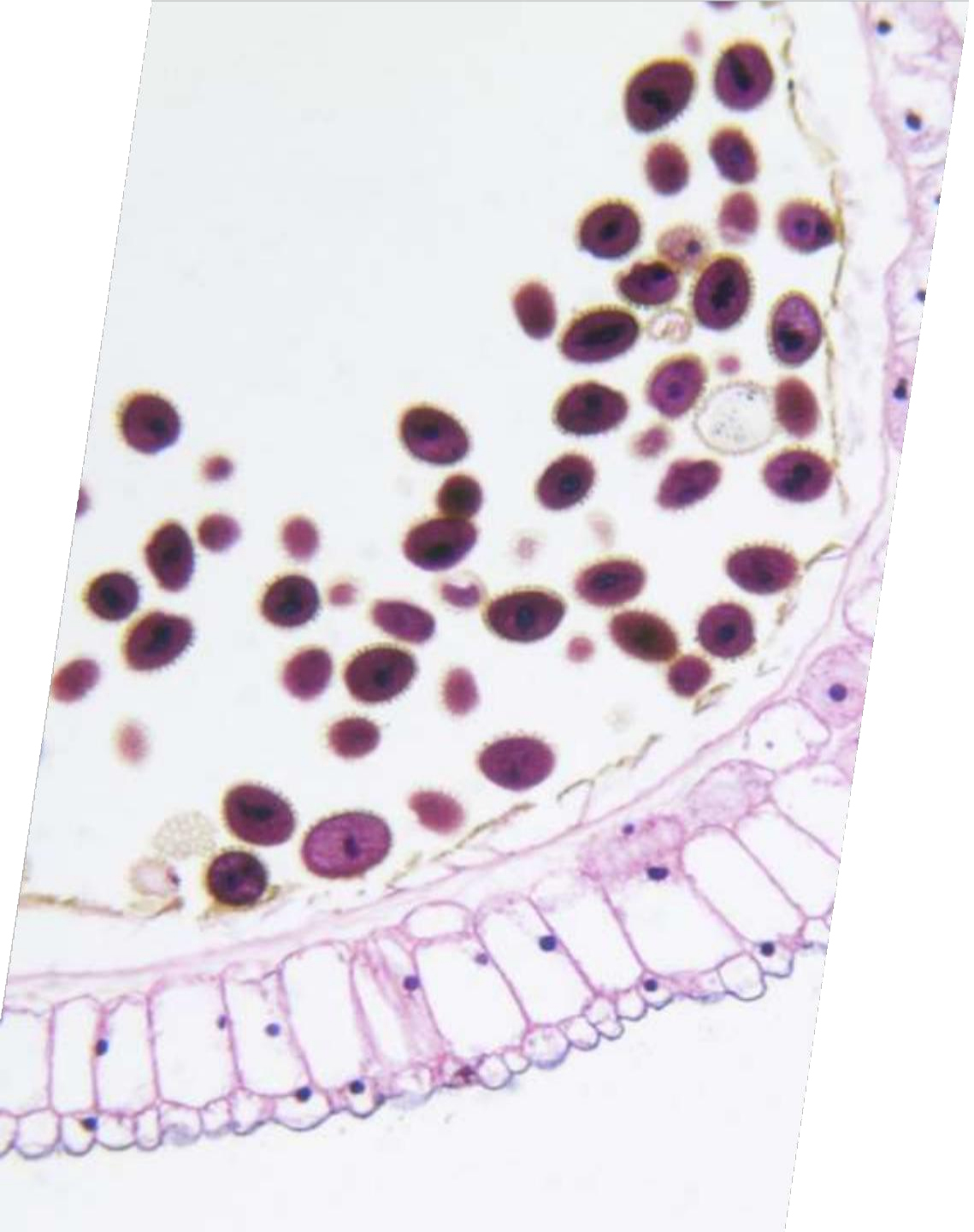

# Pathology of the stomach- 1

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University of Jordan, School of medicine

# Overview

Gastric diseases:

1-Inflammatory.

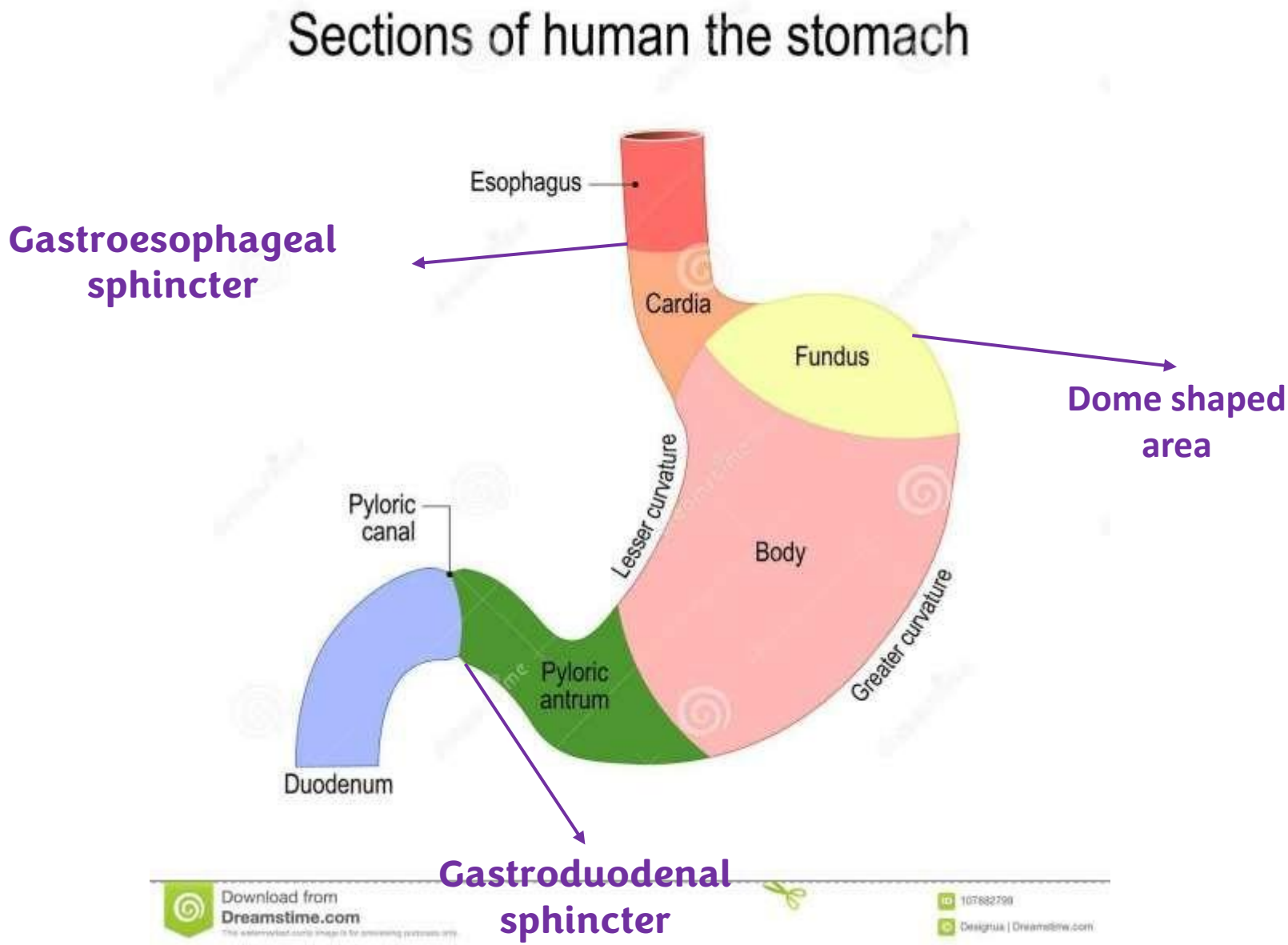
2-Neoplastic. **(Tumors)**

# Normal anatomy & histology:

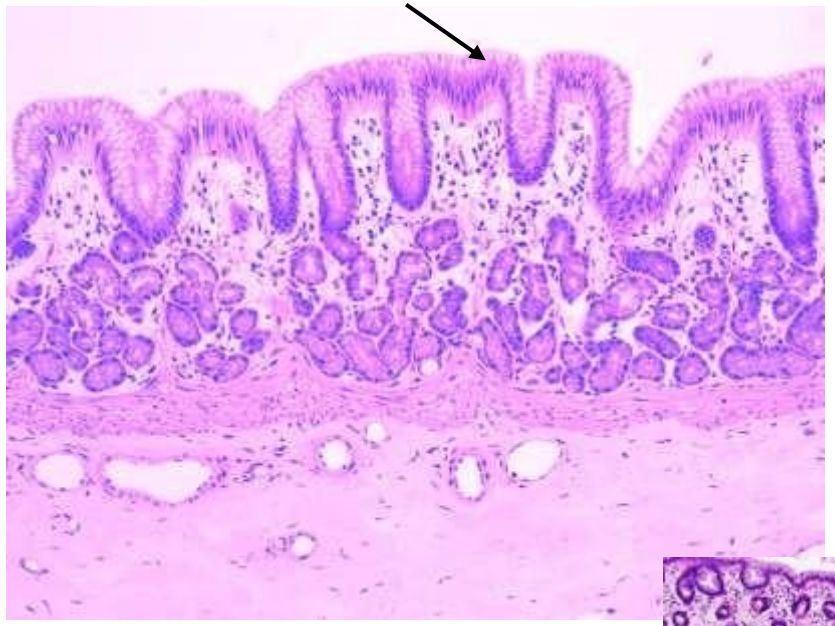
- 4 mains parts: cardia, fundus, body, antrum (pylorus).

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

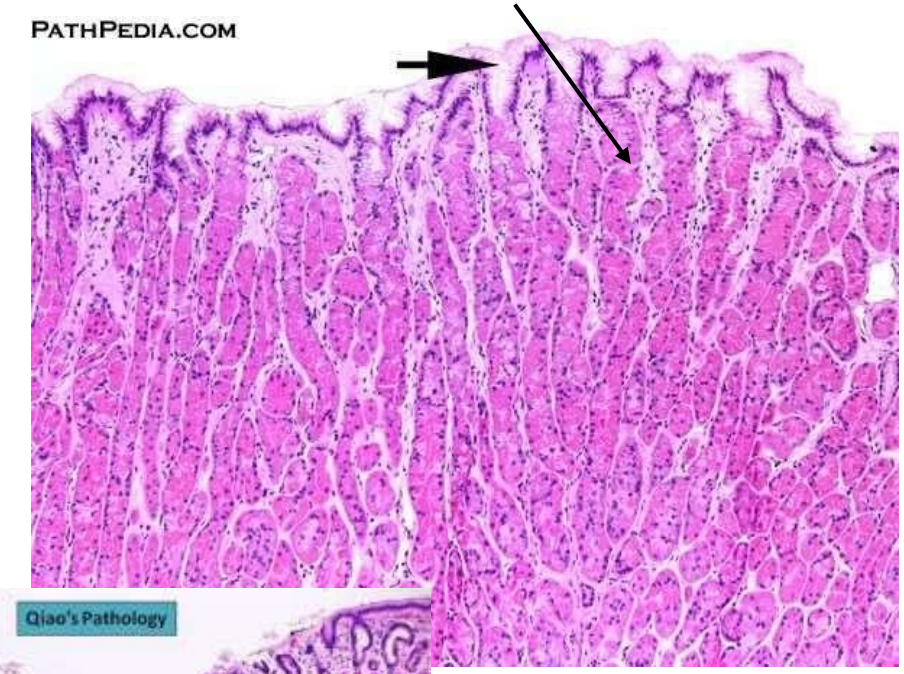
❖ **Gastrin hormone stimulates parietal cells to produce HCl acid.**

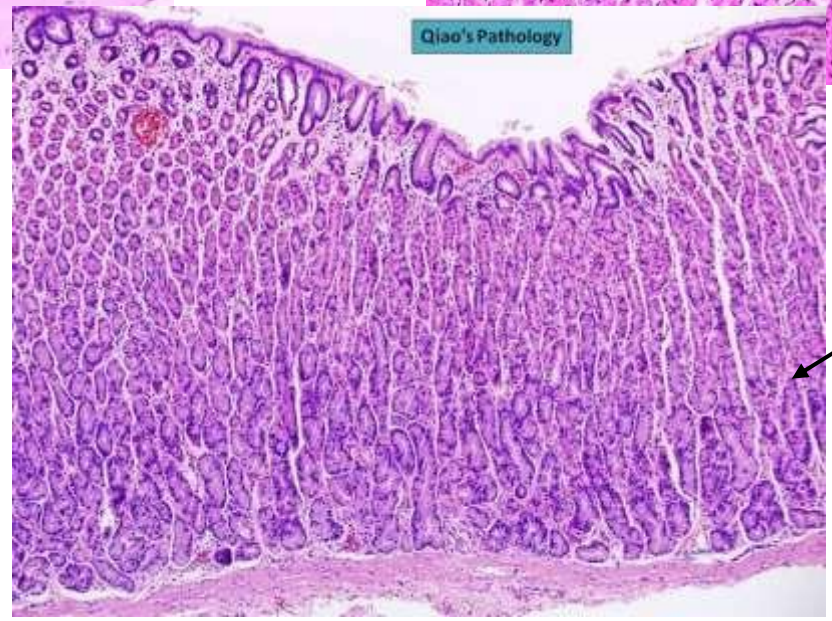

Sections of human the stomach
Esophagus
Cardia
Fundus
Body
Lesser curvature
Greater curvature
Pyloric canal
Pyloric antrum
Duodenum
Gastroesophageal sphincter
Dome shaped area
Gastroduodenal sphincter
Download from Dreamstime.com

Cardia mucosa: this light-colored superficially-located whitish cytoplasm represents foveolar cells (surface mucous cells).



Body and fundus mucosa: this pinkish color represents parietal cells.




Antrum mucosa: notice the bluish color.

The histology of stomach is much more detailed than this, if you are not satisfied with such simple explanation or are a little curious, see the references in the last slide, it shall give you better insights about this topic, because keep in mind that histology is crucial to differentiate between normal and abnormal tissue 😊 .

# Inflammatory conditions

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

# ACUTE GASTRITIS AND GASTROPATHY

- ***Acute gastritis* and *gastropathy* are almost synonymous, the only difference is that under the microscope, neutrophils are seen in the acute gastritis indicating the presence of inflammation, unlike gastropathy.**

***Causes*:**

- ***Bile reflux*: bile is normally secreted into the duodenum, if there is underlying problem causing it to reflux toward the stomach, it might cause irritation.**

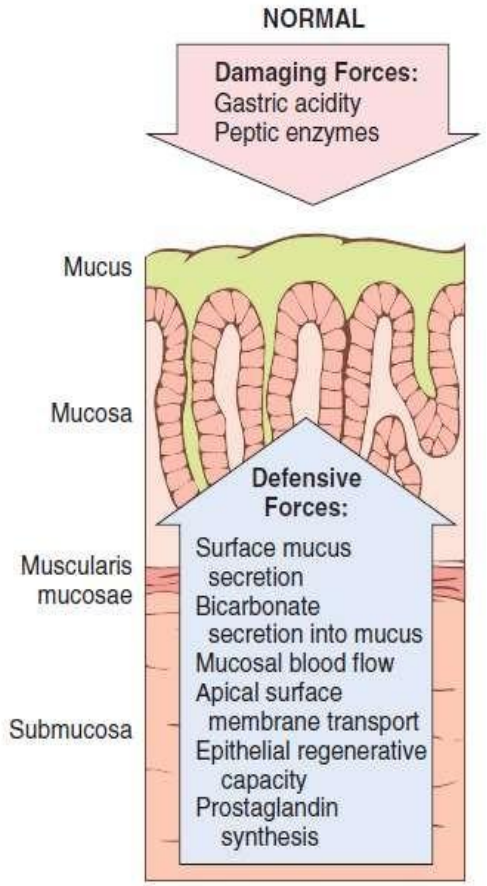
- **Acute gastritis (sudden-onset and severe symptoms) :** Mucosal injury, neutrophils present.
- **Gastropathy**: regenerative, no/rare inflammation.
- **Causes of gastropathy (causes are similar for both):**
- NSAIDs, alcohol, bile, and stress-Induced
- **Clinical features:**
- Asymptomatic **(most patient)**.
- Epigastric pain, nausea, vomiting. **(These signs are generally seen in other inflammatory and even neoplastic conditions).**
- Severe: erosions, ulcers, hematemesis **(bloody vomiting)**, melena **(black tarry stool)**.

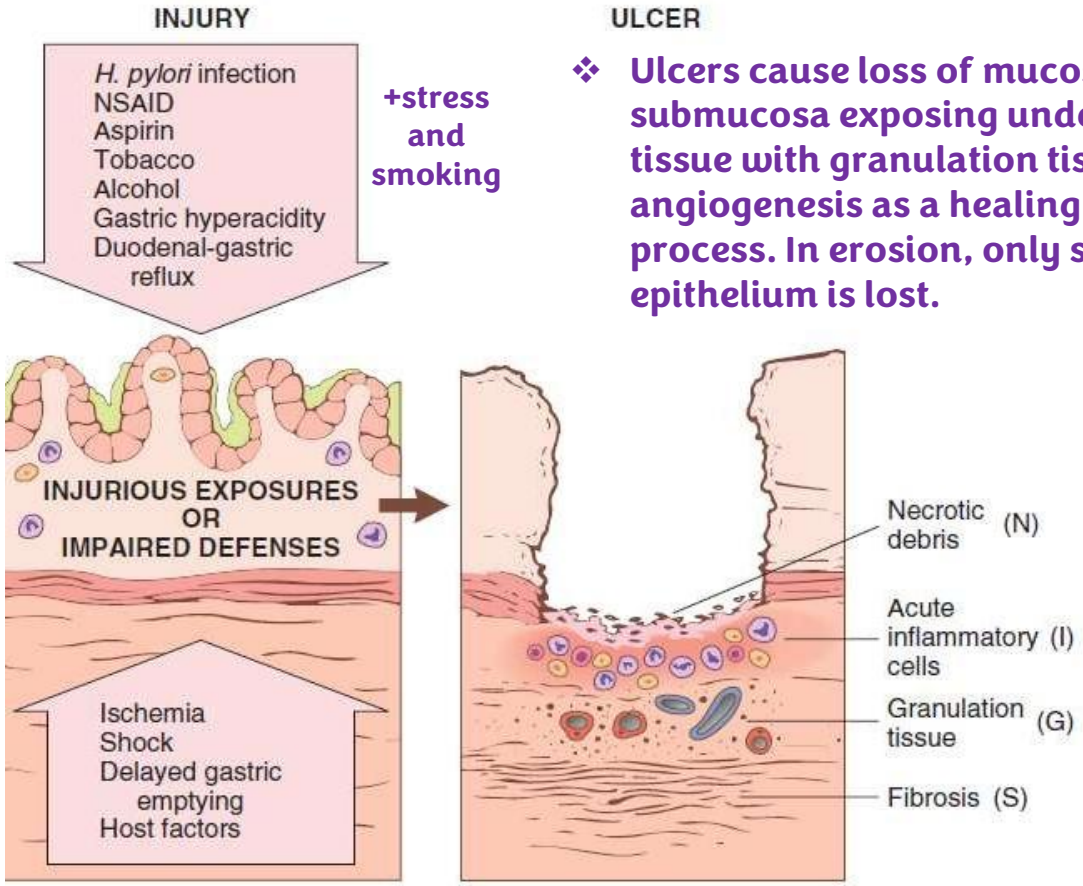
- **The clinical scenario varies from subclinical state, general clinical signs like epigastric pain etc.., to more severe erosive and ulcerative disease.**

# Pathogenesis

- **The pathogenesis arises from imbalance between protective forces and damaging forces, this imbalance either favors a decrease in the protection or increase in the injury, resulting in gastritis (acute or chronic) or ulcers.**

- **Surface mucous secretion coats the epithelial lining of the stomach alongside bicarbonate that neutralizes the acidity of the stomach.**
- **GI tract generally is rich in blood supply with great deal of anastomoses, increasing mucosal blood flow to maintain the production of mucus, bicarbonate and the regenerative process.**




- **Ulcers cause loss of mucosa and submucosa exposing underlying tissue with granulation tissue and angiogenesis as a healing process. In erosion, only surface epithelium is lost.**

- **Host factors are important, if two patients are infected with H. pylori, one might develop acute gastritis while the other might not.**

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# Pathogenesis of gastropathy, acute and chronic gastritis:

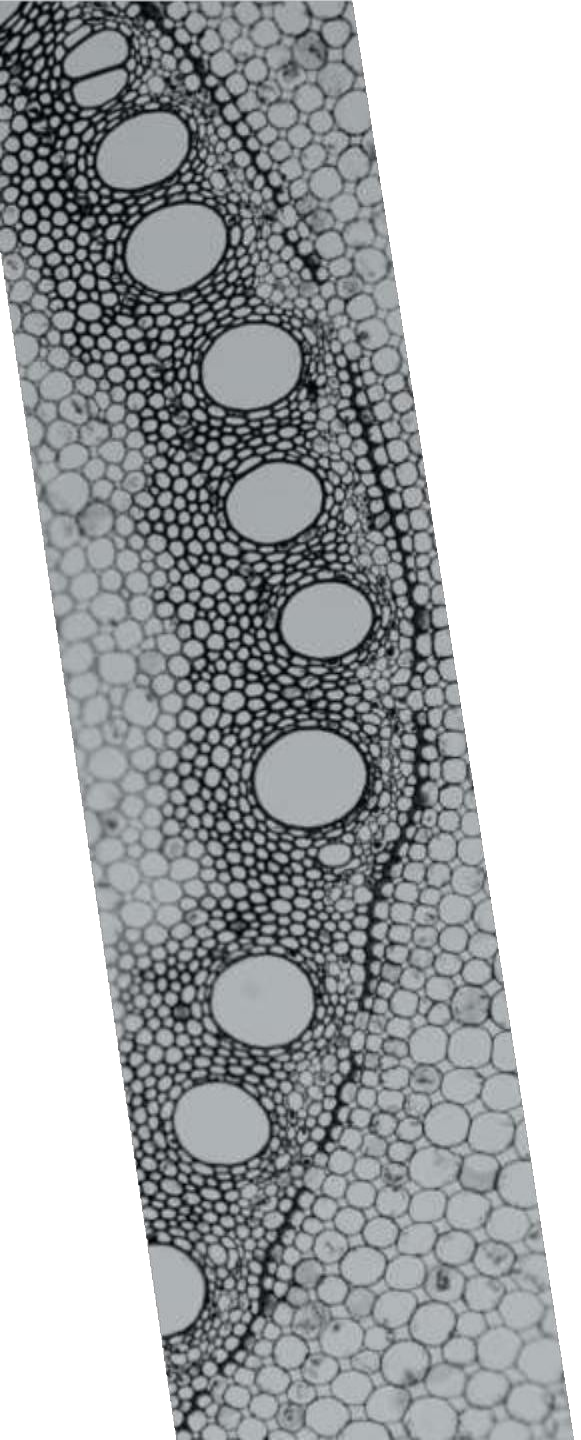
- Imbalance between protective and damaging forces
- **Main causes:**
- **NSAIDs (COX1 and COX2 inhibitors)**
- **Uremic patients with renal failure (ammonia or urea are elevated, which inhibit bicarbonate transport)**
- **H. pylori (urease produces ammonia)**
- **Aging (reduced mucin and bicarbonate secretion, also regeneration is reduced)**
- **Hypoxia (high altitudes)**
- **Harsh chemicals**, (**ingestion of** acids or bases) (direct epithelial injury)
- **Alcohol, NSAIDs, radiation therapy (direct mucosal damage)**
- **Chemotherapy (inhibit DNA synthesis and cellular renewal)**

- Notice how NSAIDs have a dual role in the pathogenesis.
- Cancer patients who undergo chemotherapy and radiotherapy can have such problems.

# prostaglandins E2 and I2:

- Stimulate nearly all the defense mechanisms including

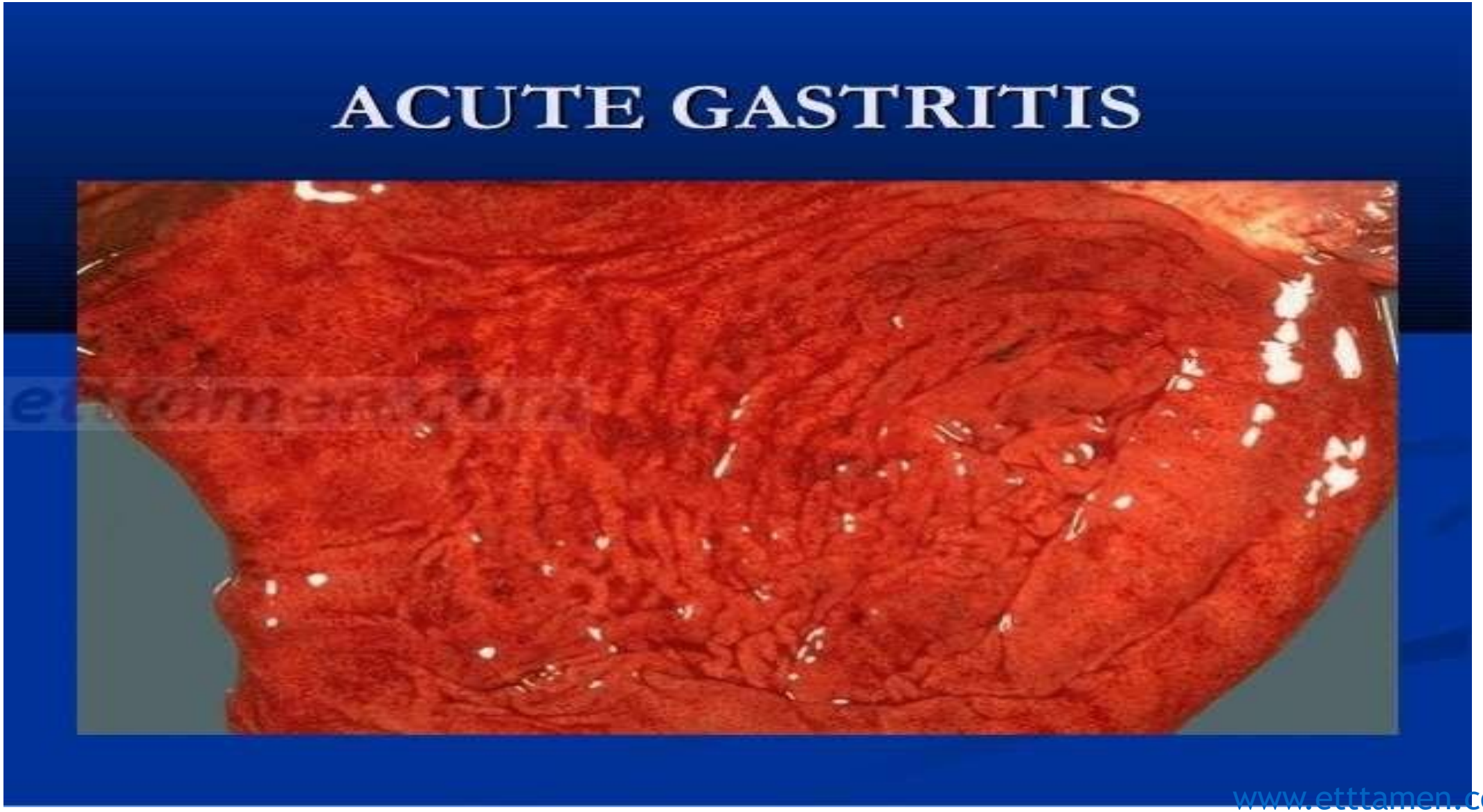
1. Mucus and bicarbonate secretion,
2. mucosal blood flow
3. Epithelial restitution.



# MORPHOLOGY **Grossly or microscopically**

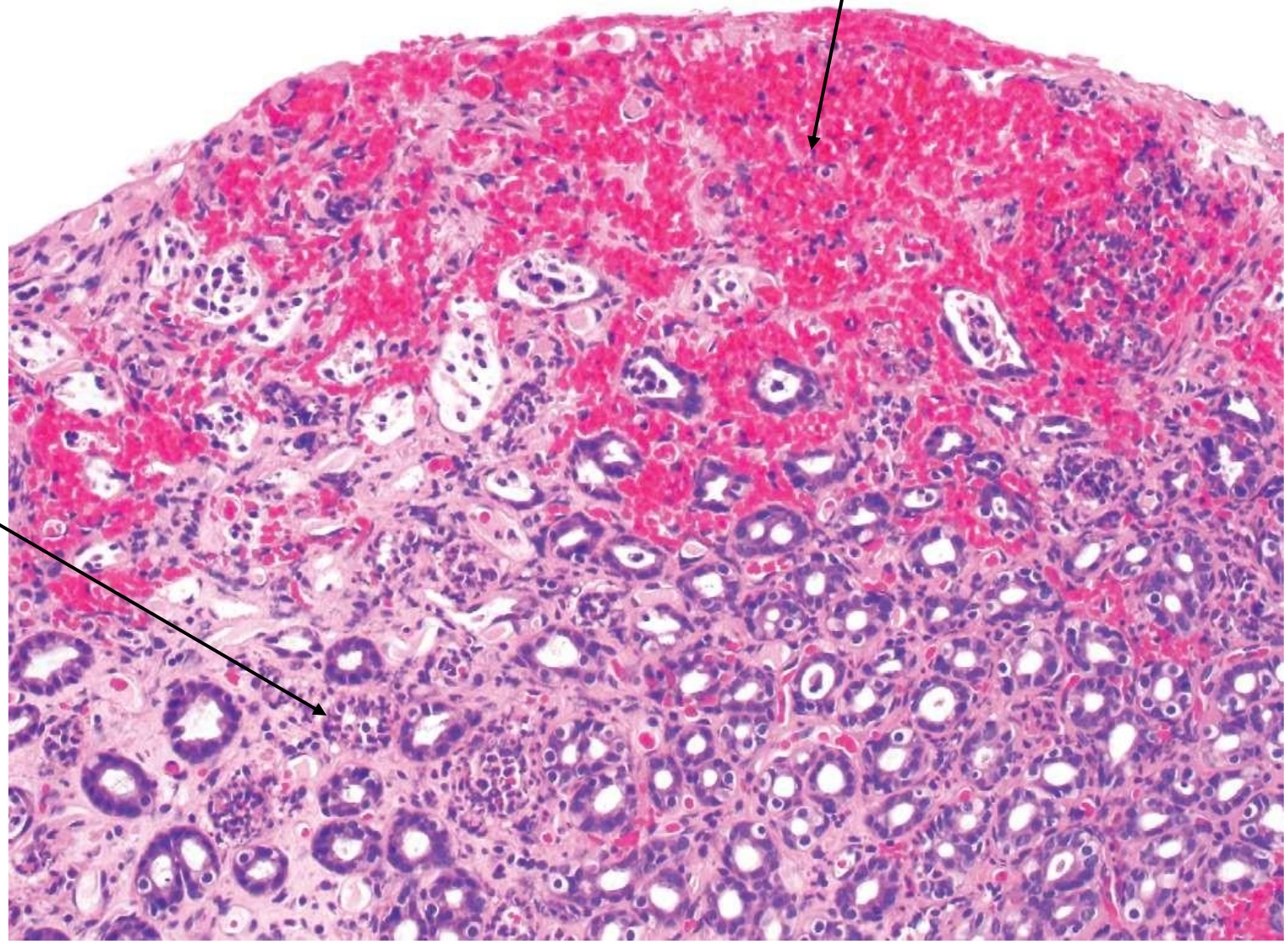
- Hyperemia (redness).
- Edema and slight vascular congestion
- Neutrophils **(the main component).** lymphocytes and plasma cells are not prominent.
- Neutrophils: Active inflammation (gastritis).
- Intact surface epithelium if mild, **and is lost in case erosions or ulcers are present**
- **Acute erosive hemorrhagic gastritis (Advanced)** **is just a descriptive name for severe acute gastritis with erosion and hemorrhage.**

❖ **Normal color of stomach after endoscopy is pinkish to brownish. In acute gastritis, it becomes inflamed and congested with erythema.**



B

Hemorrhage or extravasation of blood attributed to erosion and damage to blood vessels



Neutrophils

librepathology.org

# Stress-Related Mucosal Disease

- Severe physiologic stress **(intrinsic or extrinsic)**:

- Trauma like **wounds and fracture**
- Extensive burns
- Intracranial disease **like intracranial hypertension, tumors, hemorrhage and stroke.**
- Major surgery
- Serious medical disease
- Critically ill patients **like in ICU**

# Stress-Related Mucosal Disease

- **It manifests usually as ulcers. These ulcers look the same but have different names according to the underlying causes.**

- **Stress ulcers**: critically ill patients with shock, sepsis, or severe trauma.
- **Curling ulcers**: **occurs in the** proximal duodenum , severe burns or trauma.
- **Cushing ulcers**: **occurs in the** stomach, duodenum, or esophagus, CNS injury as stroke, high risk of perforation. **Related to intracranial diseases.**

# Pathogenesis

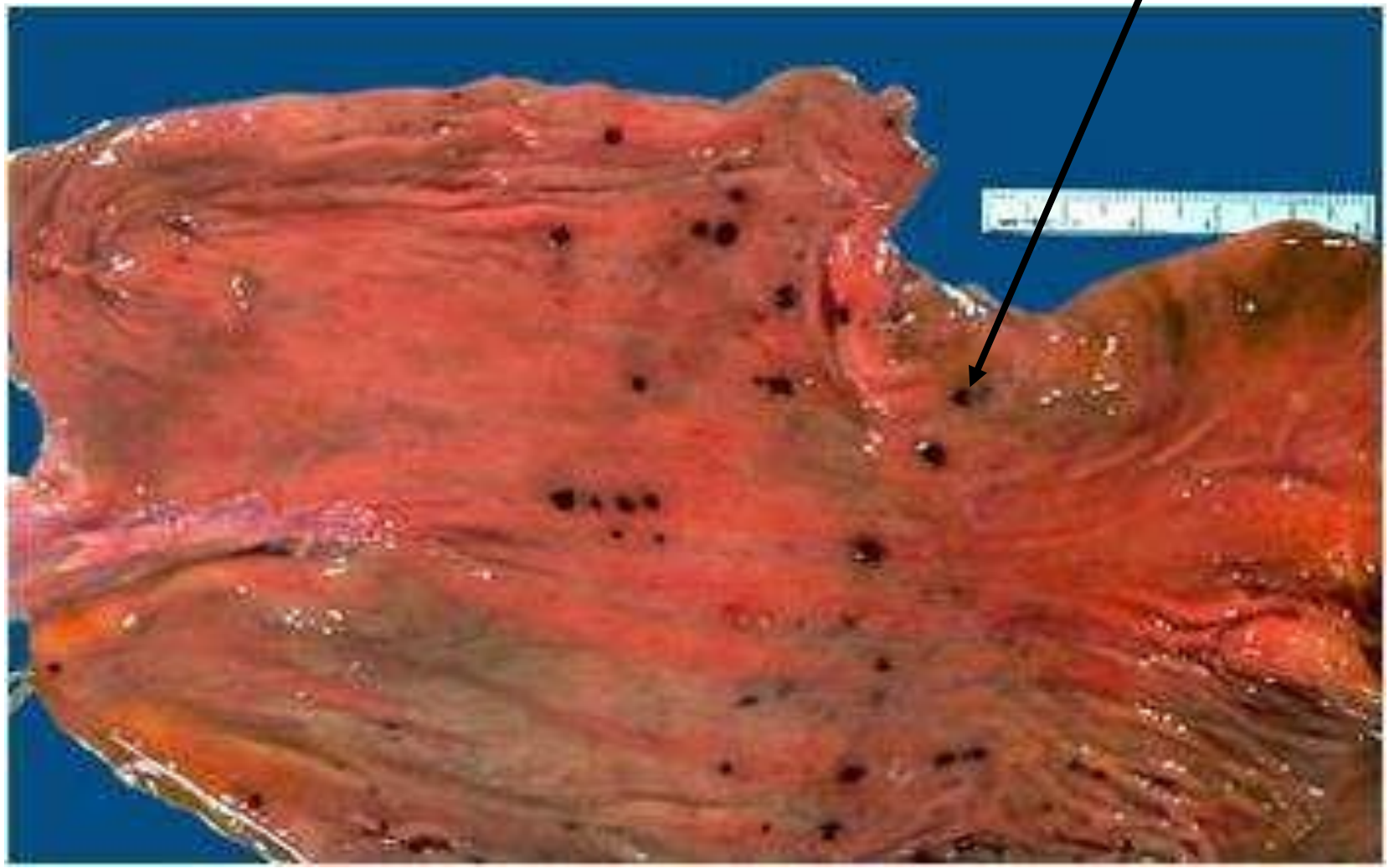
- **Stress related injury:**
- Mostly due to Local ischemia caused by.
- Systemic hypotension. **Such as in patients with severe bleeding after trauma.**
- Decreased blood flow (Splanchnic vasoconstriction)
- Systemic acidosis **in severe infections** (lower intracellular PH).
- COX2 expression is protective. **Patients must avoid NSAIDs.**
- **CNS injury and Cushing ulcers:**
- Direct vagal stimulation, acid hypersecretion.

# MORPHOLOGY

- Spectrum (Shallow to deep).
- Acute ulcers are rounded and typically **small** < 1 cm.
- Ulcer base brown to black **due to the presence of blood**.
- Multiple, anywhere in stomach
- Normal adjacent mucosa
- No scarring
- Healing with complete reepithelialization occurs days or weeks after removal of injurious factors **(treating the underlying problem with administration of proton pump inhibitors)**

# Stress ulcers

Notice the pinpoint black hemorrhages on the background of normal stomach mucosa.



# Clinical features

- Nausea, vomiting, **epigastric pain**,
- Melena
- Coffee -ground hematemesis
- Perforation complication.
- Prophylaxis with proton pump inhibitors
- Outcome depends on severity of underlying cause.

❖ **Those patients are given *proton pumps inhibitors* as prophylactic medications to prevent ulceration.** **Proton pumps inhibitors are drugs that decrease the secretion of HCl by inhibiting $H^+/K^+$ ATPase in the parietal cells that secrete HCl.**

# CHRONIC GASTRITIS

- **Symptoms are milder, gradual & persist over a long duration.**

- ***Causes:***
- *<u>Helicobacter pylori</u> associated gastritis: most common.* **Major cause (75% – 85% of cases)**
- *<u>Autoimmune atrophic gastritis</u>: less than 10% of cases.*

- **Less common**
- Chronic NSAID
- Radiation injury
- Chronic bile reflux.

- **They are considered as a cofactors, since they are less common to cause chronic gastritis**

# Clinical features

- Nausea and upper-abdominal discomfort
- Vomiting
- Hematemesis uncommon.
- Less severe but more prolonged symptoms.

❖ **These features are non-specific, since they are common in other conditions.**

# Helicobacter pylori Gastritis

- Discovery of the association of H. pylori with peptic ulcer disease was a revolution.
- **Under the microscope it appears** spiral or curved, G-ve, bacilli.
- In almost all duodenal ulcers and majority of gastric ulcers or chronic gastritis.
- **Helicobacter pylori infection increases the acidity and acid secretion in the stomach. This excess acid can reflux into the duodenum. Since the duodenum is more vulnerable and sensitive to acidic damage, the acid causes inflammation and ultimately leads to the formation of a duodenal peptic ulcer.**

- **Epidemiology:**
- Areas of poverty, poor sanitation. Acquired in childhood **(drinking or eating contaminated food or water)** , persists to adult-life, **since H. pylori can protect itself with local basic environment inside stomach.**
- Acute infection is subclinical **or asymptomatic.**

- **Pathogenesis:**
- Non-invasive, adapted to live in the mucus layer:
- **Flagella**: allow motility.
- **Urease**: split urea to ammonia, protect bacteria from acidic pH.
- **Adhesins**: bacterial adherence to foveolar cells
- **Toxins**: (CagA) mucosal damage **(erosions, ulcerations, hemorrhage)**.

❖ **Since Helicobacter pylori resides on the surface of the mucosal layer and does not penetrate the cells, when evaluating gastric biopsy for the presence of H. pylori infection, we do not look inside the cells but at the surface.**

# 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.

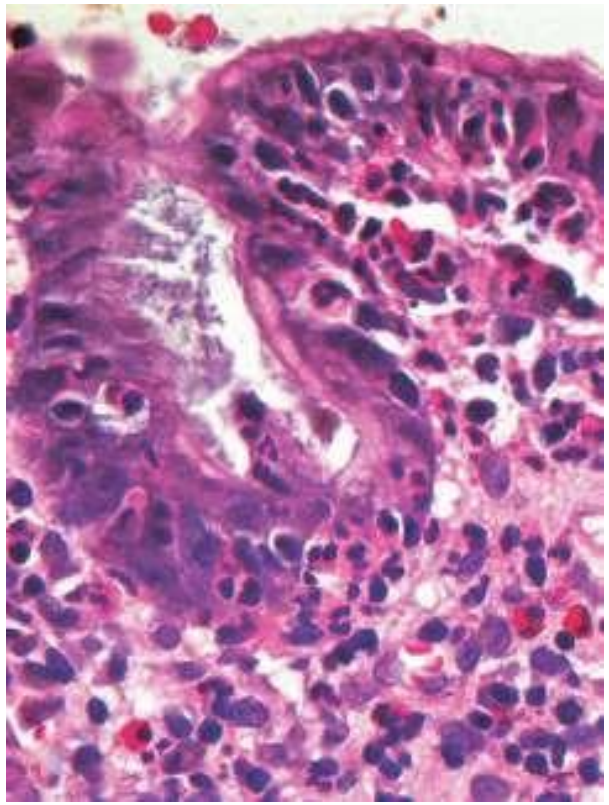
- **Remember that G cells are abundant in the antrum. These cells will produce gastrin, which will stimulate parietal cells to produce HCl acid.**

- **Metaplasia → Dysplasia → cancer**

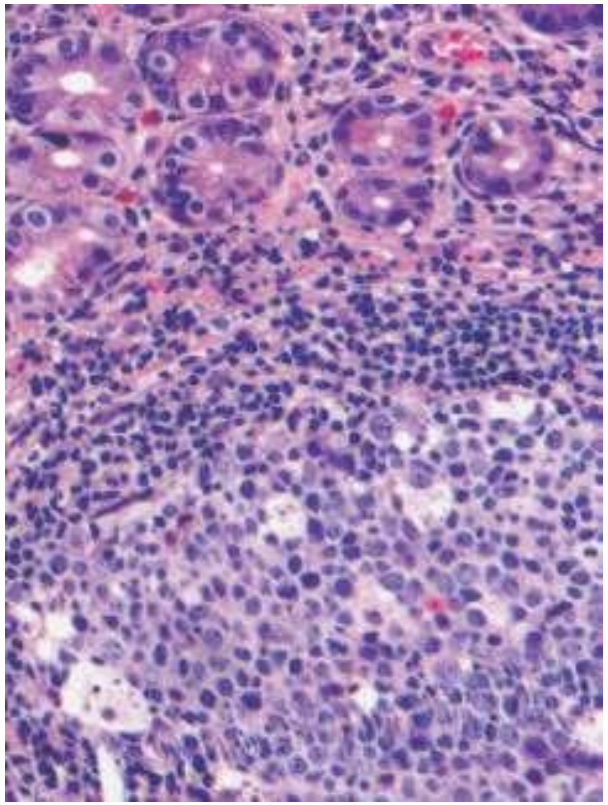
# MORPHOLOGY

- **Gastric antral biopsy**: H. pylori in mucus layer.
- Regenerative changes (hyperplastic polyps)
- Neutrophils **(in sever cases)**, Plasma cells, lymphocytes & macrophages. **Chronic inflammatory cells are the predominant.**
- **Lymphoid aggregates>>> increased risk of MALT lymphoma.**
- **Intestinal metaplasia (goblet cells)>>> dysplasia >> increased risk of gastric adenocarcinoma**

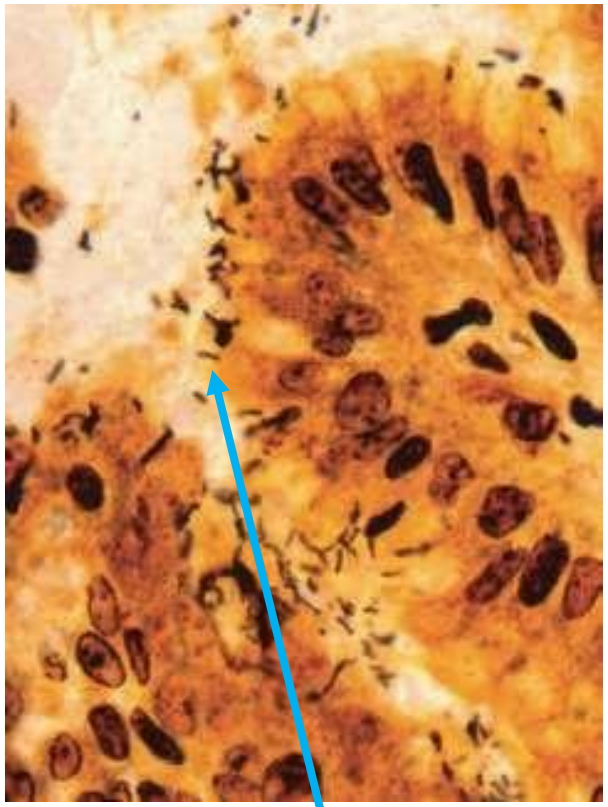
❖ **Therefore, patients with chronic gastritis should receive effective eradication therapy.**



we see a lot of neutrophiles.



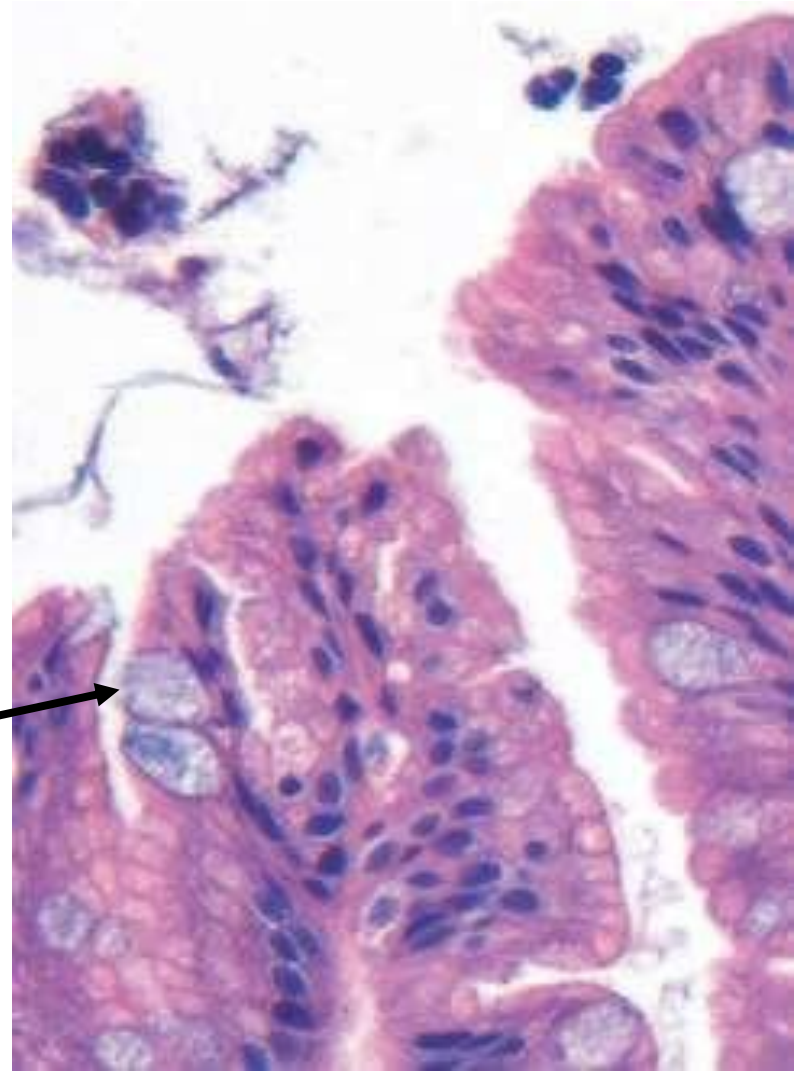
Here, we see lymphocytes mainly.



Here, we applied special stain to see Spiral-shaped H. pylori bacteria in black color.
You can note that it resides on the mucosal surface.

# Intestinal metaplasia

- **Goblet cells are normally present in the intestine, But if we see goblet cells in the stomach, this is a hallmark of intestinal metaplasia. Prompt treatment with follow-up to ensure regression of intestinal metaplasia as it is reversible.**

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# Diagnosis and treatment

See next slide for more explanation.

(1)

- Serologic test: anti-H .pylori antibodies.
- Stool test for H.pylori.
- Urea breath test. **(A)**

❖ **Serological tests might yield false positive cases as the presence of IgG especially may indicates previous infection.**

(2)

- Gastric antral biopsy (rapid urease test during endoscopy). **(B)**
- Bacterial culture.
- PCR test for bacterial DNA.
- Treatment: combinations of antibiotics and PPI (triple therapy).

❖ **H. pylori is known to be resistant (20% of cases). Resistant strains or non-compliant patient with the drug will affect the eradication of the bacteria increasing the risk for recurrence.**

# Diagnosis and treatment; further explanation

- When patients present with nausea, vomiting, abdominal pain, and hematemesis, gastritis by H .pylori infection should be considered. Initially, we should begin with non-invasive diagnostic methods (1). If needed, we can proceed to invasive diagnostic techniques (2).

- (A) In the ***urea breath test***, the patient swallows a urea tablet, H. pylori bacteria in the stomach produce the enzyme urease, which breaks down the urea into ammonia and carbon dioxide (CO2). Since the CO2 is radiolabeled, it can be detected in the patient's breath, confirming the presence of H. pylori.

- (B) In ***rapid urease test (during endoscopy)***, a gastric antral biopsy is taken. The biopsy is placed in a urea-rich environment, and if H. pylori is present, it will convert the urea into ammonia and CO2. This reaction shifts the environment to a more basic pH, causing a color change, which indicates the presence of H. pylori.

- The ***golden standard diagnosis*** is to take a gastric biopsy and then visualize it under the microscope and see the inflammation and the bacteria, H. pylori bacteria.

# Autoimmune Gastritis

- Antibodies to parietal cells and intrinsic factor in serum.
- Reduced serum pepsinogen I levels
- Antral endocrine cell hyperplasia **(G-cell hyperplasia)**
- Vitamin B12 deficiency >>> **it is called** pernicious anemia and **associated with** neurologic changes
- Impaired gastric acid secretion (*achlorhydria)*
- Marked *hypergastrinemia* **(high gastrin secretion)**
- Spares the antrum.

❖ **It mainly affects the *body* of the stomach but can extend to the antrum in case of G-cell hyperplasia remember that H.pylori gastritis mainly affects the antrum of the stomach and can extend to the body**

# Pathogenesis

- **In autoimmune gastritis, the body produces antibodies against parietal cells, leading to their damage and subsequent reduction in acid secretion. This *achlorhydria* activates G-cells to increase in gastrin production (*hypergastrinemia)* . Since the parietal cells are reduced in number initially and absent in advanced stages, this can lead to the development of G-cell hyperplasia, which may result in neuroendocrine tumors.**
- **Autoimmune gastritis is also called "*Atrophic gastritis*" because of the atrophy (absence) of the parietal cells.**

Immune-mediated loss of parietal cells >>> reductions in acid and intrinsic factor secretion.

Acid reduction >>> Hyperplasia of antral G cells >>> hypergastrinemia

Deficient intrinsic factor >> deficient ileal VB12 absorption >> pernicious anemia.

# MORPHOLOGY

- **If one takes a biopsy from the body of the stomach and notices the absence of parietal cells, autoimmune gastritis is mainly suspected.**

- Damage of the oxyntic (acid-producing) mucosa.
- Diffuse atrophy, thinning of wall **(mucosa)**, loss of gastric folds
- Lymphocytes, plasma cells, macrophages, less likely neutrophils.
- **Intestinal metaplasia >>> dysplasia >> carcinoma.**
- **G- cell hyperplasia >>> carcinoids (neuroendocrine tumors).**

# Clinical features

- 60 years, slight female predominance.
- Often associated with other autoimmune diseases **like type 1 diabetes or rheumatoid arthritis.**
- Dyspepsia.
- Anemia (VB12 or iron)

❖ **Dyspepsia is used to describe a group of symptoms that cause discomfort or pain in the upper abdomen, like epigastric pain, nausea, vomiting**

**Table 15.2 Characteristics of *Helicobacter pylori*–Associated and Autoimmune Gastritis**

| 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 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 |

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# Complication of chronic gastritis

- Peptic ulcer.
- Mucosal atrophy.
- Intestinal Metaplasia
- Dysplasia **(carcinoma)**.

Click on the GOAT to test yourself 👍 .

**Cristiano Ronaldo**

# For any feedback, scan the code or click on it.

Corrections from previous versions:

| Versions | Slide # and Place of Error | Before Correction | After Correction |
|---|---|---|---|
| V0 → V1 | | | |
| V1 → V2 | | | |

# Additional Resources:

# رسالة من الفريق العلمي:

**Stomach histology:**

1. **Medcell.org; from doctor's slides.**
2. **kenhub.**
3. **pathology outlines.**