

Pathology of the stomach

Dr. Omar Hamdan

**Gastrointestinal and liver pathologist
Mutah University**

**School of Medicine-Pathology Department
Undergraduate Lectures 2023**



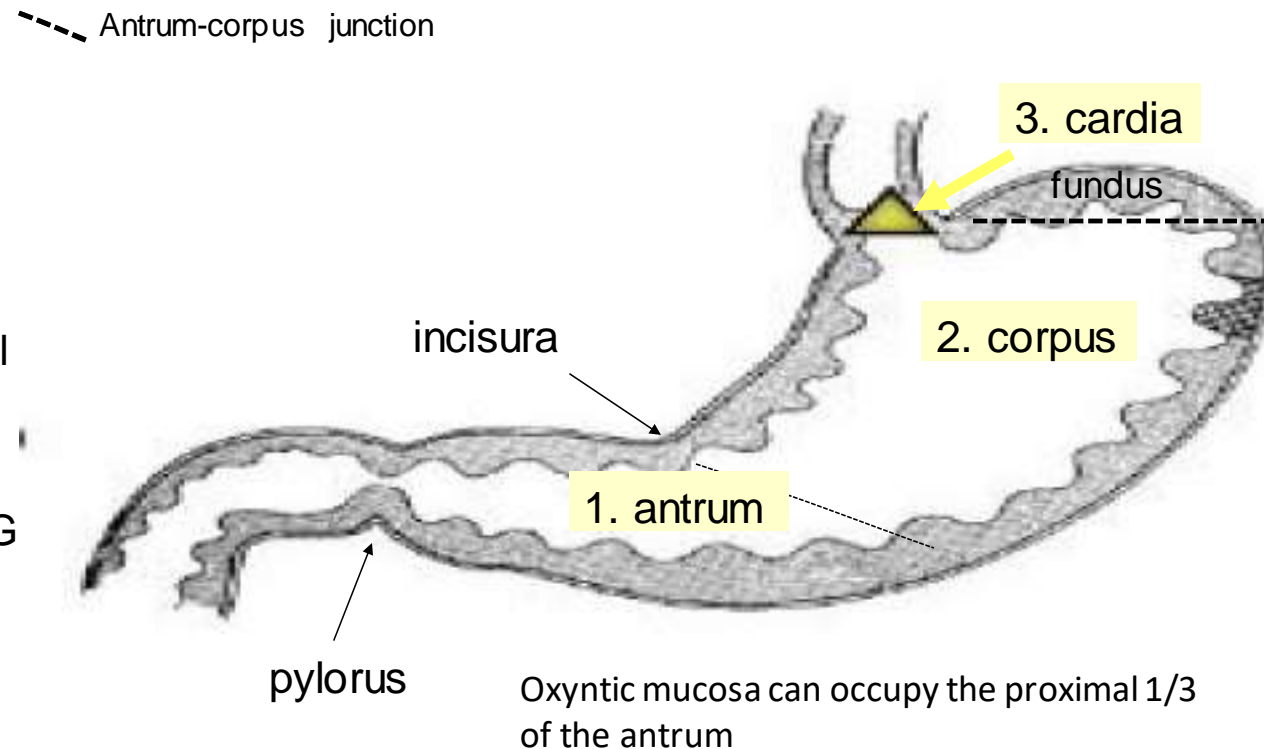
Overview

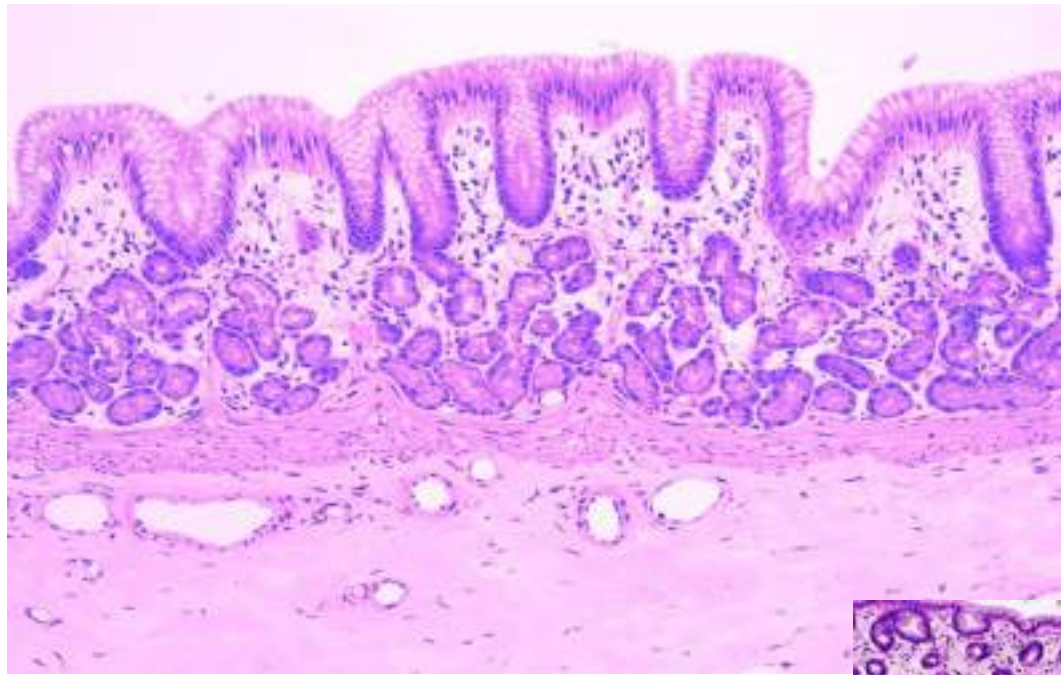
- ▶ Gastric diseases:
 - 1-Inflammatory.
 - 2-Neoplastic.
- ▶ Stomach parts: cardia, fundus, body, antrum, pylorus.

Normal Stomach

3 Regions

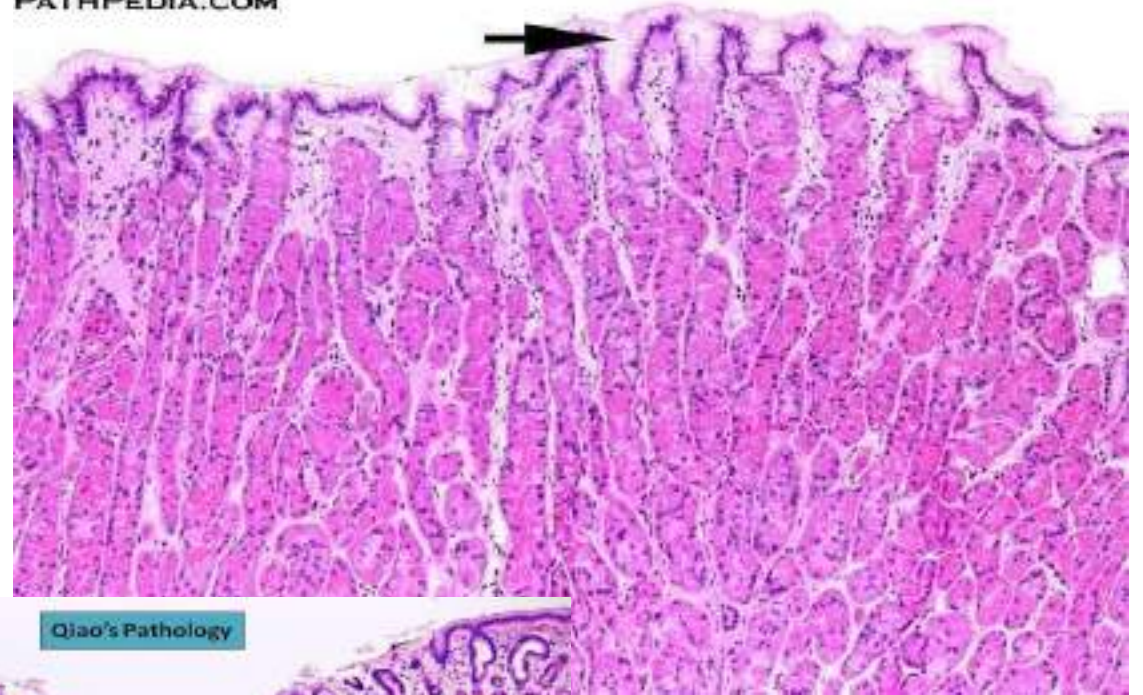
- ▶ Cardia: mucin secreting foveolar cells.
- ▶ Body and fundus: parietal cells (HCL) and chief cells (pepsin).
- ▶ Antrum: neuroendocrine G cells (gastrin)



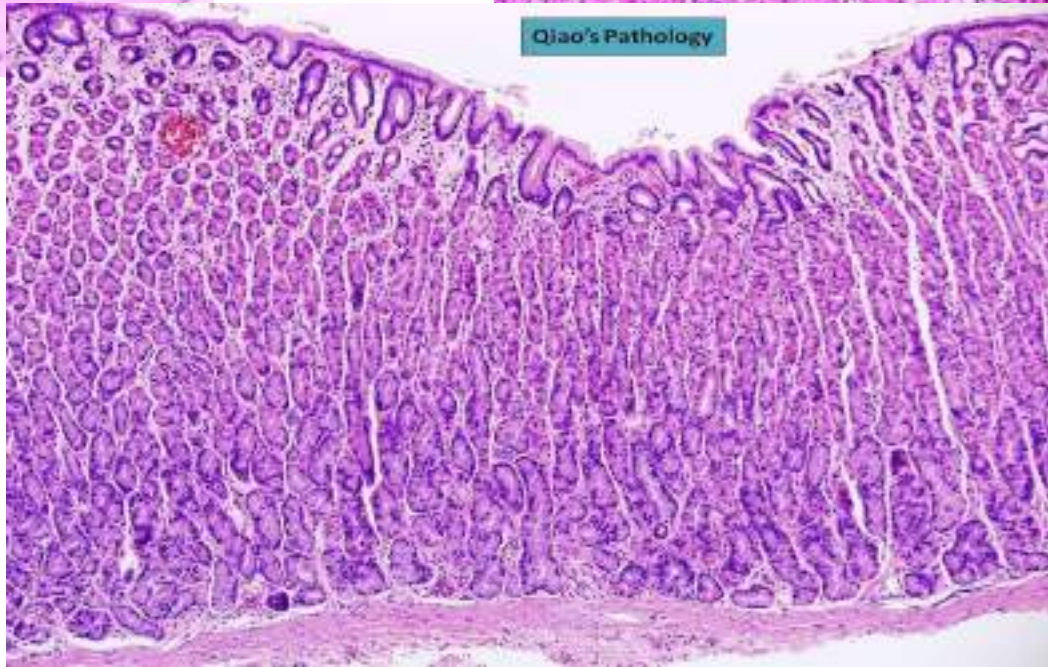


medcell.med.yale.edu

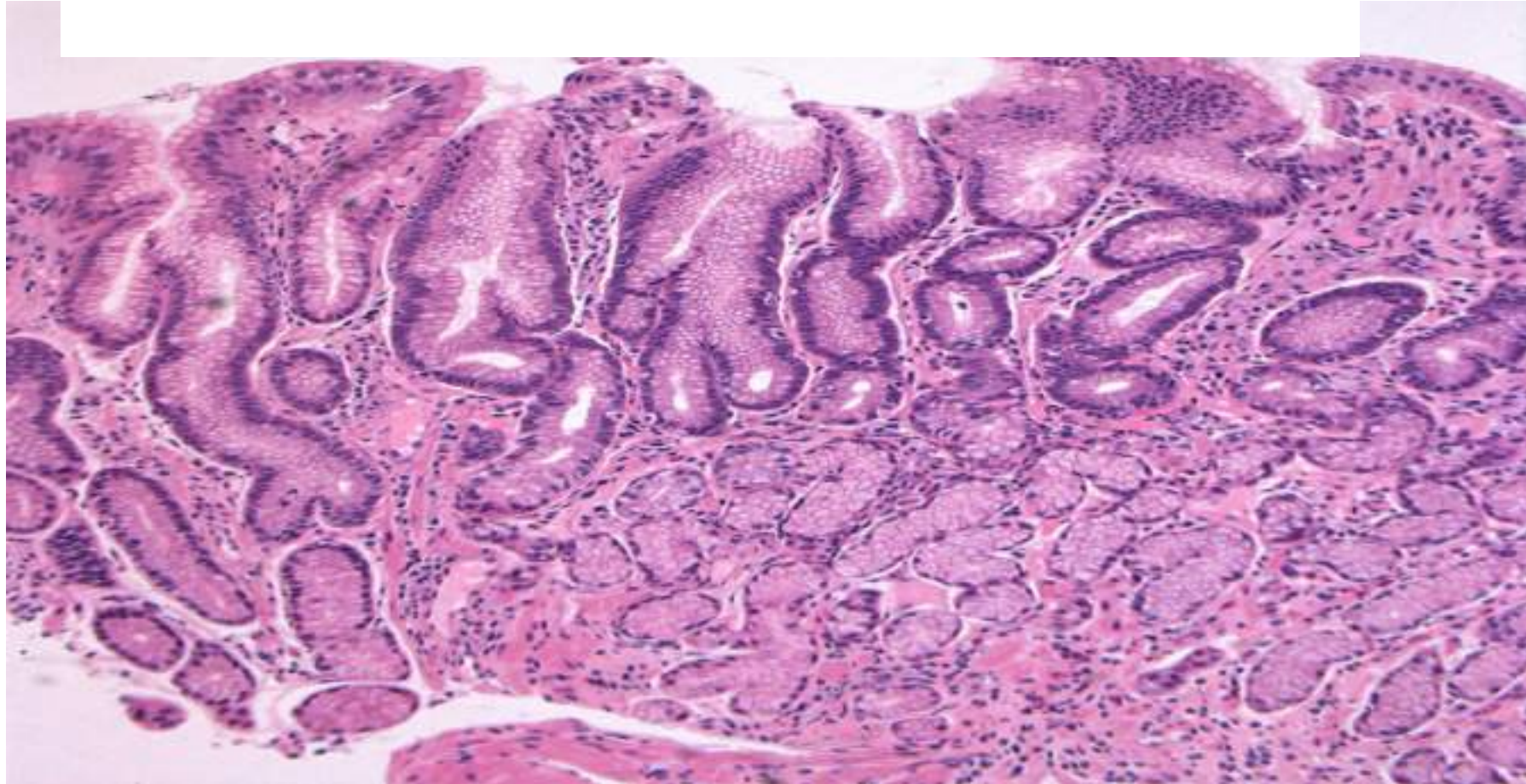
PATHPEDIA.COM



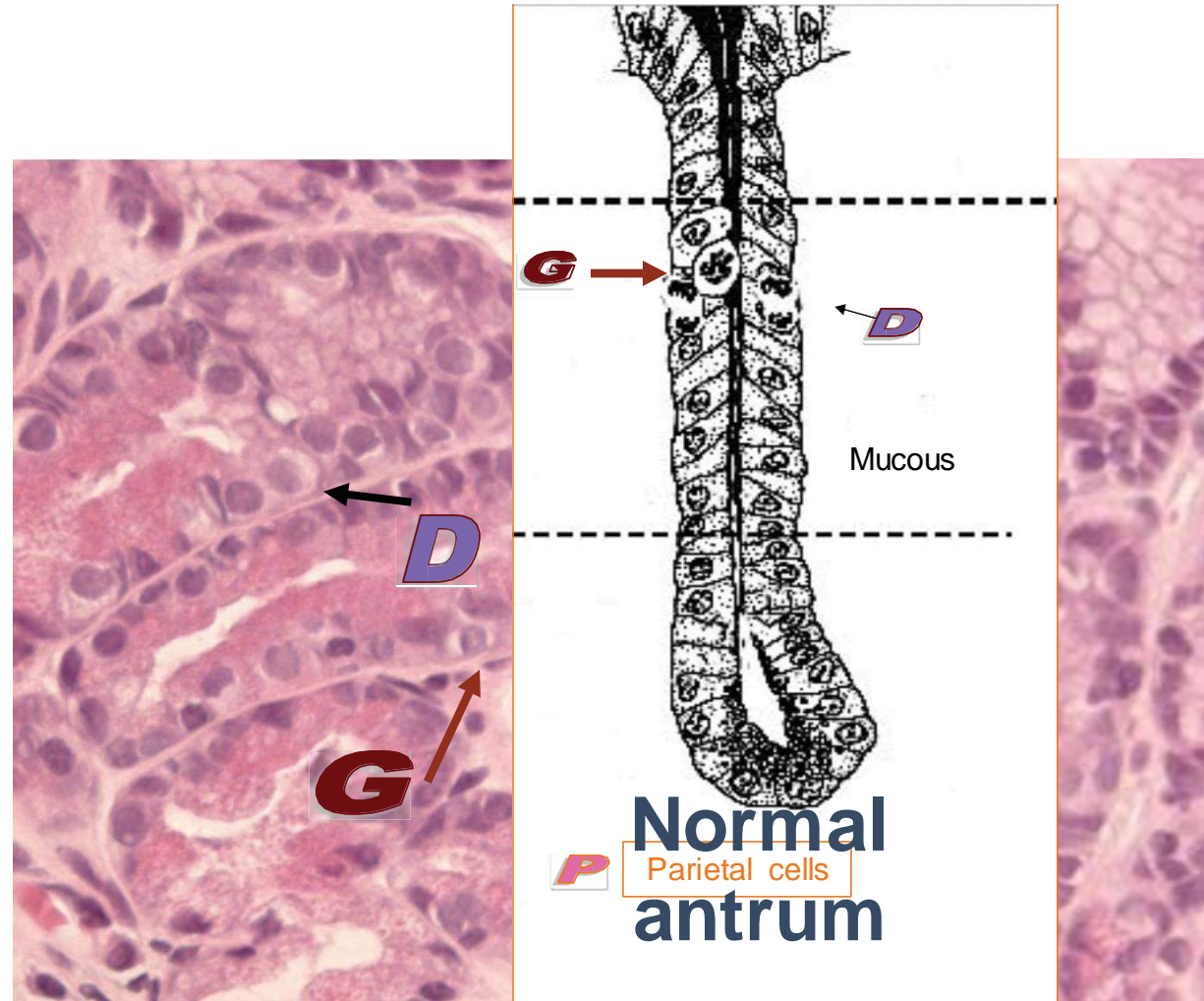
Qiao's Pathology



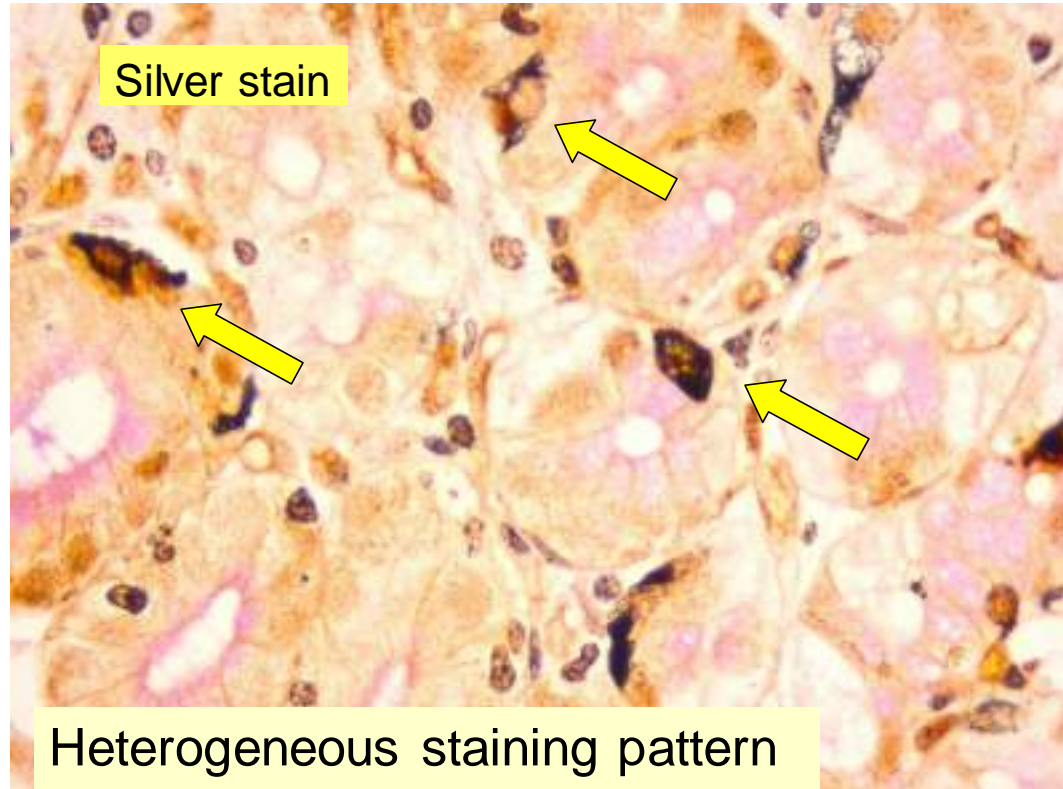
Antrum



Antrum



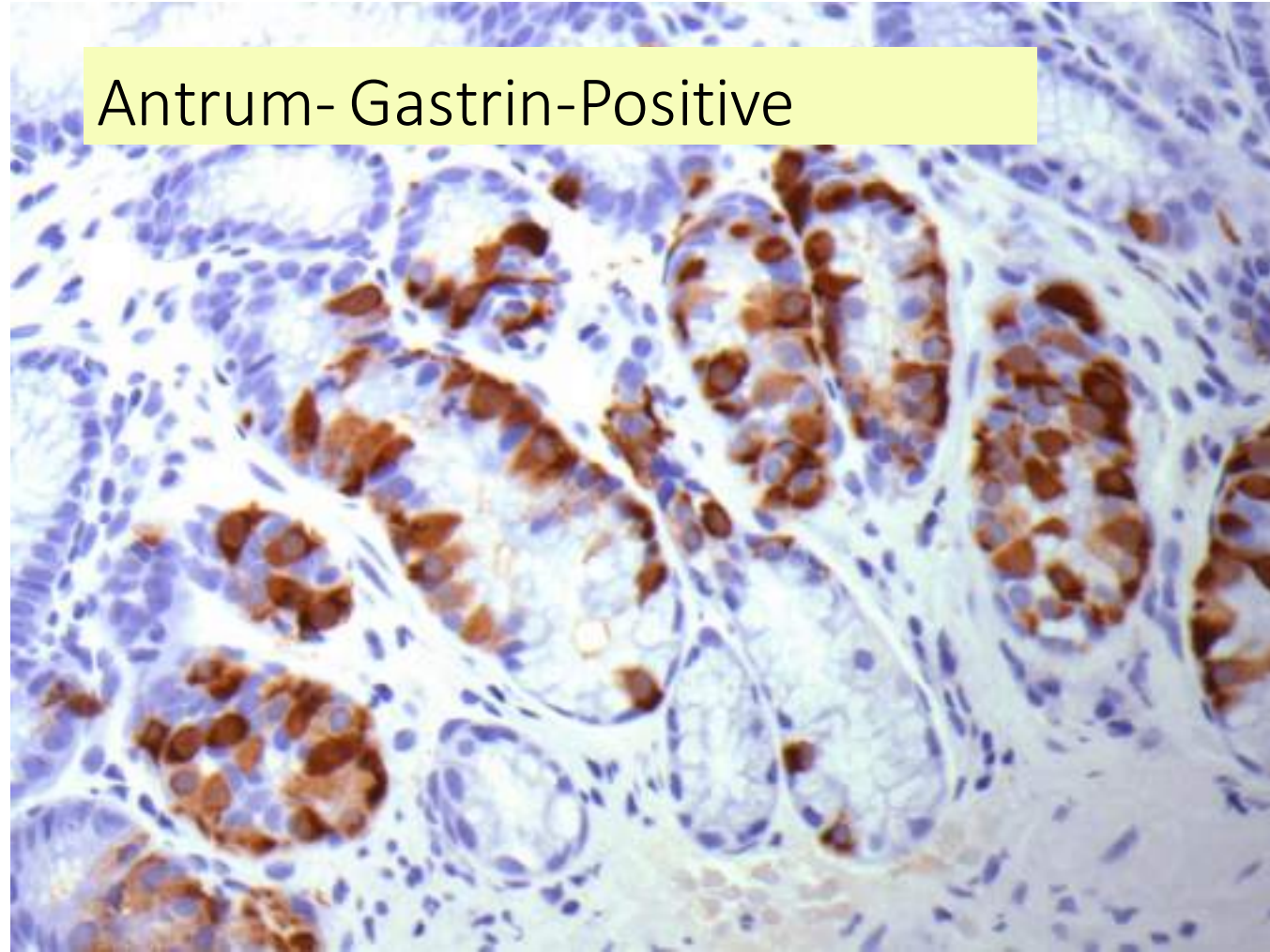
Antrum endocrine cells



Silver stain

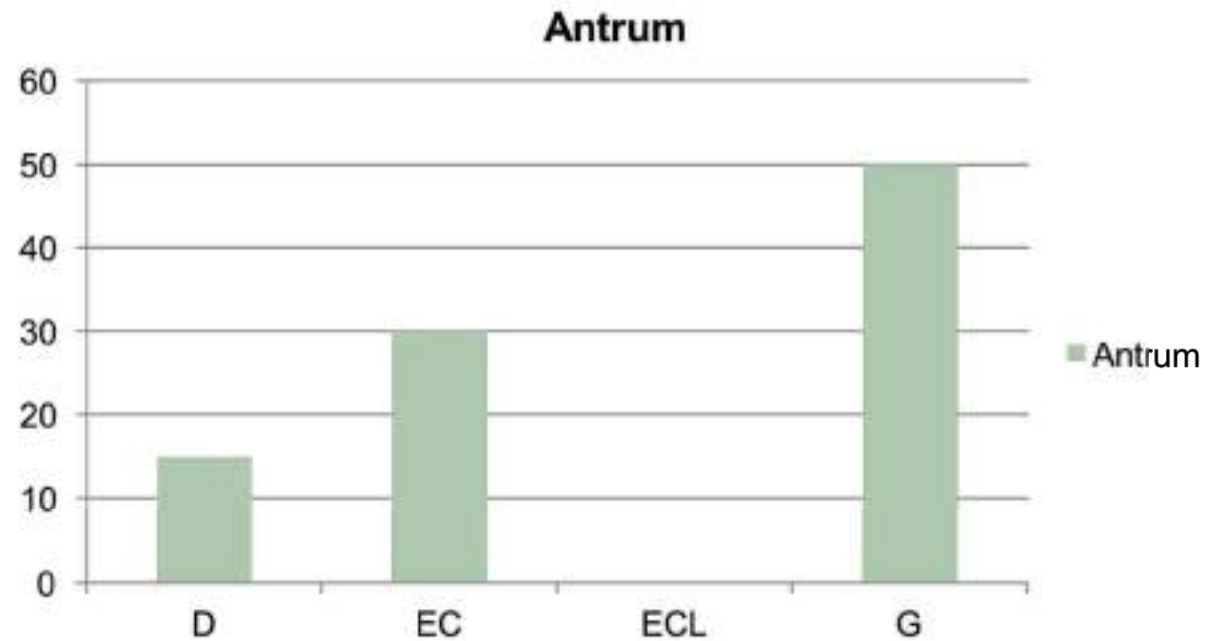
Heterogeneous staining pattern
Hence: best use immunostains

Antrum- Gastrin-Positive



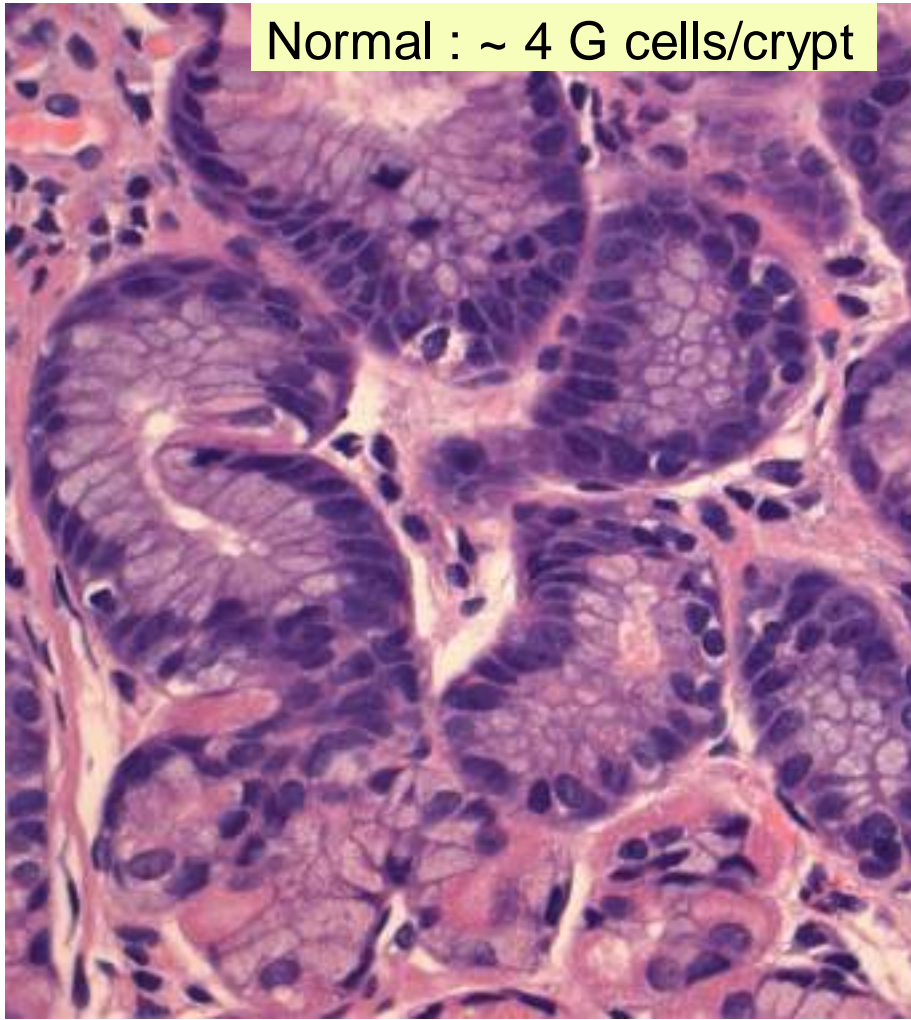
Endocrine Cells **Antrum**

D somatostatin, EC serotonin, ECL histamine or Ghrelin, G gastrin

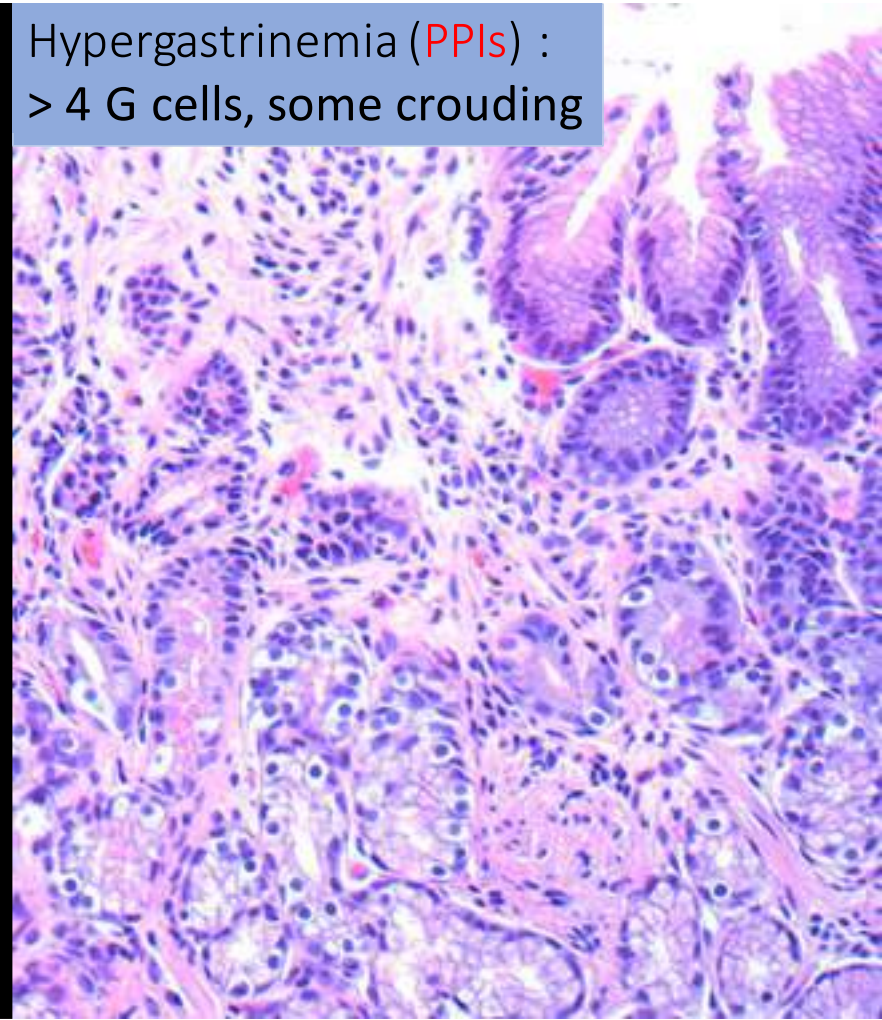


Modified from Gastroenterologia Polska 2006, 13(1): 7-10

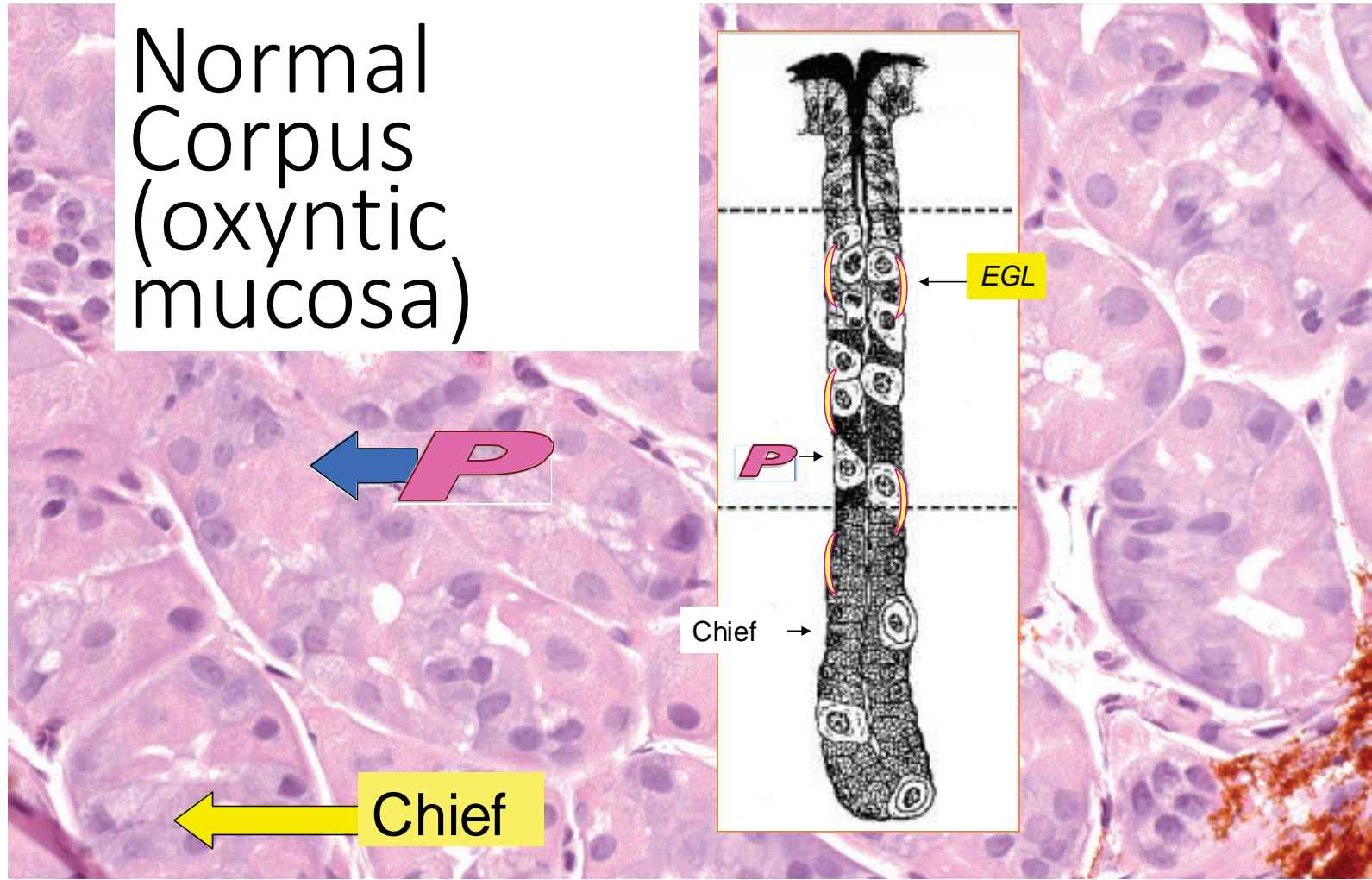
Normal : ~ 4 G cells/crypt



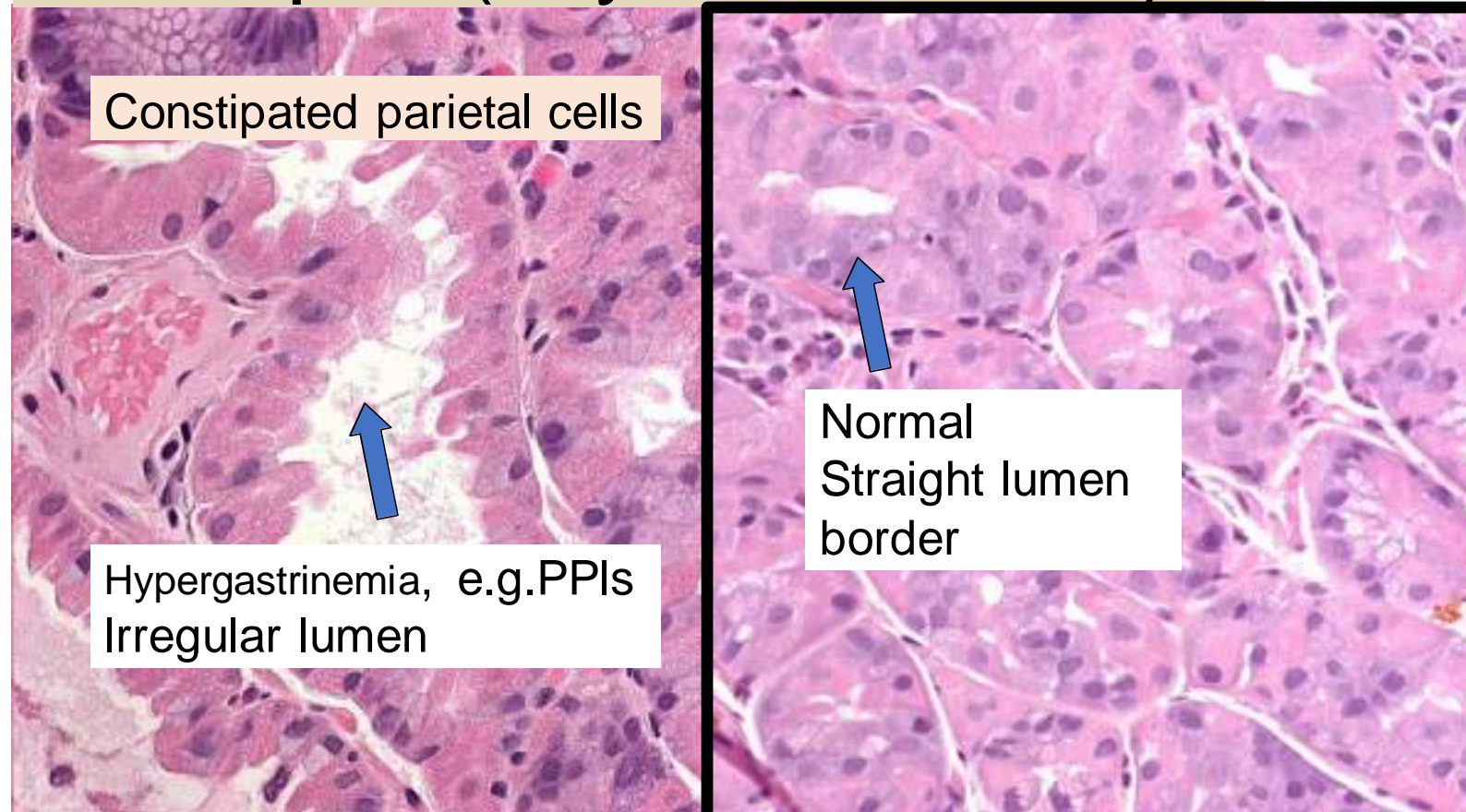
Hypergastrinemia (PPIs) :
> 4 G cells, some crowding



Normal
Corpus
(oxyntic
mucosa)



Corpus (oxyntic mucosa)



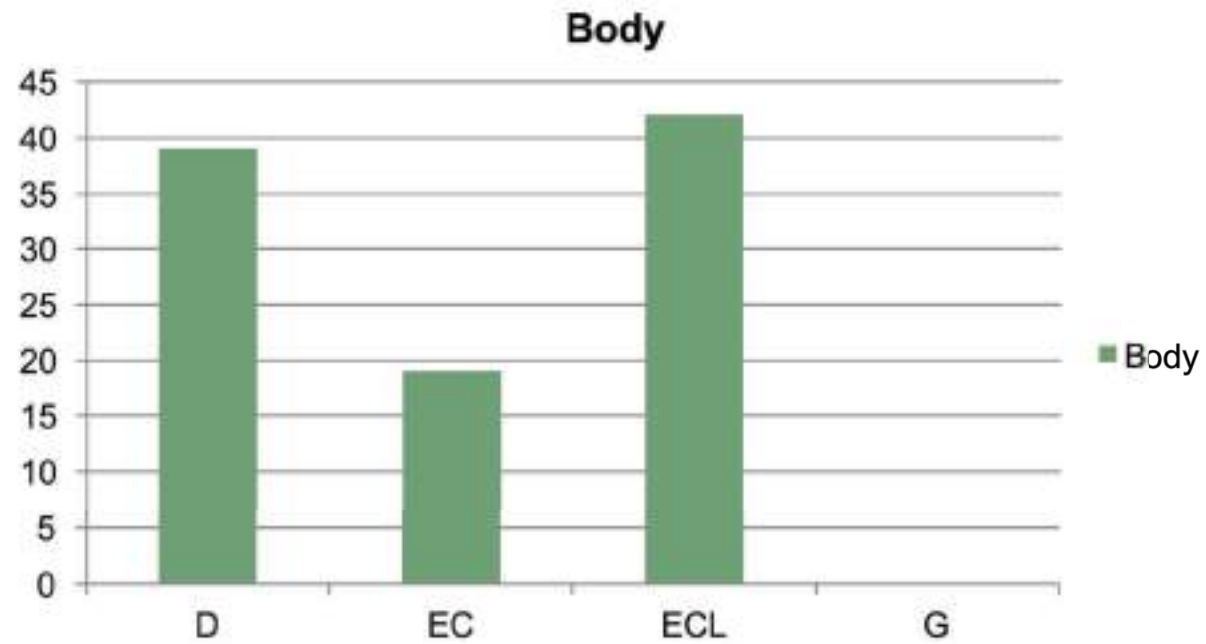
Constipated parietal cells

Hypergastrinemia, e.g. PPIs
Irregular lumen

Normal
Straight lumen
border

Endocrine Cells **body**

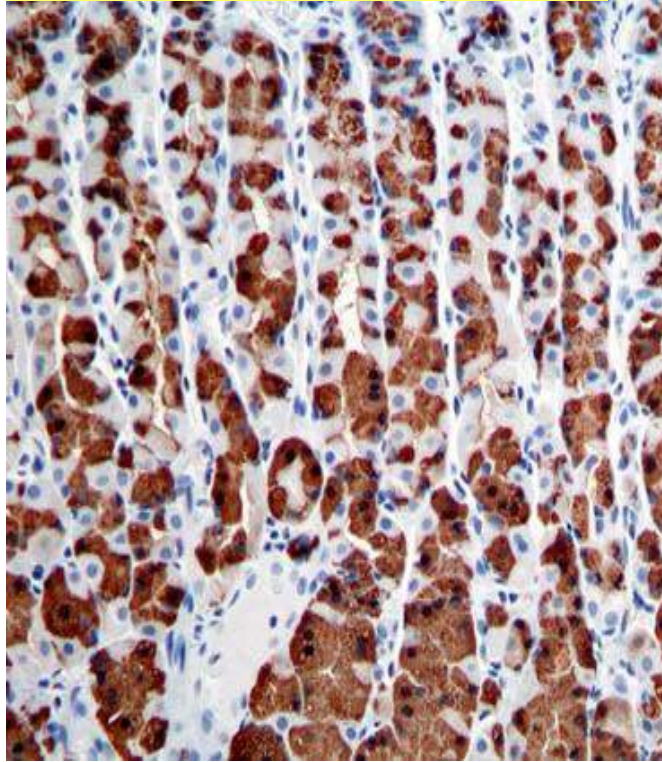
D somatostatin, EC serotonin, ECL histamine or Ghrelin, G gastrin



Modified from Gastroenterologia Polska 2006, 13(1): 7-10

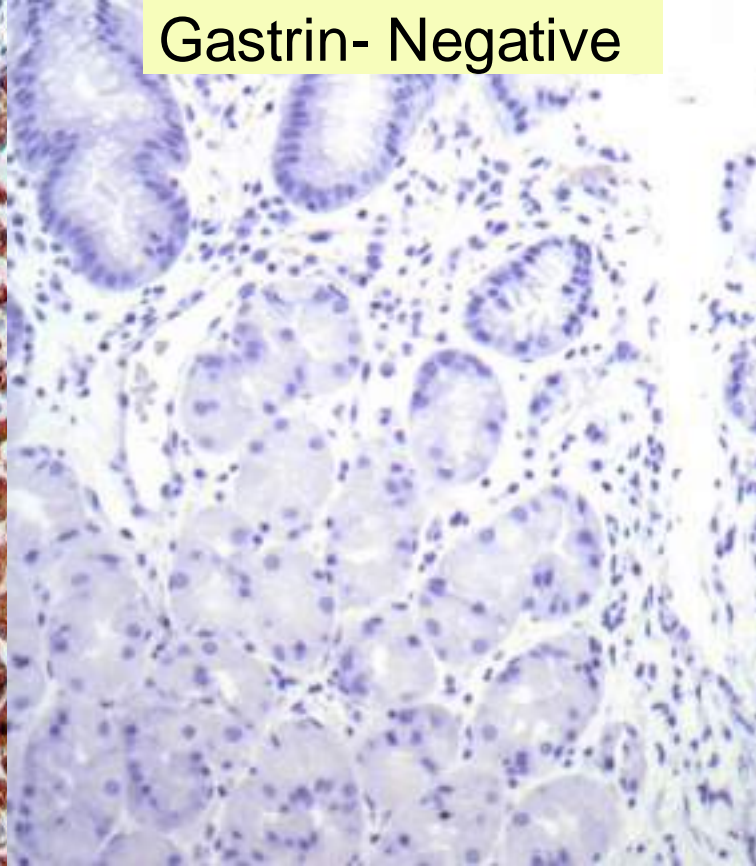
NORMAL CORPUS

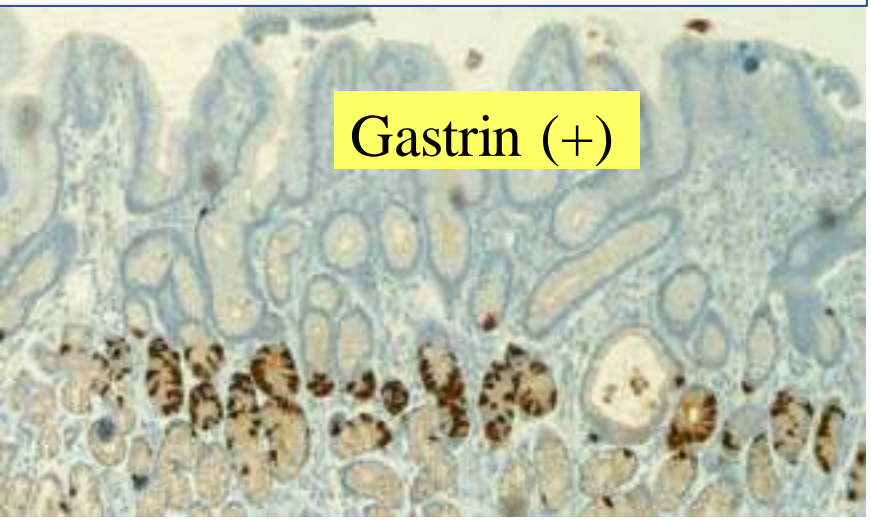
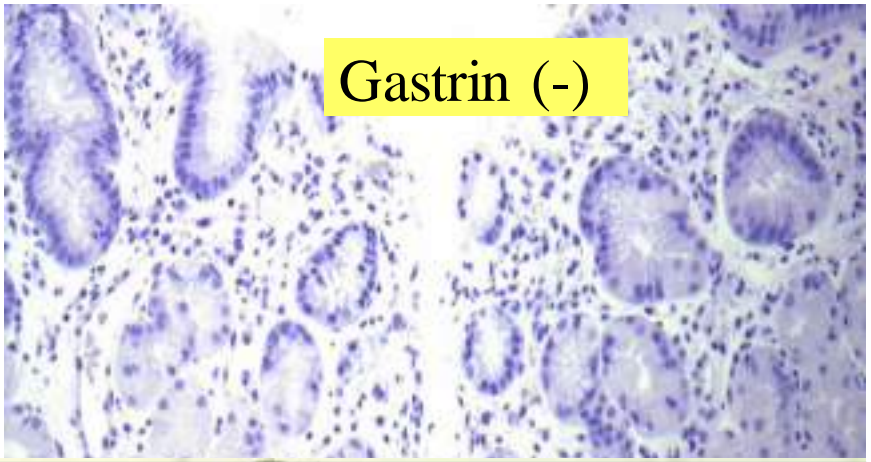
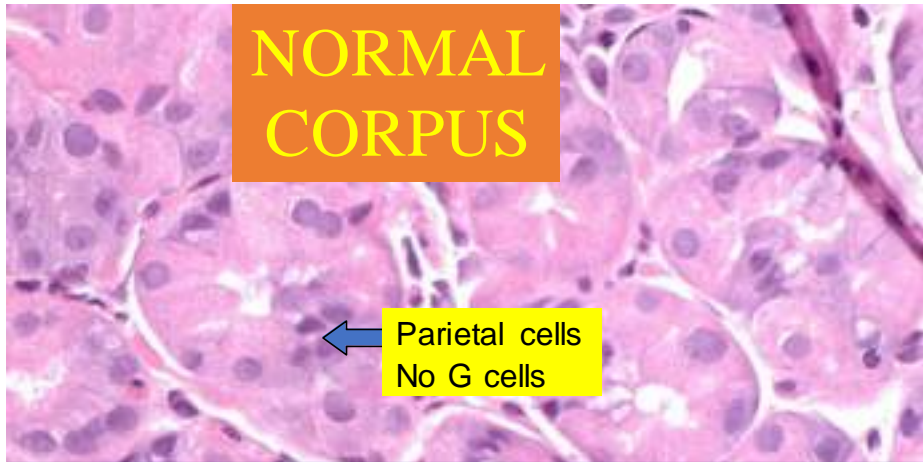
PGI (pepsinogen I) stains
Chief and mucous neck



Oxyntic endocrine cells make
histamine or **ghrelin**, not gastrin

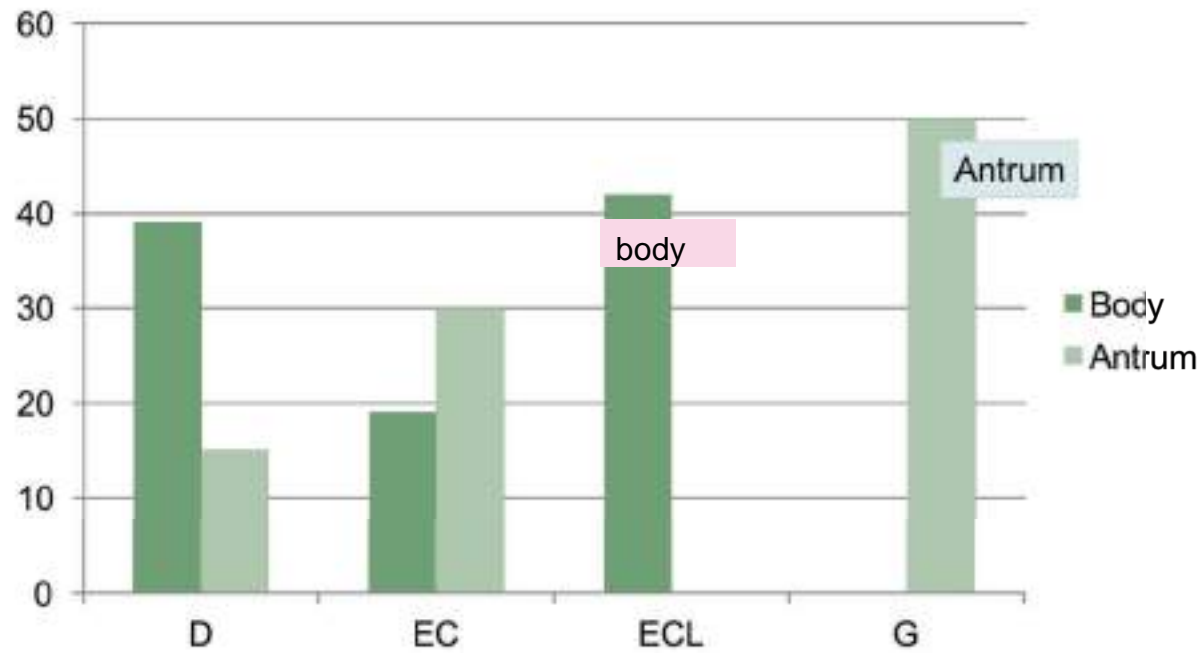
Gastrin- Negative





Endocrine Cells Stomach

D somatostatin, EC serotonin, ECL histamine or Ghrelin, G gastrin



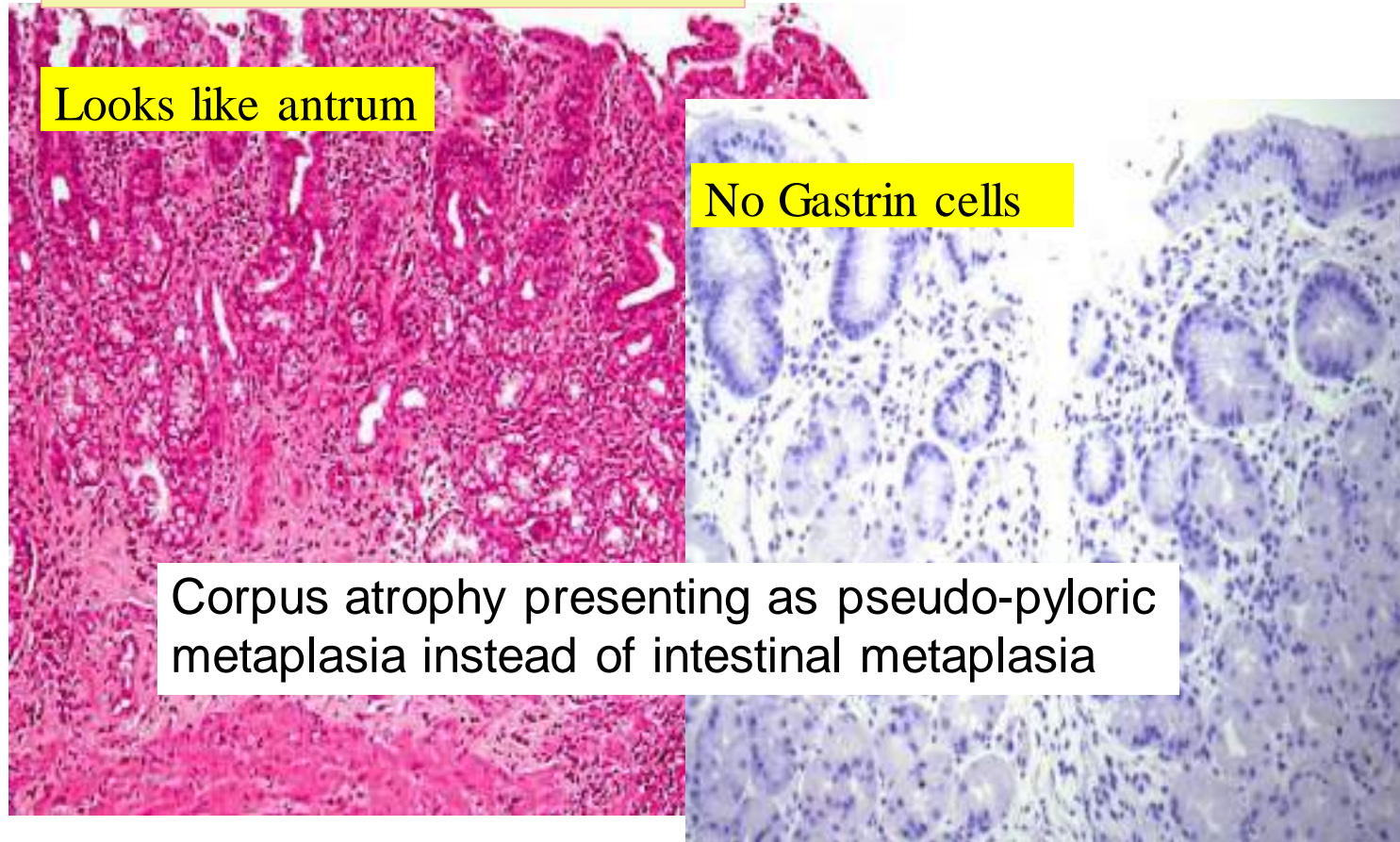
Modified from Gastroenterologia Polska 2006, 13(1): 7-10

? Clinical relevance

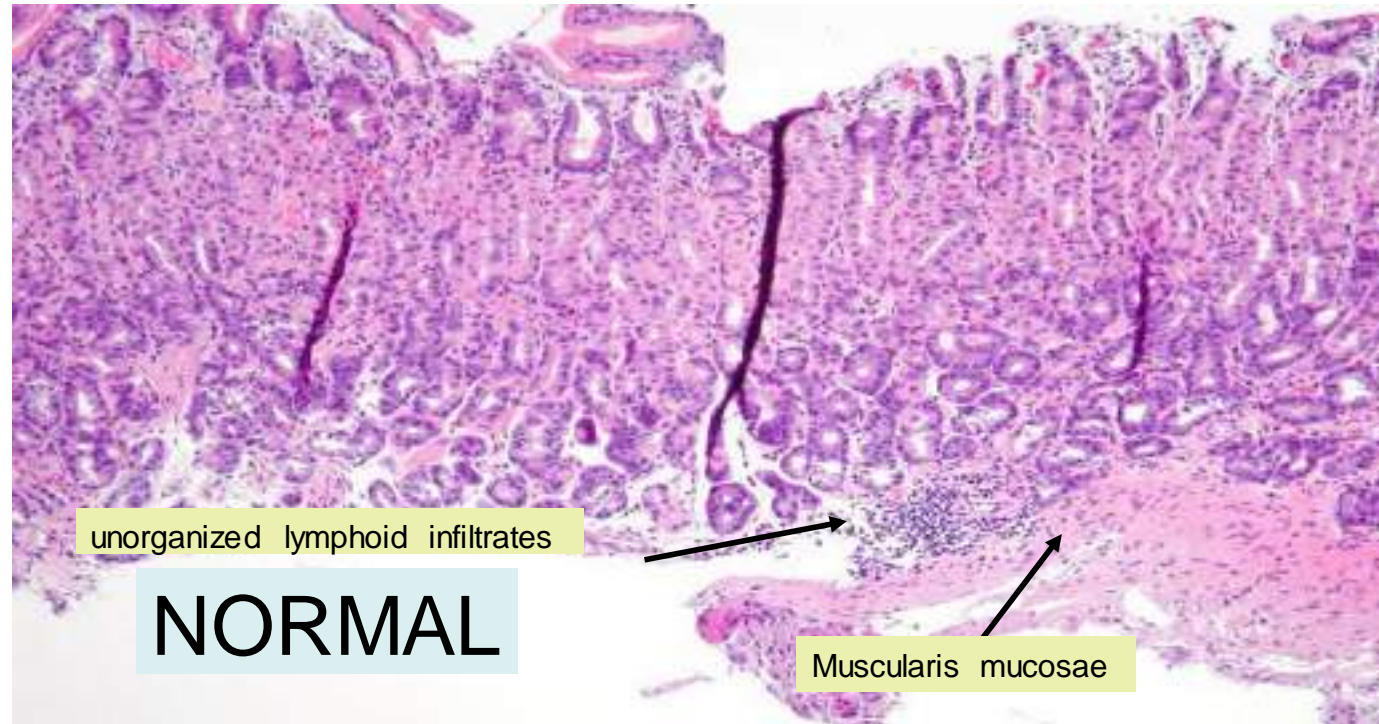
Looks like antrum

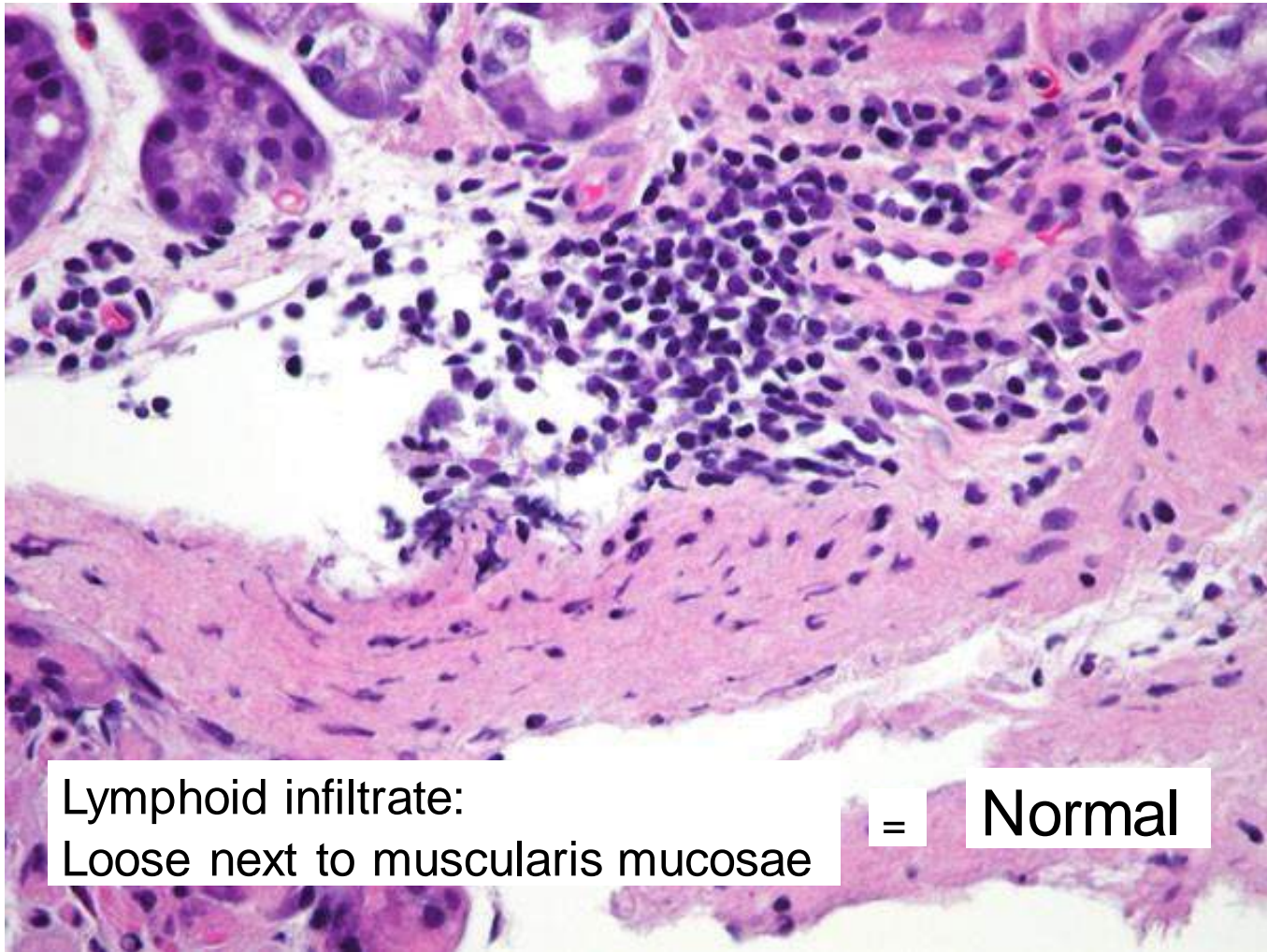
No Gastrin cells

Corpus atrophy presenting as pseudo-pyloric metaplasia instead of intestinal metaplasia



Landmark for NORMAL lymphoid infiltrates
Muscularis mucosae





Lymphoid infiltrate:
Loose next to muscularis mucosae


= Normal

OUTLINE

- I. Normal stomach
- II. Classification of gastritis**
- III. Specific types of gastritis
- IV. How to interpret gastritis

Updated Sydney System 1994

By
pattern

Type		Etiology
Non-atrophic		<i>H. Pylori</i> Other factors
Atrophic Autoimmune Multifocal		Autoimmune <i>H. pylori</i> , dietary, environmental
Special Forms Chemical Lymphocytic Eosinophilic Granulomatous Radiation Other infectious		Chemical irritation Gluten, idiopathic Food sensitivity Crohn's, sarcoid Radiation Virus, fungus, etc.

By etiology

Infectious	<ol style="list-style-type: none">1. Bacterial (<i>H. pylori</i>, T.B.)2. Viral (CMV)3. Fungal (candida)4. Parasitic
Non-Infectious	<ol style="list-style-type: none">1. Chemical/Reflux gastropathy2. Lymphocytic3. Auto-immune4. Inflammatory Bowel Disease5. Eosinophilic
Part of Systemic involvement	<ol style="list-style-type: none">1. GVHD2. Vasculitis (Churg Struss)3. Granulomatous4. collagenous
Miscellaneous	<ol style="list-style-type: none">1. Hypertrophic gastropathy2. Vascular lesions (GAVE, portal gastropathy)

My algorithm at low power

Inflammator: MNC, PMN	<ol style="list-style-type: none">1. Diffuse: infectious (+/-<i>H. pylori</i>)2. Focal: IBD, erosion
Non- Inflammator y	<ol style="list-style-type: none">1. Epithelial: Reactive (chemical/reflux gastropathy2. Vascular: GAVE & portal gastropathy
Other	<ol style="list-style-type: none">1. Eosinophilic2. Granulomatous3. Collagenous

Inflammatory conditions

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

Acute gastritis and gastropathy

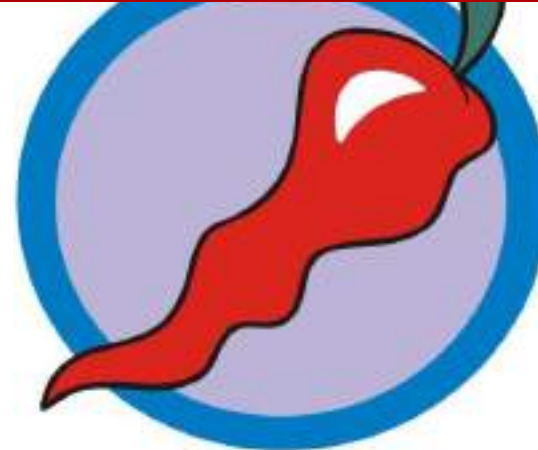
- ▶ **Acute gastritis:** Mucosal injury, neutrophils present.
- ▶ **Gastropathy:** regenerative, no inflammation.

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

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

Reactive (Chemical/Reflux) Gastropathy

- Originally described by Dixon (1990) with NSAIDs and bile reflux (1986).
- In Bile reflux: The acid causes most of the damage.



CHEMICAL GASTROPATHY

- **Triad**

chronic

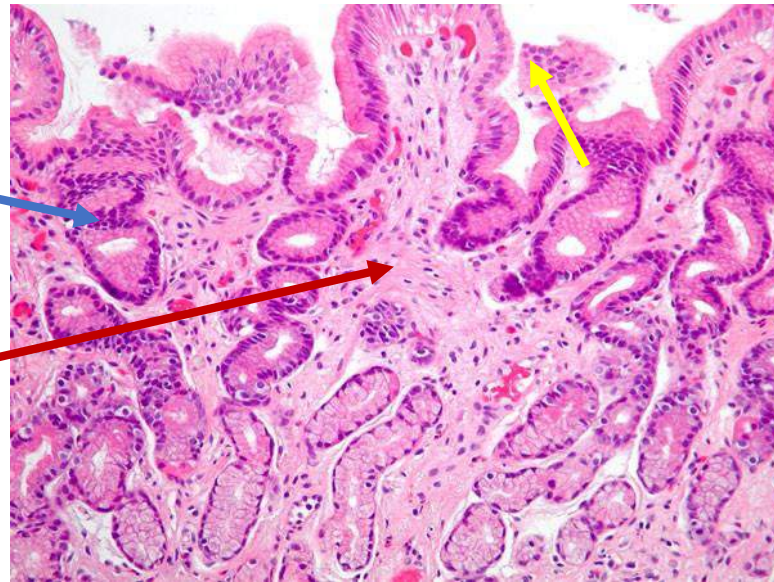
1. Foveolar hyperplasia
2. Smooth muscle fiber hyperplasia
3. Paucity of acute and chronic inflammatory cells

acute

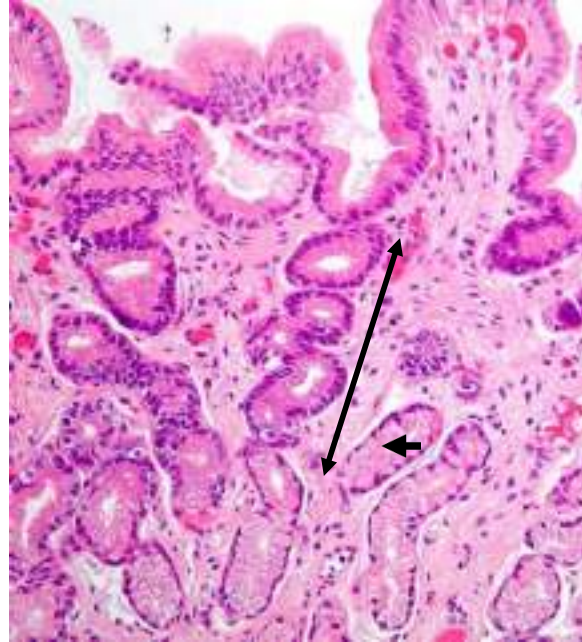
- **Other criteria:** edema, vasodilation, congestion of capillaries

Reactive/Chemical Gastropathy Triad

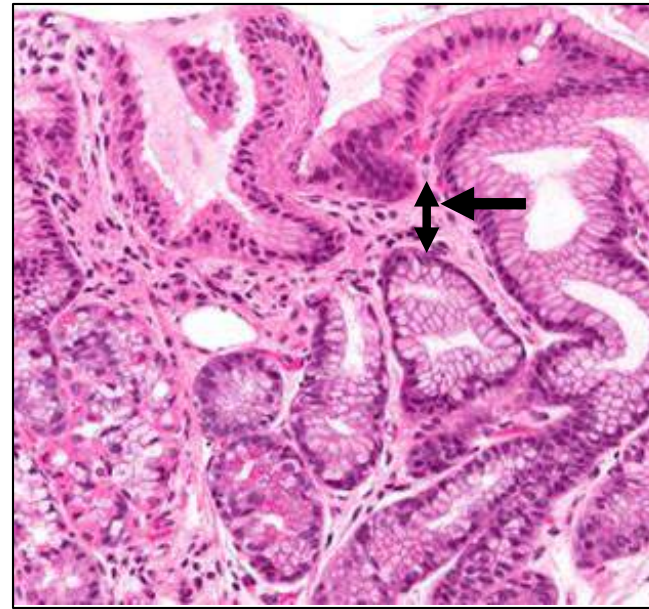
1. Foveolar hyperplasia
2. Smooth muscle fiber hyperplasia
3. Paucity of acute and chronic inflammatory cells



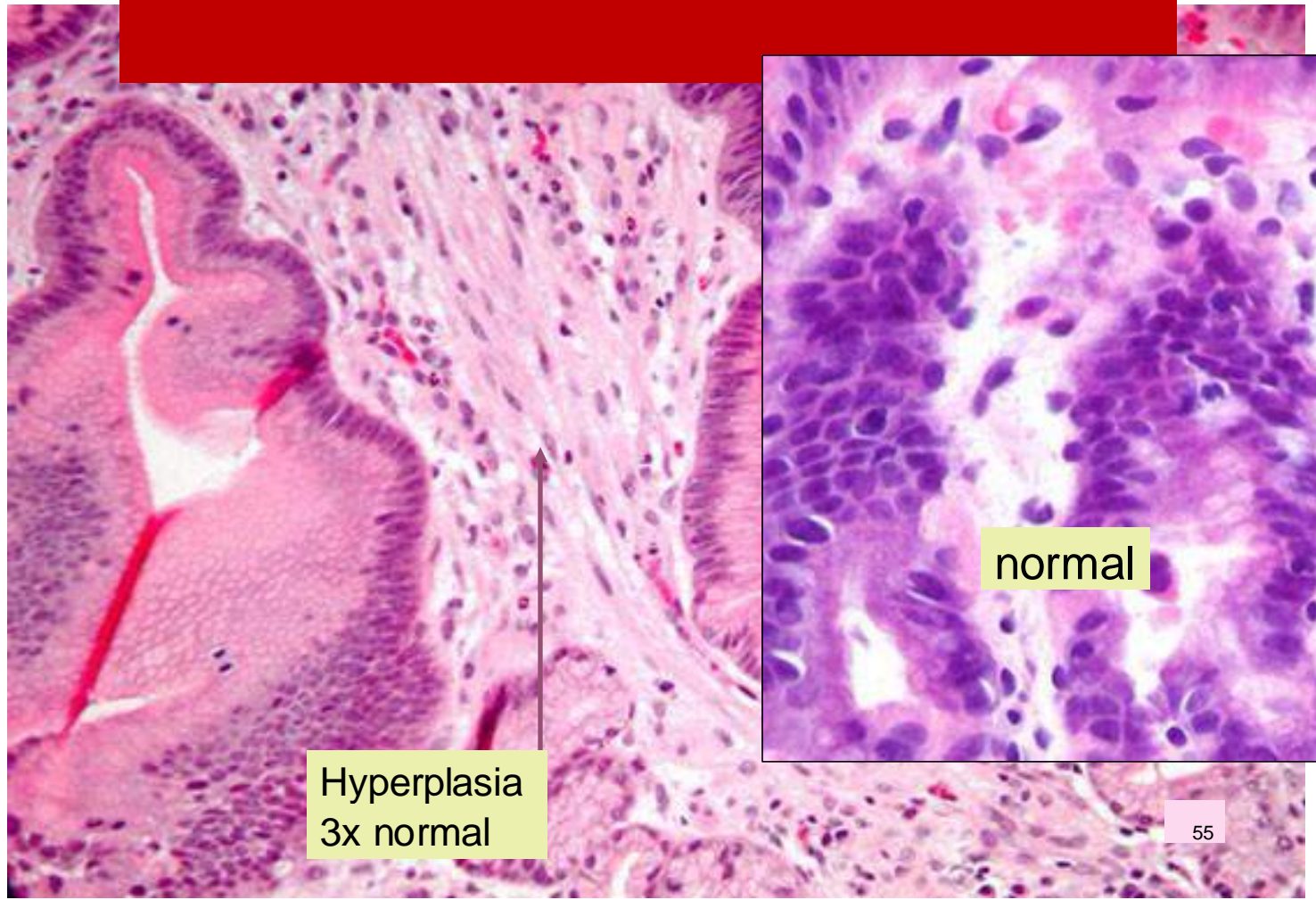
How to identify foveolar hyperplasia?
(length of neck region)



Foveolar hyperplasia
Long & tortuous
Up to 3 x normal



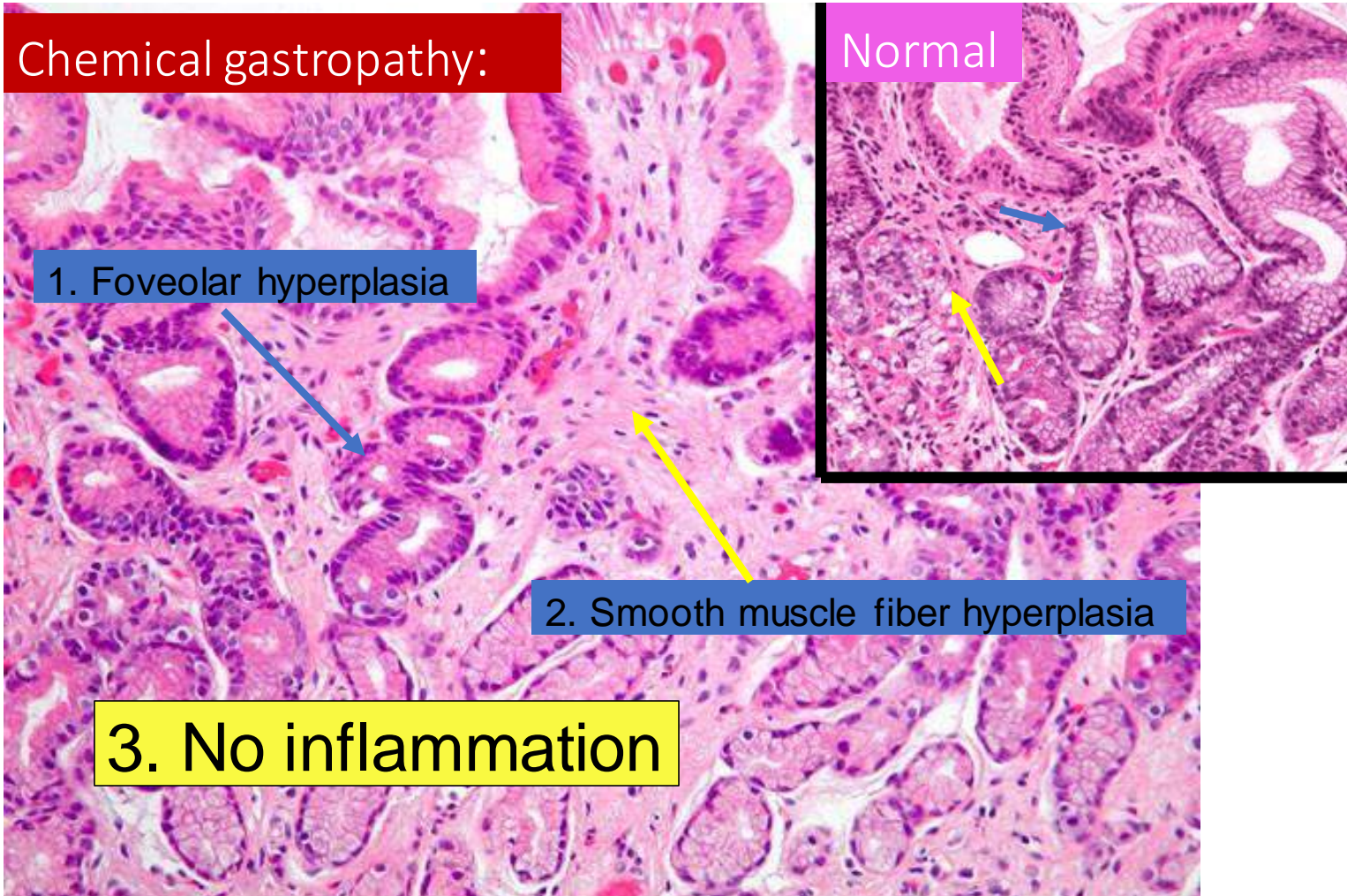
Normal



Hyperplasia
3x normal

normal

Chemical gastropathy:



1. Foveolar hyperplasia

2. Smooth muscle fiber hyperplasia

3. No inflammation

Normal

Chemical Gastropathy: A Distinct Histopathologic Entity in Children

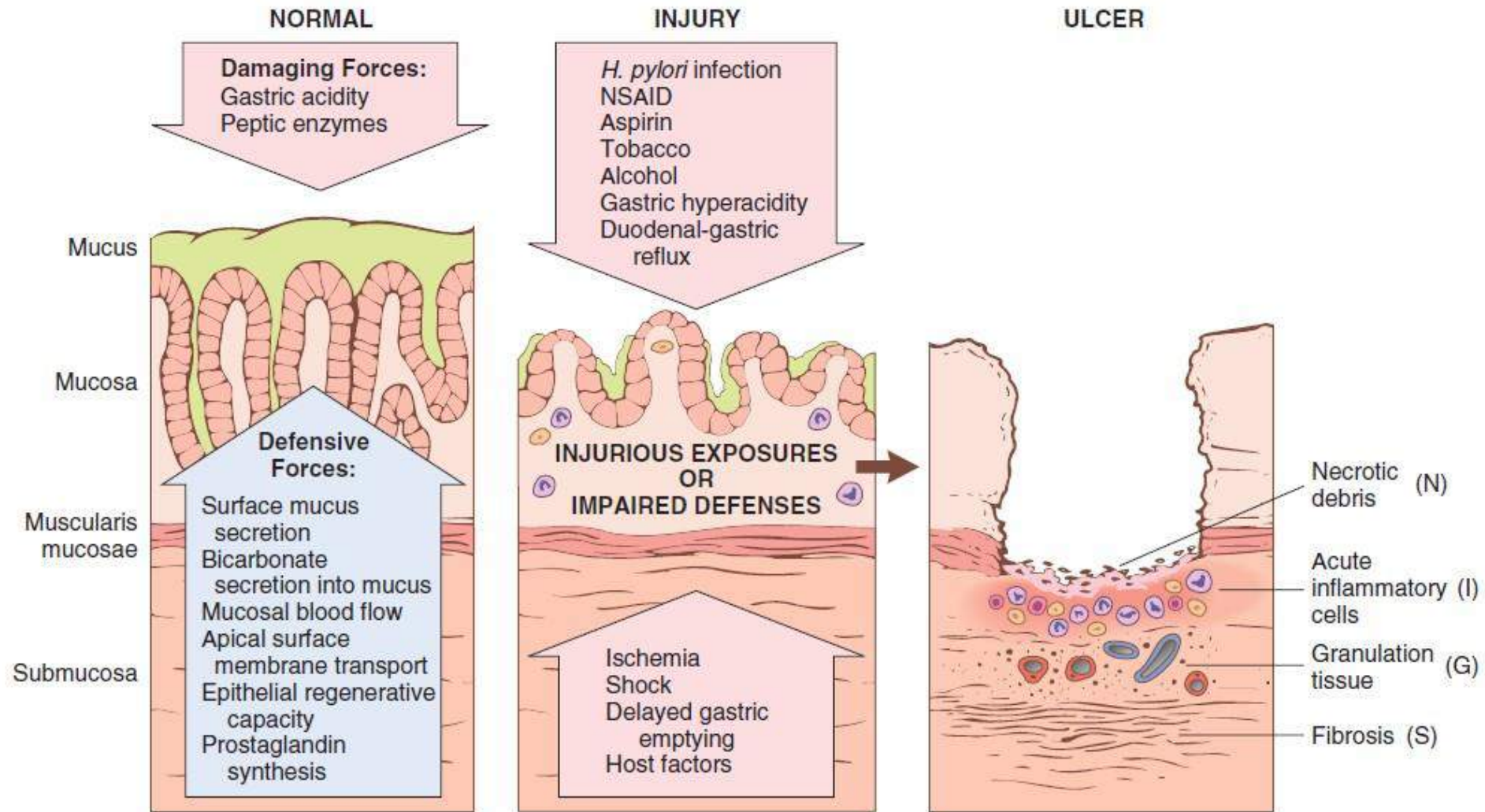
*Dinesh S. Pashankar, *Warren P. Bishop, and †Frank A. Mitros

**Division of Gastroenterology, Children's Hospital of Iowa, and †Department of Pathology, University of Iowa,
Iowa City, Iowa, U.S.A.*

TABLE 2. *Histological features of Dixon's diagnostic scoring system in 21 patients with chemical gastropathy*

Antral histological features	Number	Percent
Foveolar hyperplasia	19	90
Lamia propria edema/smooth muscle fibers	16	76
Vascular congestion	20	95
Paucity of acute inflammatory cells	21	100
Paucity of chronic inflammatory cells	19	90

Pathogenesis



Pathogenesis

▶ Imbalance between protective and damaging forces

▶ **Main causes:**

1. **NSAIDs**
2. **Uremic patients, H pylori infected patients**
3. **Old age.**
4. **Hypoxia**
5. **Harsh chemicals, (acids or bases)**
6. **Alcohol, radiation therapy:**
7. **Chemotherapy.**

Morphology

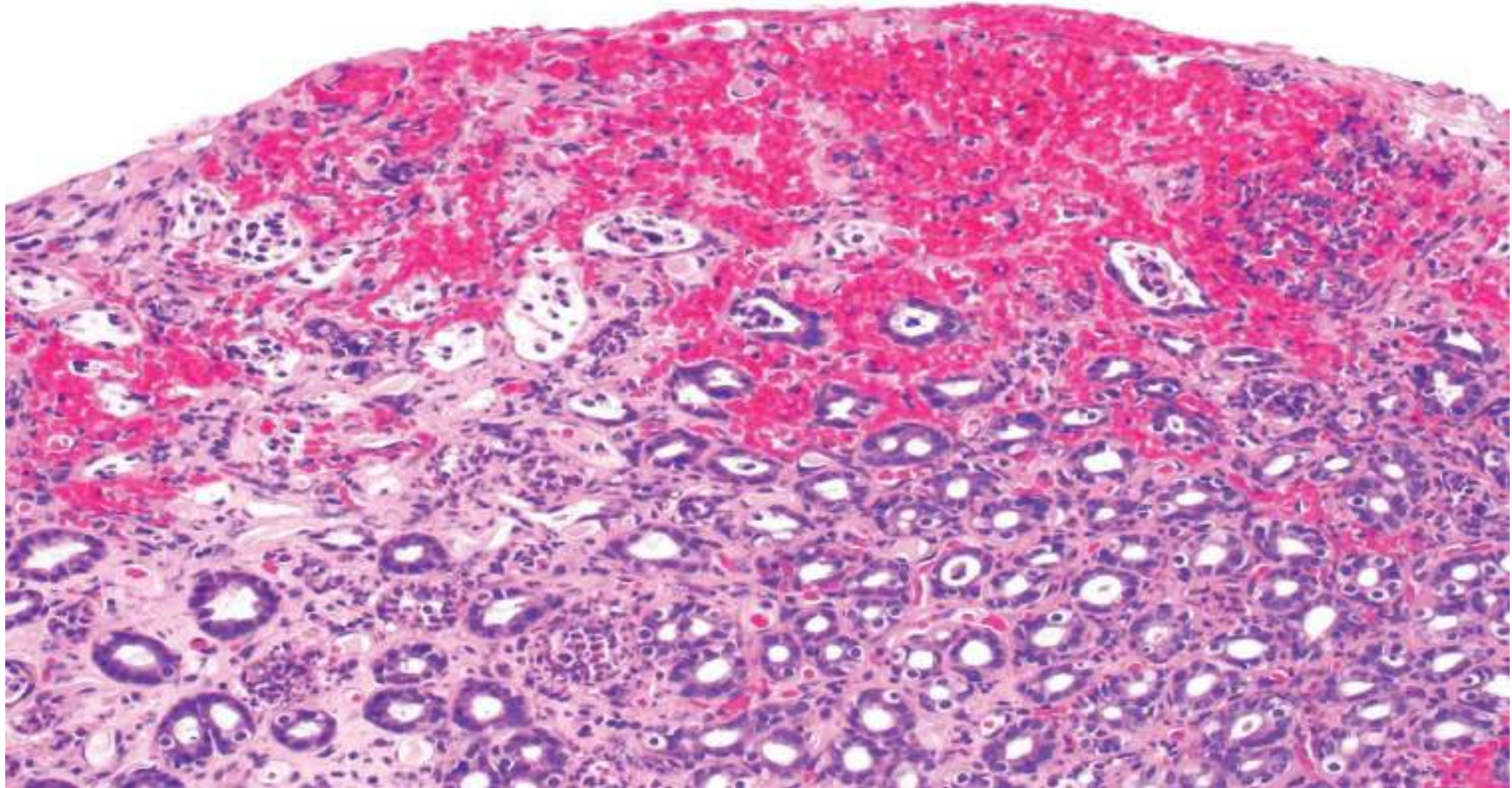
- ▶ Hyperemia.
- ▶ Edema and slight vascular congestion
- ▶ Neutrophils, lymphocytes, and plasma cells are not prominent.
- ▶ Intact surface epithelium.
- ▶ Advanced: Erosions and hemorrhage, acute erosive hemorrhagic gastritis.

- ▶ Active inflammation (neutrophils) is not necessary.

Acute gastritis



B



Stress-Related Mucosal Disease

acute gastric ulcers

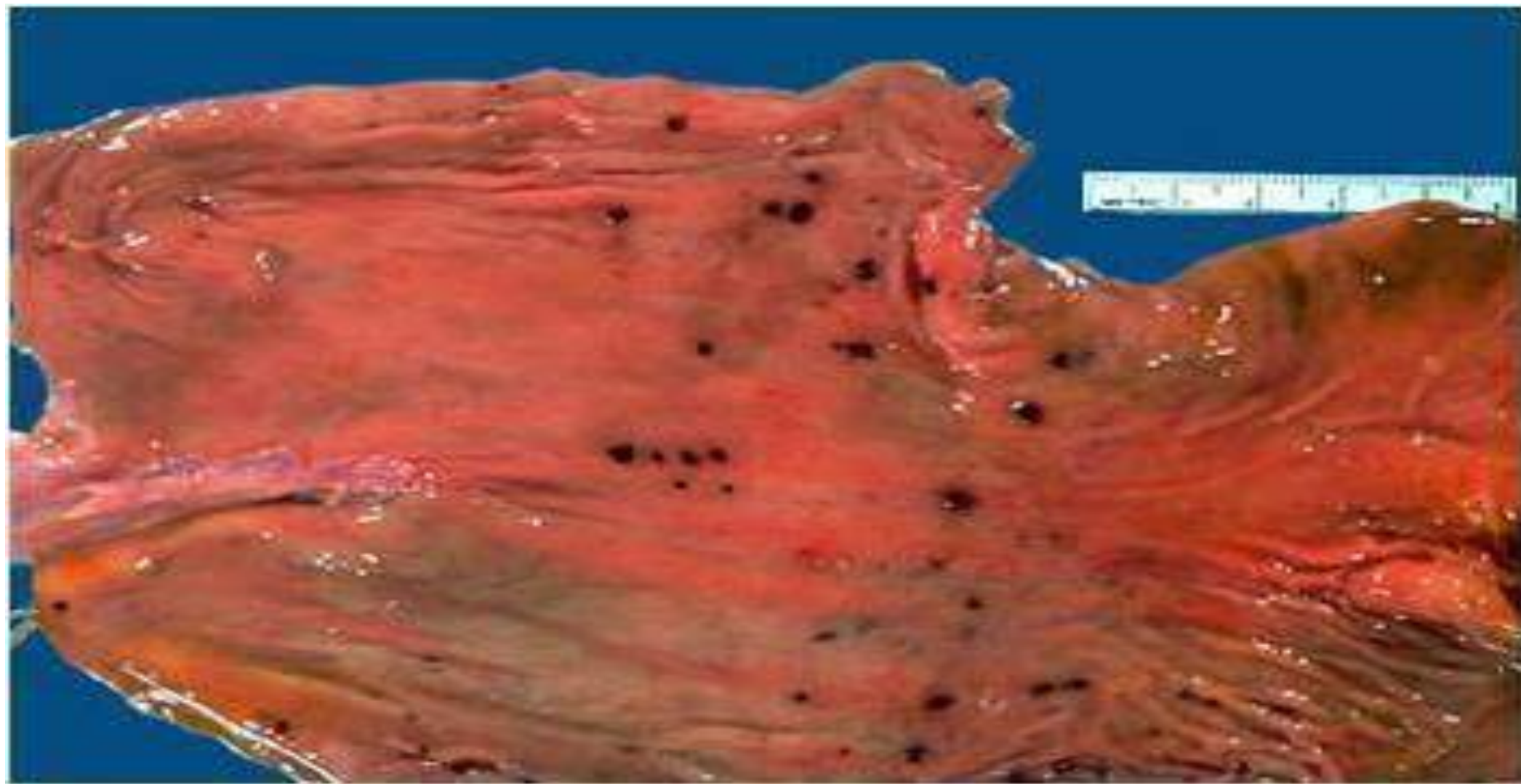
- ▶ Severe physiologic stress:
 - ▶ Trauma
 - ▶ Extensive burns
 - ▶ Intracranial disease
 - ▶ Major surgery
 - ▶ Serious medical disease
 - ▶ Critically ill patients

Acute gastric ulcers:

- ▶ ***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, intracranial disease, high risk of perforation.

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 reepithelialization occurs days or weeks after removal of injurious factors



Clinical features

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

Chronic gastritis

- ▶ *Causes:*
- ▶ ***Helicobacter pylori associated gastritis: most common.***
- ▶ ***Autoimmune atrophic gastritis: less than 10% of cases.***

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

Clinical features

- ▶ Nausea and upper-abdominal discomfort
- ▶ Vomiting
- ▶ Hematemesis uncommon.

- ▶ Less severe but more prolonged symptoms.

Diffuse Ghronic Inflammation

H. pylori

1. Gastritis Patterns
2. Special presentations
3. Diagnosis (stains)



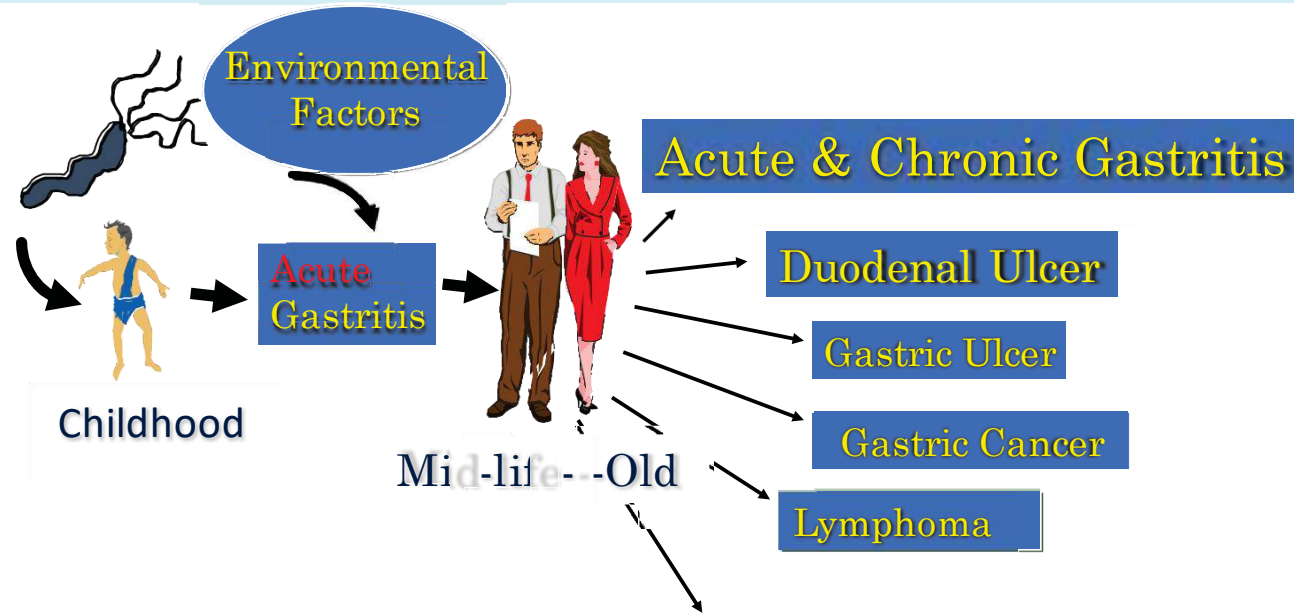
Helicobacter pylori Gastritis

- ▶ Discovery of the association of H.pylori with peptic ulcer disease was a revolution.
- ▶ Spiral or curved, G-ve, bacilli.
- ▶ Present in almost all duodenal ulcers.
- ▶ Majority of gastric ulcers or chronic gastritis.
- ▶ Acute infection is subclinical.
- ▶ ***Antral gastritis with increased acid production >> peptic ulcer***
- ▶ **Intestinal metaplasia and increased risk of gastric cancer.**

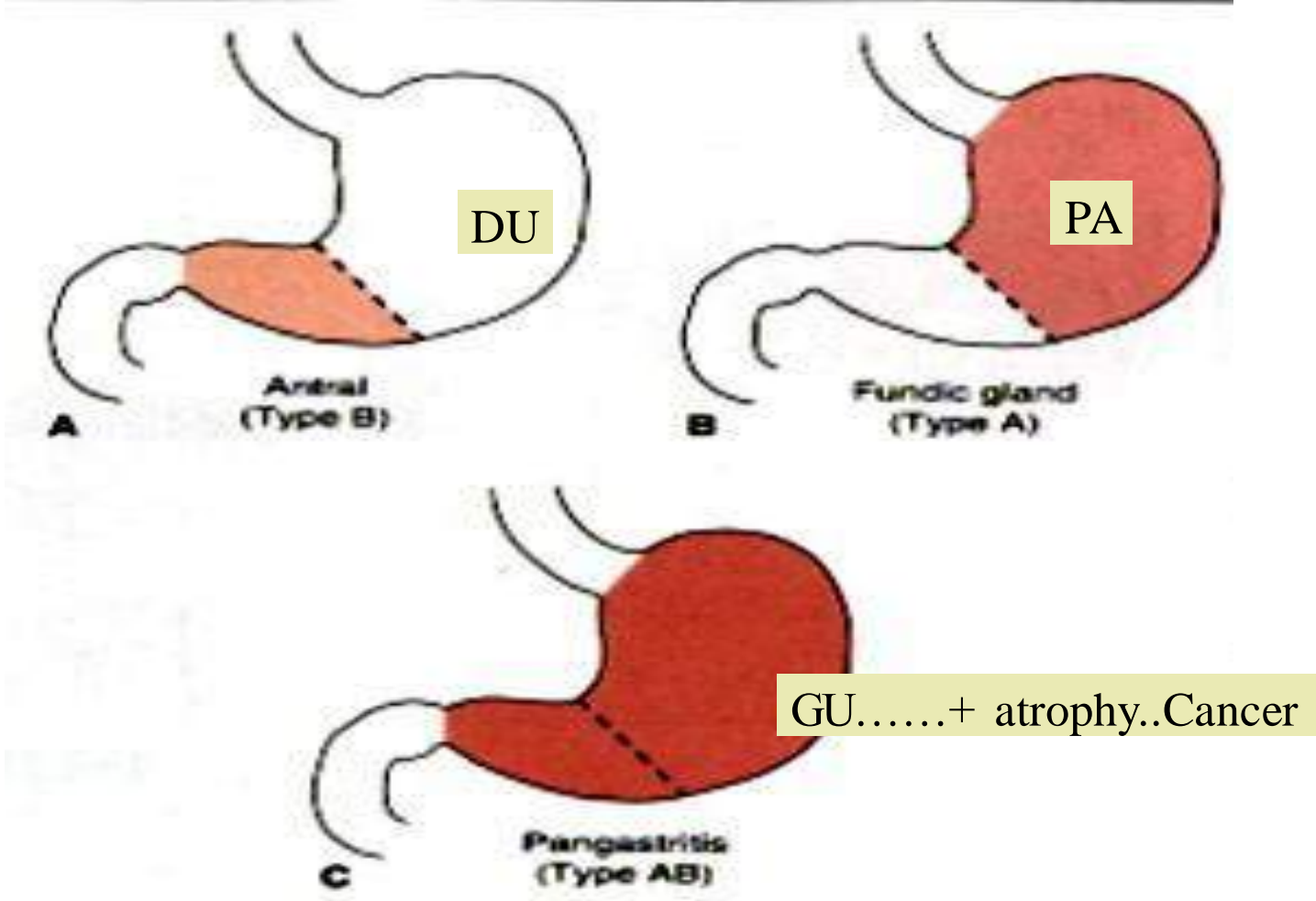
- ▶ Poverty, household crowding, limited education, poor sanitation
- ▶ Infection is typically acquired in childhood, persists to adult-life.

- ▶ **Pathogenesis:**
- ▶ H.pylori adapted to live in the mucus layer, non-invasive, by
- ▶ **Flagella:** allow motility.
- ▶ **Urease:** *split urea to ammonia*, protect bacteria from acidic pH.
- ▶ **Adhesins:** bacterial adherence to foveolar cells
- ▶ **Toxins:** *CagA*, for ulcer or cancer development

OUTCOMES OF *H. PYLORI* INFECTION



GASTRITIS PATTERN

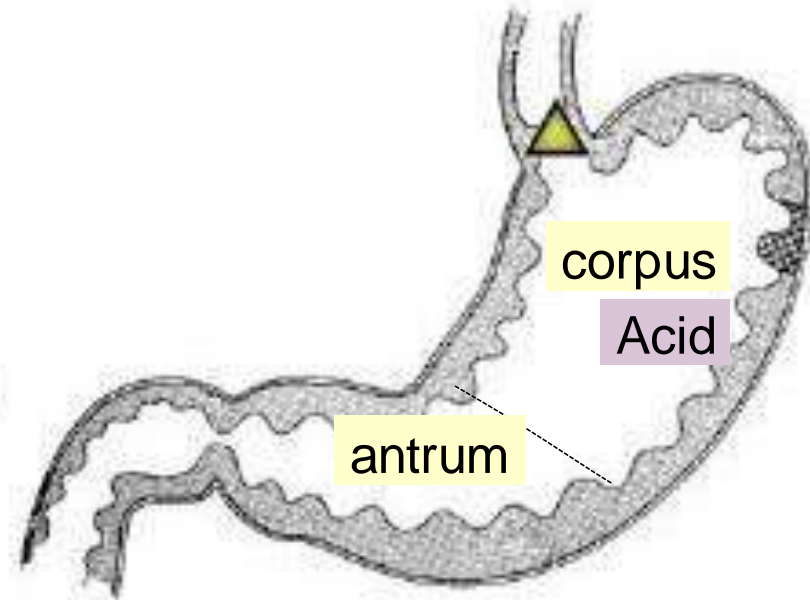


Q: How do we explain different gastritis patterns with *H. pylori* infection?

Q: How do bugs in the stomach cause ulcers in the duodenum?

No bacteria likes too much acid including *H. pylori*

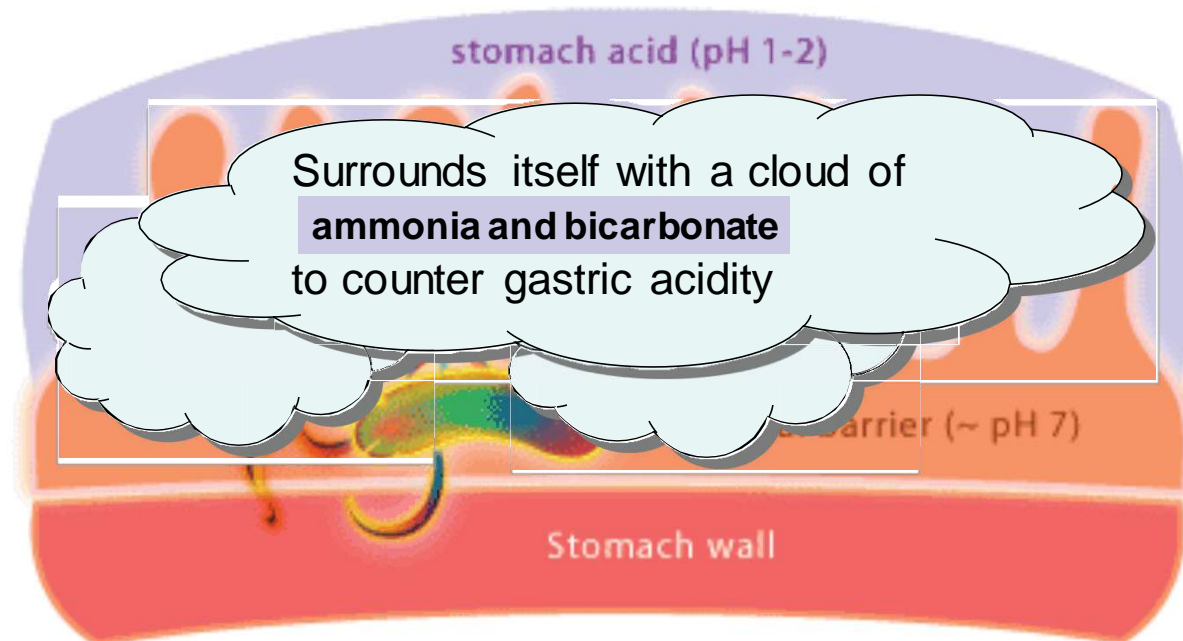
H. pylori prefers neutral pH and dies below 4.0 or above 8.2



H. pylori starts its life in the antrum where it is less acidic

No bacteria likes acid

Starts in the antrum



Surrounds itself with a cloud of
ammonia and bicarbonate
to counter gastric acidity

(it produces urease which converts urea (abundant in saliva & gastric juices) to ammonia and bicarbonate)



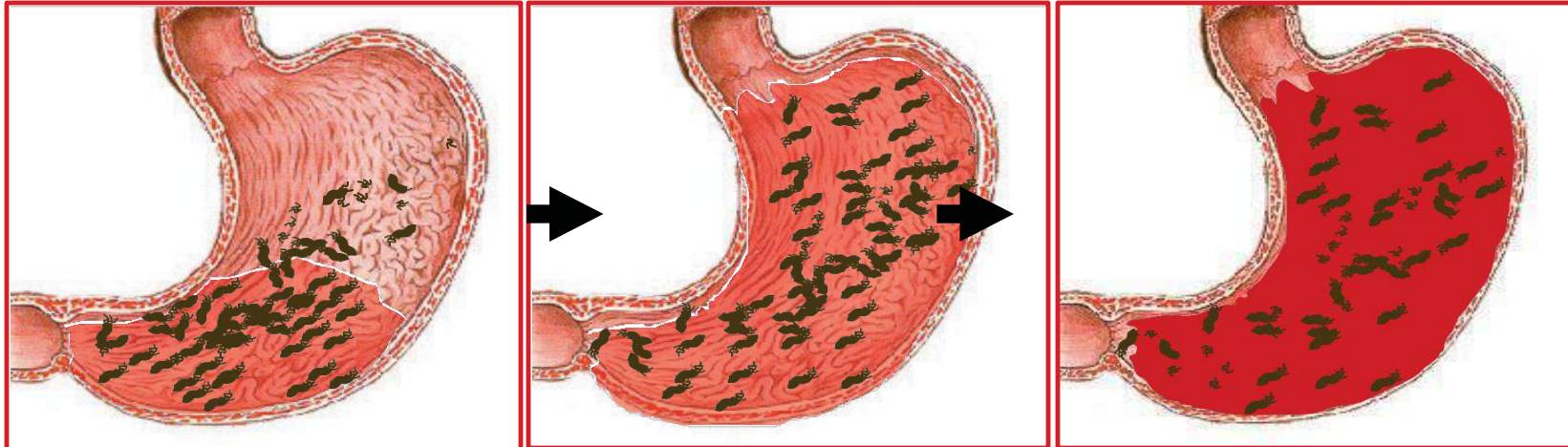
Gastritis Stages

proximal migration of *H. pylori*

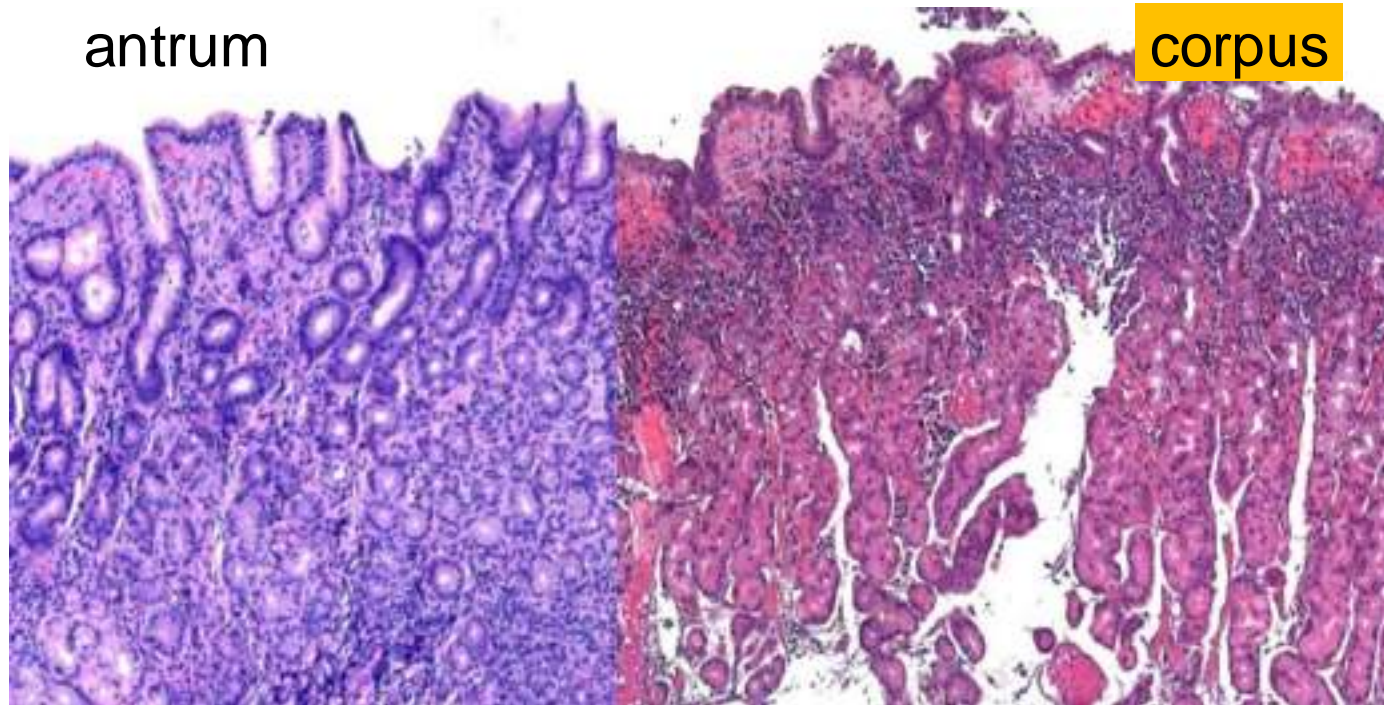
Antral Predom.

Corpus gastritis

Pan-atrophic

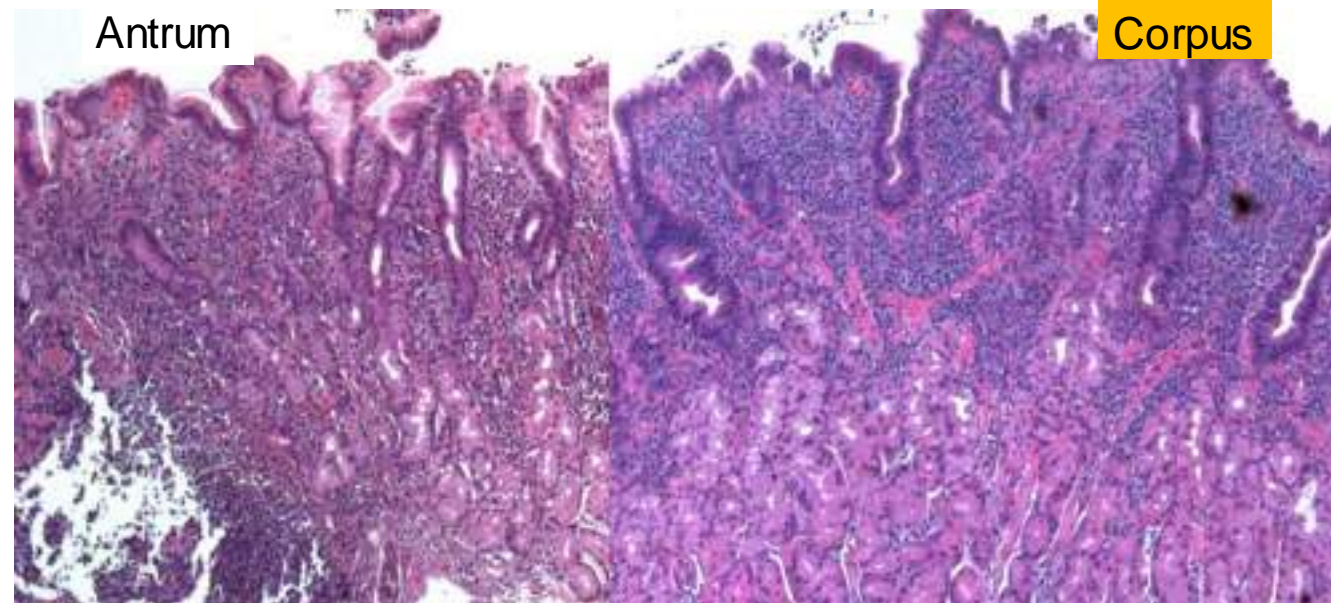


Sustained *H. Pylori* Gastritis



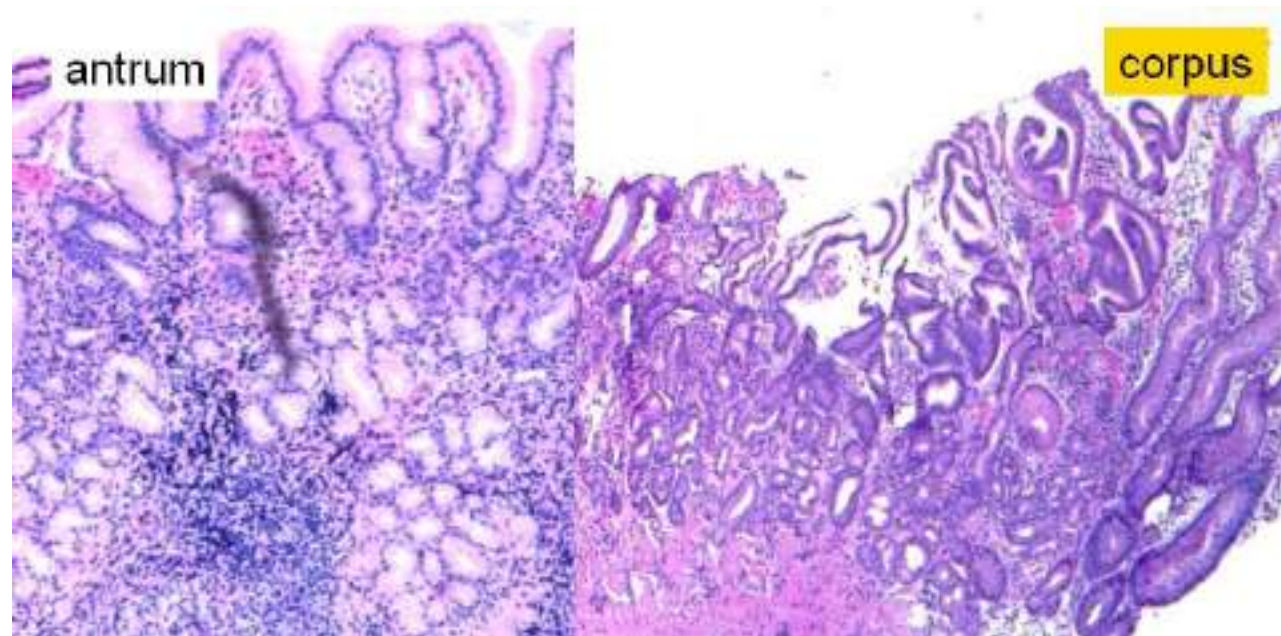
Pan Gastritis with superficial inflammation in the corpus

And *later* H. Pylori Gastritis



Pan-Gastritis with deeper inflammation in ! corpus

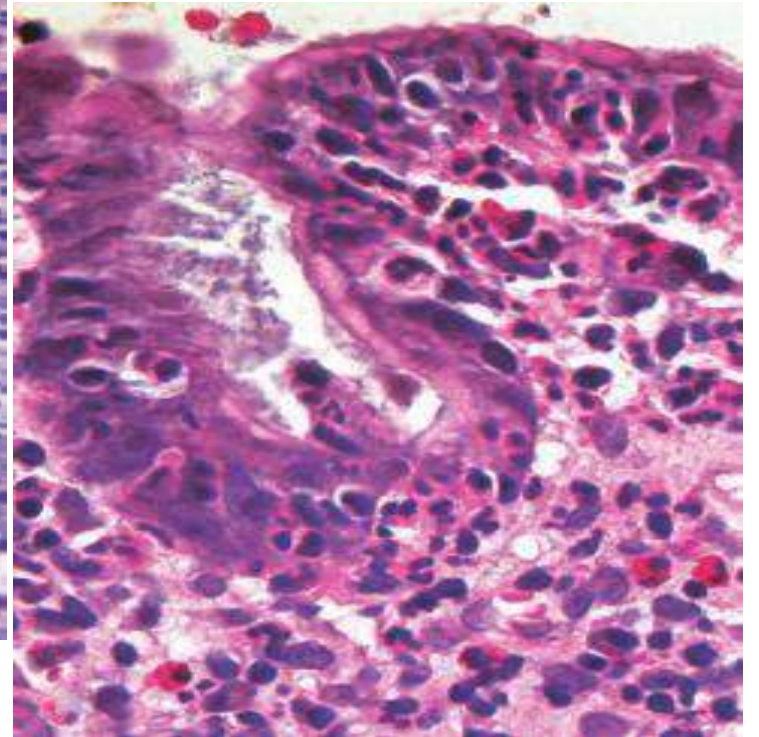
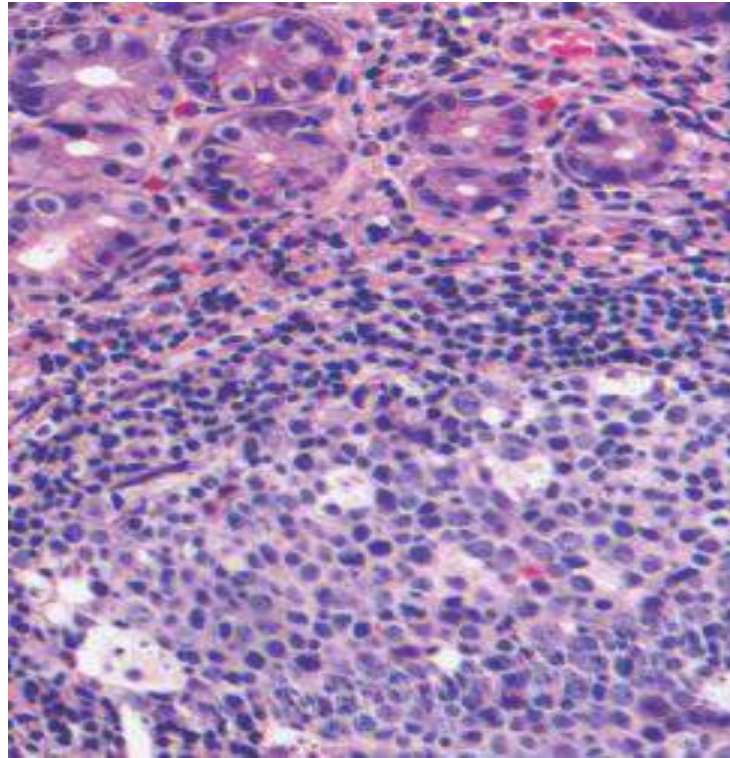
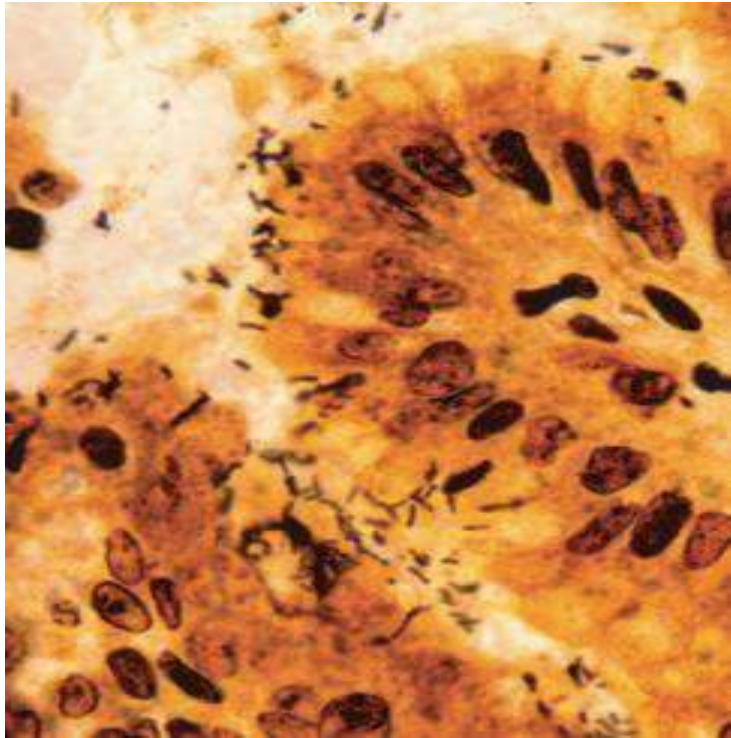
Too Late *H. Pylori* gastritis



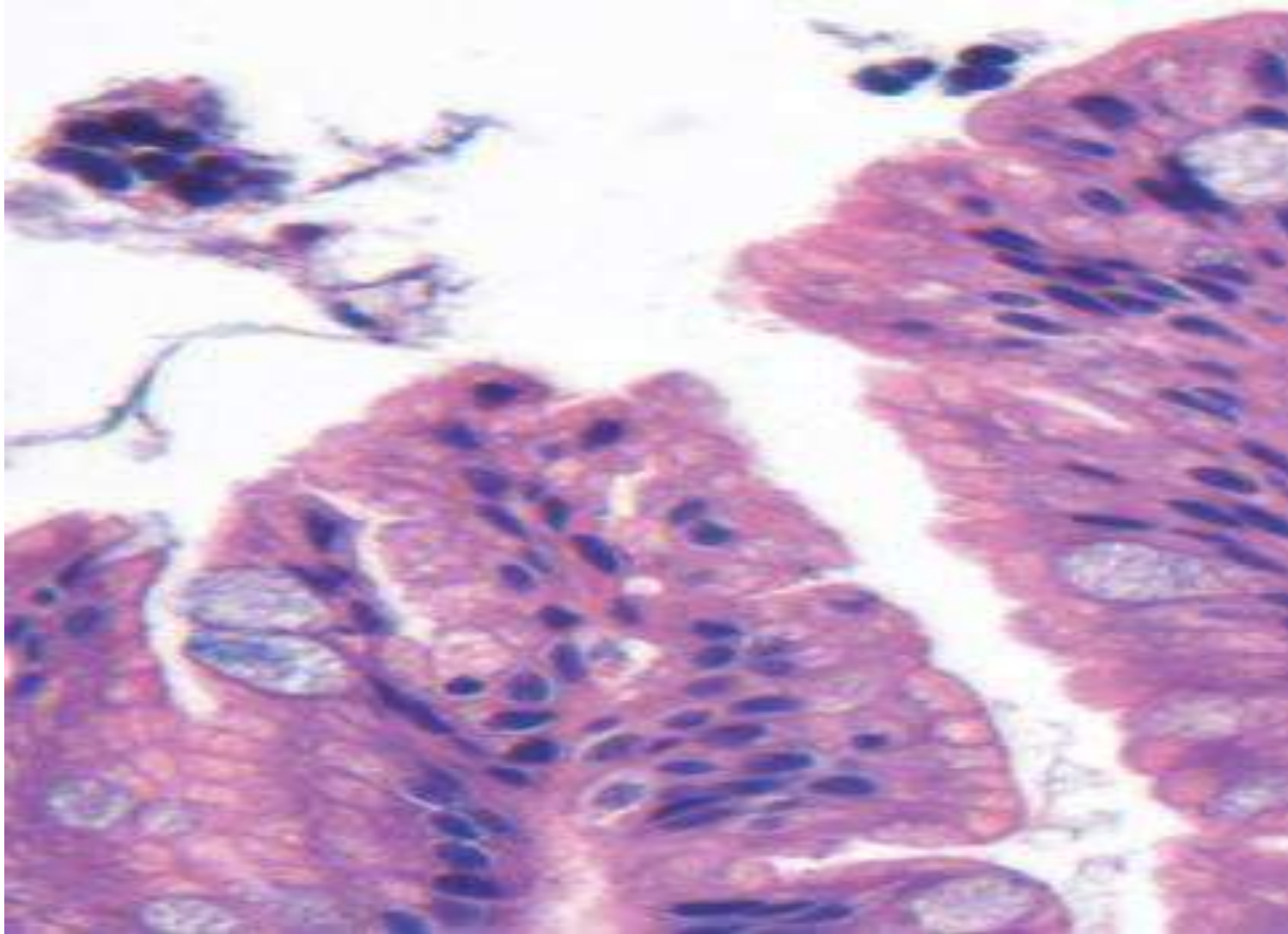
Pan Gastritis with corpus atrophy
With increased risk for gastric carcinoma

Morphology

- ▶ Gastric biopsy: H. pylori in mucus layer, antrum.
- ▶ Neutrophils within the lamina propria
- ▶ Plasma cells, lymphocytes & macrophages.
- ▶ **Lymphoid aggregates>>> increased risk of MALT lymphoma.**
- ▶ **Intestinal metaplasia (goblet cells)>>> dysplasia >> increased risk of adenocarcinoma**



Intestinal metaplasia



Diagnosis and treatment

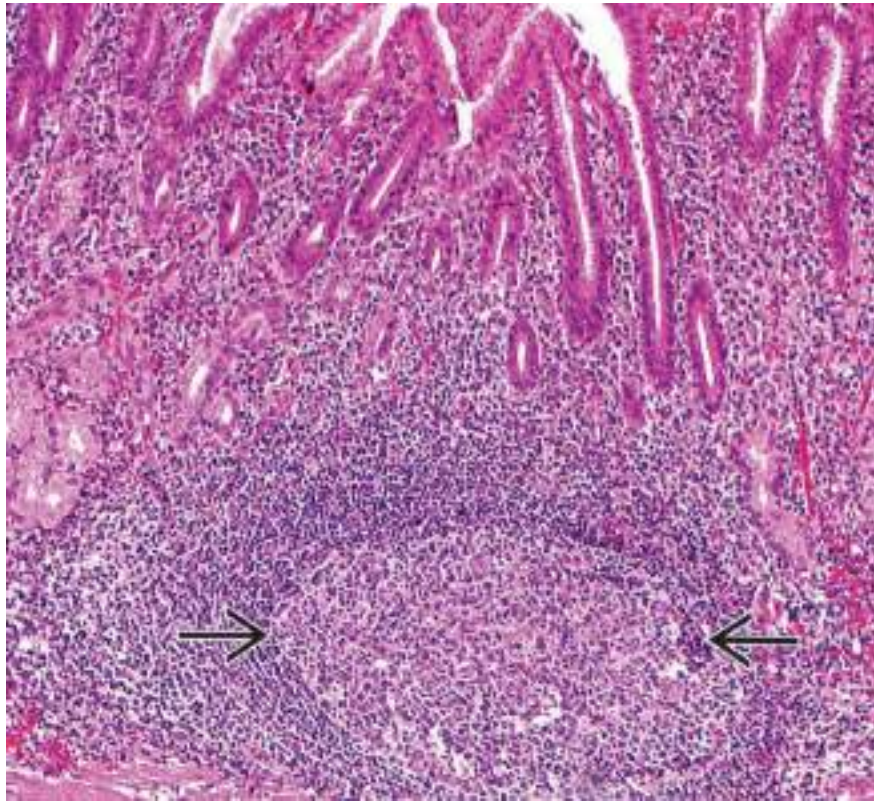
- ▶ Serologic test: anti-H .pylori antibodies.
- ▶ Stool test for H.pylori.
- ▶ Urea breath test.

- ▶ Gastric biopsy
- ▶ Bacterial culture.
- ▶ PCR test for bacterial DNA.

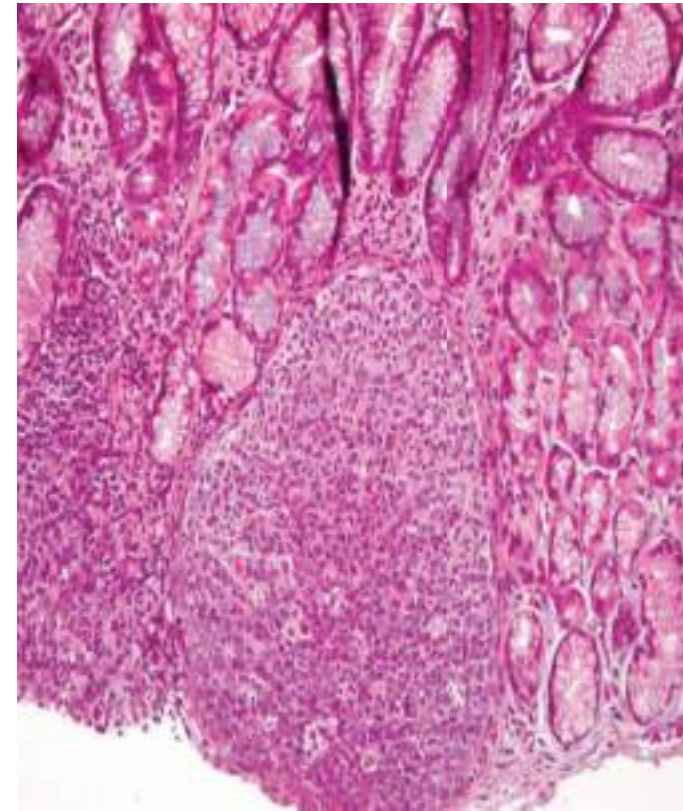
- ▶ Treatment: combinations of antibiotics and PPI.

Lymphoid Follicles in *H. pylori* infection

Pre-treatment



Post treatment



Autoimmune Gastritis

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

Pathogenesis

- ▶ Immune-mediated loss of parietal cells >>> reductions in acid and intrinsic factor secretion.
- ▶ Acid reduction leads to hypergastrinemia
- ▶ Hyperplasia of antral G cells
- ▶ Deficient intrinsic factor >> deficient ileal VB12 absorption >> megaloblastic anemia.
- ▶ Some chief cell damage >> reduced pepsinogen

Morphology

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

Clinical features

- ▶ 60 years, slight female predominance.
- ▶ Often associated with other autoimmune diseases

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

Feature	<i>H. pylori</i> -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 <i>H. pylori</i>	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