Lec4 :

GASTROPATHY AND ACUTE GASTRITIS

Is a term used when there's a minimal inflammatory cells espically neutrophils leukocytes associated with non-steroidal anti-inflammatory drugs (NSAIDs), alcohol, and bile reflex (from duodenum to stomach and bile is very irritant to the stomach mucosa)

Gastropathy= chemical gastritis or gastritis (espically when it related to NSIDs or alcohol consumption

Note :Acute and chronic always related to time but in pathology we replace acute by the word Active

In stomach there are aggressive factors (Pepsin and acid) and there are a protective mechanisms(mucus layer phospholipid rich in bicarbonate secretion + the high generation activity so Surface epithelium each 3 days it's replaced by a new layer of epithelia cells + rich vasculature for nitrations ,oxygen and for support the regeneration activity) and between them there's a balance when if the aggressive or damaging factors overwhelm the protective ones some diseases as (peptic ulcer , acute gastritis ,stress mucosal diseases)

The disruption of the protective mechanism is done by :

1- Inhibition of cyclooxygense (COX) by NSAIDs. NSAIDs inhibit COX-dependent synthesis of prostaglandins E2 and I2
2-Inhibition of gastric bicarbonate transporters by ammonium ions can result in gastric injury in uremic patients and those infected with urease-secreting H. pylori.
3-Reduced mucin and bicarbonate secretion have been suggested as factors that explain the increased susceptibility of older adults to gastritis.
4-Decreased oxygen delivery may account for an increased incidence of acute gastritis at high altitudes.
5-cohesive damage as Ingestion of harsh chemicals, particularly acids or bases, either accidentally or as a suicide attempt, causes severe gastric injury.
6-Direct cellular damage also contributes to gastritis induced by alcohol consumption, NSAIDs, radiation therapy, and chemotherapy (radiotherapy and chemotherapy lead to decrease the cell proliferation)
The presences of neutrophils more than normal and the presence of neutrophils spreading through the basement membrane into the epithelium (columanr epithelium وصلت لل basement membrane كانها عدت ال)that mean there's an active inflammatory process which in this case is active gastritis

acute erosive hemorrhagic gastritis:

Description term of acute gastritis

Note 🤓

Erosion is sloughing of the epithelial layer

Ulceration : sloughing of epithelium lamina prpria and underlying c.t

STRESS-RELATED MUCOSAL DISEASE

Stress-related mucosal disease occurs in patients with severe trauma, extensive burns, intracranial disease, major surgery, serious medical disease, and other forms of severe physiologic stress. Stree affected stomach lead to ulceration

For example:

- Stress ulcers are most common in the setting of shock, sepsis, or severe trauma.
- Curling ulcers refer to ulcers occurring in the proximal duodenum in the context of severe burns or trauma.
- Cushing ulcers refer to gastric, duodenal, and esophageal ulcers arising in those with intracranial disease(related to the root of vagus never caused by trauma or haemorrhage in CNS will stimulate the vagus and the secretion of acid lead to ulcer formation). They have an elevated risk of perforation

The pathogenesis of stress-related gastric mucosal injury is most often related to local ischemia. This may be due to systemic hypotension or reduced blood flow caused by stress-induced splanchnic vasoconstriction. Which mean that the damaging factors overwhelm the protective mucosa

Peptic ulcer may located in stomach (antral part) or the duodenum

ulcer that related to stress is a one single ulcer Is a limited ulcer when the underlying condition is managed it ends But peptic ulcer is more resistant to the treatment (in the past it treated by gastrectomy but nowadays there's a PPI and other treatment

CHRONIC GASTRITIS AND ITS COMPLICATIONS

Chronic gastritis is most often caused by H. pylori infection. Other causes include autoimmune gastritis; radiation injury; chronic bile reflux; mechanical injury (e.g., an indwelling nasogastric tube); and involvement by systemic diseases such as Crohn disease(affect from the oral cavity to the anus and the most commonly location is the terminal ileum) , amyloidosis, or graft-versus-host disease

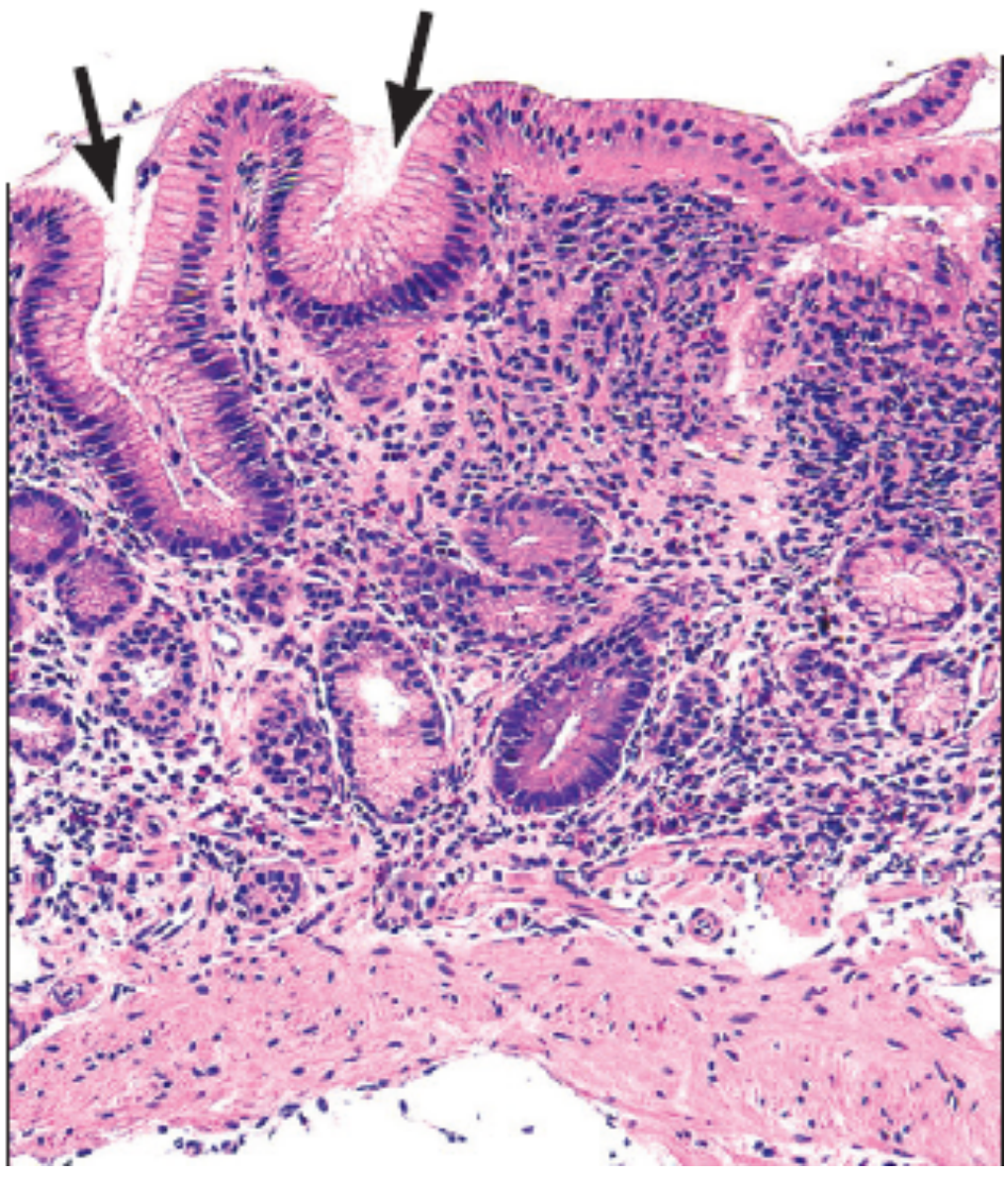
H. pylori organisms are present in the majority of individuals with chronic antral gastritis. (at the antral area there's oxyntic mucusa that contain parietal and secretion of acid and pepsin)

H. pylori infection is associated with poverty, household crowding, limited education, residence in rural areas. Is asymptomatic for a long time and transmitted oral-fecal rotue

Infection is typically acquired in childhood and persists for life without treatment. Improved sanitation explains the marked reduction in H. pylori infection rates among younger people but is present in up to 50% of those older than 65. Due to the socioeconomic development

H. pylori infection most often presents as a predominantly antral gastritis with normal or increased acid production. And it’s a chronic or long duration after a time the infection may transfer to somewhere else as the oxyntic mucusa , fungus and corpus and by years may it lead to atrophy —-> the acid secretion decreased and a reflex increase of gastrin but there’s a parietal cell atrophy and no mucus secreation

The atrophy lead to metaplasia which mean the replacement of the gastric mucusa by intestinal type mucusa that contain columnar cells with microvilli and goblet cells that is the start of dysplastic changes and acquired mutations till cance formation



It’s a gastric mucosa after a years of h.pylori infection and the atrophy stat try to appear Atrophy(decrease the thickness of mucosa and lamina propria infiltrated by dense inflammatory process lymphocytes plasma cells and neutrophils . Glands not closed to each other + increas lamina prpria thicknesses

In contrast to autoimmune gastritis there's no antibodies (in autoimmune gastritis there's antibodies against **2 elements**

📍**intrinsic factors** and 📍**parietal cells)**

In H.pylori gastritis —> patchy atrophy but in autoimmune gastritis —>diffuse atrophy and in most cases the atrophy is in all the mucosa

In H.pylori gastritis the acid secretion is low so that mean there's a reduction is gastrododenual ulcers formation

H.pylori virulence is linked to the following factors:

- Flagella, which allow the bacteria to be motile in viscous mucus
- Urease, which generates ammonia from endogenous urea and thereby elevates local gastric pH and enhances bacterial survival
- Adhesins that enhance bacterial adherence to surface foveolar cells
- Toxins, such as cytotoxin-associated gene A (CagA)

the CagA gene is present in 50% of H. pylori isolates overall

but in 90% of H. pylori isolates in populations with an increased prevalence of gastric cancer.
This may, in part, be because CagA-expressing strains colonize the gastric body and induce proinflammatory cytokine secretion, atrophy, and intestinal metaplasia more effectively than CagA-negative H. pylori.

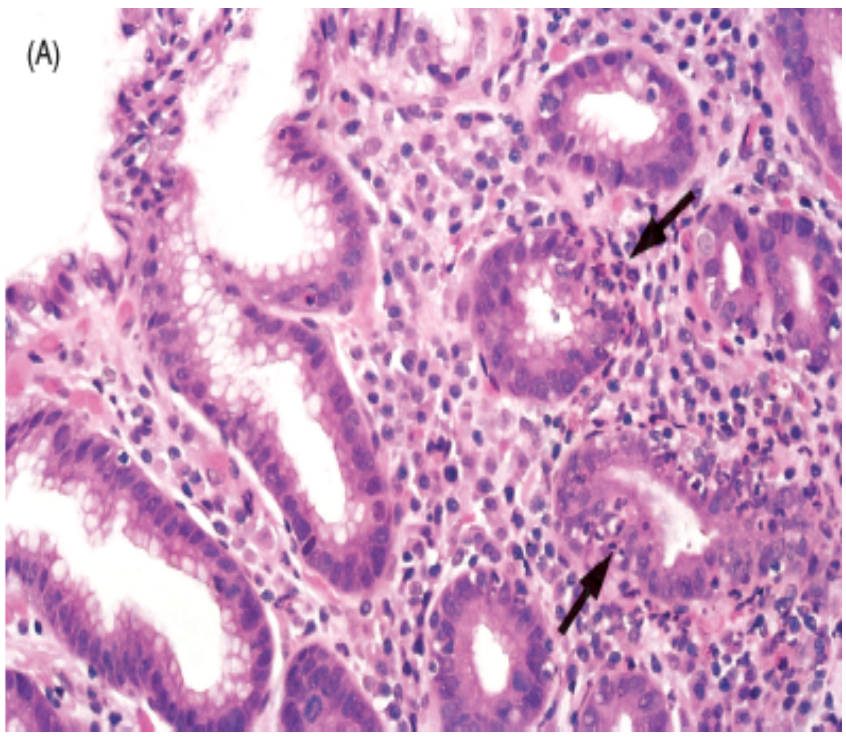
Genetic polymorphisms that lead to increased expression of the proinflammatory cytokines tumor necrosis factor (TNF) and interleukin (IL)-1β or decreased expression of the anti-inflammatory cytokine IL-10 seem to be associated with development of pangastritis, atrophy, intestinal metaplasia, and gastric cancer.

Morphology :
The microorganisms is in the mucus layer
Neutrophils passed through the basement membrane
Microscoplly: inflammatory material closer to the surface epithelium (just beneath it)but in autoimmune gastritis the inflammatory material is more deep

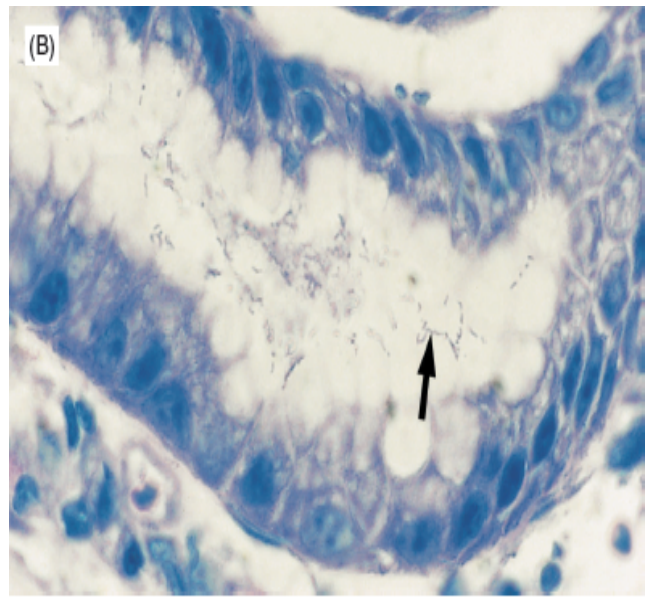
The distribution can be irregular, with areas of heavy colonization adjacent to those with few organisms.
Mainly in the antrum
By endoscopy: Congestion and Edema and hyperaemic changes

In cagA positive there's a diffuse acute gastritis in entire gastric mucosa
In sever case may show a disruption of ruge organization and more promenant (cancer ممكن يعتقدو ها)

chronic H. pylori gastritis is associated with increased risk of both gastric adenocarcinoma and lymphoma.



Neutrophils leukocytes in the epithelial layer after it passes the basement membranes inside the lamina propria there's a mixture of inflammatory cells



H.pylori it's a curved bacilli

The changes seen in atrophic H. pylori gastritis are sometimes referred to as environmental metaplastic atrophic gastritis, to distinguish it from autoimmune metaplastic atrophic gastritis

Autoimmune Atrophic Gastritis

Self immune reaction against intrinsic factor or parietal cell

Spares the antrum (it in the oxyntic mucosa in the fundus and corpus)

associated with marked hypergastrinemia more than that in the h.pylori related gastritis

Hypergatrinemia is caused by increase the G-cells activity and proliferation (hyperplasia and nodule structure formation and it may cause a neoplasticism formation)

Autoimmune atrophic gastritis is characterized by:

- Antibodies to parietal cells and intrinsic factor that can be detected in serum and gastric secretions
- Reduced serum pepsinogen I concentration
- Endocrine cell hyperplasia
- Vitamin B12 deficiency
- Defective gastric acid secretion(achlorhydria)

Autoimmune atrophic gastritis is associated with loss of parietal cells, which are responsible for secretion of gastric acid and intrinsic factor. The absence of acid production stimulates gastrin release, resulting in hypergastrinemia and hyperplasia of antral gastrin-producing G cells. Intrinsic factor loss results in defective ileal vitamin B12 absorption, which ultimately leads to vitamin B12 deficiency and pernicious anemia a form of megaloblastic anemia (another form of megaloblastic anemia associated with folic acid deficiency)

The high frequency of associated intestinal metaplasia has led to the term autoimmune metaplastic atrophic gastritis.

CD4+ T cells directed against parietal cell components, including hydrogen potassium adenosine triphosphatase (H+,K+-ATPase)
There is no evidence of an autoimmune reaction to chief cells, If autoimmune destruction is controlled by immunosuppression, the glands can repopulate, demonstrating that gastric stem cells survive and are able to differentiate into parietal and chief cells.

antibodies are not thought to be pathogenic because neither secreted intrinsic factor nor the luminally oriented proton pump is accessible to circulating antibodies

MORPHOLOGY

1- Autoimmune atrophic gastritis is characterized by diffuse damage to the oxyntic (acid-producing) mucosa within the body and fundus.
2- thinning of mucosal layer + predominant submucosal blood vessels
3- reduced gland consantration
4- inflammatory cells in the lamina propria
5-intestinal metaplasia
6-eosinophilia gastritis rarely lymphocytic and granulomatous gastritis

Peptic Ulcer Disease

It's frequency and complications reduced due to some treatment as PPIs

In stomach antrum or proximalduodenum almost always associated with H.pylori infection

which is associated with increased gastric acid secretion and decreased duodenal bicarbonate secretion

Risk Factors for Peptic Ulcer Disease

- Helicobacter pylori infection
- Cigarette use (due to blood supply defect +chemical defect)
- NSAIDs

Ectopic gastric mucosa : the presence of gastric mucosa in anatomical location outside the stomach also called hetrotopic gastric mucosa it happened in mecekel's diverticulm that there's a gastric mucosa as a finger like projection with the small intestine lead to ulceration(peptic ulcer) due to acid secretion and no presence of protective mechanism

Epidemiology. The incidence of PUD is falling along with reduced prevalence of H. pylori infection. However, PUD in patients older than 60 years has increased due to growing NSAID use.

PUD is also associated with cigarette use and cardiovascular disease, likely due to reduced mucosal blood flow, oxygenation

→ Pud = peptic ulcer disease

Pathogenesis

PUD results from imbalances between defense mechanisms and damaging factors that cause chronic gastritis (discussed earlier). Thus, PUD generally develops on a background of chronic gastritis. The H. pylori gastritis, is also a factor

Morphology:

Sings of inflammation and hyperemia +loss of the tissue and epithelium and the underlying C.T so there's an exudate covered it's deep yellowish material (pus +neutrophils + fibrin+ necrotic cells)under it there's a granulation tissue (proliferation of bnewly formed blood vessel) under it there's a fibrosis (repair mechanism)

Microscoplly: ulcer [loss of tissue] surrounded by hyperemic edematous mucosa , and the normal mucosa surround the ulcer engaged in the inflammatory process with edema and swelling but ulcer cancer is an ulcerated mass rather than ulcer called heaped-up margins which are more characteristic of cancers.

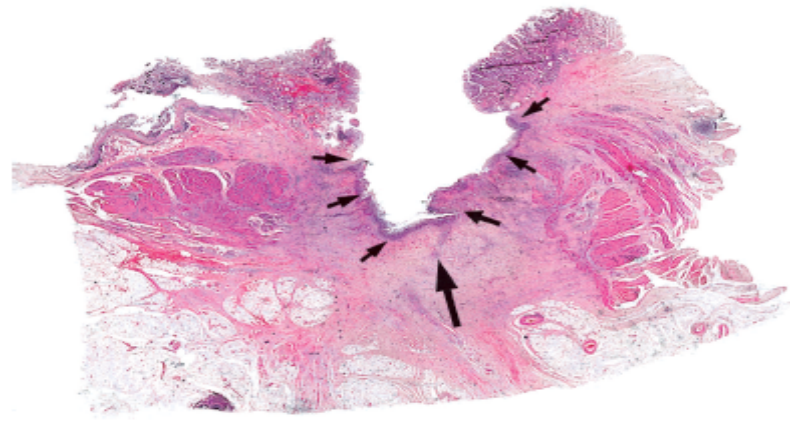
Ulcer in duodenum so the surrounding tissues contain foveolar metaplasia (foveolar=gastric pits) to adapt the new environmental changes as the presence of acid in the duodenum

80% of peptic ulcer is solitary (single) + have no elevated margins

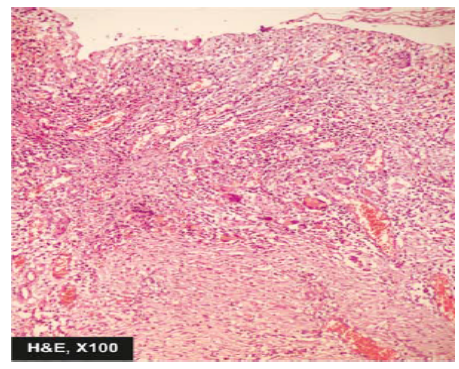
The ulcer depth related to the time and treatment when the ulcer depth increas that lead to perforation

PUD complications:

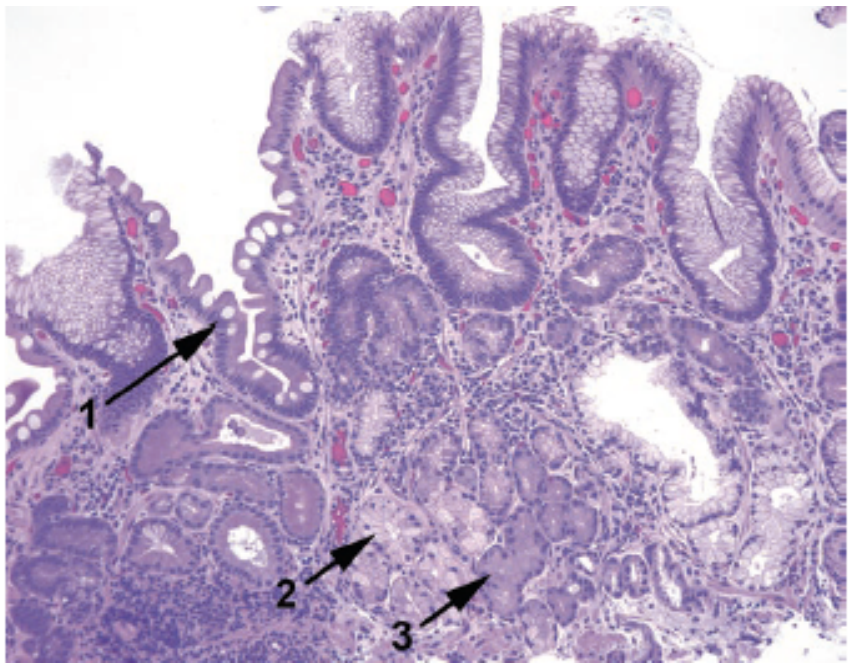
Perforation,
hemorrhage
scarring
(when it depth reach the blood vessel and make erosion then perforation and massive life threatening bleeding)
obstruction



Ulcer : gastric mucosa interrupted by deep ulceration

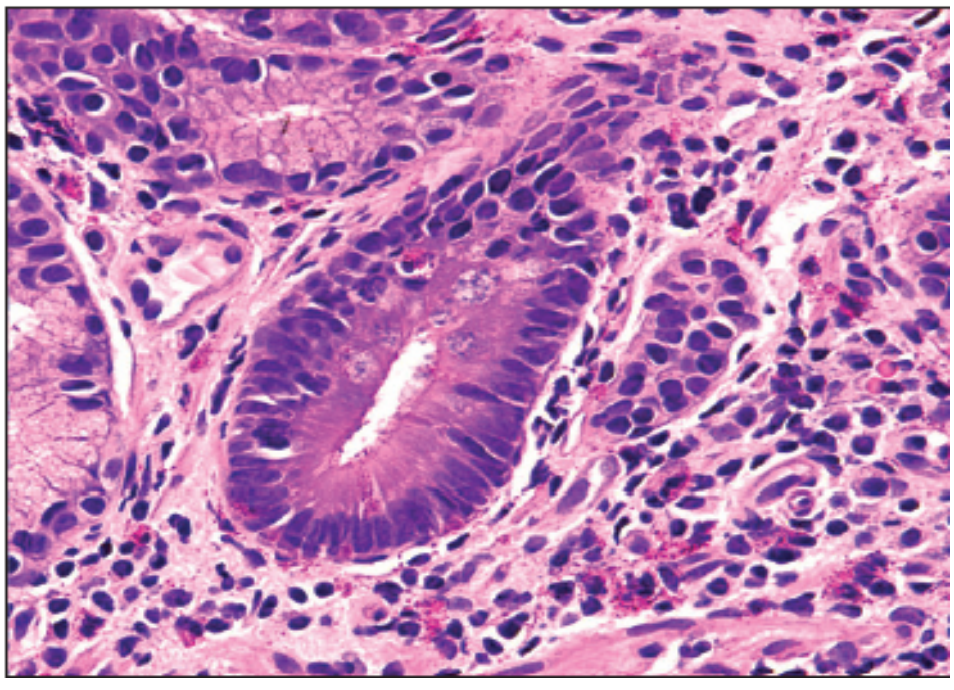


morphologyنفس ال
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Normal stomach mucosa with mucin secreting cells and gastric pits linked to gastric gland

There's changes in the epithelial cells and the cells become absorptive columnar cells with microvills and goblet cells disparesed among the columnar epithelium



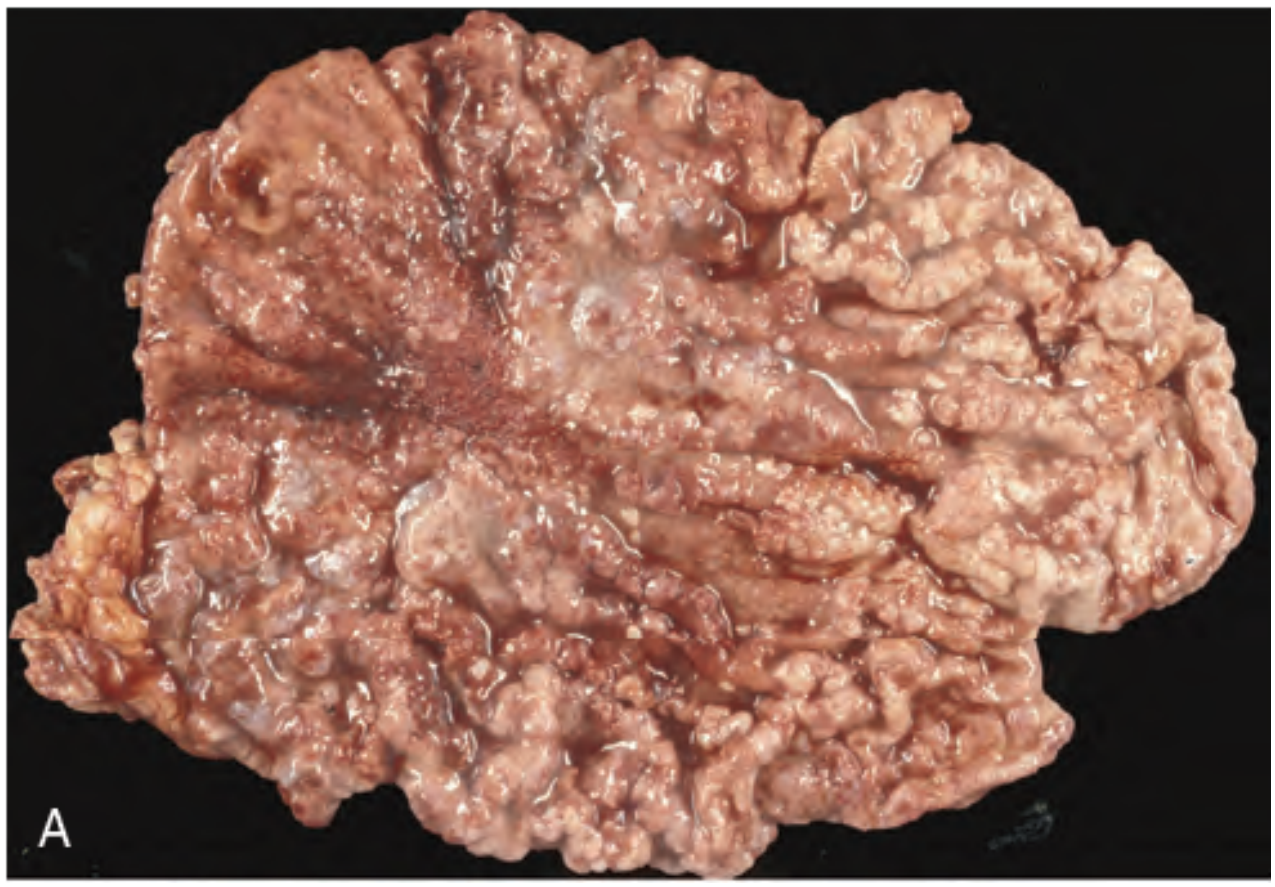
Dysplasia

There's a nuclei stratification and the cytoplasm become more eosinophilia

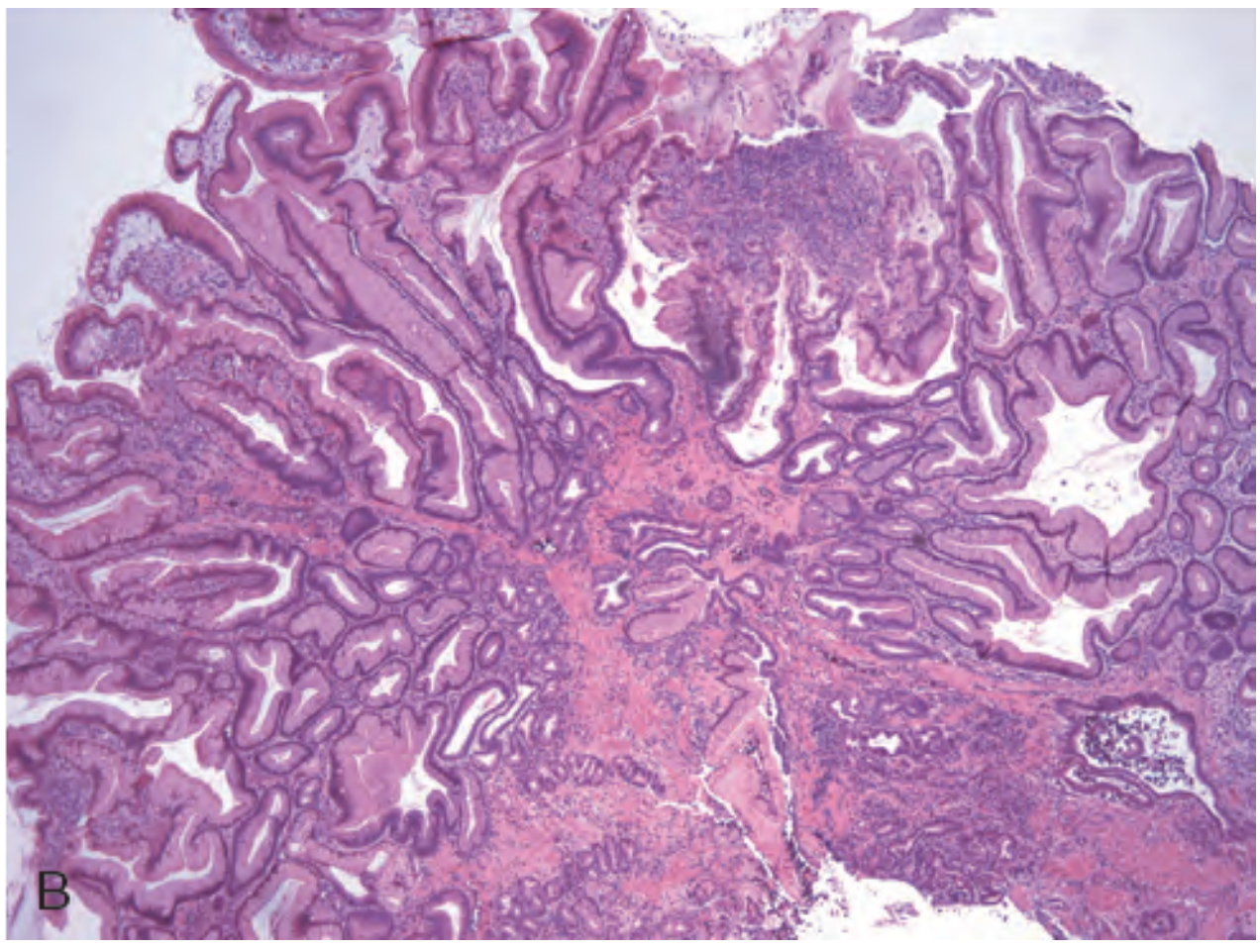
Hypertrophic gastropathies

Two well-defined examples are Ménétrier disease and Zollinger-Ellison syndrome

Hypertrophic gastropathies are uncommon diseases characterized by giant "cerebriform" enlargement of the rugal folds due to epithelial hyperplasia without inflammation. the hypertrophic gastropathies are linked to excessive growth factor release with diffuse hyperplasia
Also they will have hypoprotinemia



Stomach of Ménétrier disease. Marked hyperplasia of rugal folds.



Mucosal thinking + angulation

Zollinger-Ellison Syndrome

Zollinger-Ellison syndrome is caused by gastrin-secreting neuroendocrine tumors.
Due to acidity they will have multiple ulceration in extraordinary locations

Treatment is very hard ☹️ may use the PPIs or by surgery if the place determine