Azerbaijan Medical University
Department of Pathological Anatomy

PATHOLOGICAL ANATOMY OF GASTROINTESTINAL TRACT DISEASES

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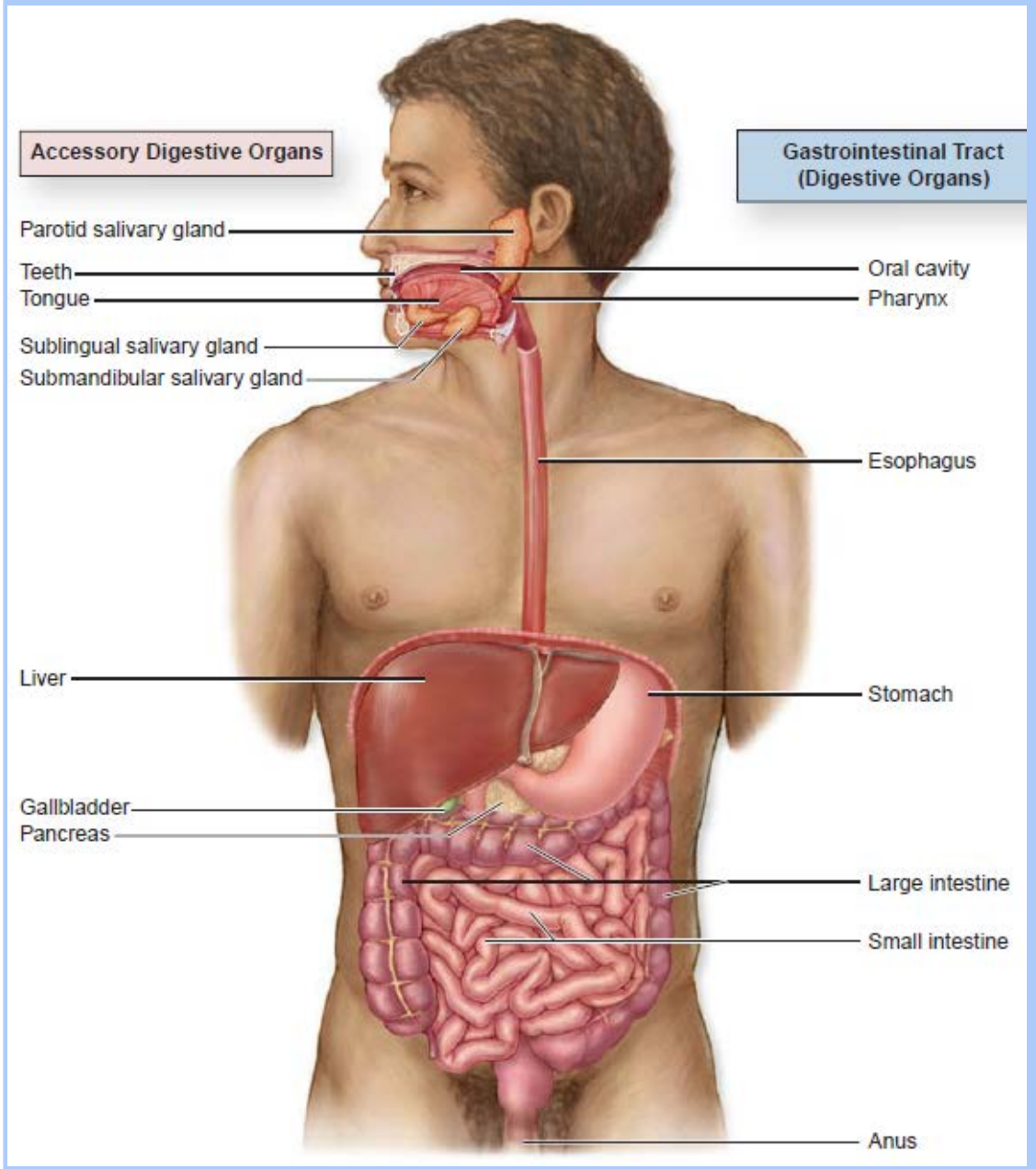
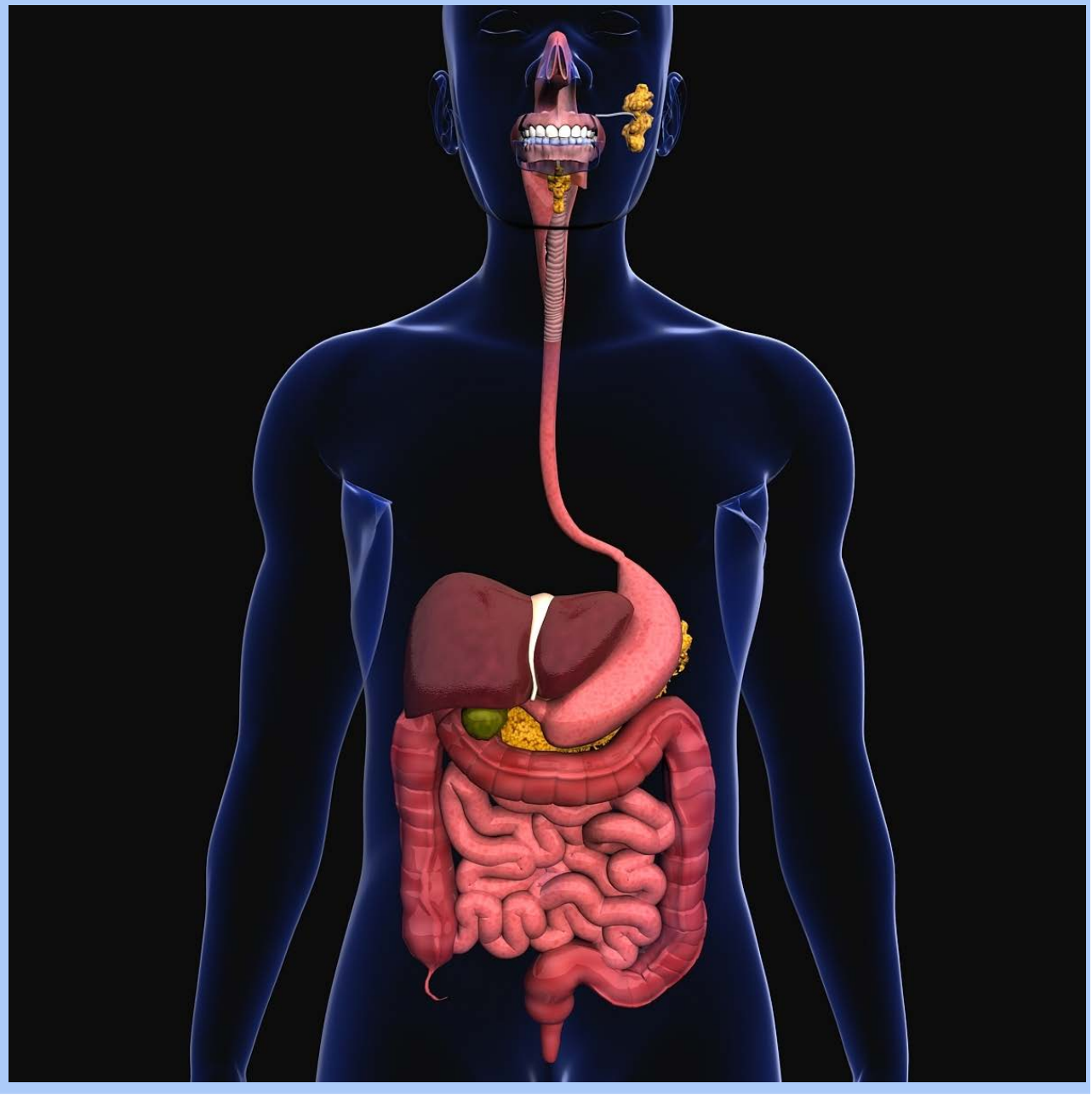
Plan of the Lecture 4 on “Pathological Anatomy-2”

- ✓ Anatomy and Physiology of Gastrointestinal tract
- ✓ Tonsillitis: acute and chronic
- ✓ Barret’s esophagus
- ✓ Esophagitis
- ✓ Gastritis: acute and chronic
- ✓ Peptic ulcer disease
- ✓ Enteritis: acute and chronic
- ✓ Whipple disease
- ✓ Appendicitis: acute and chronic
- ✓ Colitis: acute and chronic
- ✓ Ulcerative colitis
- ✓ Crohn’s disease

Digestive System Anatomy

- The digestive system is composed of two separate categories of organs: digestive organs and accessory digestive organs.
- **The digestive organs** collectively make up the **gastrointestinal (GI) tract,** also called the **digestive tract or alimentary canal**.
- The GI tract organs are the oral cavity, pharynx, esophagus, stomach, small intestine and large intestine.
- These organs form a continuous tube from the mouth to the anus.
- **Accessory digestive organs** are not part of the long GI tube, but often develop as outgrowths from and are connected to the GI tract.
- The accessory digestive organs assist the GI tract in the digestion of material.
- Accessory digestive organs include the teeth, tongue, salivary glands, liver, gallbladder and pancreas.





https://www.turbosquid.com/3d-models/3d-model-human-digestive-organs-small-intestine-1279199

Digestive System Functions

- **Ingestion** (*ingero* = to carry in) is the introduction of solid and liquid materials into the oral cavity.
- It is the first step in the process of digesting and absorbing nutrients.
- **Digestion** is the breakdown of large food items into smaller structures and molecules.
- There are two aspects to digestion:

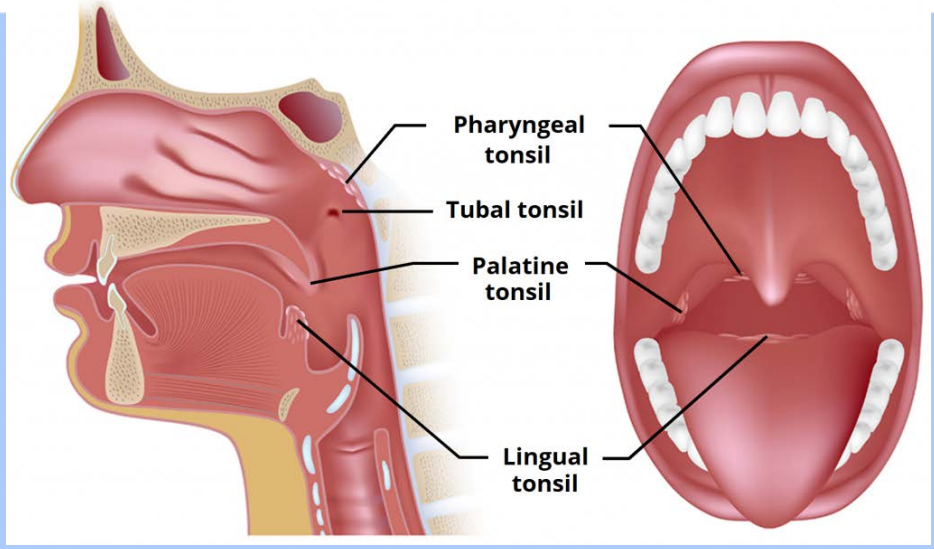
1) ***mechanical digestion*** physically breaks down ingested materials into smaller pieces,
2) ***chemical digestion*** breaks down ingested material into smaller molecules by using enzymes.

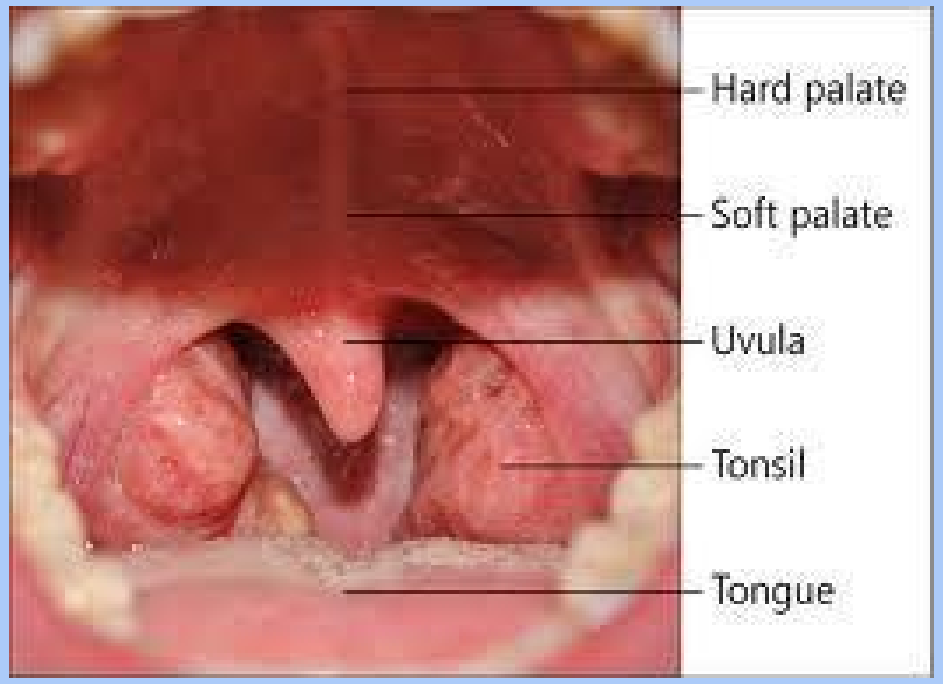
- The first part of mechanical digestion is ***mastication*** (*mastico* = to chew), the chewing of ingested material by the teeth in the oral cavity.
- After the materials are swallowed, they move through the GI tract by a process termed **propulsion** (*propello* = to move forth).
- Two types of movement are involved in propulsion: peristalsis and segmentation.
- ***Peristalsis*** (*stalsis* = constriction) is the process of muscular contraction that forms ripples along part of the GI tract and forces material to move further along the tract.
- Churning and mixing movements in the small intestine, called ***segmentation*** help disperse the material being digested and combine it with digestive organ secretions.

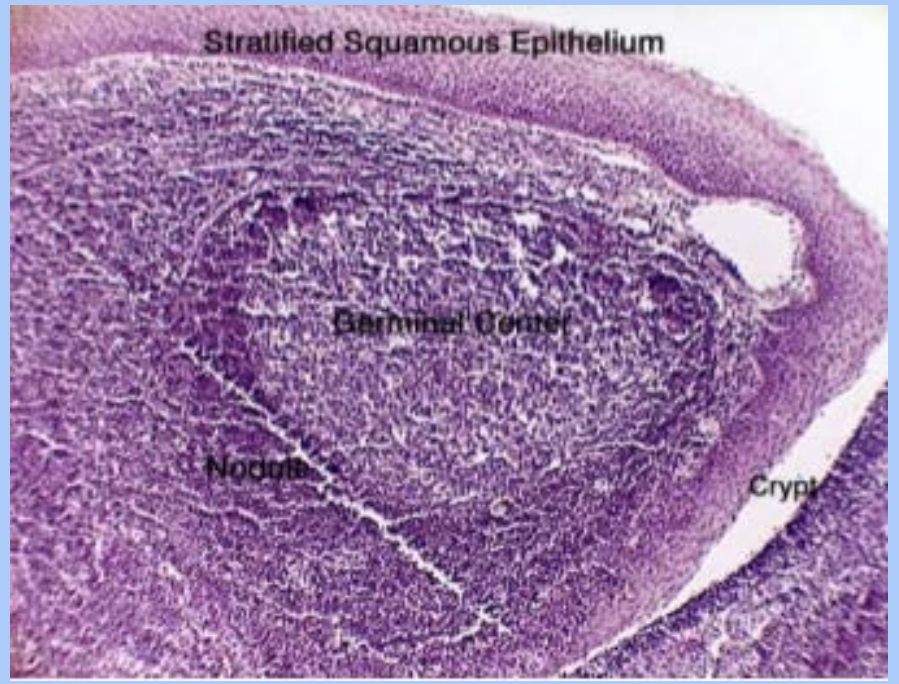
Digestive System Functions (cont...)

- **Secretion** (*secerno* = to separate) is the process of producing and releasing mucin or fluids such as acid, bile, and digestive enzymes.
- When these products are secreted into the lumen of the GI tract, they facilitate chemical digestion and the passage of material through the GI tract.
- Some of these products (e.g., acid, bile, digestive enzymes) help digest food.
- Mucin secretions serve a protective function.
- Mucin mixes with water to form mucus and the mucus coats the GI wall to protect and lubricate it against acidic secretions and abrasions by passing materials.
- **Absorption** (*absorptio* = to swallow) involves either passive movement or active transport of electrolytes, digestion products, vitamins and water across the GI tract epithelium and into GI tract blood and lymph vessels.
- The final function of the digestive system is the **elimination of wastes**.
- Our bodies utilize most, but not all, of the components of what we eat.
- All undigestible materials as well as the waste products secreted by the accessory organs into the GI tract are compacted into feces (*faex* = dregs) or fecal material and then eliminated from the GI tract by the process of ***defecation*** (*defaeco* = to remove the dregs).

Waldeyer's lymphoid ring



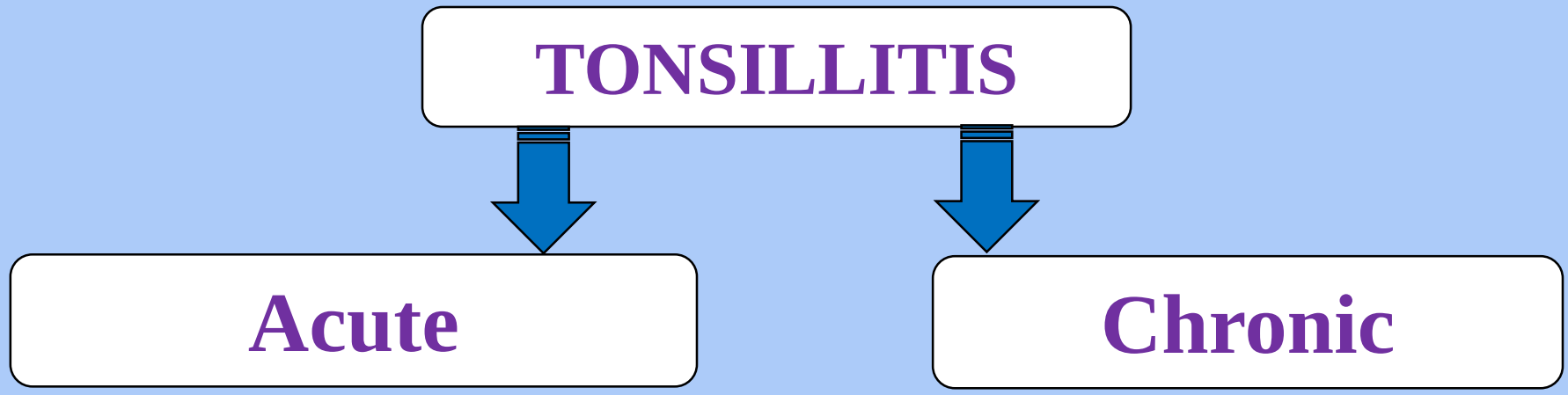




https://teachmeanatomy.info/neck/misc/tonsils-and-adenoids/
https://www.slideshare.net/vandanavalluri/tonsillitis-48105665

TONSILLITIS

- It is the **infectious disease** accompanied by hyperplasia and other inflammatory changes of the lymphoid tissues of the tonsils, pharynx and tongue (Pirogov-Waldeyer's lymphoid ring).
- Earlier it was called ***angina*** (Latin: angere - *"suffocation"*).
- It is very common in preschool and school age children.



Acute tonsillitis

- The tonsils are composed of lymphatic tissue and are a component of Waldeyer's ring along with the adenoids (nasopharyngeal tonsil), tubal tonsil, and lingual tonsil.
- They serve as an important defense against inhaled or ingested pathogens by providing the initial immunological barrier to insults.
- **Tonsillitis** is a common disease and makes up approximately 1.3% of outpatient visits.
- It is predominantly the result of a viral or bacterial infection and, when uncomplicated, presents as a *sore throat*.
- **Acute tonsillitis** is a clinical diagnosis.
- Differentiation between bacterial and viral causes can be difficult; however, this is crucial to prevent the overuse of antibiotics.

https://www.ncbi.nlm.nih.gov/pubmed/31335062

Acute tonsillitis

Etiology

Infectious agents: Staphylococci, pneumococci, adenovirus and various microbial associations

Pathogenic factors

Exogenic

Common cold, consumption of cold water and substances, traumas of the mucous membranes of tonsils.

Endogenic

Weakened immune system, age features of the lymphoid ring, autoinfection - caries, chronic pulpitis, chronic laryngitis / pharyngitis, retropharyngeal infection, etc.

Complications

Local

Peritonsillar abscess, retropharyngeal abscess, pharyngeal phlegmon, thrombophlebitis, acute otitis media, etc.

General

Tonsillogenic sepsis, post-streptococcal glomerulonephritis, rheumatic fever, etc.

Clinical-morphological types of Acute tonsillitis

- ***Catarrhal tonsillitis.*** Serous, serous-mucous exudate appears on the mucous membrane of the tonsils.
- Catarrhal tonsillitis is a part of generalized pharyngitis and seen in viral infections.
- ***Fibrinous (membranous) tonsillitis*** is characterized by the formation of a whitish-yellowish diphtheritic fibrinous membrane on the surface of the mucous membrane.
- ***Purulent tonsillitis.*** Occurs as a result of neutrophil-mixed lympho-leukocytic infiltration of the tonsils.
- ***There are 2 types of Purulent tonsillitis:***

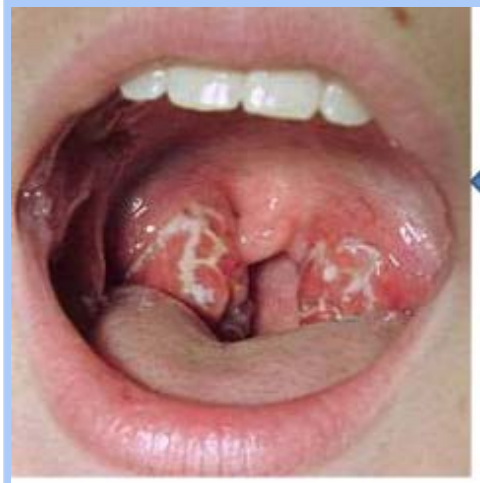
  a – Phlegmonous tonsillitis – the purulent process is diffuse in the tonsils.

  b – Apostematous tonsillitis - small abscesses in the tonsils - ***apostemas*** appear.
- ***Lacunar tonsillitis -*** serous, mucous or purulent exudate accumulates in the tonsils lacunae. *False membranes* are formed.

Clinical-morphological types of Acute tonsillitis

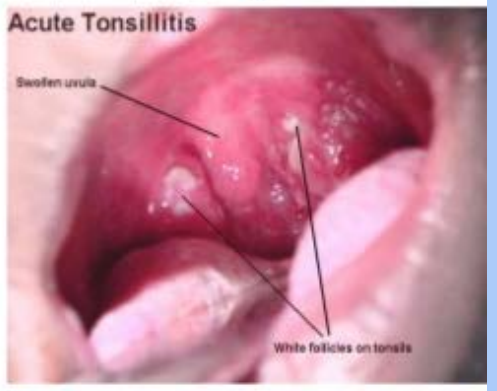
- ***Follicular tonsillitis -*** in which tonsillar crypts become filled with purulent materials.
- Both lacunar and follicular tonsillitis are distinguished by the localization of the inflammatory process.
- ***Necrotic tonsillitis -*** foci of necrosis in the mucosa of the tonsils.
- Wounds are formed when necrotic masses rupture ***- necrotic-ulcerative tonsillitis.***
- ***Gangrenous tonsillitis -*** usually found in children with acute leukemia or scarlet fever.
- At this time, the tonsils grow in size and appear greenish-black.
- ***Vincent's tonsillitis (Vincent's angina - ulcerative-membranous tonsillitis - Simanovski-Plaut-Vincent tonsillitis)*** - is usually epidemic.
- It is caused by the combined action of *spirochetes (Borrelia vincentii)* and *fusobacteria (Fusobacterium fusiforme).*

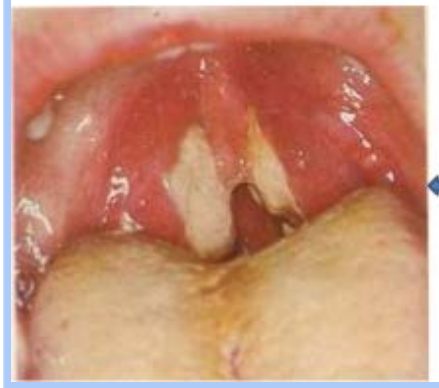
Pathology of Acute tonsillitis



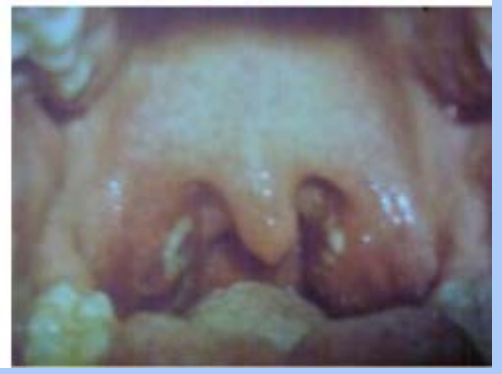
Acute catarrhal or superficial tonsillitis

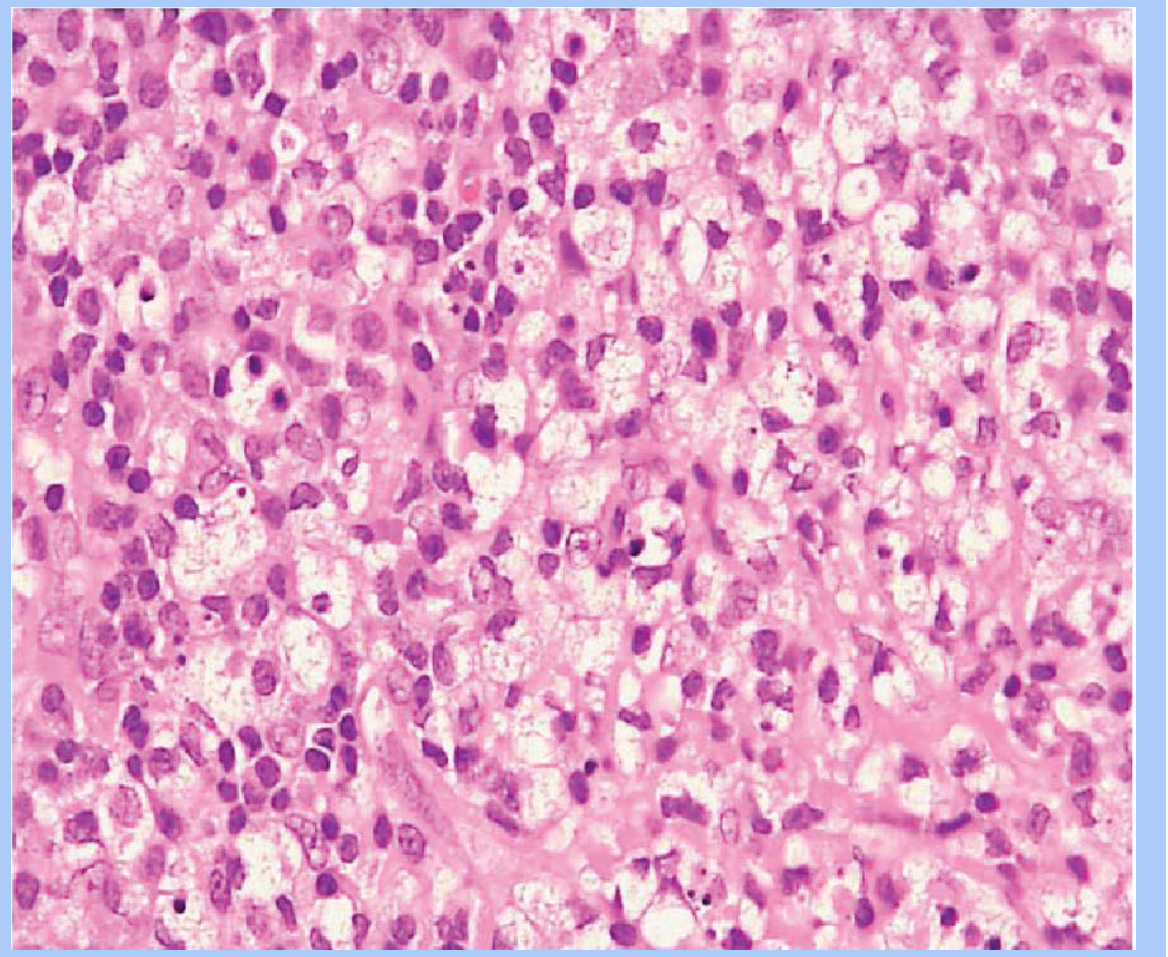
Acute follicular tonsillitis





Acute membranous tonsillitis





Acute Tonsillitis With Concurrent Kikuchi's Disease

Karyorrhectic area composed of apoptotic bodies, foamy histiocytes and phagocytic histiocytes (H&E, 300x)

https://www.slideshare.net/vandanavalluri/tonsillitis-48105665

https://www.semanticscholar.org/paper/Acute-Tonsillitis-With-Concurrent-Kikuchi's-Disease-Sawali-Athar/e00b1e351283868ee7f2c865f37de1161db8d36d

Chronic tonsillitis

- May be a complication of acute tonsillitis.
- Subclinical infection of tonsils without acute attack.
- Allergic factors play an important role in the pathogenesis.
- Chronic infection of sinuses or teeth may be a predisposing factor.
- Often accompanied by recurrence.
- The palatine tonsils are deformed by diffuse sclerosis, often shrinking in size.
- There are numerous sclerotic adhesions with surrounding soft tissues.
- Chronic tonsillitis is sometimes accompanied by *purulent pharyngitis* or *pharyngo-laryngitis*.
- Chronic tonsillitis acts as a source of endogenous infection.

Chronic tonsillitis

Types:

- Chronic Follicular Tonsillitis
- Chronic Parenchymatous Tonsillitis
- Chronic Fibroid Tonsillitis

Chronic tonsillitis

Clinical features

- recurrent attacks of acute tonsillitis
- chronic irritation in throat and cough
- bad taste in mouth and foul breath *(halitosis)*

Histopathology of Chronic tonsillitis

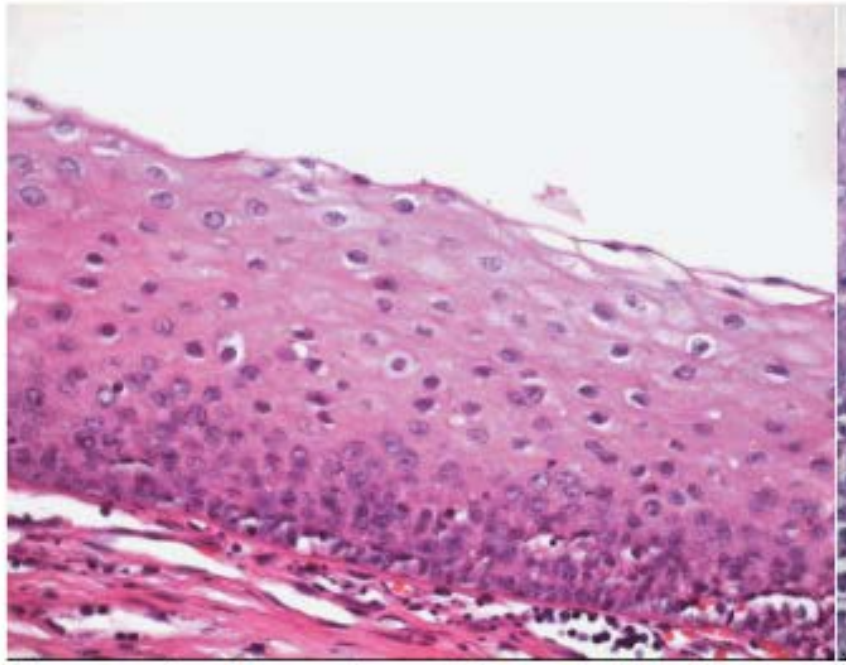


Figure 1. Normal surface epithelium: The stratified squamous nonkeratinized surface epithelium and no lymphocyte. (Hematoxylin-eosin stain, original magnification X 40)

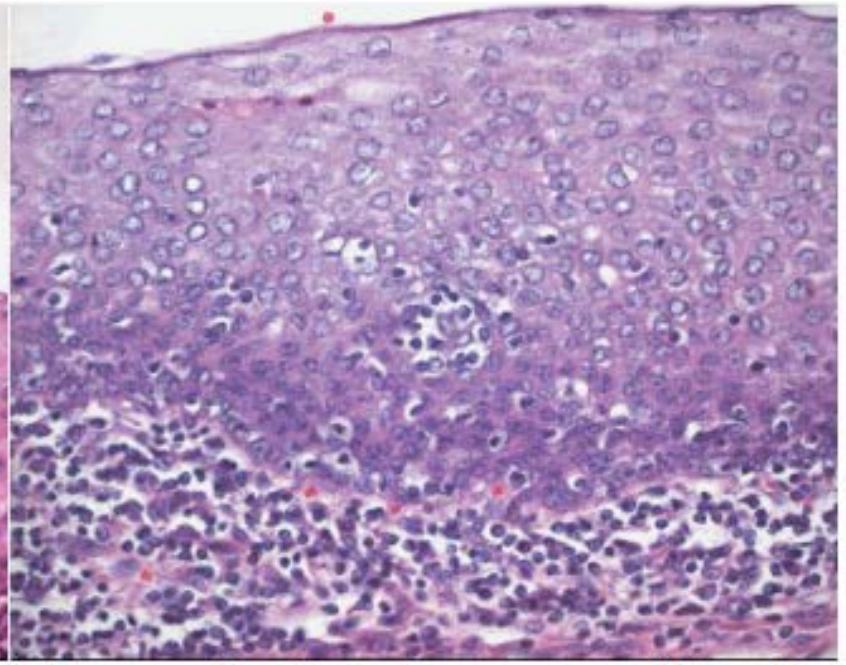
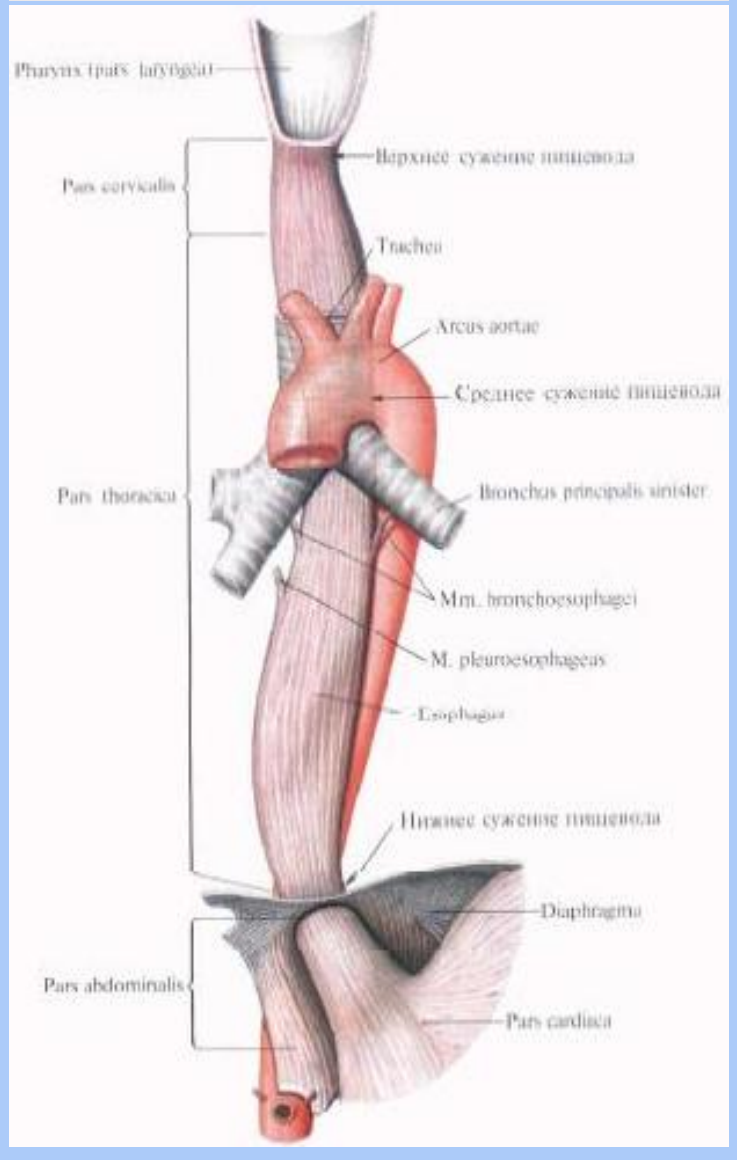
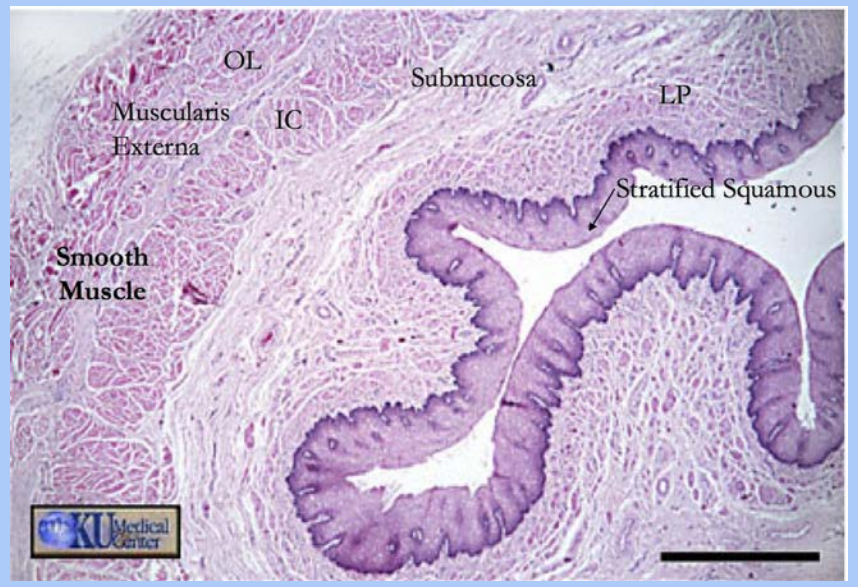


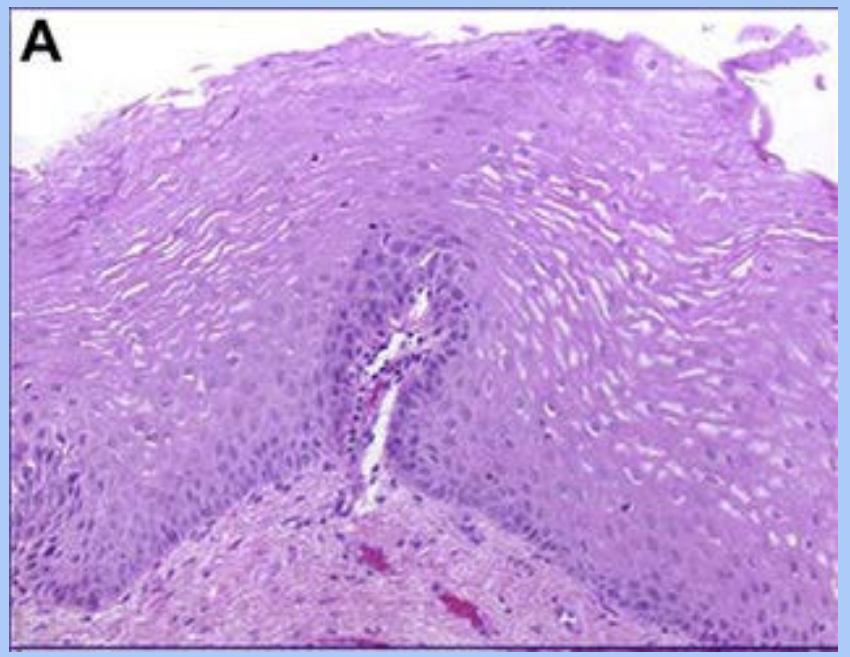
Figure 2. The presence within the surface epithelium of scattered small lymphocyte groups in moderate lymphocyte infiltration in the surface epithelium and lymphocytes in the subepithelial region. (Hematoxylin-eosin stain, original magnification, X 40)

http://www.bioline.org.br/pdf?gm08018

Esophagus







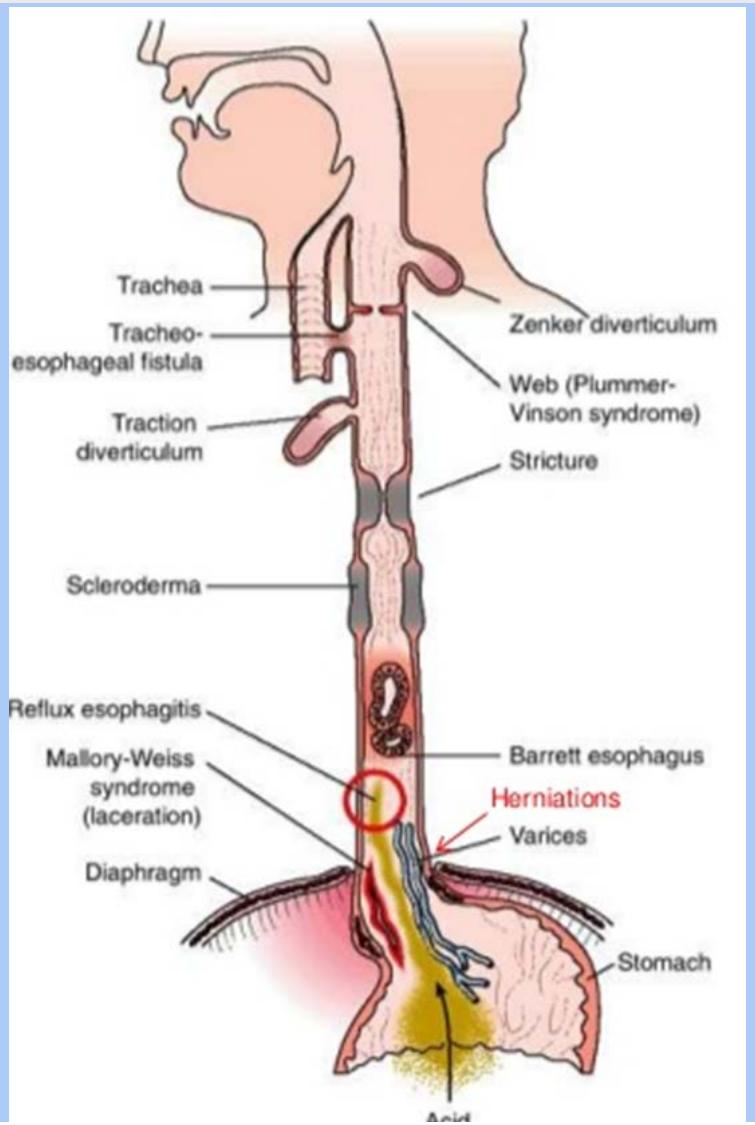
https://www.researchgate.net/publication/51036881_Eosinophilic_esophagitis_Updated_consensus_recommendations_for_children_and_adults/figures?lo=1

https://www.pinterest.com/pin/369928556873825884/

Diseases of Esophagus

- Reflux esophagitis
- Barrett’s esophagus
- Stricture

- Mallory-Weiss syndrome (Bleeding due to rupture of the mucous membrane of the transition zone between the esophagus and stomach with severe vomiting)
- Varices
- Hernia
- Zenker diverticulum
- Tracheo-Esophageal fistula
- Plummer-Vinson syndrome (rare disease characterized by difficulty swallowing, iron-deficiency anemia, glossitis, cheilosis and esophageal webs)



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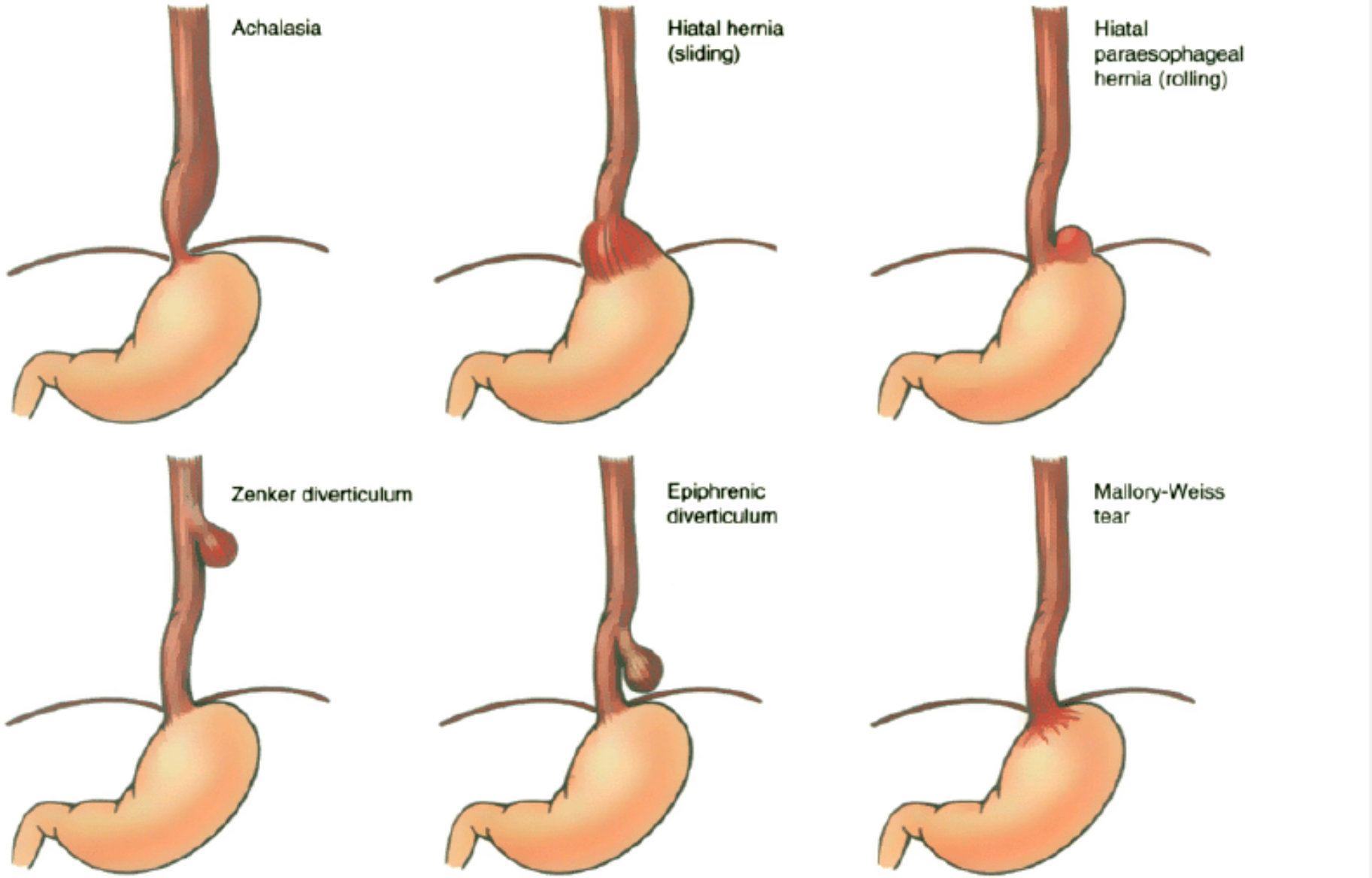

Figure 17-3 Esophageal laceration (Mallory-Weiss tears). Gross view demonstrating longitudinal lacerations extending from esophageal mucosa into stomach mucosa *(arrow)*. *(Courtesy of Dr. Richard Harruff, King County Medical Examiner's Office, Seattle, WA.)*

Esophagitis

- It is characterized by damage and inflammation of the epithelial lining of the esophagus.
- There are 3 major etiological groups of esophagitis:
- **Infectious esophagitis**, **chemical esophagitis** (most common form) and **esophagitis as a manifestation of other disease**.
- **The main cause is gastroesophageal reflux** - reflux of the contents of the stomach (sometimes the duodenum) into the lower esophagus.
- Another cause may be **infectious factors.**
- Histological features are not entirely sensitive and specific for esophagitis.
- Clinical and endoscopic information can be very useful in the diagnosis of esophagitis.
- ***Clinical signs:*** dysphagia (63%), nausea, vomiting, chest pain, stenosis, and eating disorders.

https://www.archivesofpathology.org/doi/full/10.5858/arpa.2014-0132-RA

Clinical-morphological types of esophagitis

- Reflux esophagitis
- Eosinophilic esophagitis
- Lymphocytic esophagitis
- Necrotic esophagitis *(Sloughing esophagitis/Esophagitis dissecans superficialis)*
- Crohn’s disease affecting the esophagus
- Pill esophagitis *(antibiotics (especially of the tetracycline family), nonsteroidal anti-inflammatories, bisphosphonates, slow-release potassium medications, and iron supplements.)*
- Infectious esophagitis
- Skin disorders affecting the esophagus

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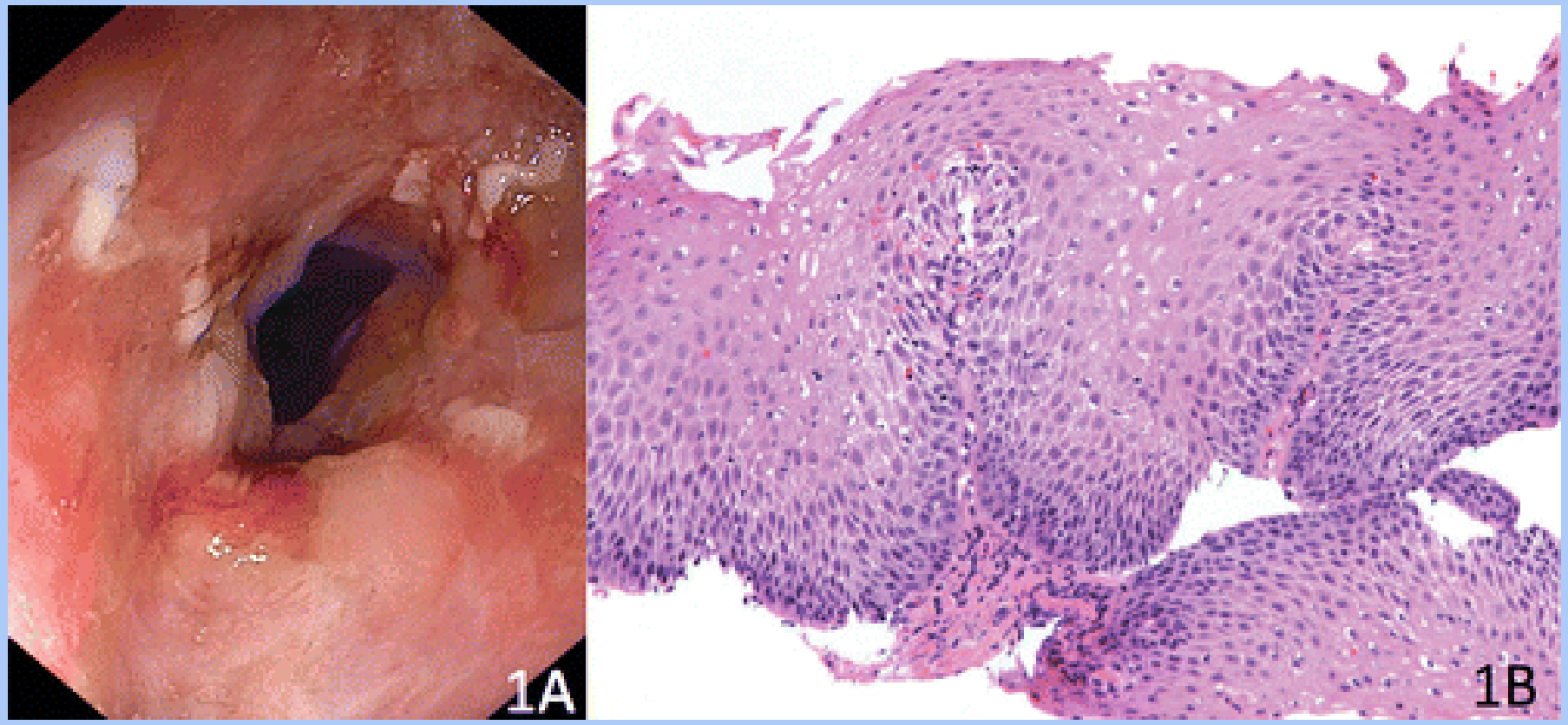
Reflux esophagitis



A - Endoscopic appearance of ulcerative esophagitis secondary to severe gastroesophageal reflux disease (GERD).

B - Histologically, GERD is characterized by increased basal layer thickening, elongated papillae, and mild inflammation with occasional eosinophils.

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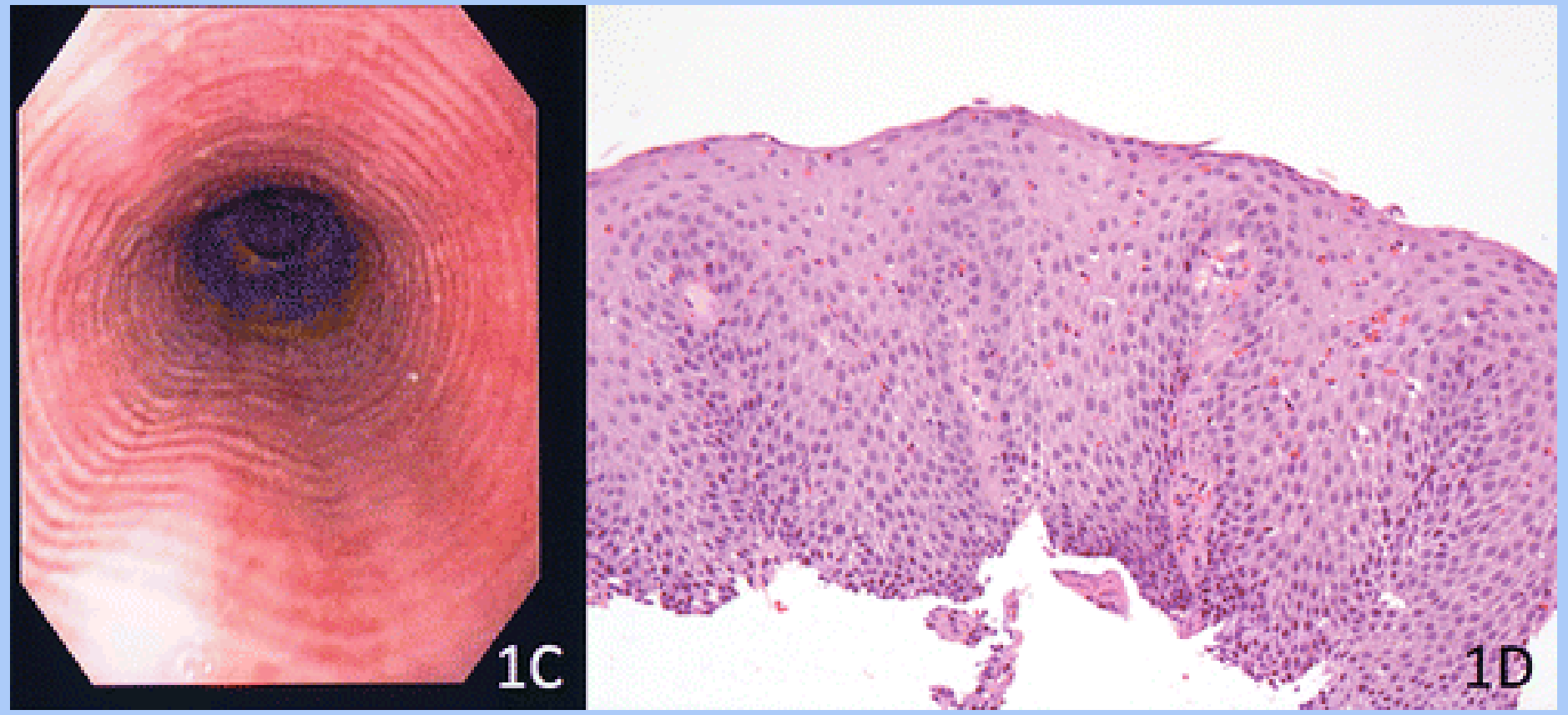
Eosinophilic esophagitis



C - Eosinophilic esophagitis with characteristic rings known as *trachealization* visible endoscopically.

D - Histologically, eosinophilic esophagitis also has basal cell hyperplasia and elongated papillae, but contains a marked increase in intraepithelial eosinophils (>15/high-power field).

https://www.archivesofpathology.org/doi/full/10.5858/arpa.2014-0132-RA

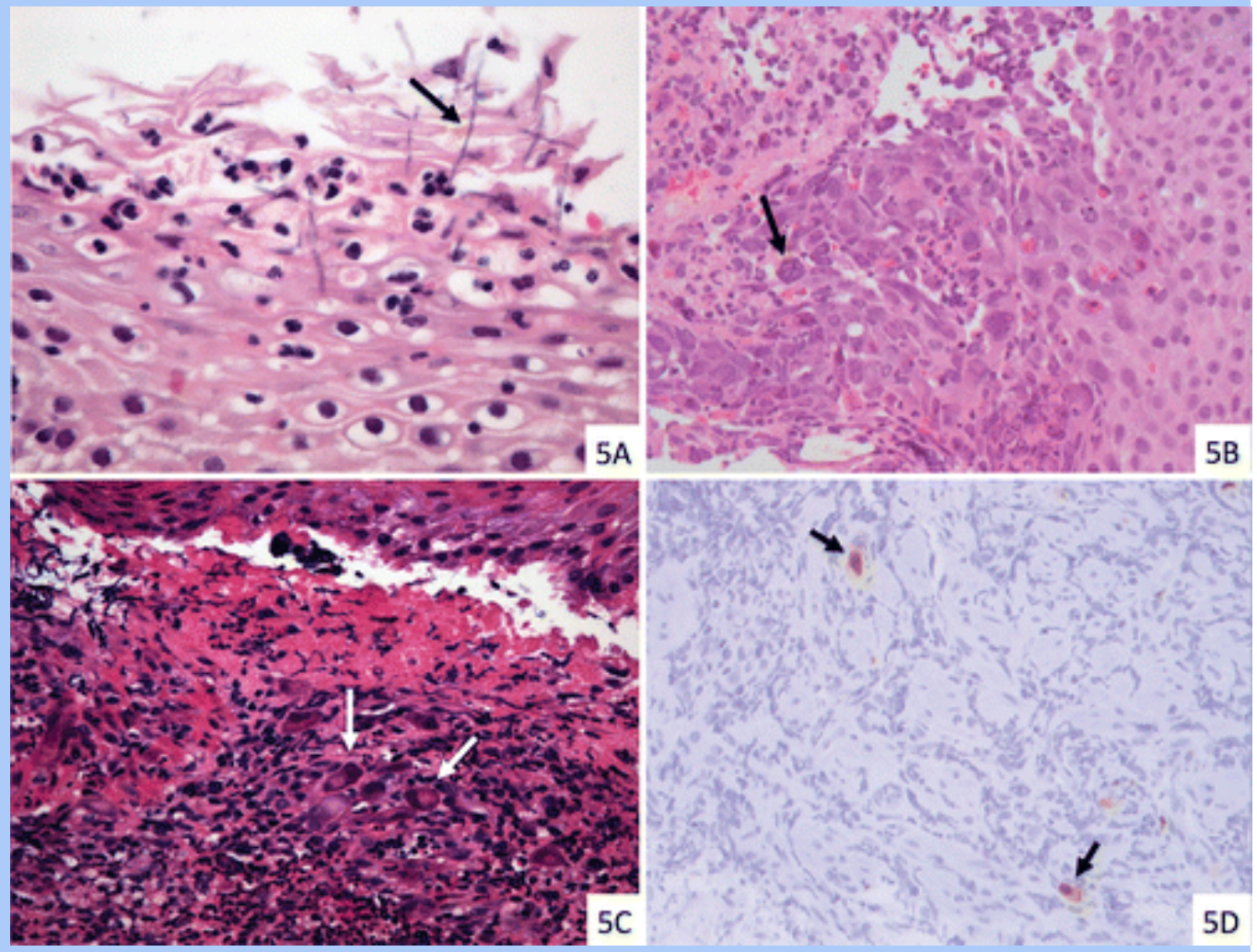
Infectious esophagitis

A - *Candida hyphae* (arrow) are present within squamous mucosa.

B - Herpes esophagitis. Arrow points to a *multinucleated ground-glass inclusion* with chromatin margination and molding.

C - Cytomegalovirus infection. Arrows point to *inclusions* within stromal cells.

D - Immunohistochemistry for cytomegalovirus highlights *multiple inclusions* (arrows)



https://www.archivesofpathology.org/doi/full/10.5858/arpa.2014-0132-RA

Barret's esophagus (BE)

American College of Gastroenterology (ACG) 2016 BE **definition**: Extension of salmon colored mucosa into the tubular esophagus extending ≥ 1 cm proximal to the gastroesophageal (GE) junction with biopsy confirmation of intestinal metaplasia (goblet cells).

Etiology:

- **Known risk factors:**
  - Chronic (> 5 years) GERD symptoms
  - Advancing age (> 50 years)
  - Male gender
  - Tobacco usage
  - Central obesity
  - Caucasian race
- More common in first degree relatives of subjects with known BE

Sites:

- Distal esophagus, GE junction

http://www.pathologyoutlines.com/topic/esophagusBarrettsgeneral.html

Barret’s esophagus (BE)

Pathophysiology:

- **Metaplasia in BE** presumably results from cellular reprogramming
- GERD induced **tissue damage** reprograms immature progenitor cells to express **columnar development transcription factors**
- Tissue injury activates **signaling pathways** such as Hedgehog, BMP4 and NF-KB, and downregulates **Notch signaling**
- Signals lead to **increased expression of SOX9** (induces columnar differentiation), FOXA2, CDX1 and CDX2 (induces intestinal differentiation)
- **Transdifferentiation** (distinctive type of multilayered epithelium at the squamocolumnar junction with features of both squamous and columnar epithelium) may occur in BE

http://www.pathologyoutlines.com/topic/esophagusBarrettsgeneral.html

Barret’s esophagus (BE)

Clinical features:

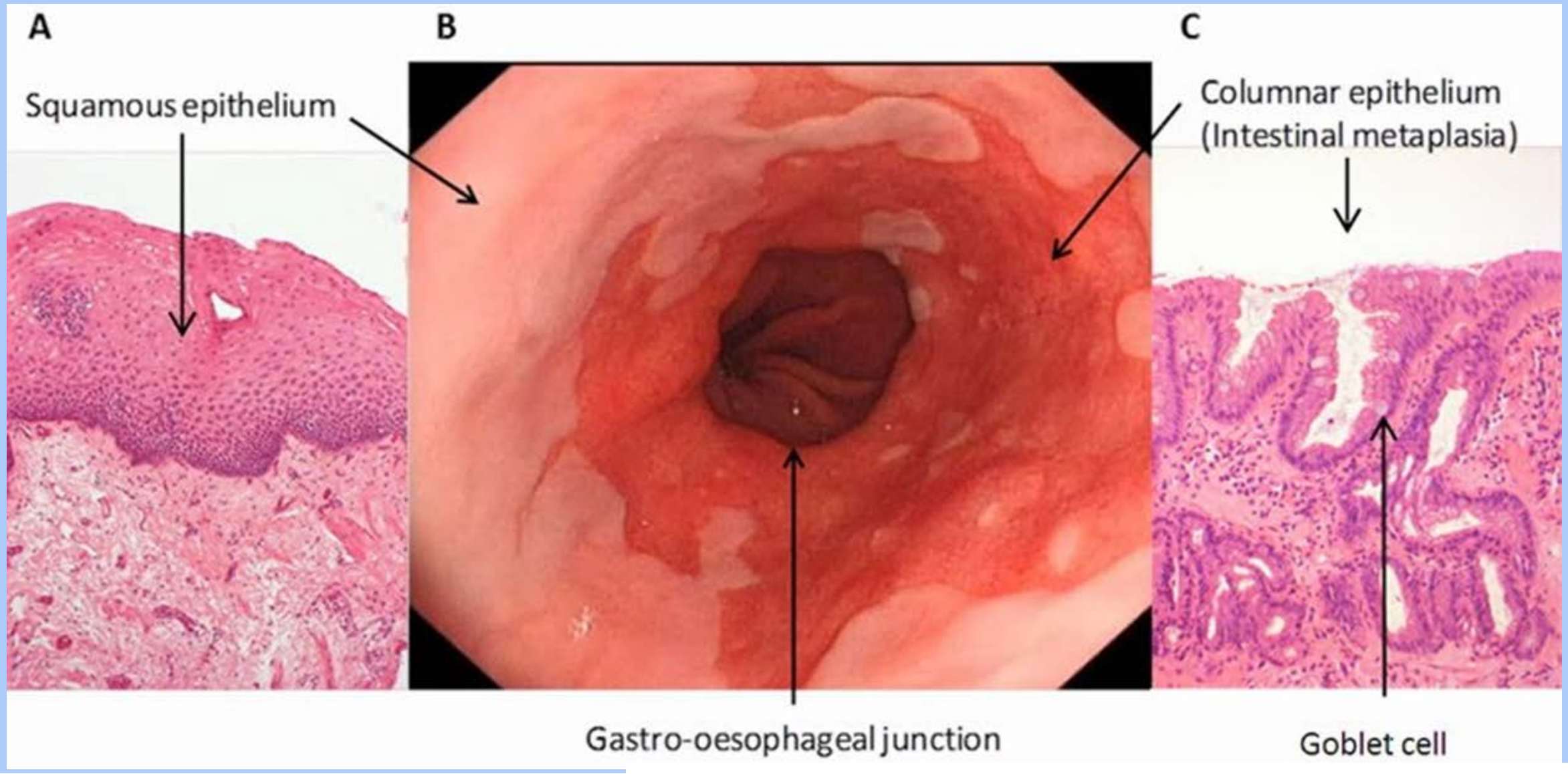
- **GERD** symptoms

Gross description:

- **Red / salmon colored mucosa** between pale squamous mucosa of lower esophagus and lush pink gastric mucosa; may have tongues extending up from GE junction
- Endoscopists utilize the **Prague classification** to describe disease extent (include circumferential and maximal segment length) in Barrett mucosa

http://www.pathologyoutlines.com/topic/esophagusBarrettsgeneral.html

Barret's esophagus (BE)

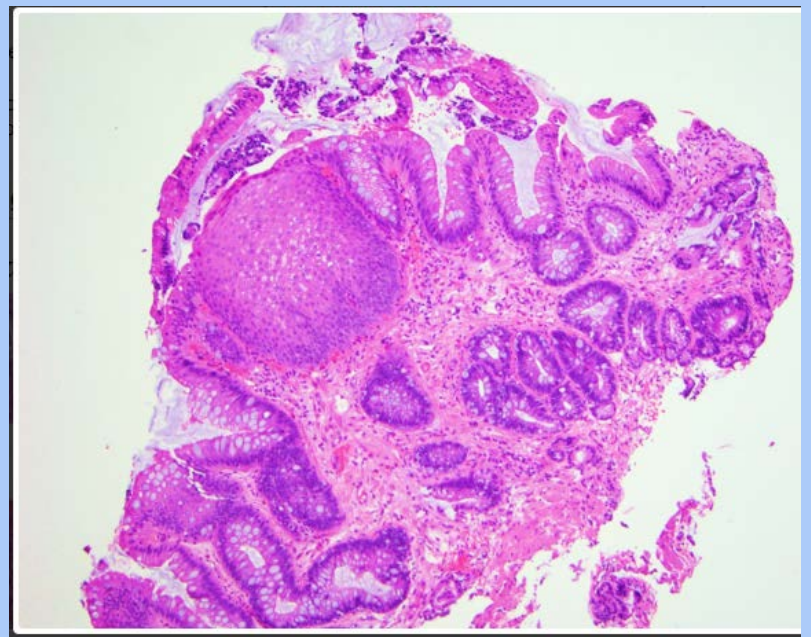


http://gastroenterologymaster.blogspot.com/2012/11/barretts-oesophagus.html

Barret's esophagus (BE)

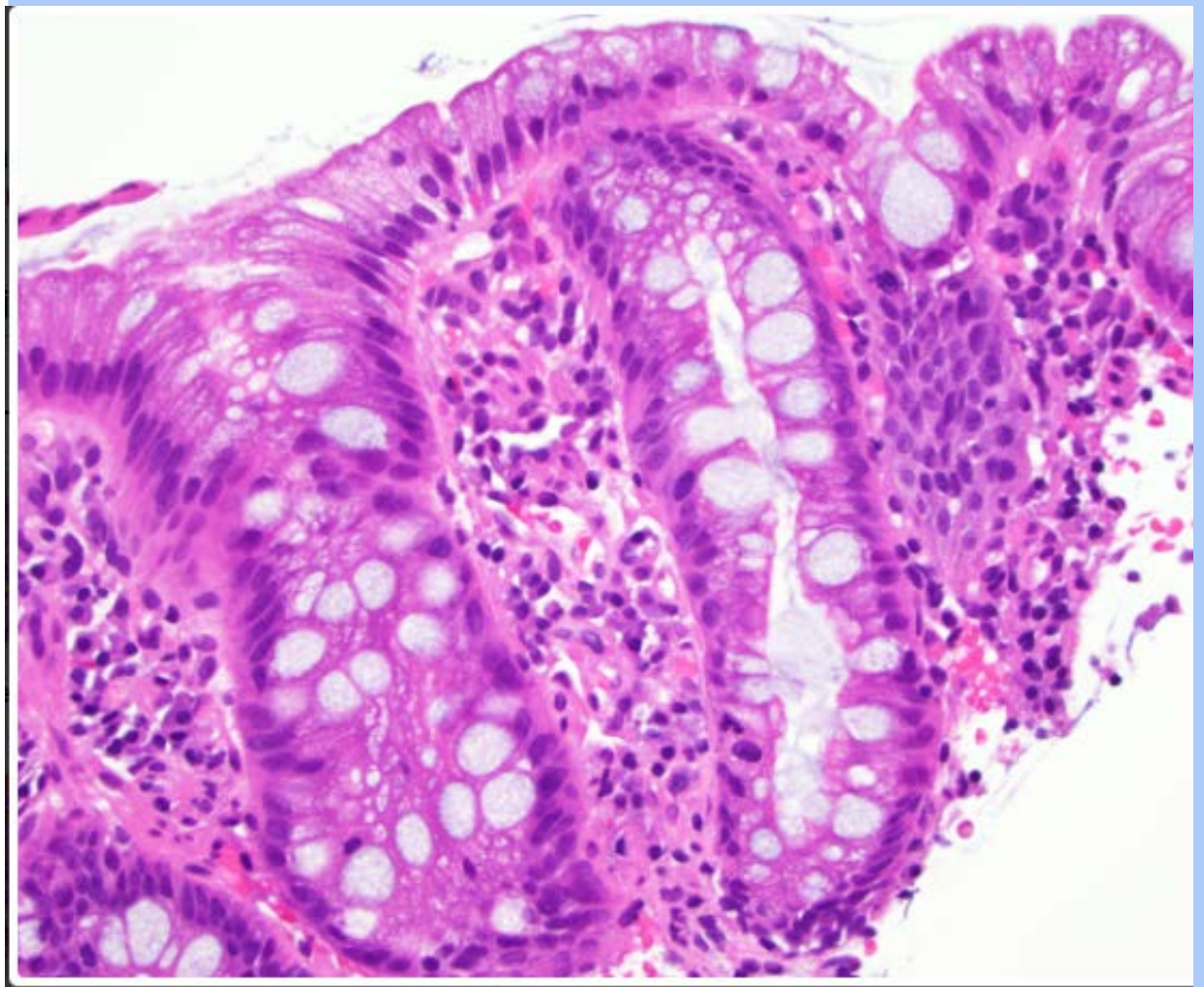
Microscopic (histologic) description:

- Esophageal squamous epithelium replaced by columnar epithelium of intestinal type with goblet cells
- ***True goblet cells***: rounded shape, clear to bluish cytoplasmic mucin, randomly scattered, mucin usually indents nucleus
- Nondysplastic reactive BE shows the presence of **four lines**:
  - **1st line**: gastric foveolar type mucin droplet
  - **2nd line**: base of the foveolar mucin vacuole
  - **3rd line**: cytoplasm below the mucin vacuole
  - **4th line**: row of nuclei
- **Baseline atypia of Barrett mucosa** – some basal glands may show nuclear enlargement and stratification but there is complete surface maturation; this is considered ***negative for dysplasia***
- **Duplication of muscularis mucosae** characteristic finding in BE; observed in 92% of BE resections, involving 5% of the Barrett segment
- ***Squamous overgrowth*** over metaplastic epithelium, ***hybrid glands***, presence of esophageal ducts have high specificity for BE
- **Postablation histology**: replacement of columnar mucosa to squamous (neosquamous) mucosa; residual metaplastic epithelium may persist beneath the squamous epithelium (known as **buried Barrett's**) and progress to dysplasia or carcinoma

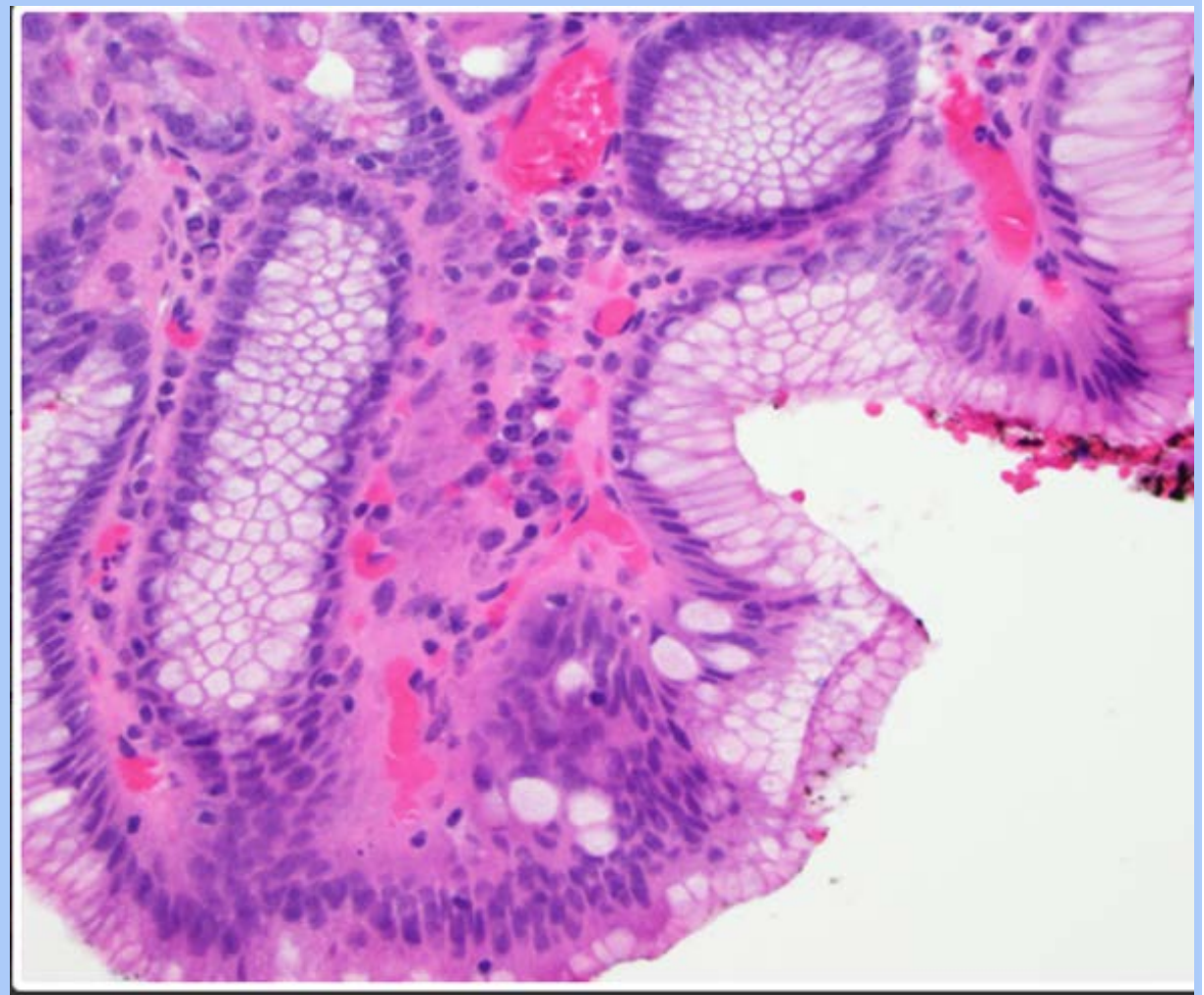


Barrett esophagus characterized by columnar epithelium with intestinal metaplasia (goblet cells) in a biopsy taken from "distal esophagus" with endoscopically recognizable abnormal

http://www.pathologyoutlines.com/topic/esophagusBarrettsgeneral.html

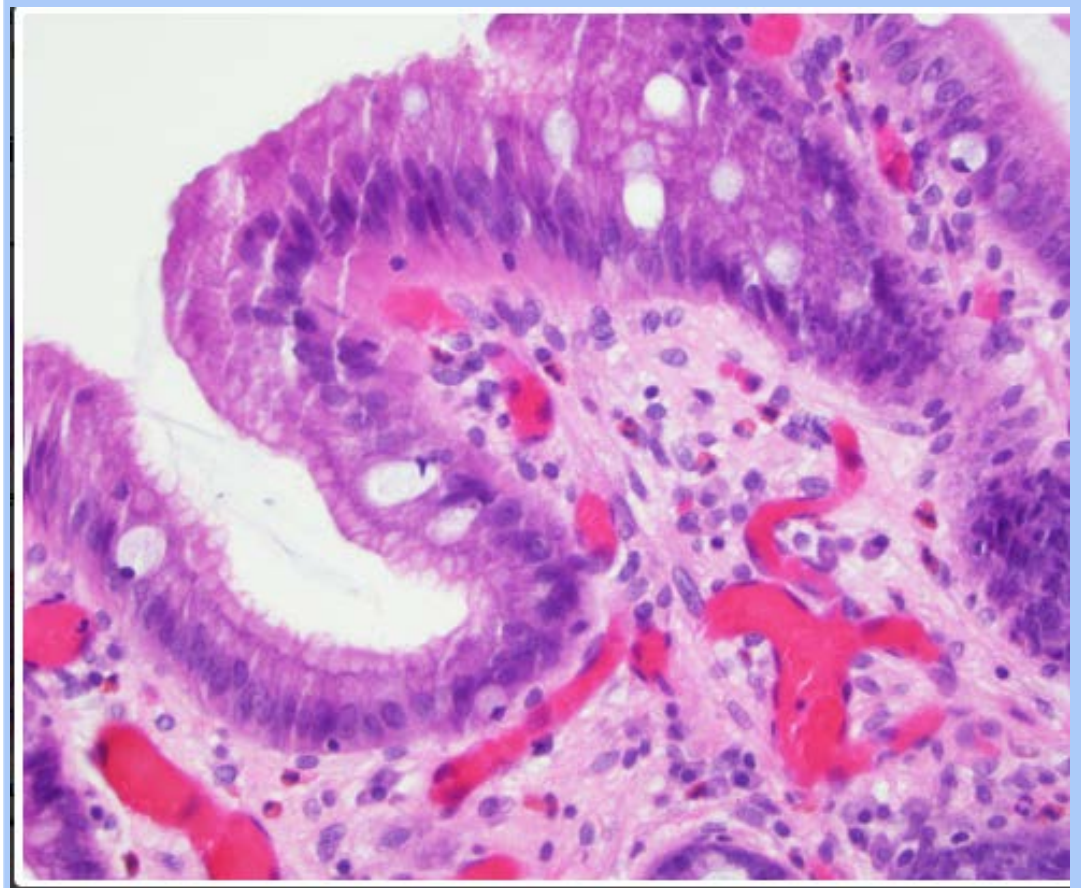


Barrett esophagus characterized by goblet cells. True goblet cells are randomly scattered, barrel shaped or circular with a bluish cytoplasmic hue.

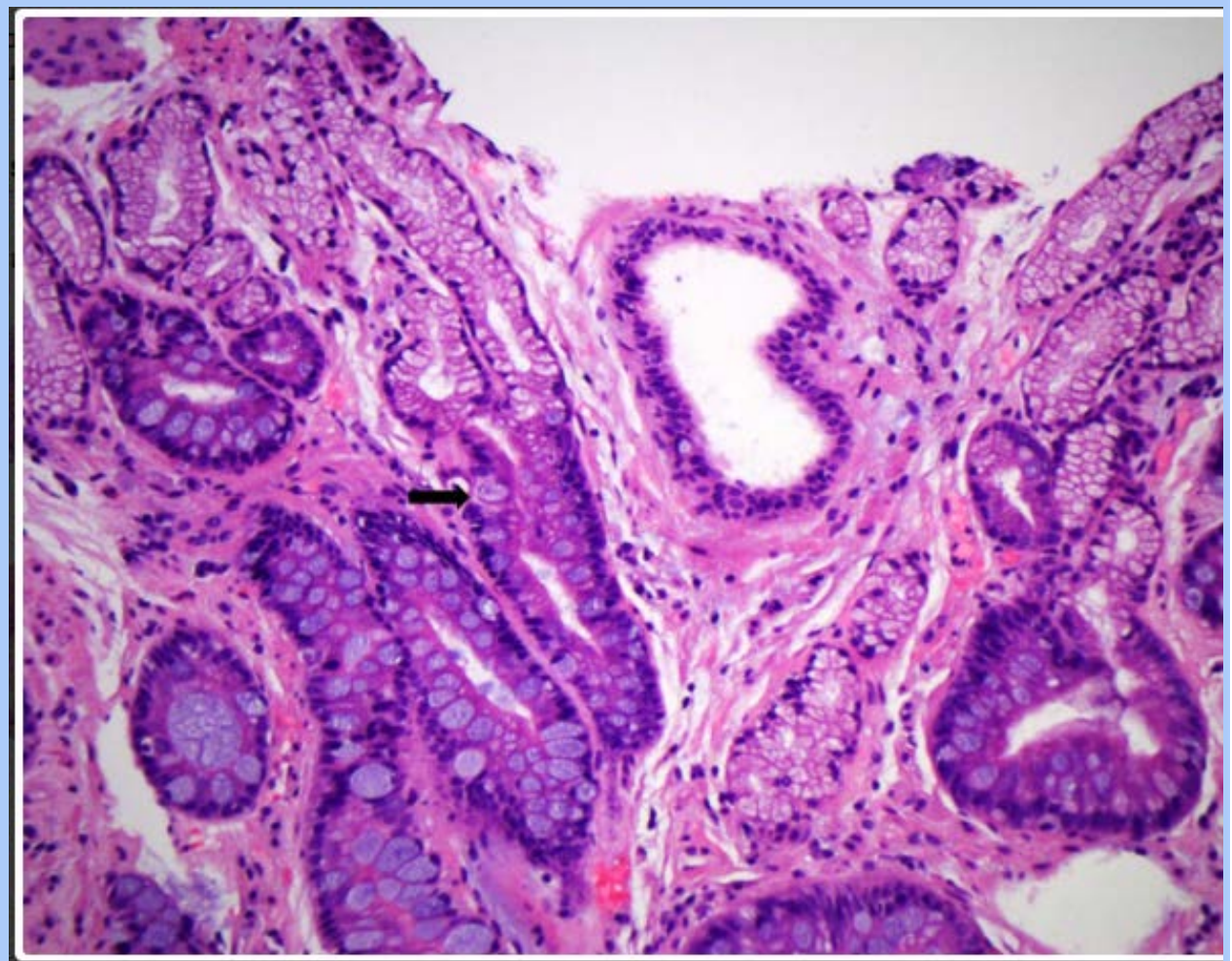


In contrast to true goblet cells, pseudogoblet cells are goblet shaped gastric foveolar cells. They are clustered and characteristically arranged in a linear or a back-to-back array

http://www.pathologyoutlines.com/topic/esophagusBarrettsgeneral.html

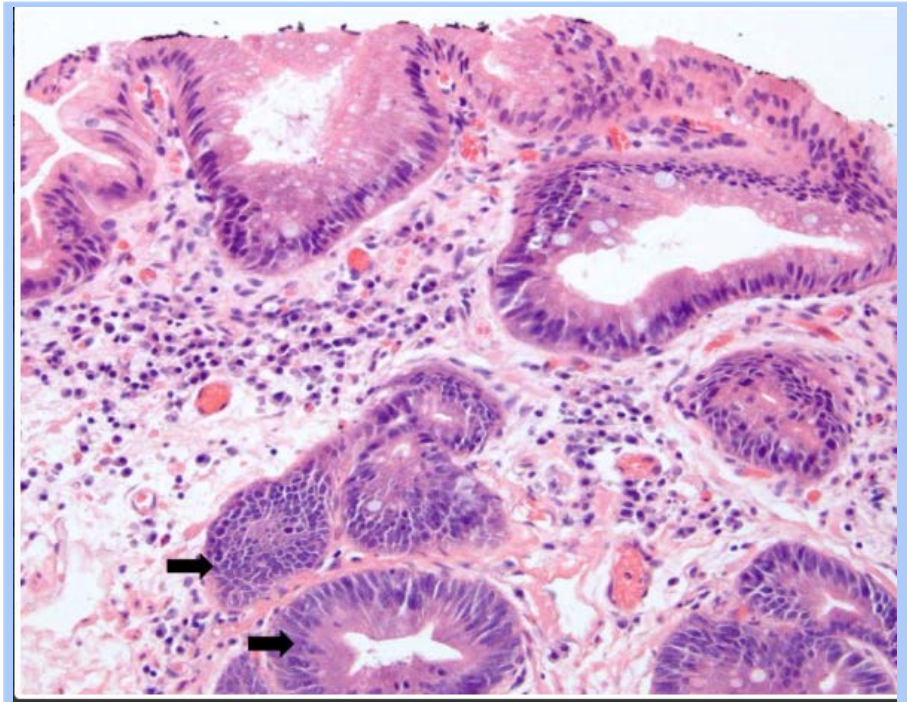


Reactive Barrett mucosa shows 4 lines:
First line: gastric foveolar type mucin droplet
Second line: base of the foveolar mucin vacuole
Third line: cytoplasm below the mucin vacuole
Fourth line: row of nuclei

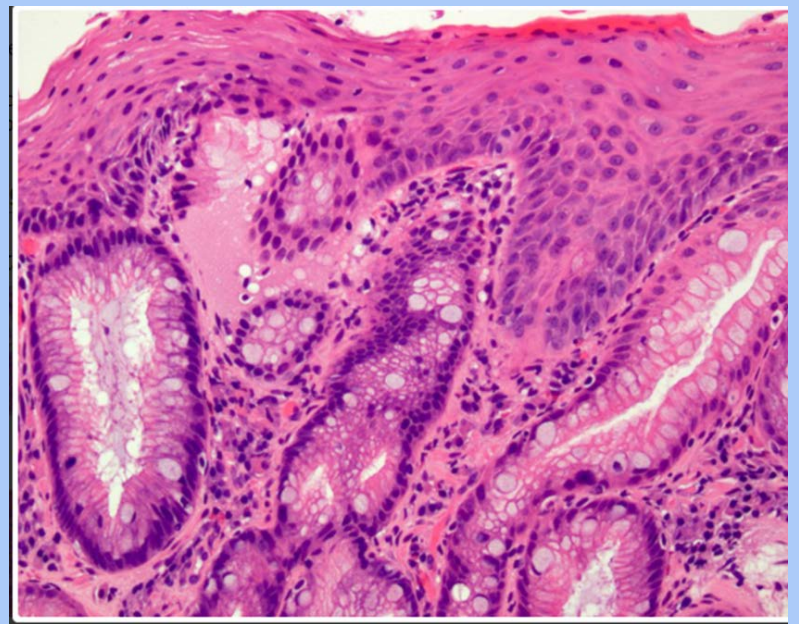


Hybrid glands (shown by an arrow) consist of mixed metaplastic (with goblet cells) and mucinous epithelium and has high specificity for Barrett mucosa.

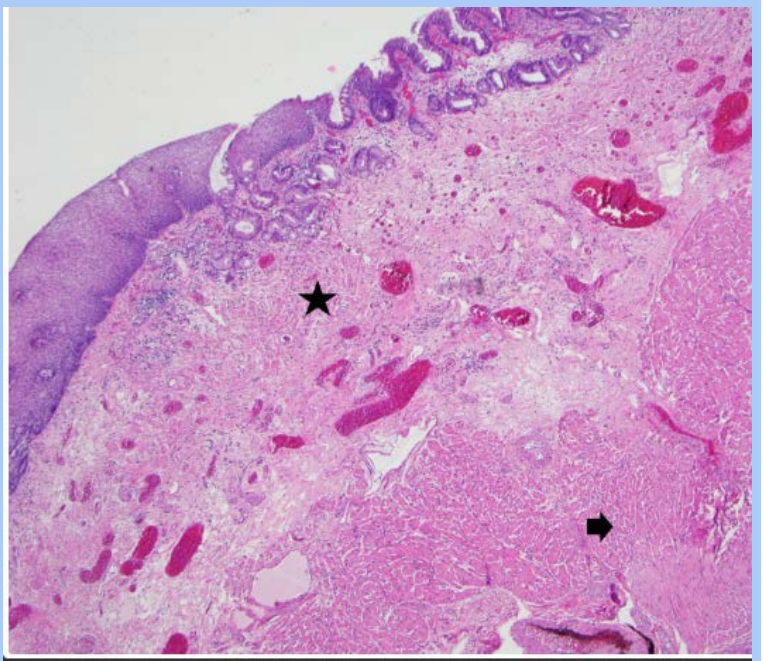
http://www.pathologyoutlines.com/topic/esophagusBarrettsgeneral.html



The basal glands in Barrett mucosa (highlighted by arrow) can show nuclear stratification and elongation; however there is complete surface maturation. This atypia is referred to as "baseline atypia" and is considered as a reactive response and is negative for dysplasia.



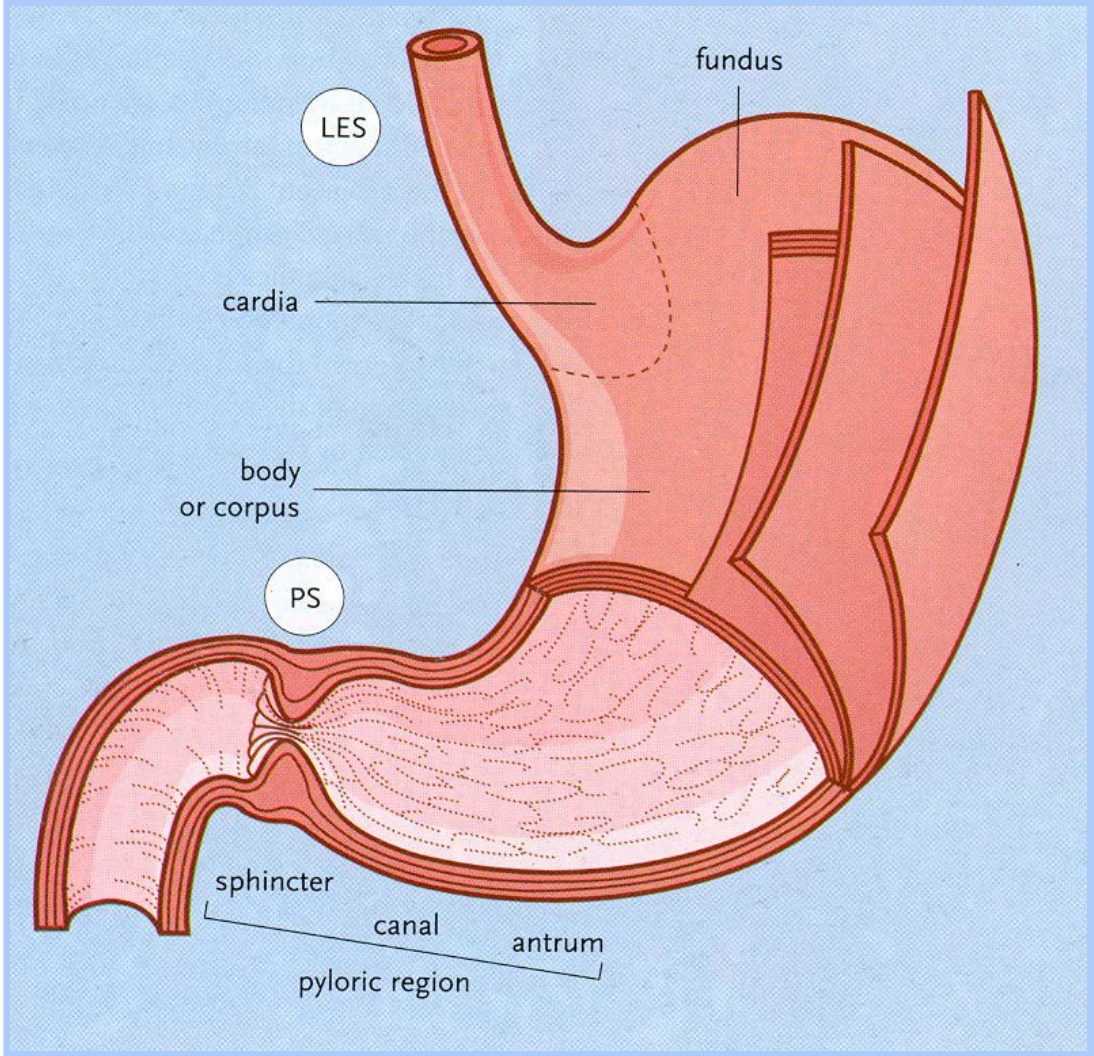
Squamous epithelium overlying the glands with intestinal metaplasia is another feature with high specificity for Barrett mucosa. If seen, it is recommended to mention in report.

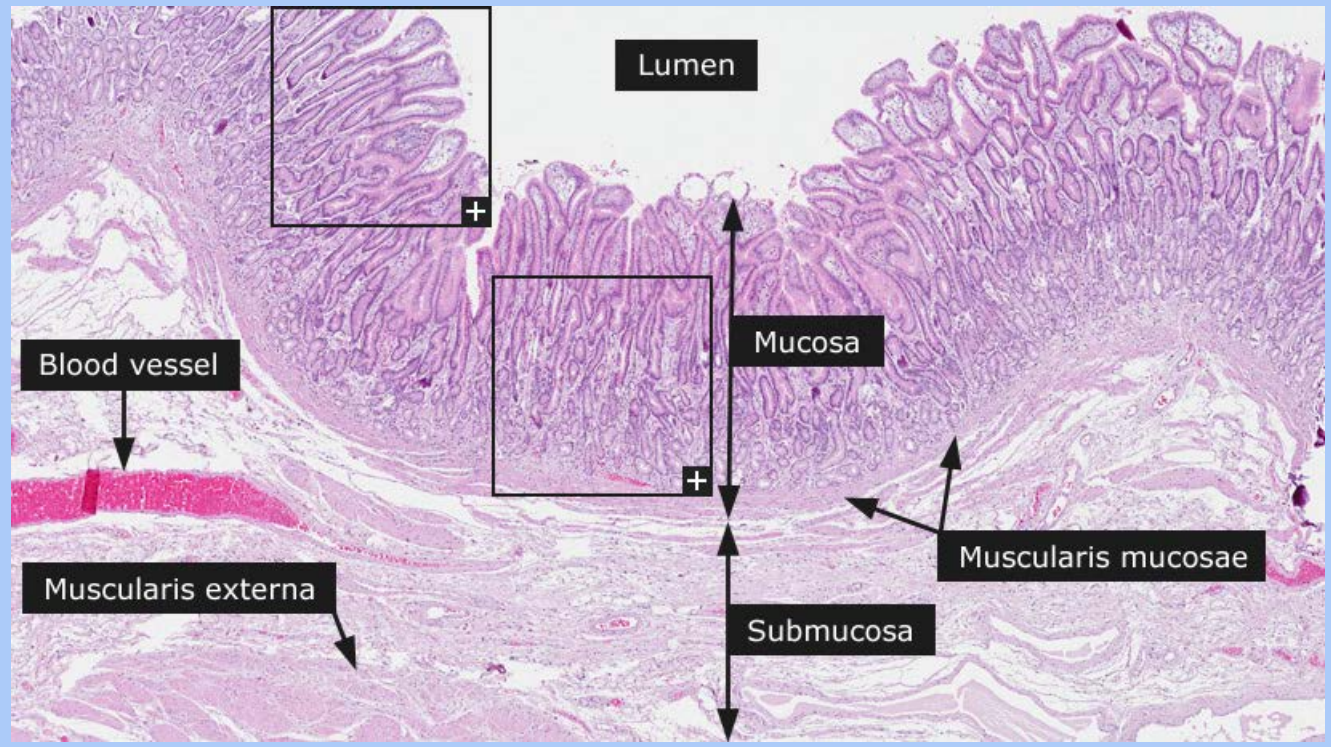


Duplication of muscularis mucosae (MM) is a characteristic feature seen in specimens from BE (star highlights inner or neo MM, arrow highlights native or outer MM).

http://www.pathologyoutlines.com/topic/esophagusBarrettsgeneral.html

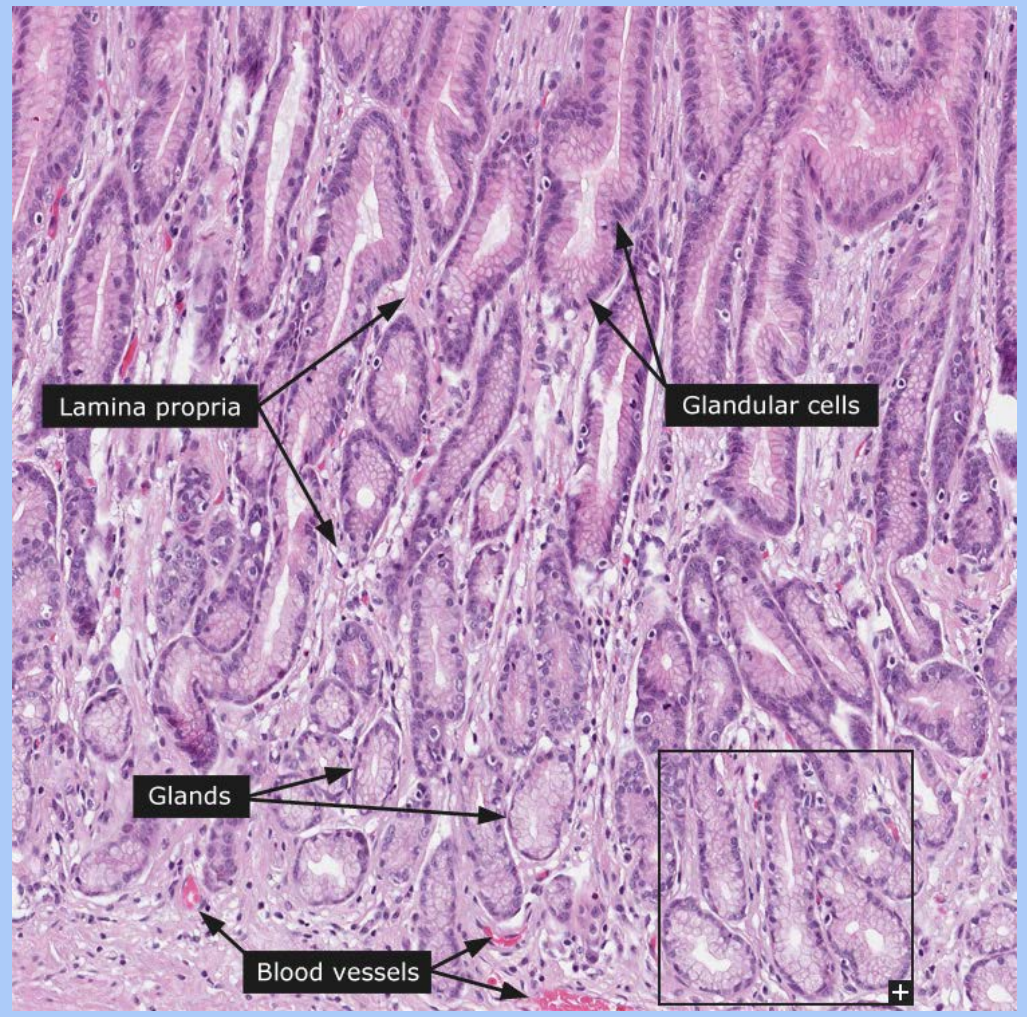
Anatomical structure of the stomach

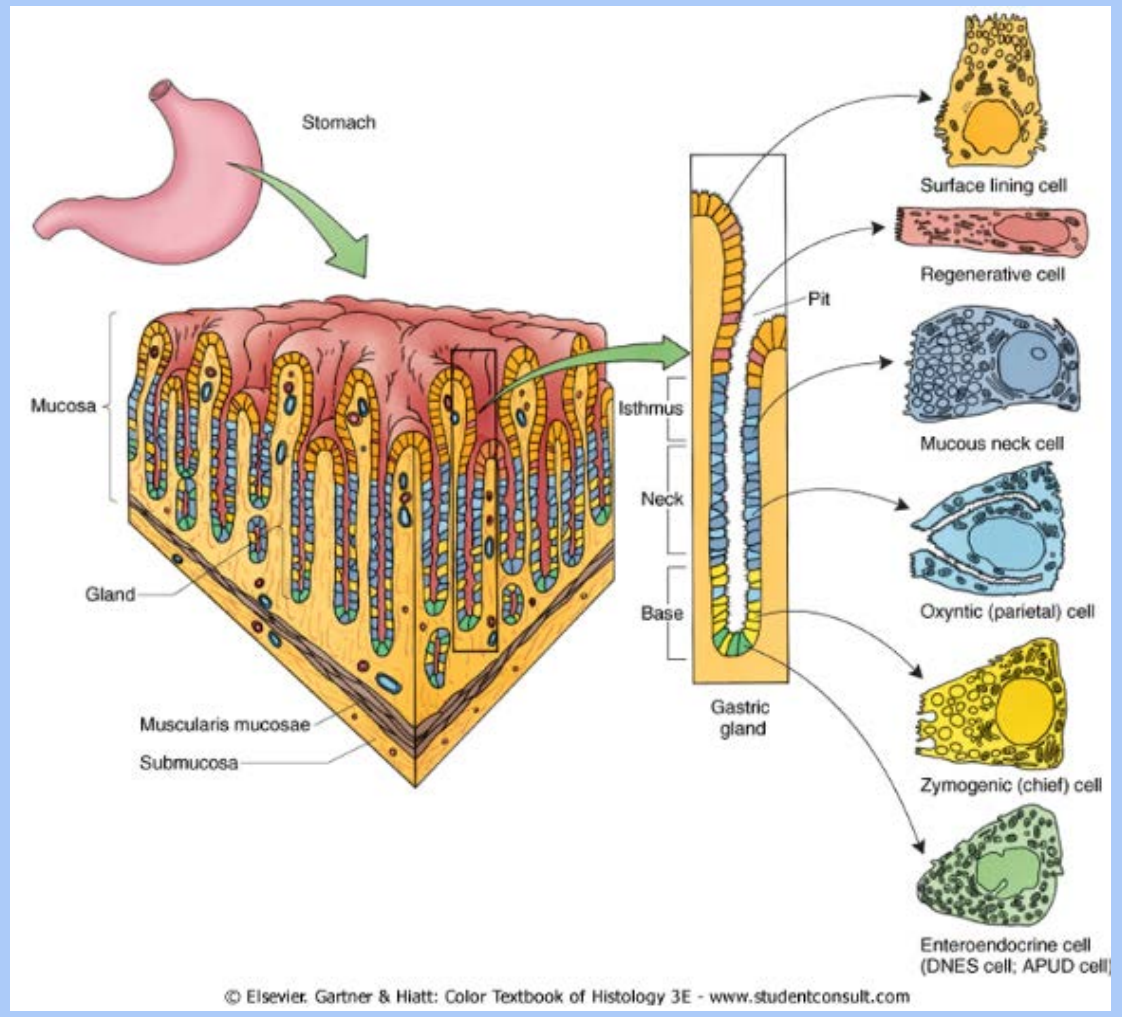




https://www.proteinatlas.org/learn/dictionary/normal/stomach+2

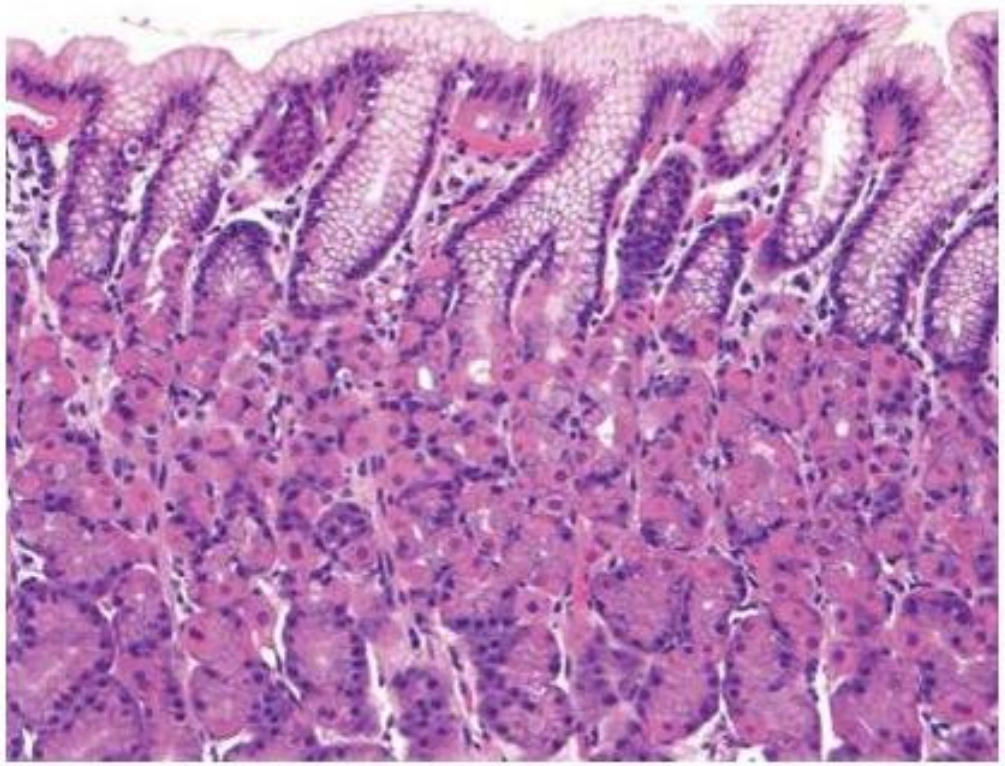
Histological structure of the gastric mucosa



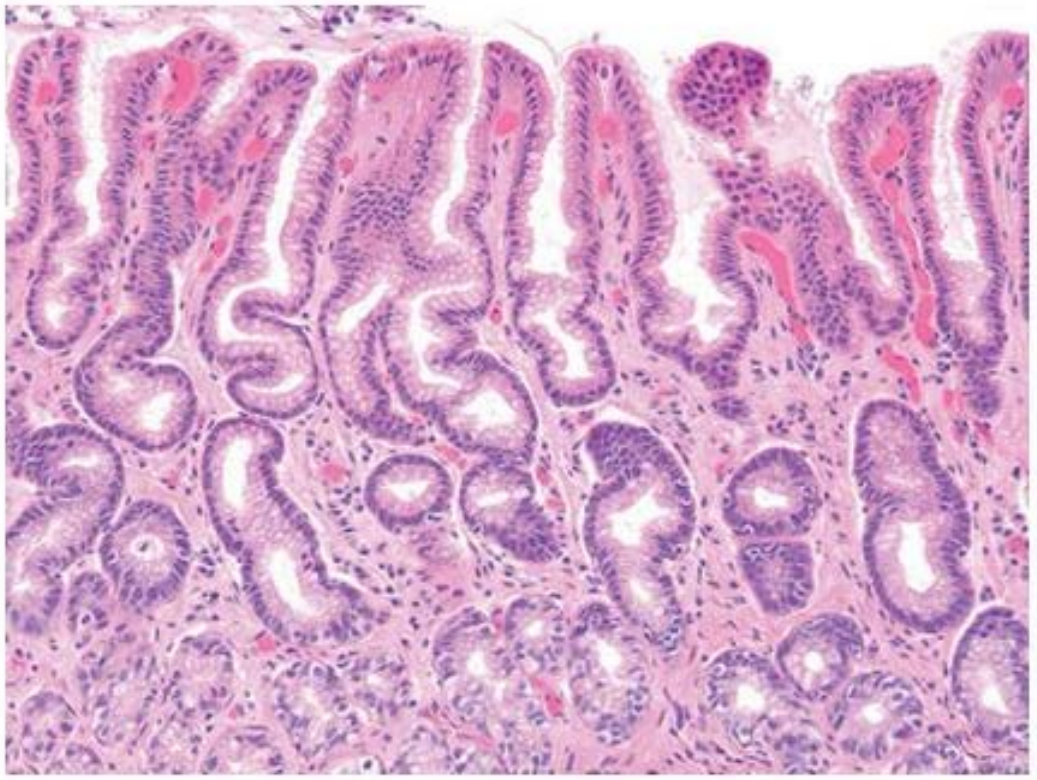


https://www.proteinatlas.org/learn/dictionary/normal/stomach+2/detail+2

Histological structure of the gastric mucosa



Fundic mucosa with parietal & chief cells



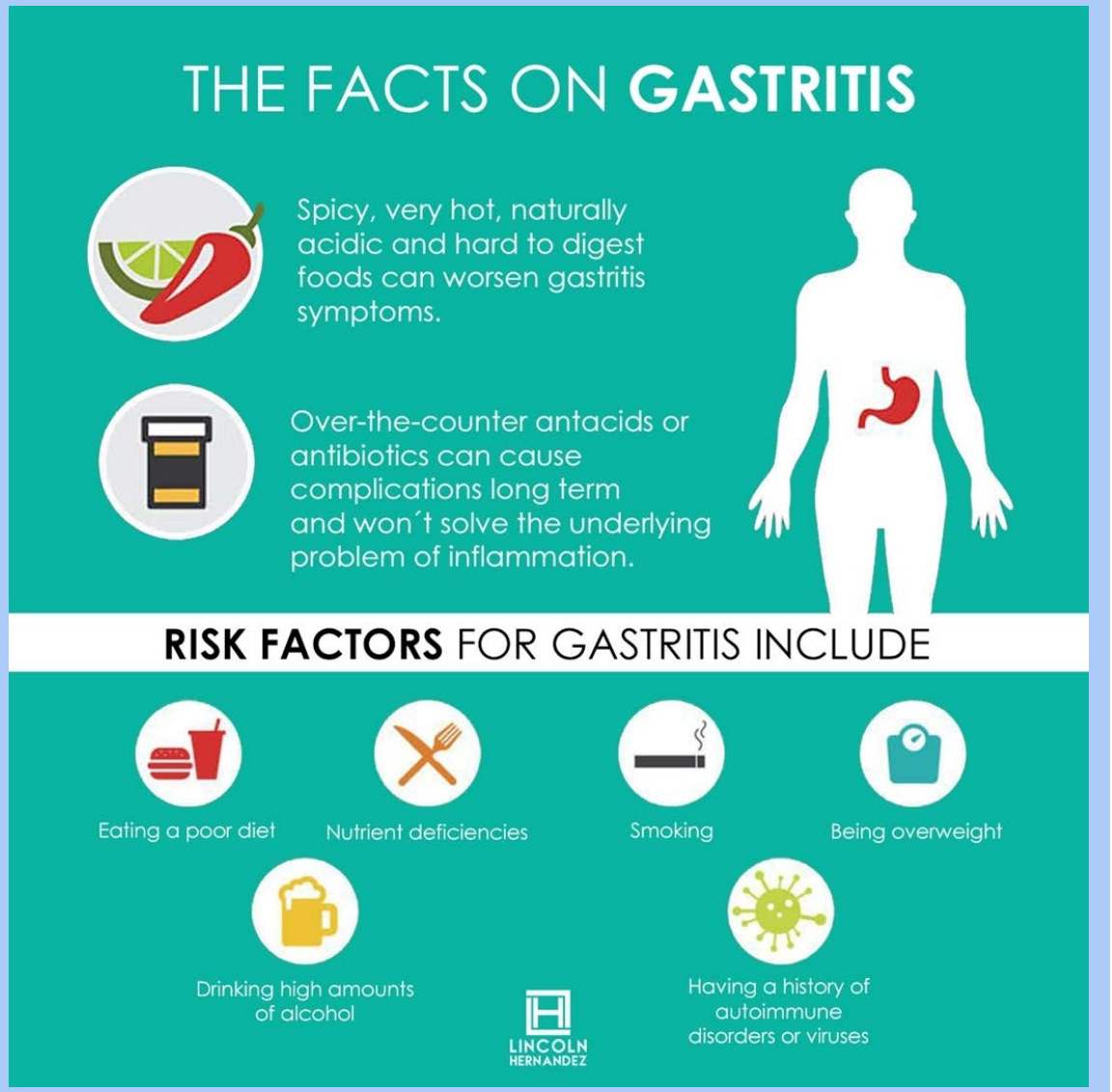
Antral mucosa with mucin secreting glands

https://slideplayer.com/slide/11343049/

Gastritis

Risk factors

- **Drugs**
  - Direct irritating effect on gastric mucosa
  - Aspirin, NSAIDs, and corticosteroids
- **Diet**
  - Alcohol, spicy food
- **Microorganisms**
  - *Helicobacter pylori*
    - Important cause of chronic gastritis
    - Promotes breakdown of gastric mucosal barrier
  - Staphylococcus organisms
- **Environmental factors**
  - Radiation, smoking
- **Pathophysiologic conditions**
  - Burns, renal failure, sepsis
- **Other factors**
  - Psychological stress, NG tube



https://www.picuki.com/media/2224168352904337825

Acute gastritis

- It is the acute inflammation of the gastric mucosa.

Depending on the region of occurrence:

Diffuse

Focal

Etiology

Exogenic

- ***Alimentary***
- ***Toxic***
- ***Medicamentous***
- ***Infectious***
- ***Erozive***

Endogenic

- ***Endemic intoxication***
- ***Ischemic***
- ***Circulatory***
- ***Neurotic***
- ***Sepsis***

Acute gastritis

Catarrhal

Dystrophy, necrobiosis, necrotic changes and ***erosions*** develop in the of the mucosal epithelium.

Fibrinous

If the necrotic layer is thin - **croupous**, if deep - **diphtheritic gastritis.**

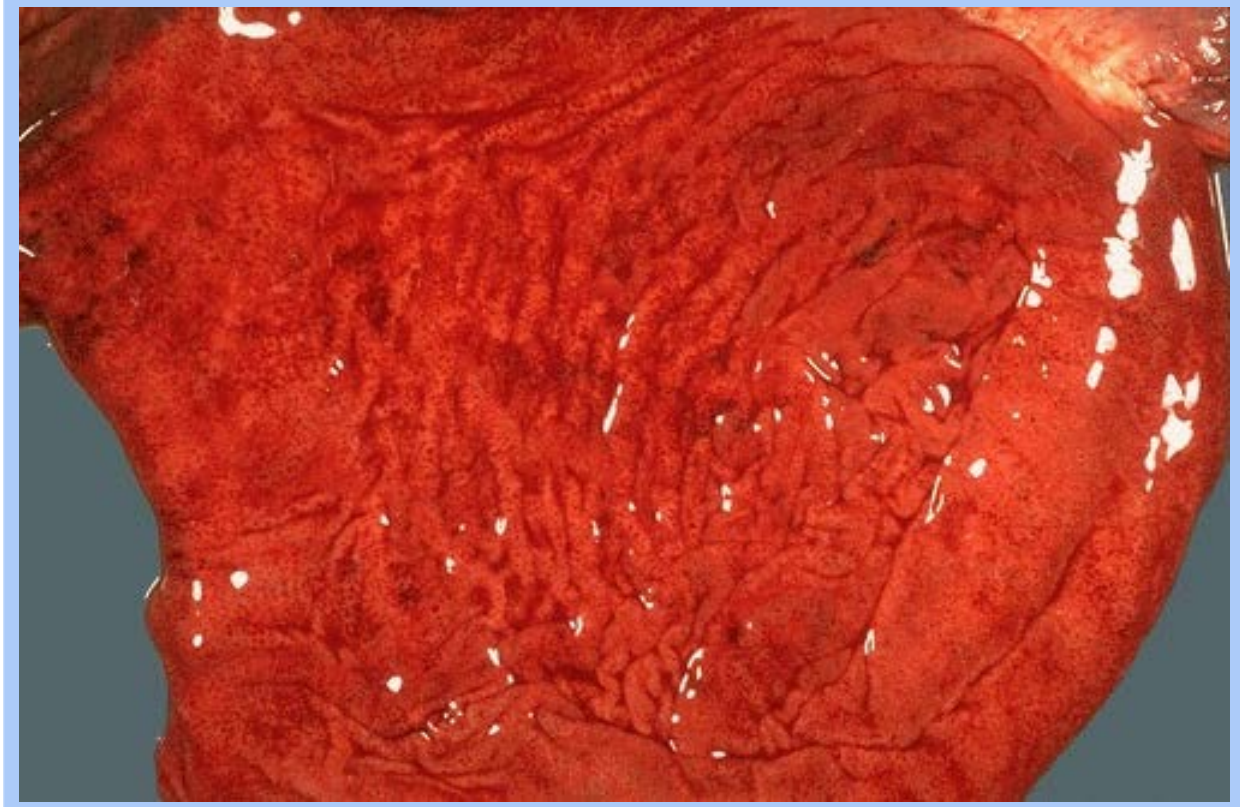
Phlegmonous

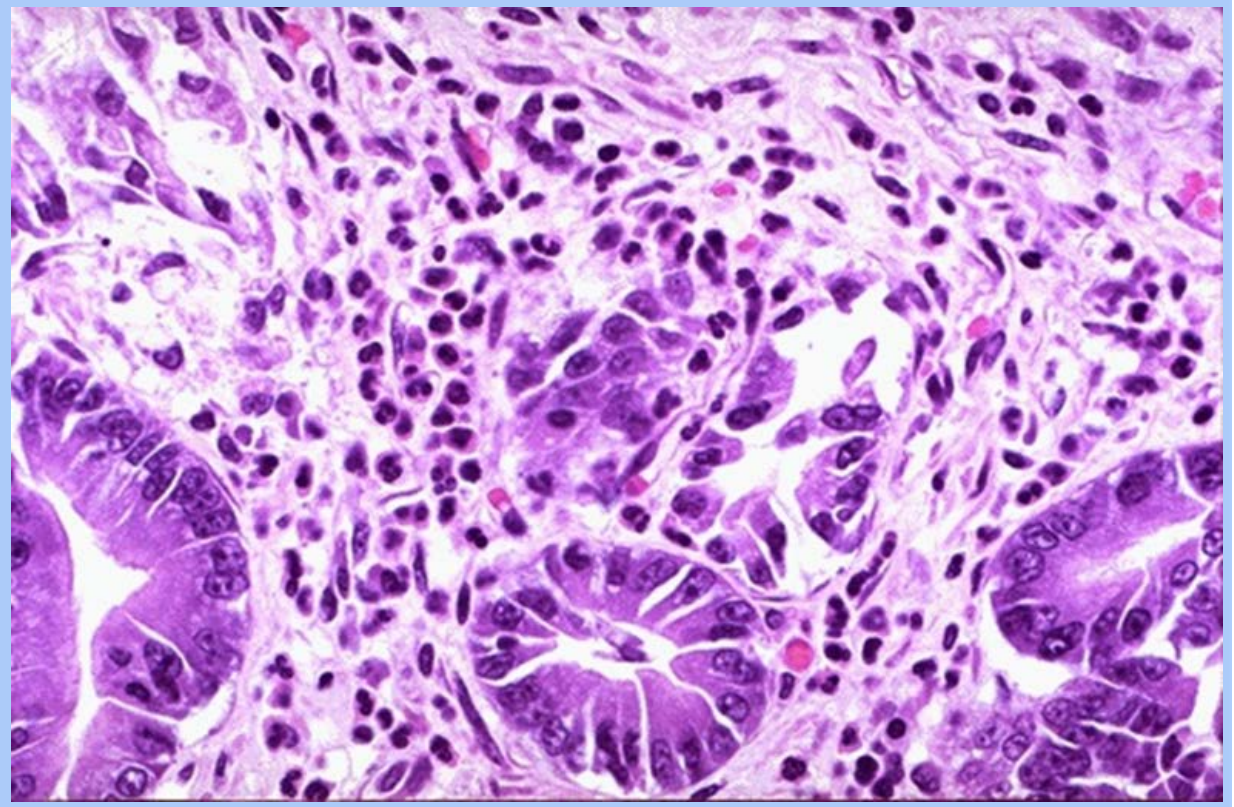
Purulent exudate is formed in the mucosa and submucosa.

Necrotic

Necrosis of the gastric wall due to destructive substances - **corrosive gastritis**

Acute gastritis





https://webpath.med.utah.edu/GIHTML/GI016.html

https://webpath.med.utah.edu/GIHTML/GI017.html

Chronic gastritis

- **Chronic gastritis** is defined as the presence of chronic mucosal inflammatory changes leading eventually to mucosal atrophy and intestinal metaplasia, usually in the absence of erosions.
- ***Etiology:***
- Chronic infection by *H. pylori*
- Immunologic (in association with pernicious anemia)

Classification of Chronic gastritis

According to the Pathogenetic mechanism:

A gastritis

- **Autoimmune gastritis -** autoimmune disease, forms the autoantibodies against the parietal cells of gastric glands.
- 15-20% of all chronic gastritis.
- Also known as **Fundal or hypoacid** gastritis.
- The B_{12}-deficiency anemia **(pernicious anemia)** is developed.

B gastritis

- **H. pylori gastritis -** 80% of all chronic gastritis.
- **Antral gastritis.**
- ***Caused by Helicobacter pylori.***

C gastritis

- Duodeno-gastral reflux occurs in the patients after gastric resection.
- In 30% of such patients is developed the **antral chronic gastritis**.

Classification of Chronic gastritis according to the localization

- **Fundal**
- **Pangastritis**
- **Antral**

According to the activity

- **Active**
- **Non-active**

According to the clinical course

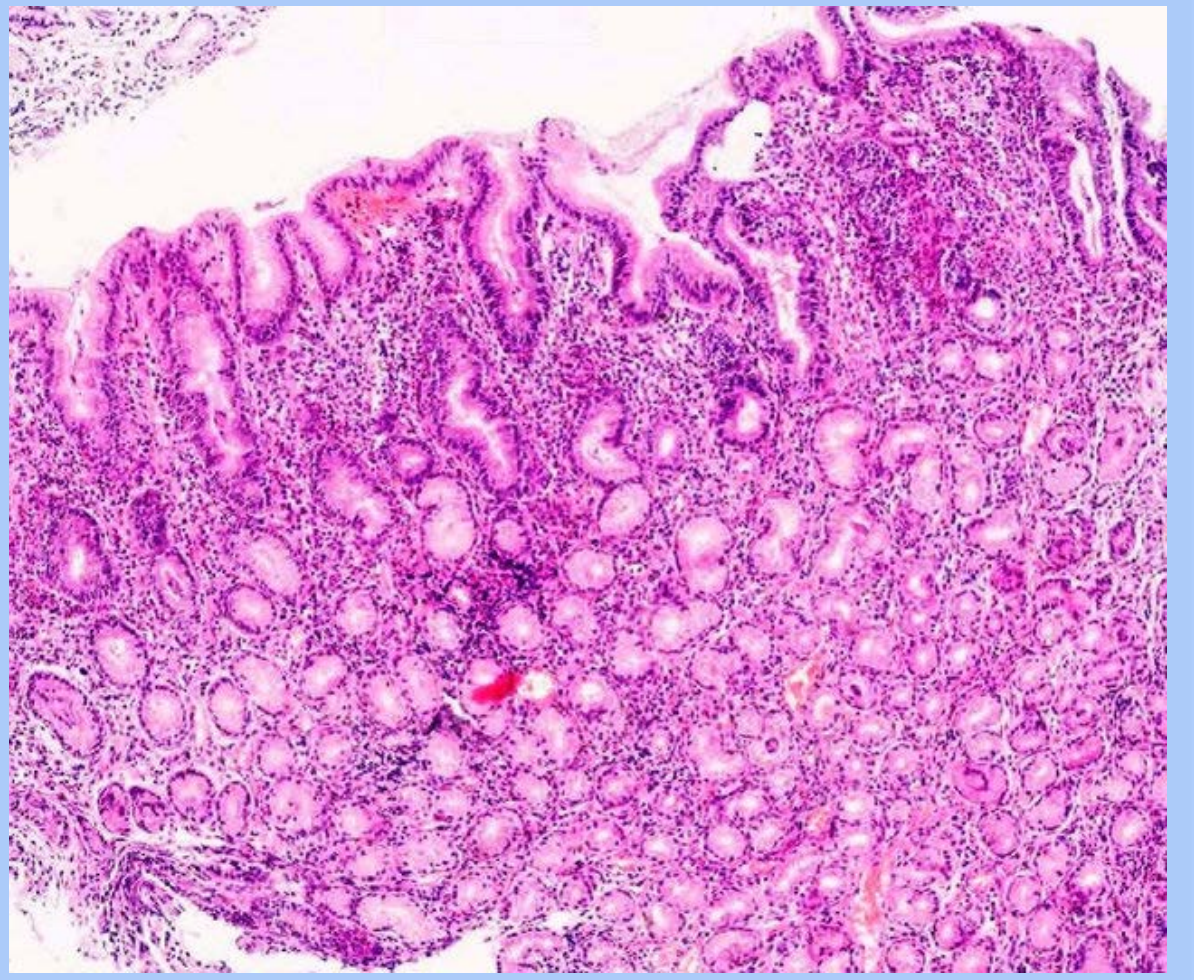
- **Mild**
- **Moderate**
- **Severe**

According to the morphologic features

- **Superficial**
- **Atrophic**
- **Hypertrophic**

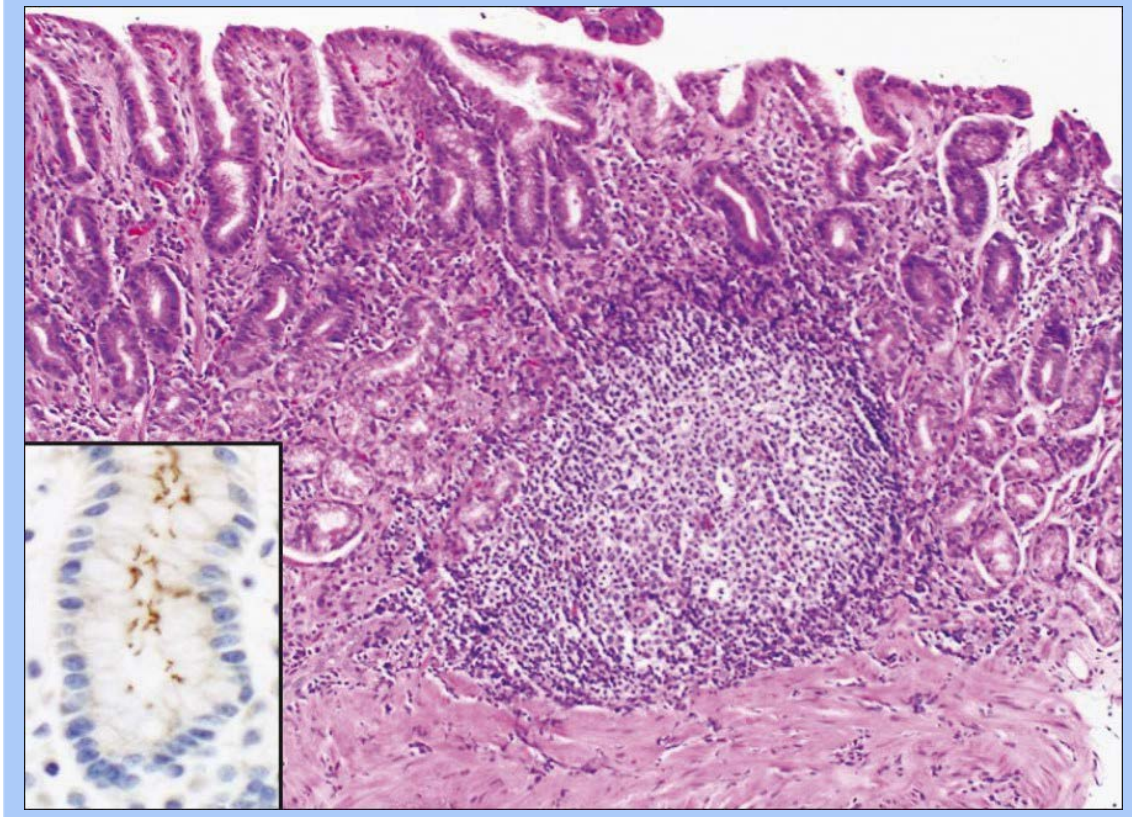
Chronic superficial gastritis

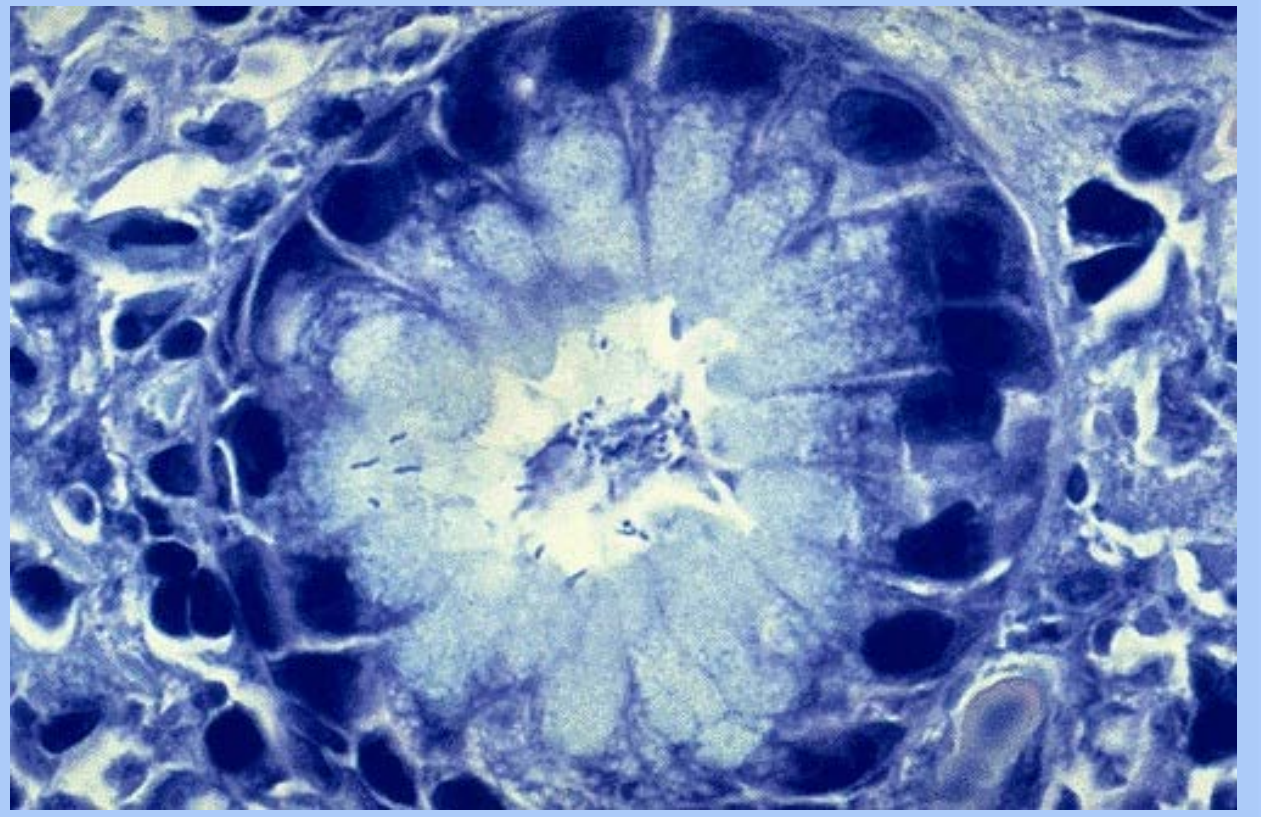
• The mucosa is of normal thickness, ***the main morphological changes*** occur in the upper 1/3 - in the surface layers.
• **Degenerative changes** in the epithelium, and sometimes *metaplasia* are noted.
• **Lympho-leukocytic infiltration and edema** occur in the lamina propria.
• Chronic superficial gastritis can remain in the same condition for many years **without progression.**



https://www.researchgate.net/publication/294106169_Expression_of_cagA_virBD_Complex_andor_vacA_Genes_in_Helicobacter_pylori_Strains_Originating_from_Patients_with_Gastric_Diseases/figures?lo=1

Histopathology of Chronic H. pylori gastritis

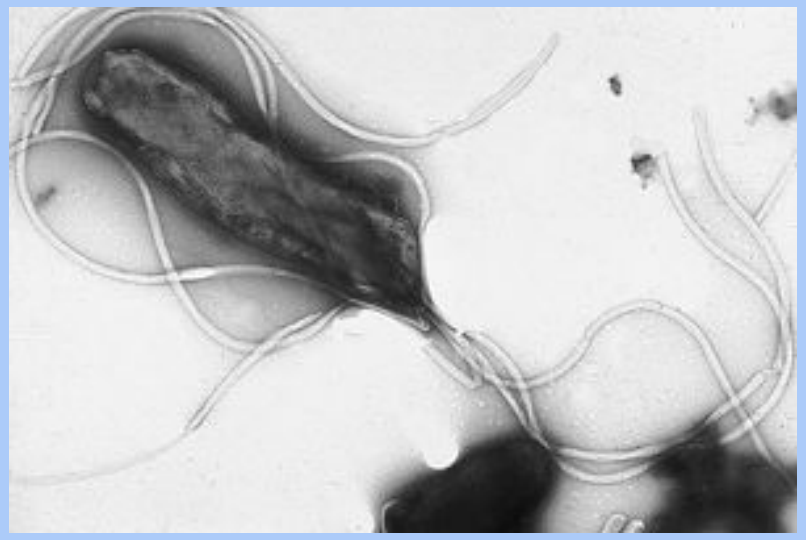


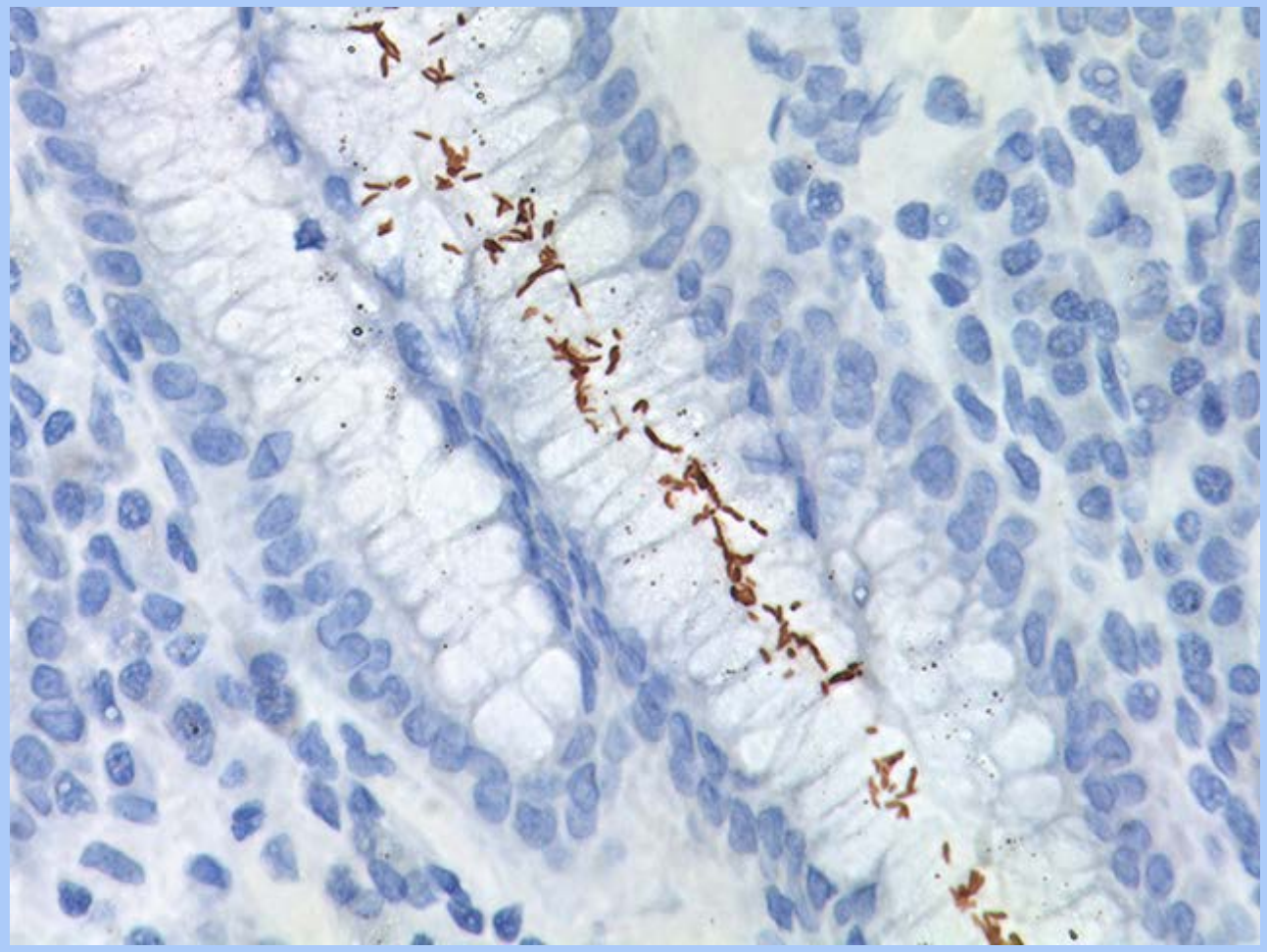


http://www.ijpmonline.org/viewimage.asp?img=IndianJPatholMicrobiol_2012_55_1_1_94847_f7.jpg

https://webpath.med.utah.edu/GIHTML/GI023.html

Helicobacter Pylori
Morphology





https://biocare.net/product/helicobacter-pylori-antibody/

https://www.ueg.eu/education/latest-news/article/article/mistakes-in-the-management-of-helicobacter-pylori-infection-and-how-to-avoid-them/

https://microbewiki.kenyon.edu/index.php/Helicobacter_pylori_as_a_causative_agent_of_Gastric_Cancer

Chronic atrophic gastritis

• ***Atrophy and sclerosis*** occur in the mucosa and its glandular structures.

• The mucosa becomes thinner and smoother, mucus secretion is sharply reduced,

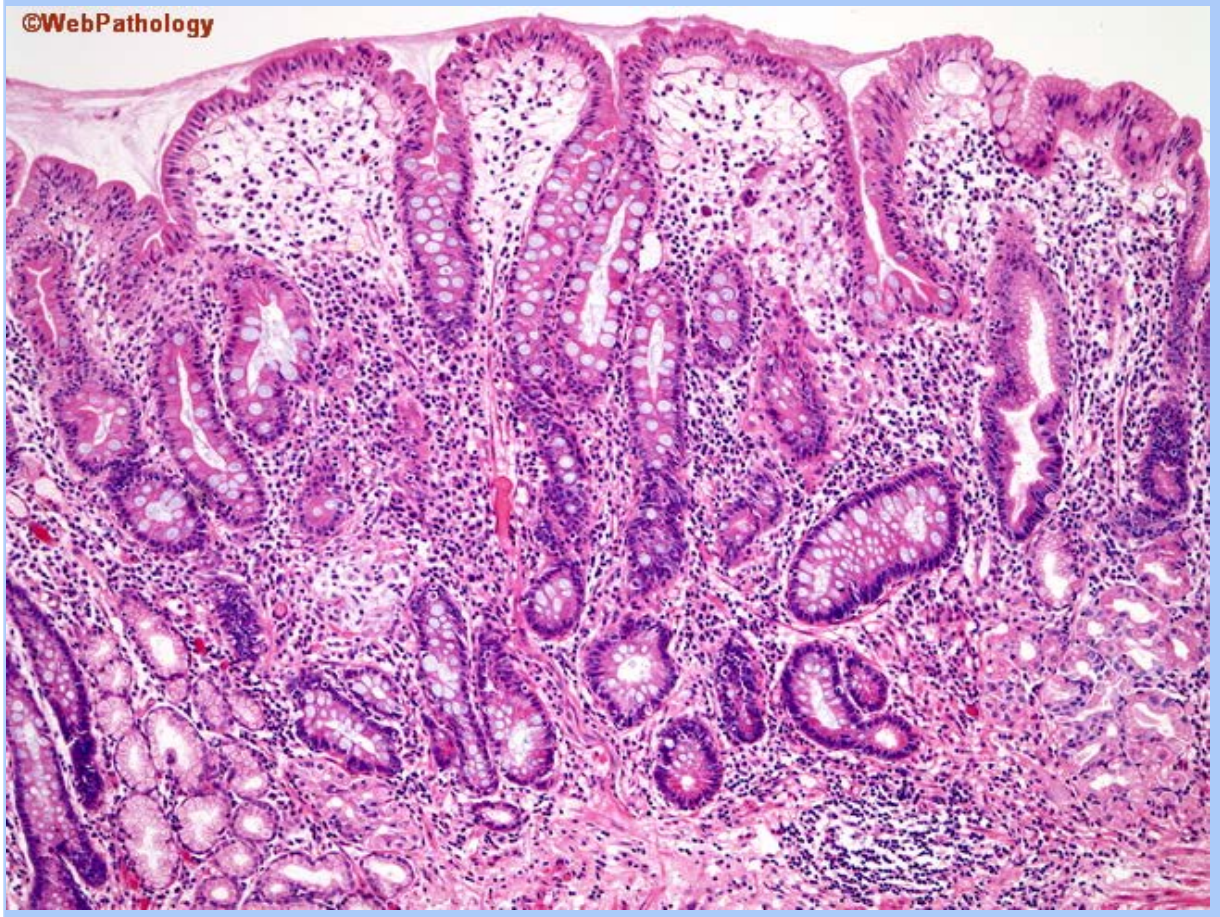
metaplasia - ***“enteralization”*** occurs in the covering and glandular epithelium, where **goblet cells** populate large stretches of the mucosa.

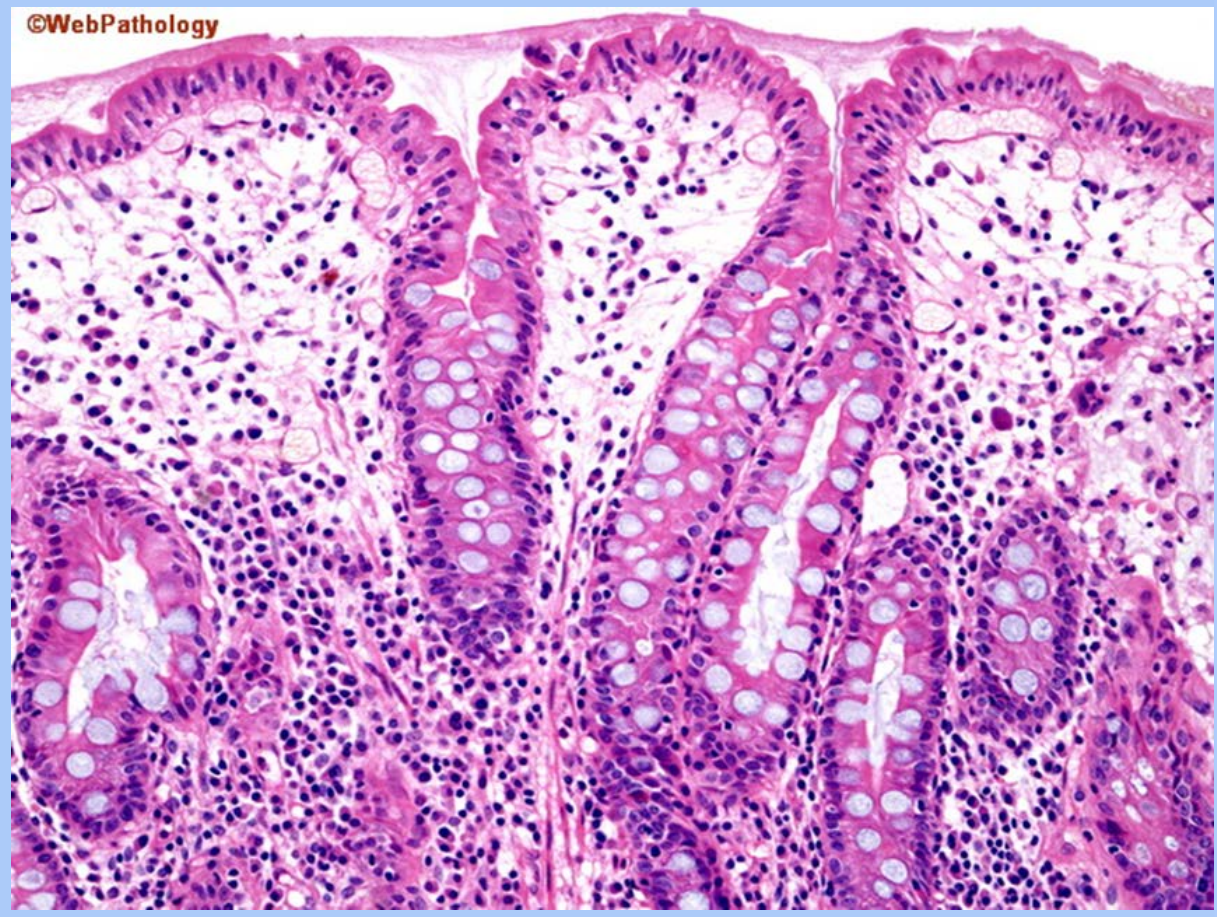
• Additionally, **pseudopyloric metaplasia** can be seen toward the base of the glands.

• The surface of the mucosa demonstrates hyperplastic changes.

• It is a ***precancerous disease***.

Chronic atrophic gastritis





https://www.webpathology.com/image.asp?case=196&n=6

Sydney System of Grading Chronic Gastritis

1. Site: Antral, Corporal mucosa
2. Grading of: (Mild, Moderate, Marked)

- ✓ H-Pylori
- ✓ Chronic inflammation
- ✓ Activity
- ✓ Atrophy
- ✓ Intestinal metaplasia

*Normal lymphocytes & plasma cells in lamina propria = up to 5/HPF

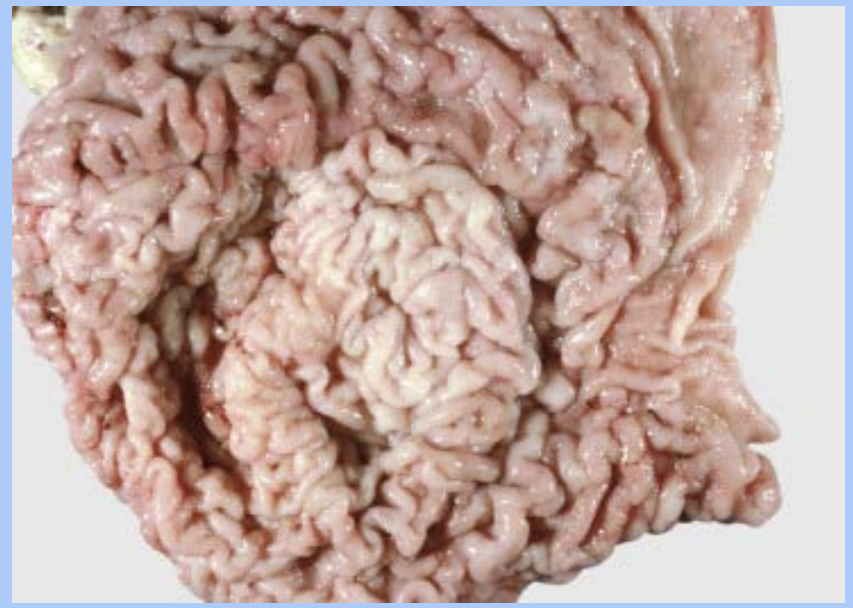
*No Neutrophils in lamina propria

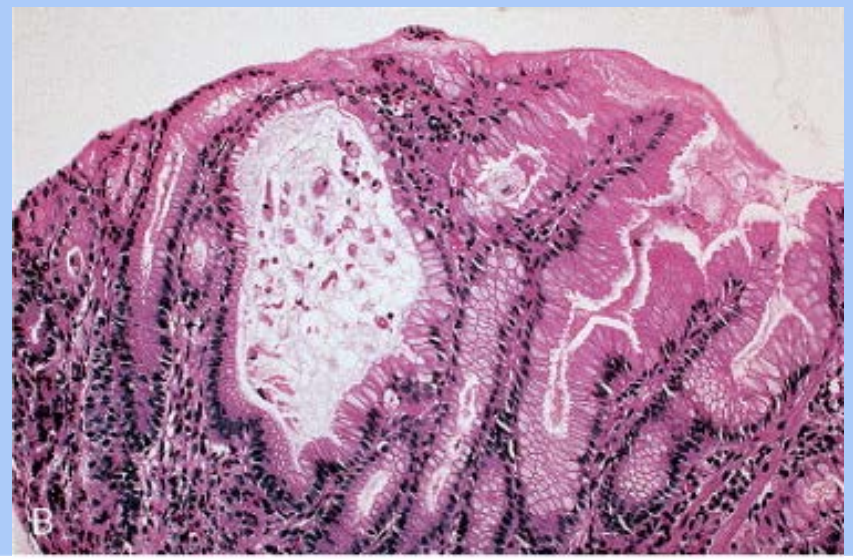
https://www.slideshare.net/drsapnablore/stomach-pathology-lecture

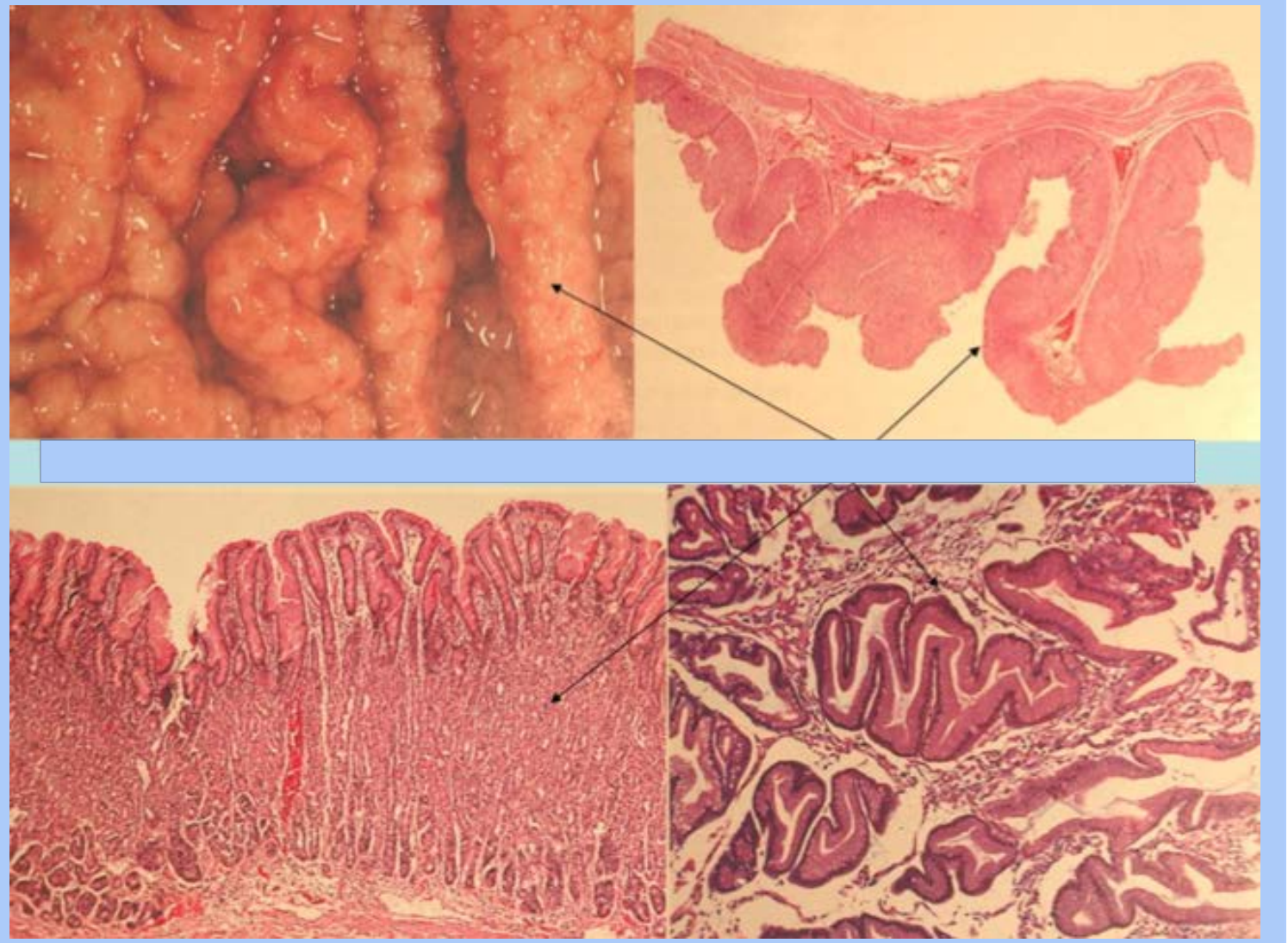
Chronic hypertrophic gastropathy

- Inaccurate name “hypertrophic gastritis”.
- ***Menetrier disease,*** resulting from profound hyperplasia of the surface mucous cells with accompanying glandular atrophy.
- ***Hypertrophic-hypersecretory gastropathy,*** associated with hyperplasia of the parietal and chief cells within gastric glands.
- ***Gastric gland hyperplasia secondary to excessive gastrin secretion,*** in the setting of a gastrinoma (Zollinger-Ellison syndrome).

Chronic giant hypertrophic gastropathy







https://www.sciencedirect.com/topics/medicine-and-dentistry/menetrier-disease

Symptomatic ulcers develops as a signs of other diseases

- **Endocrine ulcers:** Ellison-Zollinger syndrome, thyrotoxic goiter, parathyreosis
- **Congestion ulcers:** during the cardiovascular insufficiencies and different vasculitis
- **Medicamentous ulcers:** treatment with steroids and aspirin
- **Toxic ulcers:** exo- and endogenic intoxication
- **Chronic infectious ulcers:** in some specific inflammations *(tuberculosis, syphilis, leprosy etc.)*
- **Stress ulcers:** shocks, burn disease *(Curling ulcers)*, sepsis, severe operations, CNS lesions *(Cushing ulcers)*
- **Allergic ulcers, etc.**

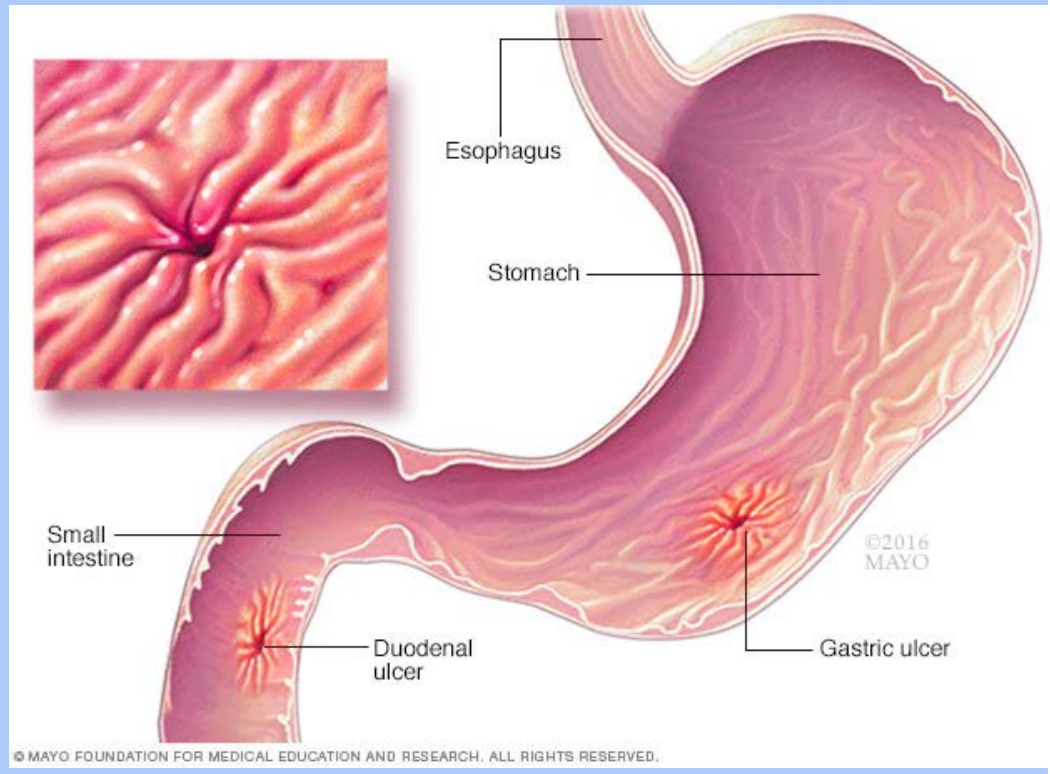
Peptic (Chronic) Ulcer Disease

- Peptic ulcers are chronic, relapsing, usually solitary lesions
- Most often diagnosed in middle-aged to older adults
- Occur in any portion of the GIT exposed to the aggressive action of acidic peptic juices
- There are 3 characteristic localization of peptic ulcers:

1. Ulcer of gastric body – ***Mediogastral ulcer***
2. Pyloric ulcer of stomach – ***Pyloroantral ulcer***
3. Ulcer of duodenum - ***Duodenal ulcer: bulbar and postbulbar***

- There are 2 types of peptic ulcers according to the pathogenetic features:

1. Ulcer of gastric body – ***Mediogastral ulcer***
2. ***Pyloroduodenal ulcer*** (most common type)



Peptic (Chronic) Ulcer Disease
Etiology and Pathophysiology

- Some acid does seem to be essential for a gastric ulcer to occur.
- Under specific circumstances the mucosal barrier can be broken and HCL freely enters the mucosa and injury to tissues occurs.
- This results in cellular destruction and inflammation.
- Histamine is released:

 - vasodilatation, increasing capillary permeability

 - further secretion of acid and pepsin

Peptic (Chronic) Ulcer Disease

Pathogenetc factors:

- **Infection:** *H. pylori* is found in 90% of duodenal and 65% of gastric ulcer patients.
- **Neuroendocrine factors:** The secretion of gastric juices is under the neuroendocrine control, which becomes dysregulated in peptic ulcer patients.
- **Local mucosal factors:** Drugs such as NSAIDs reduce the secretion of prostaglandins and damage the mucosal barrier.
- Alcohol, spicy food, and substances that stimulate acid secretion may play a pathogenetic role.

	Pyloro-duodenal	Mediogastral
Appearance	More than 4 times	Few time
Age	Young and middle-age	Older adults
Sex	Mainly males	Mainly females
Condition of adjacent tissue	Normal	Chronic gastritis
Gastric acidity	High acidity	Low acidity
Blood group	Persons with usually I blood group	Persons with usually II blood group

Peptic Ulcer Disease
Morphogenesis

EROSION — Damage of the covering mucosal epithelium

↓

ACUTE ULCER — Develops as a result of penetration of the necrotic process into the deep layers of gastric wall

↓

CHRONIC ULCER — Last phase of disease

Peptic Ulcer Disease

- Pathological changes have penetrated and destroyed the **muscular layer**, with alternation of recidivating and remission periods.
- Have a **typical distribution**: 95% are found on the *posterior end of the lesser curvature* and most occur in the *pylorus*.
- Almost is *solitary*, but in 5-10% a second ulcer may be found on the anterior aspect of the pyloric canal.

Gross pathology:

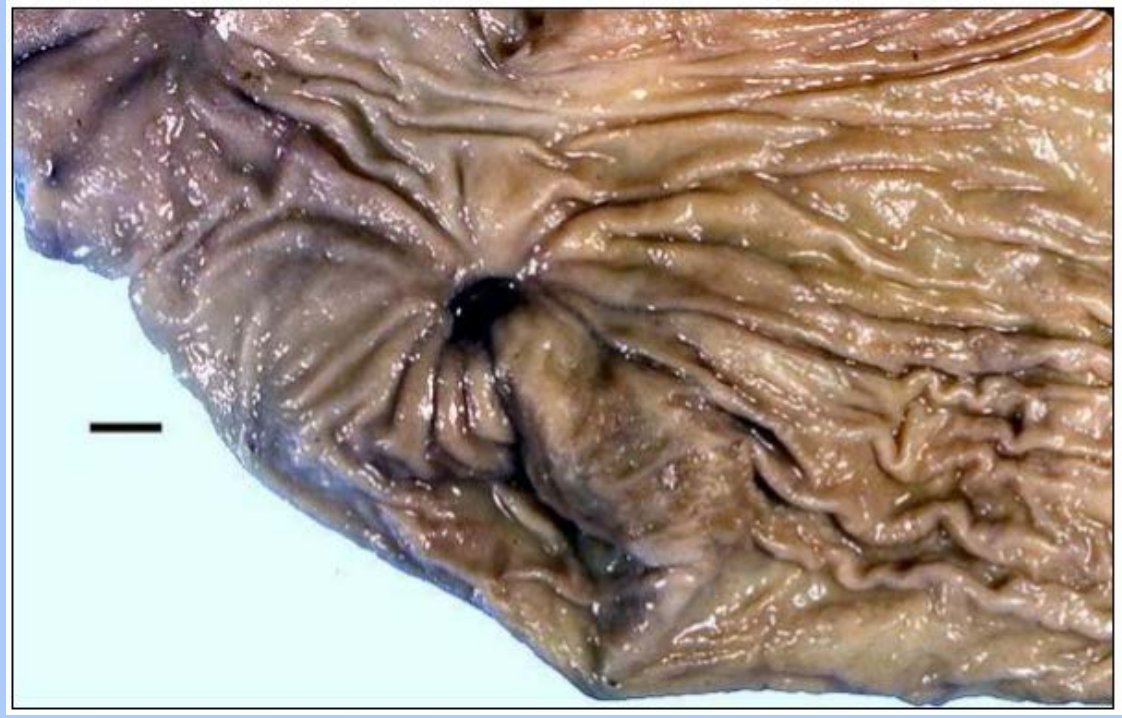
- Sharply demarcated round or oval defect of mucosa - ***ulcus rotundum***
- Most ulcers are small, ~ 1.5-2 cm.
- The bottom is smooth (HCL and pepsin keep it “clean”), but it may be covered by blood.
- Borders are sharp, but around the long-lasting lesions, the adjacent mucosa may show some puckering due to fibrosis.

Peptic Ulcer Disease
Morphology

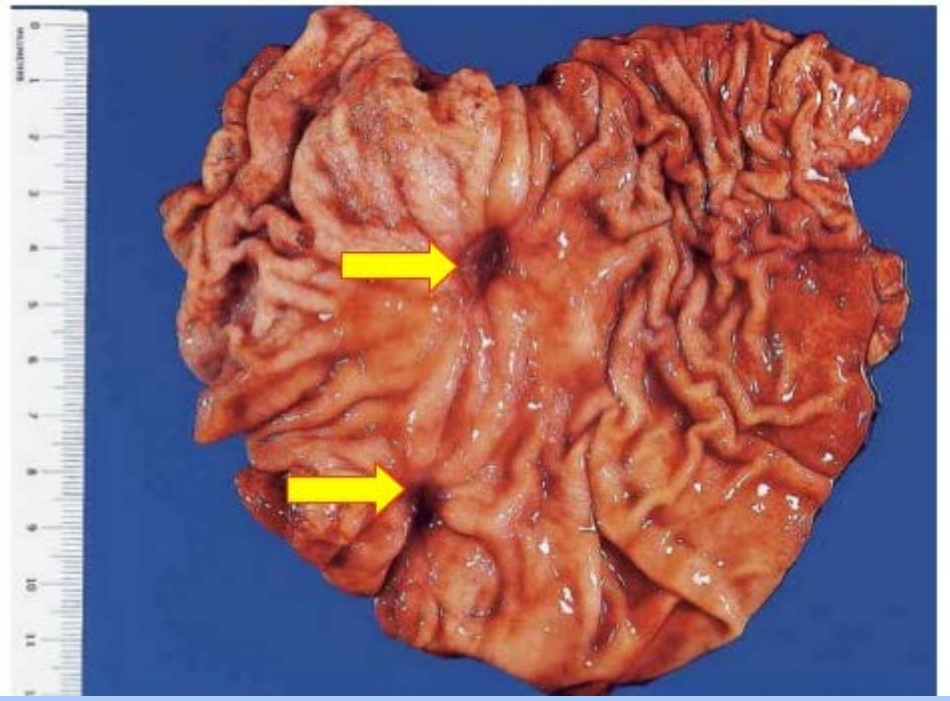
- Vessels trapped within the dense scar tissue replacing muscles, show **endarteritis.**
- The crater fills with granulation tissue, followed by *reepithelization* from the margins by healing.
- Extensive *fibrous scarring* occur.
- The fibrozed ulcer margins can be evaluated above the surface, and give rise to phenomenon ***"callous ulcer".***
- Frequently the ulcerative process extends to the serosa or even beyond it.
- Extension of the inflammation to the serosa may result in adhesion to adjacent organs, such as *pancreas.*
- The ulceration may burrow into the affected organ.
- The remainder of the stomach frequently shows the features of *chronic atrophic gastritis.*
- *Healing* appears in 6-8 weeks.

Peptic Ulcer Disease
Gross Pathology

Gastric Peptic Ulcer



Double Benign, Chronic, Gastric Peptic Ulcer



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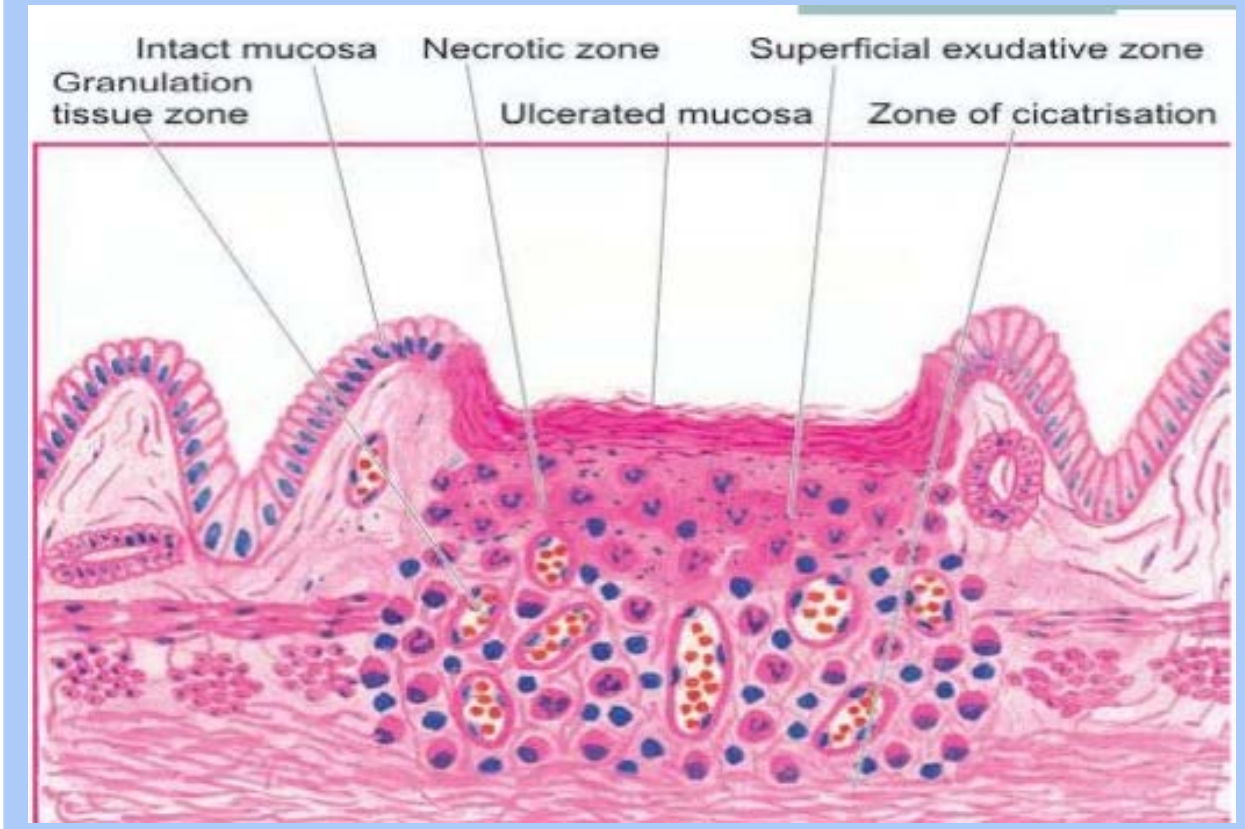
Histological layers of Chronic Peptic Ulcer during activation period

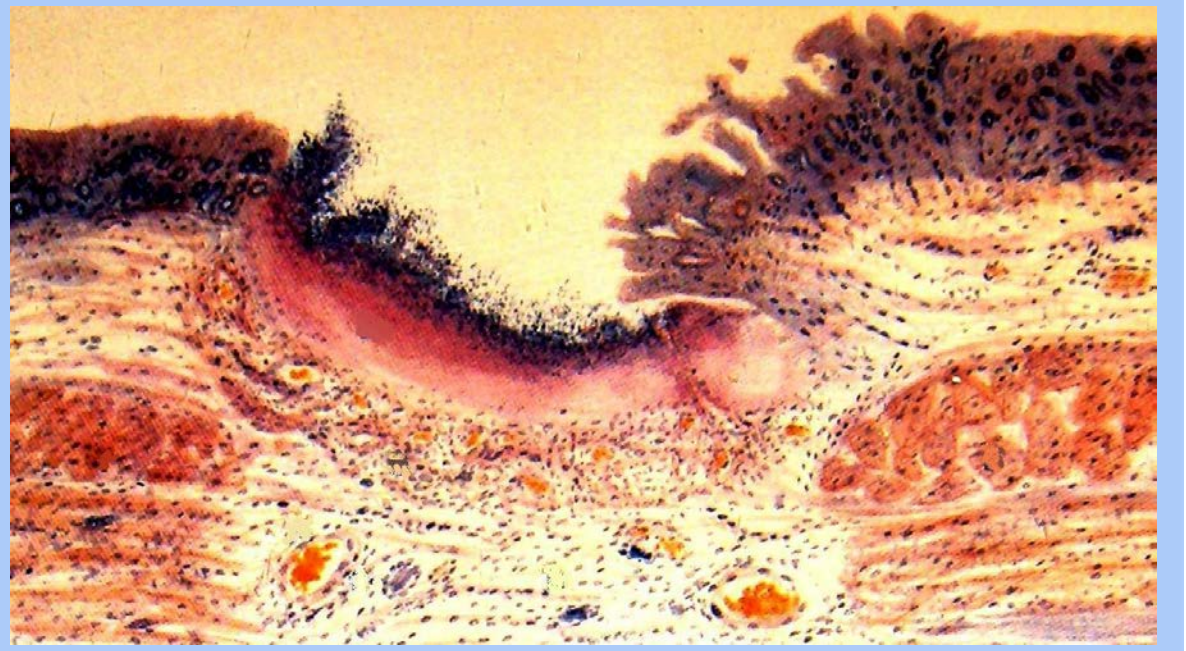


1 – **Superficial exudative zone** – purulent-necrotic zone or ″dusty layer″

2 – Wide zone of **fibrinoid necrosis**

3 – **Granulation tissue zone** – clinically related to the **red scar**

4 – Fibrous, collagenous **scar** – clinically related to the **white scar**



https://www.slideshare.net/utsav1712/peptic-ulcer-pathology

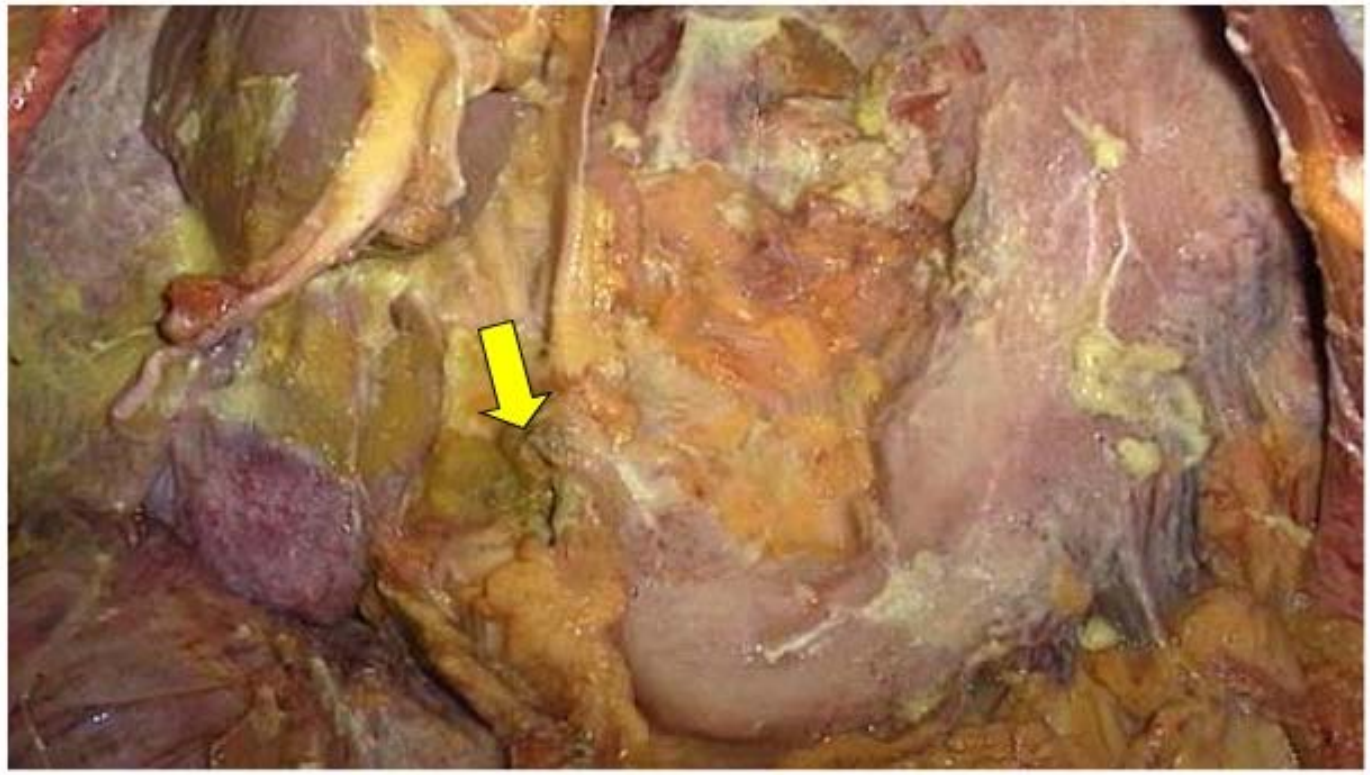
Peptic Ulcer Disease
Complications

I. **Destructive (necrotic) complications: hemorrhage, *perforations and penetration*.**

- **Hemorrhage –** bleeding is the chief complication, occurring due to fibrinoid necrosis of the vessels in the base of ulcer.
- It is evident in 1/3 of patients and may be life-threatening.
- Most commonly it is of minor degree, which can only be detected by testing the faeces for iron.
- Such the chronic bleeding leads to ***anemia***.
- More marked hemorrhage may actually cause discoloration of the faeces – ***"tarry stools"*** or ***melena*** due to the formation of iron sulphides.
- ***"Coffee-grounds"*** vomiting may also occur.

Peptic Ulcer Disease
Complications

Perforation Peritonitis



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Peptic Ulcer Disease
Complications

II. Inflammatory complications: *periulcerous gastritis, perigastritis; duodenitis and periduodenitis.*

III. Sclerotic complications.

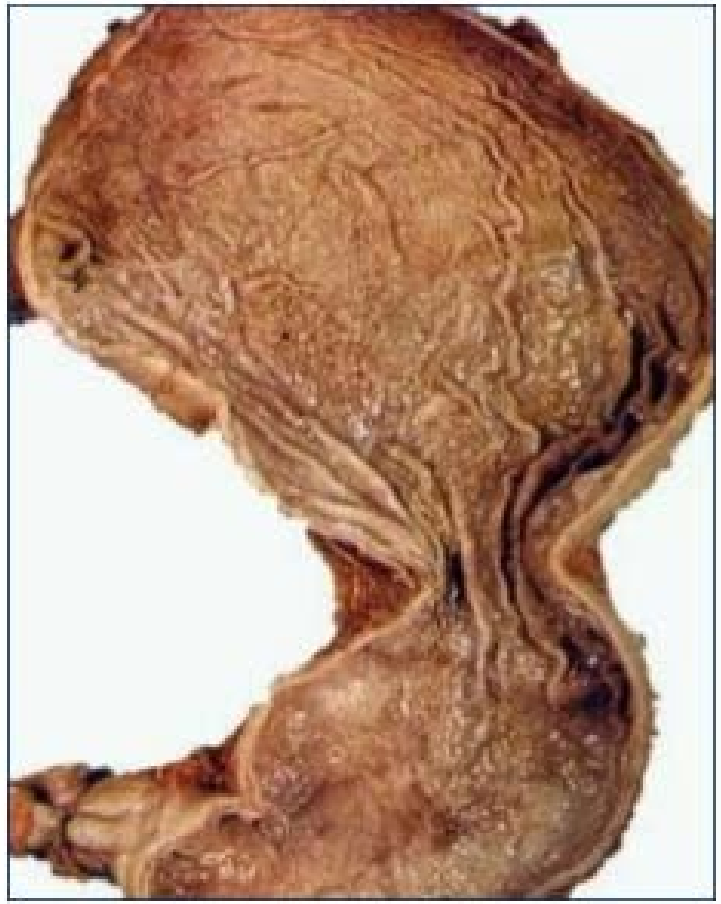
- Healing of large ulcers may result in muscle drawing up by scar tissue, which shows the stellate contractions.
- *"Hourglass"* stomach
- Pylorostenosis (obstruction)
- Duodenostenosis
- Deformation of duodenum

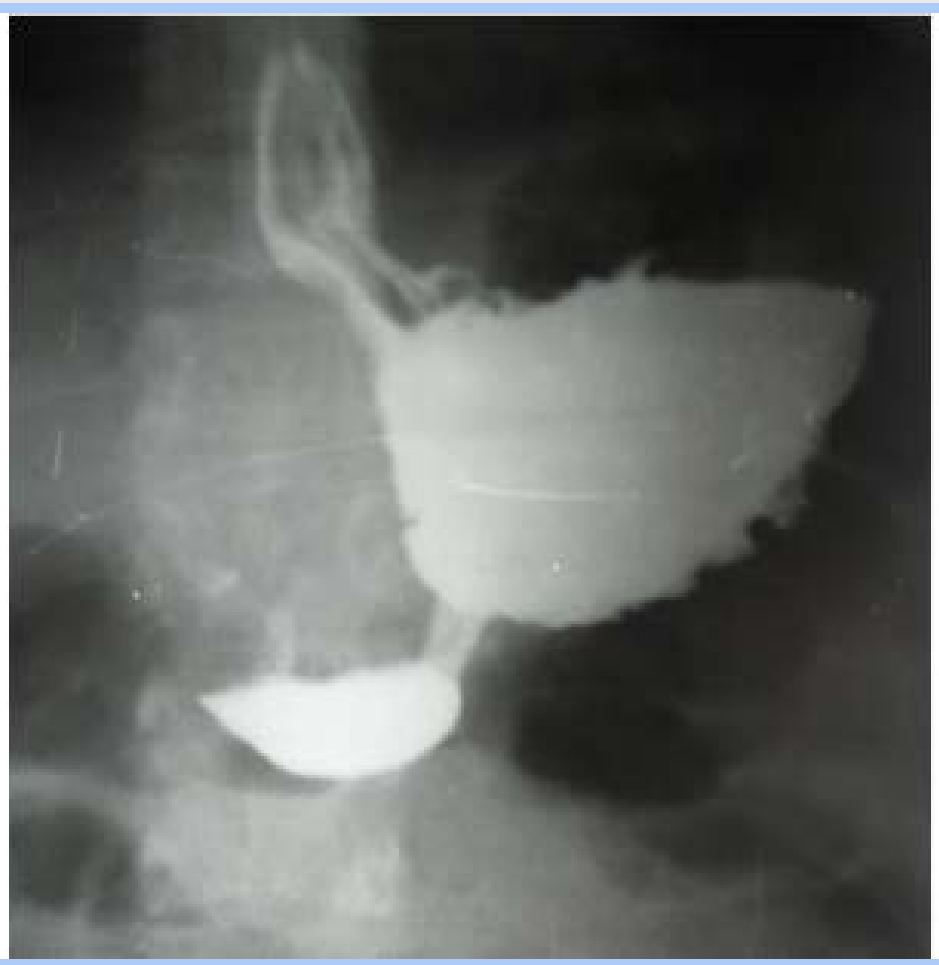
IV. Malignisation – development of the carcinoma.

V. Common and alimentary complications: alimentary cachexia, peptic disorders, metabolic disturbances, etc.

VI. Combined complications.

Complications of the Peptic Ulcer Disease
"Hourglass" stomach





Due to chronic peptic ulceration there is fibrosis and contracture of the stomach leading to *an* ***hourglass shape*** as well as altered mobility.

https://www.slideshare.net/mohamedmouradaly/imaging-53086508

Intestinal diseases

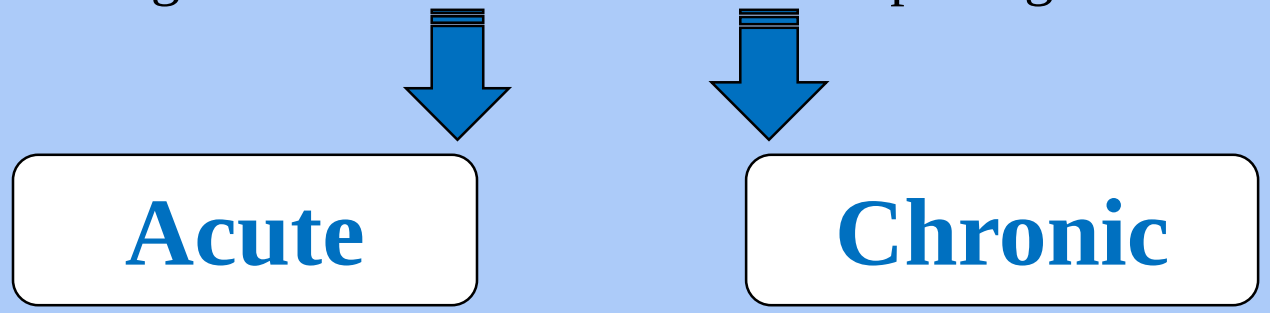
- **Inflammatory diseases** *(enteritis, colitis, appendicitis)*
- **Degenerative diseases** *(enteropathies)*
- **Vascular diseases** *(acute and chronic ischemic diseases, angiodysplasia, hemorrhoid, etc.)*
- **Tumors** *(polyps, carcinomas)*
- **Developmental abnormalities** *(megacolon, megasigma, diverticules, stenosis, atresia)*

Enteritis

- Inflammation of the small intestine

Classification

According to the clinical course and morphological features:



According to the localization of the inflammatory process:

- **Duodenitis**
- **Jejunitis**
- **Ileitis**

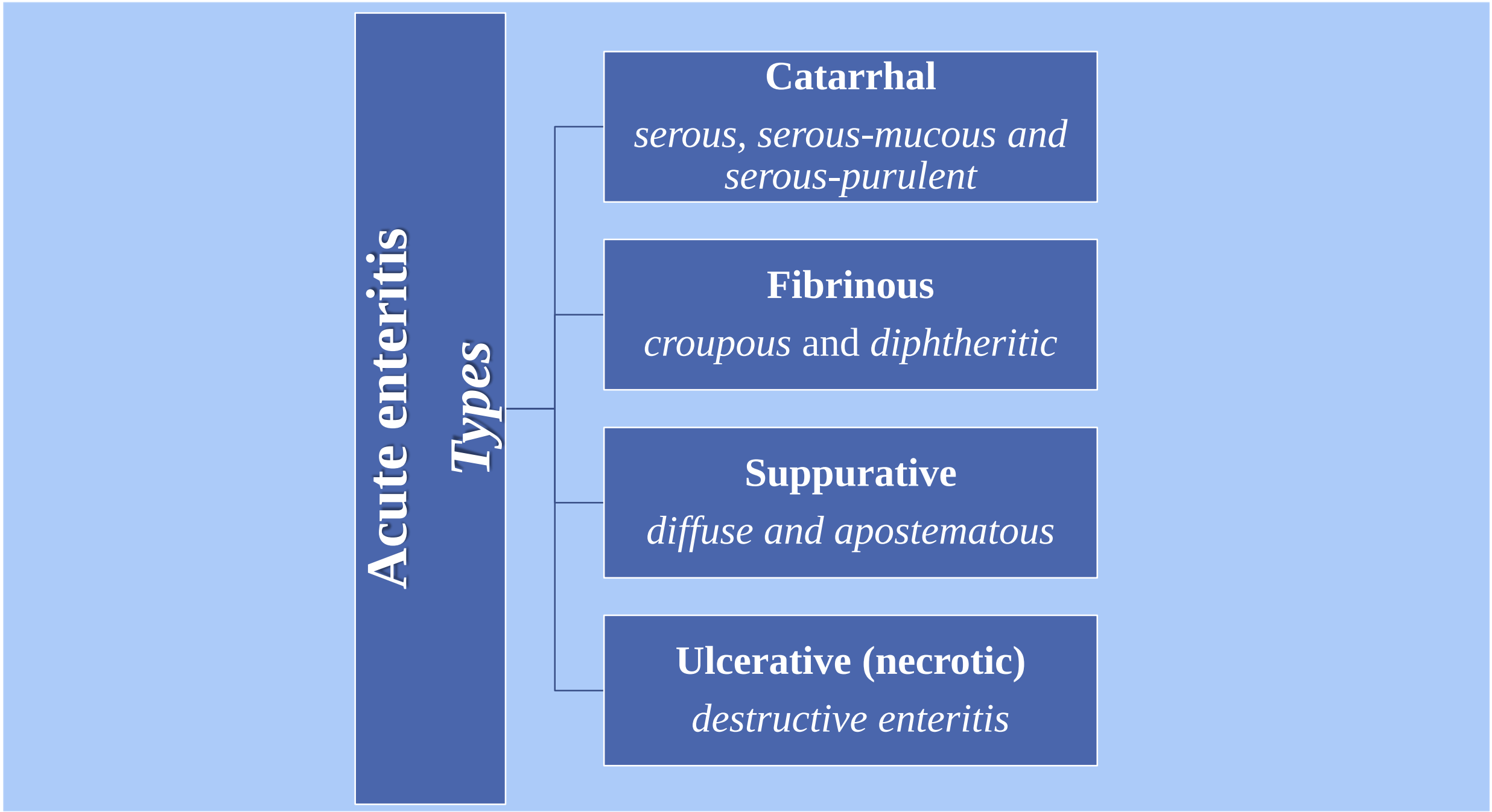
Acute enteritis
Etiology

- **Infections** – typhoid, cholera, staphylococcal and viral infections, sepsis, etc
- **Toxic agents** – alimentary toxinfections *(salmonellosis, botulism), poisoning (chemical poisons, toxicant funguses, etc)*
- **Alimentary agents** – hyperalimentation, the use of rasping food, spices, strong alcohol drinks
- **Allergic agents** – idiosyncrasy to foodstuff, medicines

Acute enteritis
Signs and Symptoms

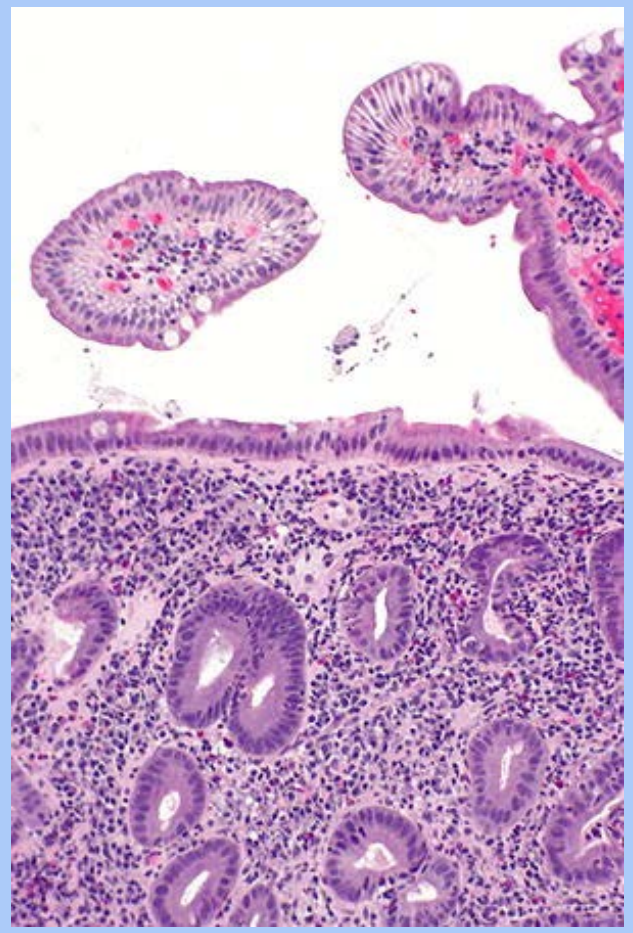
- Diarrhea
- Nausea and vomiting
- Loss of appetite
- Abdominal cramps and pain
- Pain, bleeding, or mucus-like discharge from rectum
- Fever
- Dehydration
- Weight loss

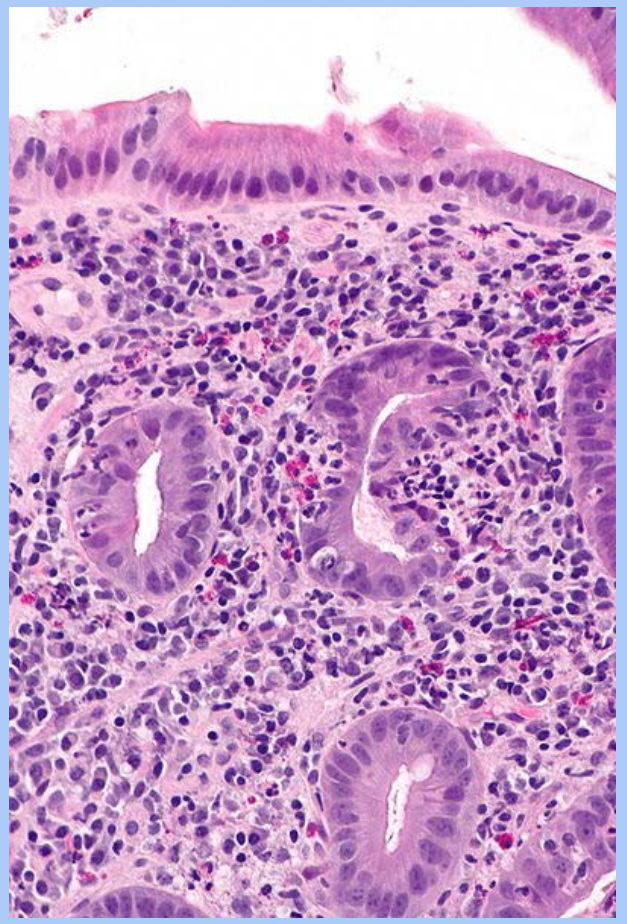
https://www.healthgrades.com/right-care/digestive-health/enteritis

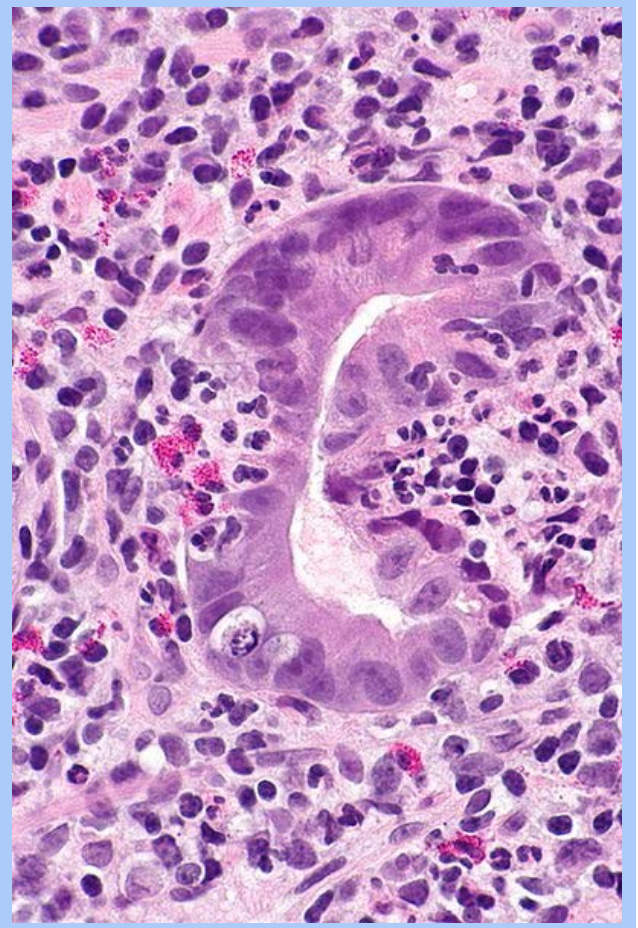

Acute enteritis
Types
Catarrhal
serous, serous-mucous and serous-purulent
Fibrinous
croupous and diphtheritic
Suppurative
diffuse and apostematous
Ulcerative (necrotic)
destructive enteritis

Acute duodenitis
Histopathology

neutrophils - "found without searching",
eosinophils - "found without searching",
plasma cells (increased),
intraepithelial lymphocytes







https://librepathology.org/wiki/File:Acute_duodenitis_--_high_mag.jpg

Chronic enteritis
Etiology

- Irregular alimentation
- Dietary disturbances
- Alcohol abuse
- Industrial, domestic and medicamentous poisoning
- Food allergy
- Helmintosis
- Endogenic autointoxications, etc.

Chronic enteritis

Chronic non-atrophic enteritis

Chronic superficial enteritis

- degenerative changes
- destruction of basement membrane
- sclerotic adhesions
- lymphocytic infiltration of the villi stroma

Chronic diffuse enteritis

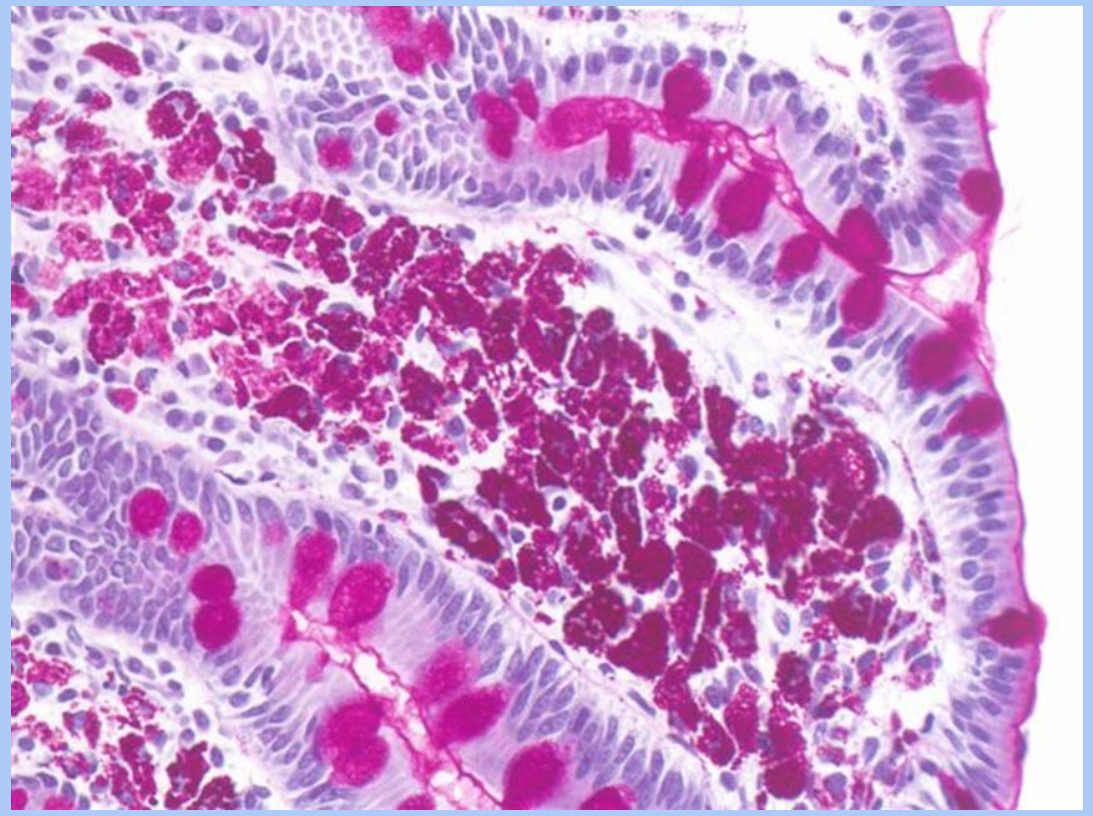
morphological changes occupy all of the mucosa

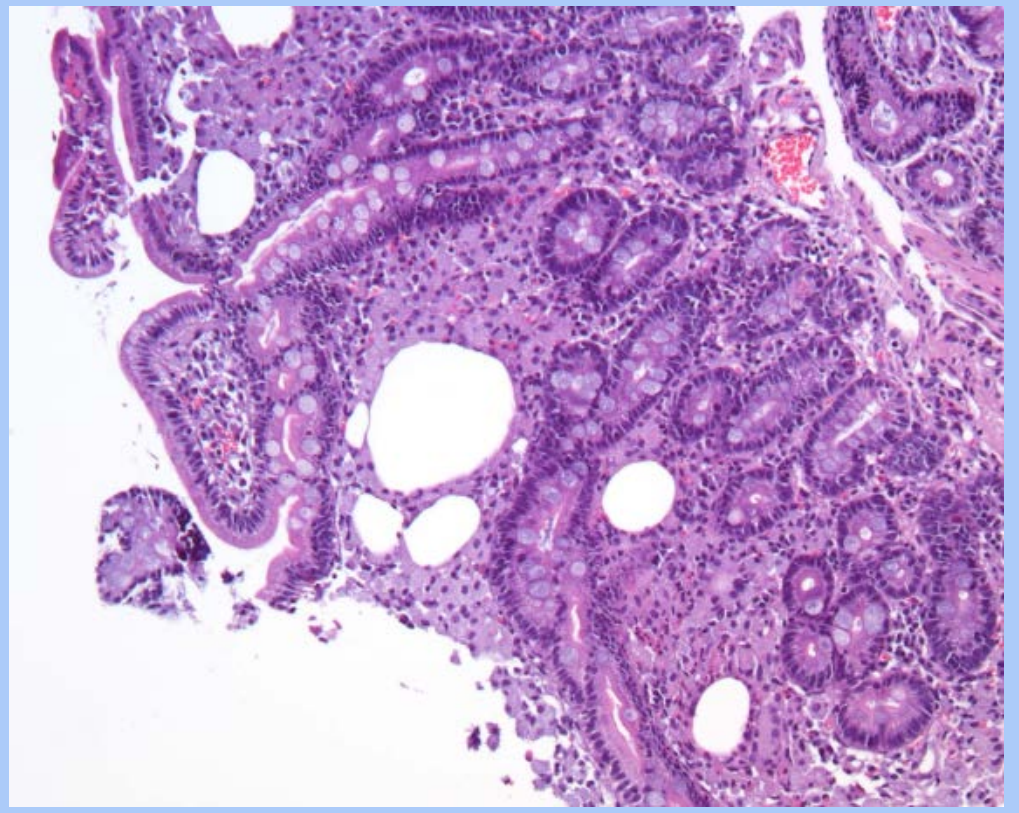
Chronic atrophic enteritis

Whipple's disease
(Intestinal lipodystrophy or Idiopathic steatorea)

- **Whipple's disease** is a rare, systemic infectious disease caused by the bacterium ***Tropheryma whipplei*.**
- First described by **George Hoyt Whipple** in 1907.
- Whipple’s disease typically presents in middle-aged Caucasian patients, with a striking **male to female predominance of 8:1.**
- Can affect virtually any organ system.
- **Typical signs and symptoms:** low-grade fever, chronic weight loss, arthritis, malabsorption, and lymphadenopathy.
- Many patients also have significant **neuropsychiatric manifestations**.
- The **polyarthritis** of Whipple’s disease is often the first manifestation and may precede gastrointestinal symptoms by years.
- **Immunosuppressive therapy** may significantly exacerbate both the intestinal and systemic manifestations of the disease.

Whipple's disease
Histopathology





- Characteristic lesion is massive infiltration of the lamina propria and submucosa by **foamy macrophages**, that are packed with bacilli, which are strongly ***PAS-positive.***
- The lamina propria often contains **small foci of fat** and overlying **vacuolization of enterocytes.**

http://www.pathologyoutlines.com/topic/smallbowelwhipple.html

Appendicitis

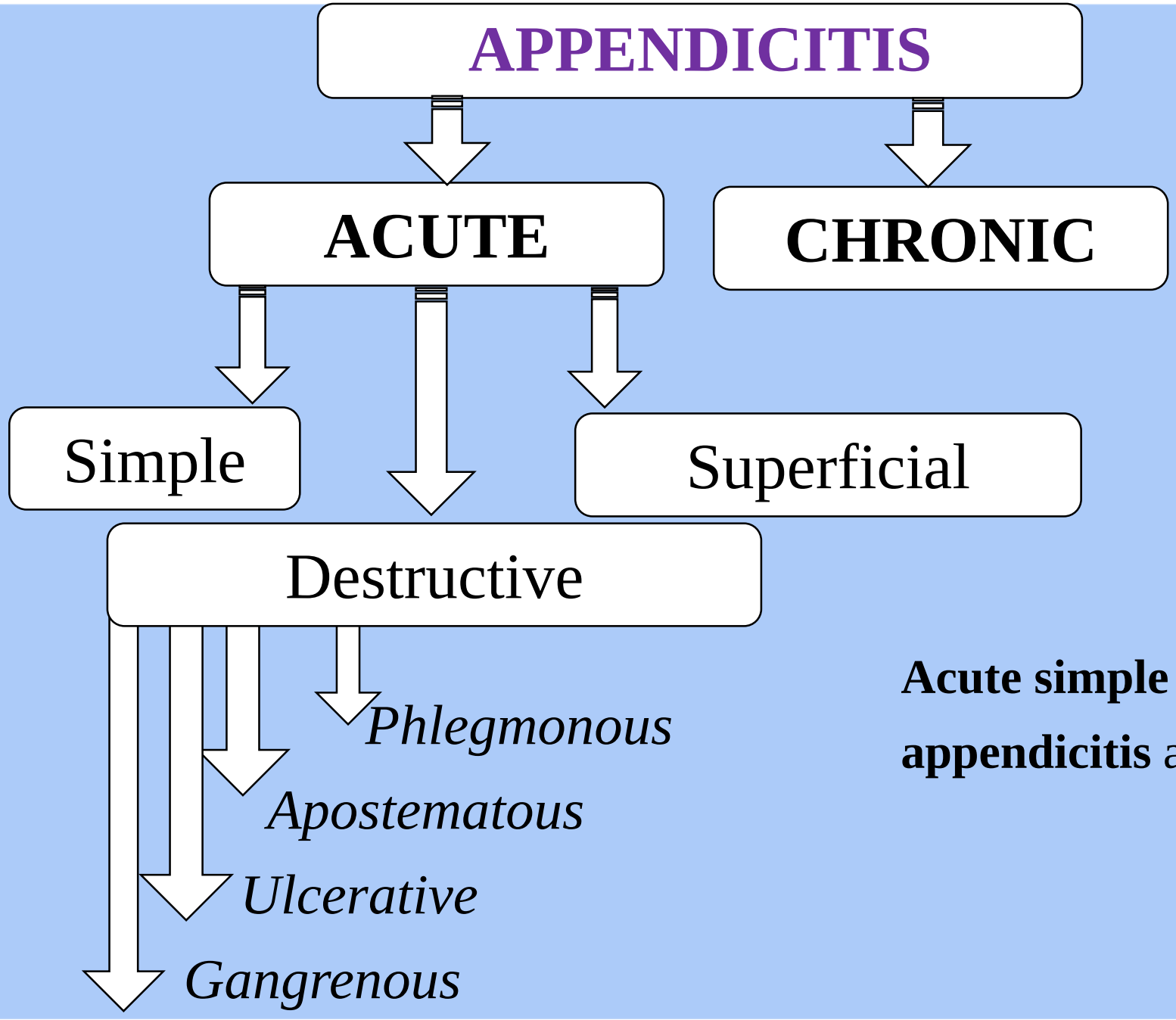
◦ Inflammation of the appendix vermiformis

Etiology

Autoinfection, is related with intestinal microflora (especially *E. coli*, *enterococci*, etc.)

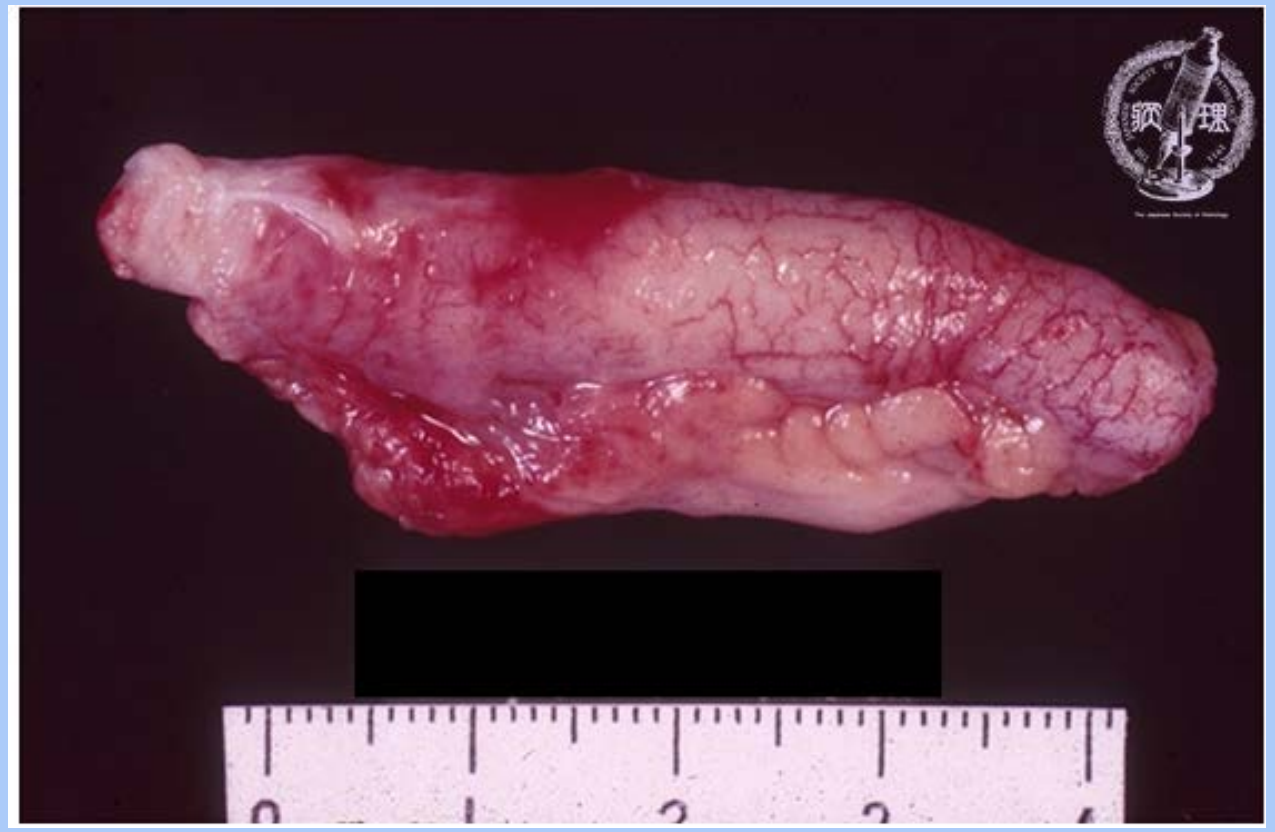
Background

• Impaction of lumen by the fecal and bile concretions, rasping food, foreign bodies, wound accumulation and etc.
• Disturbances in blood and nerve supply of mucosa
• Spasm of the lumen or entering



Acute simple and Acute superficial appendicitis are reversible processes

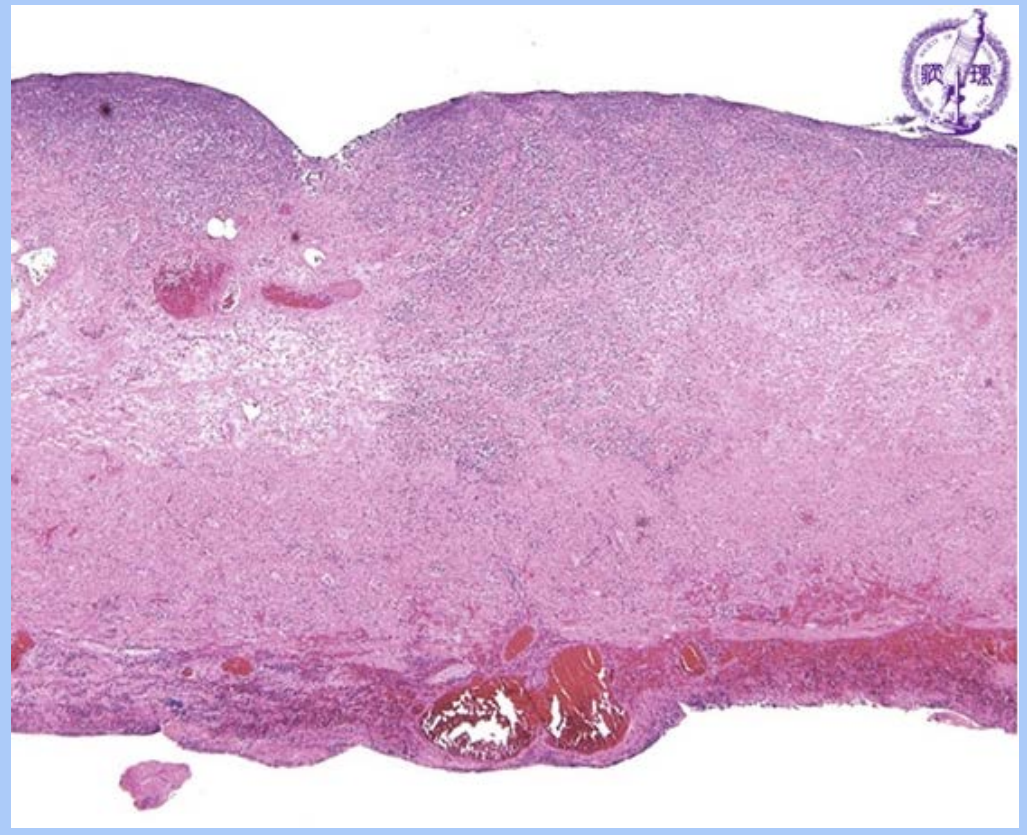
Acute phlegmonous appendicitis



Gross appearance (unfixed specimen):

- The appendix is swollen and red due to hemorrhage.

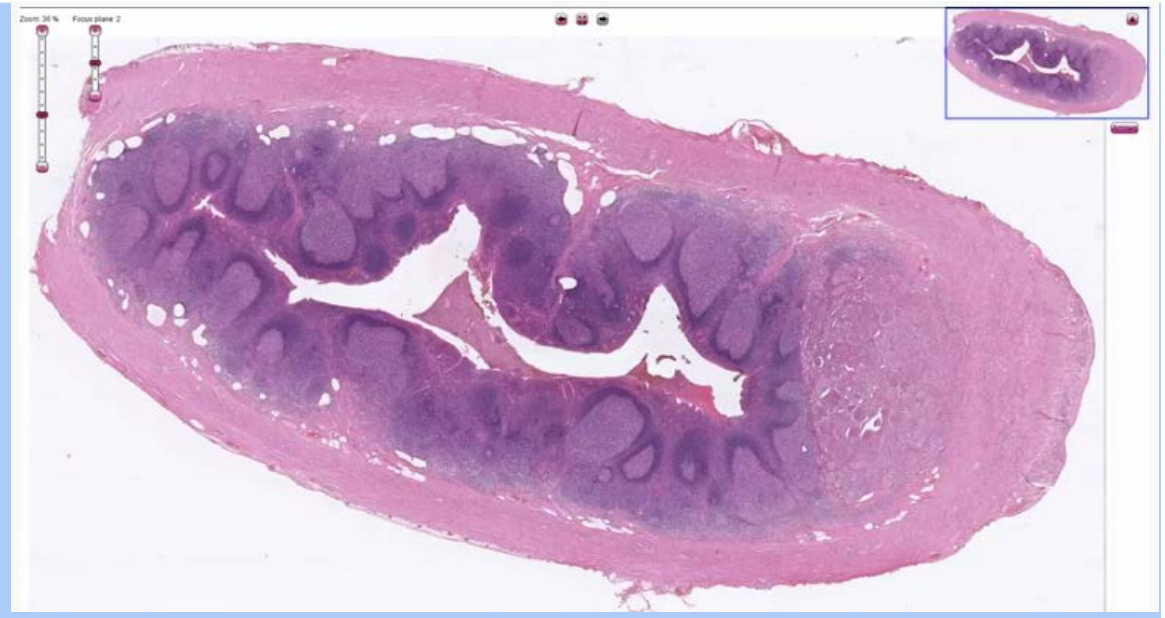
http://pathology.or.jp/corepicturesEN/09/c07/01.html

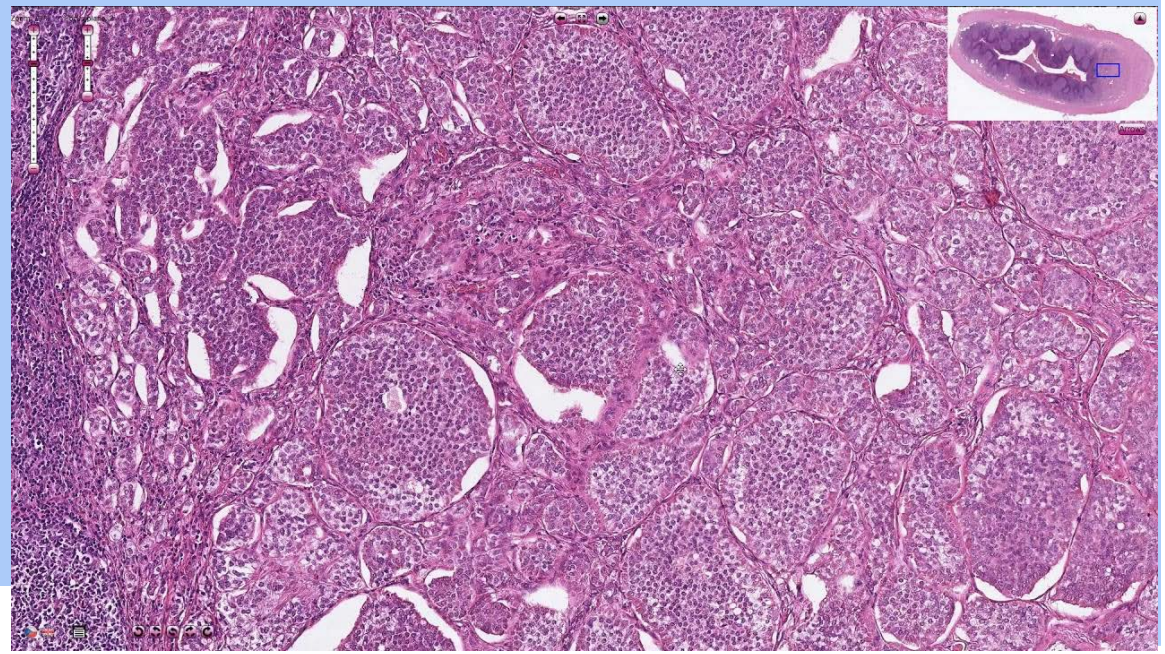


Microscopic view (H&E stain, low power):
The epithelium is denuded and there is marked severe inflammation. Inflammation and hemorrhage spans the entire appendix wall.

http://pathology.or.jp/corepicturesEN/09/c07/03.html

Appendiceal carcinoid

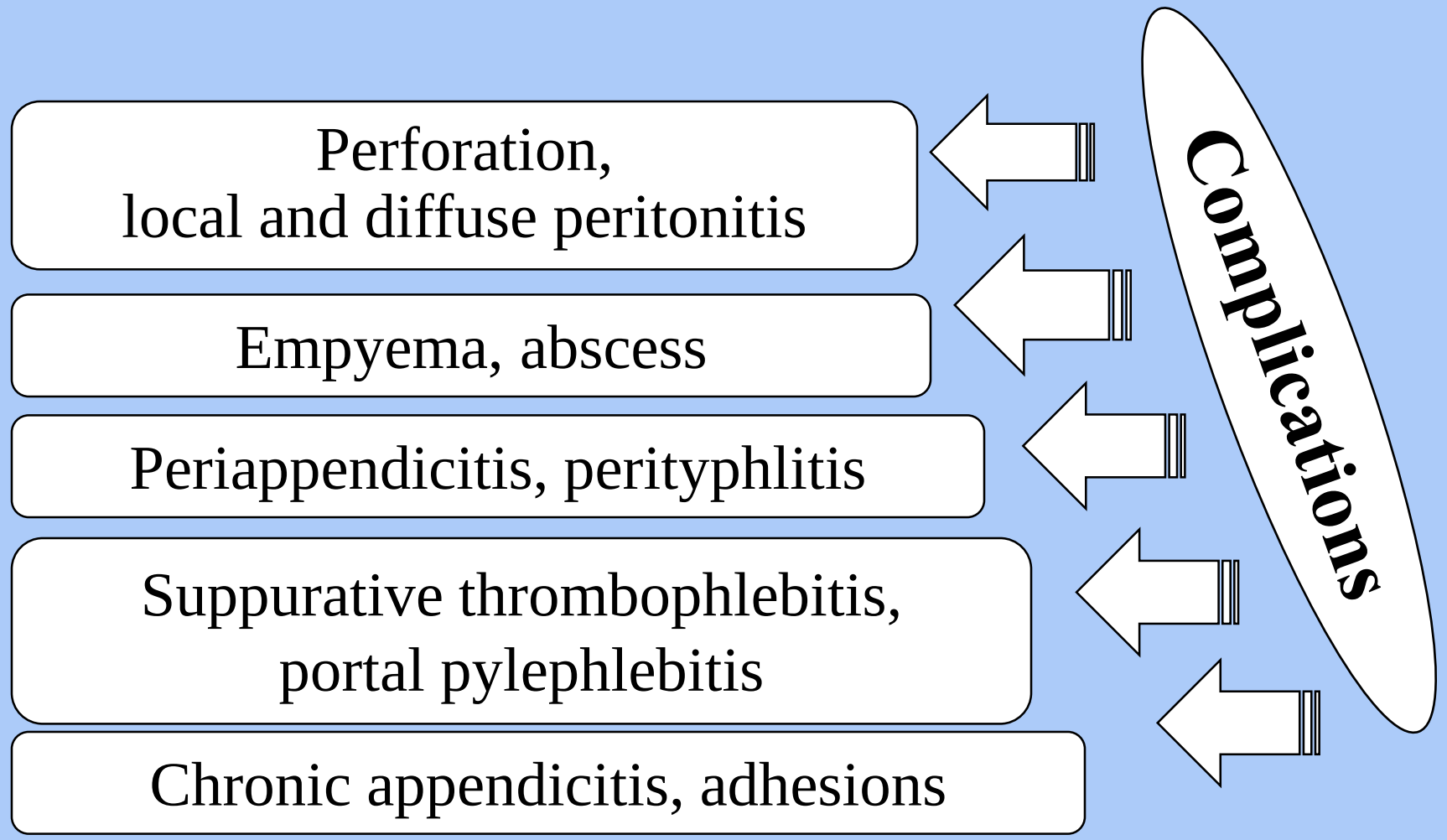




https://www.youtube.com/watch?v=aHY9h1k1W18

https://commons.wikimedia.org/wiki/File:Appendiceal_carcinoid_1.JPG

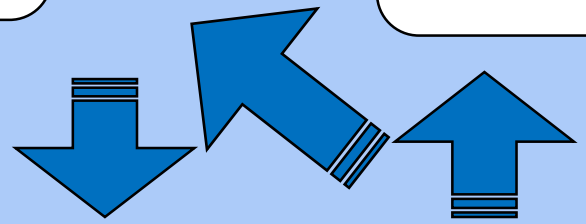
Complications of acute appendicitis due to the progression of destructive processes and the spread of the purulent process to other nearby organs and tissues.



Chronic appendicitis - develops as a complication of acute appendicitis.

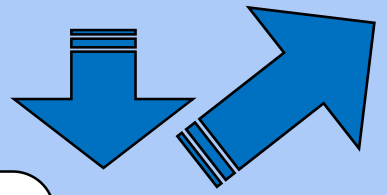
Atrophy of the tunics, sclerosis

Gangrene of the appendix

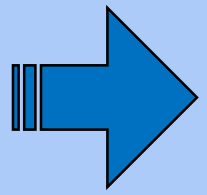


Dyskinetic disturbances

Activation of the inflammation

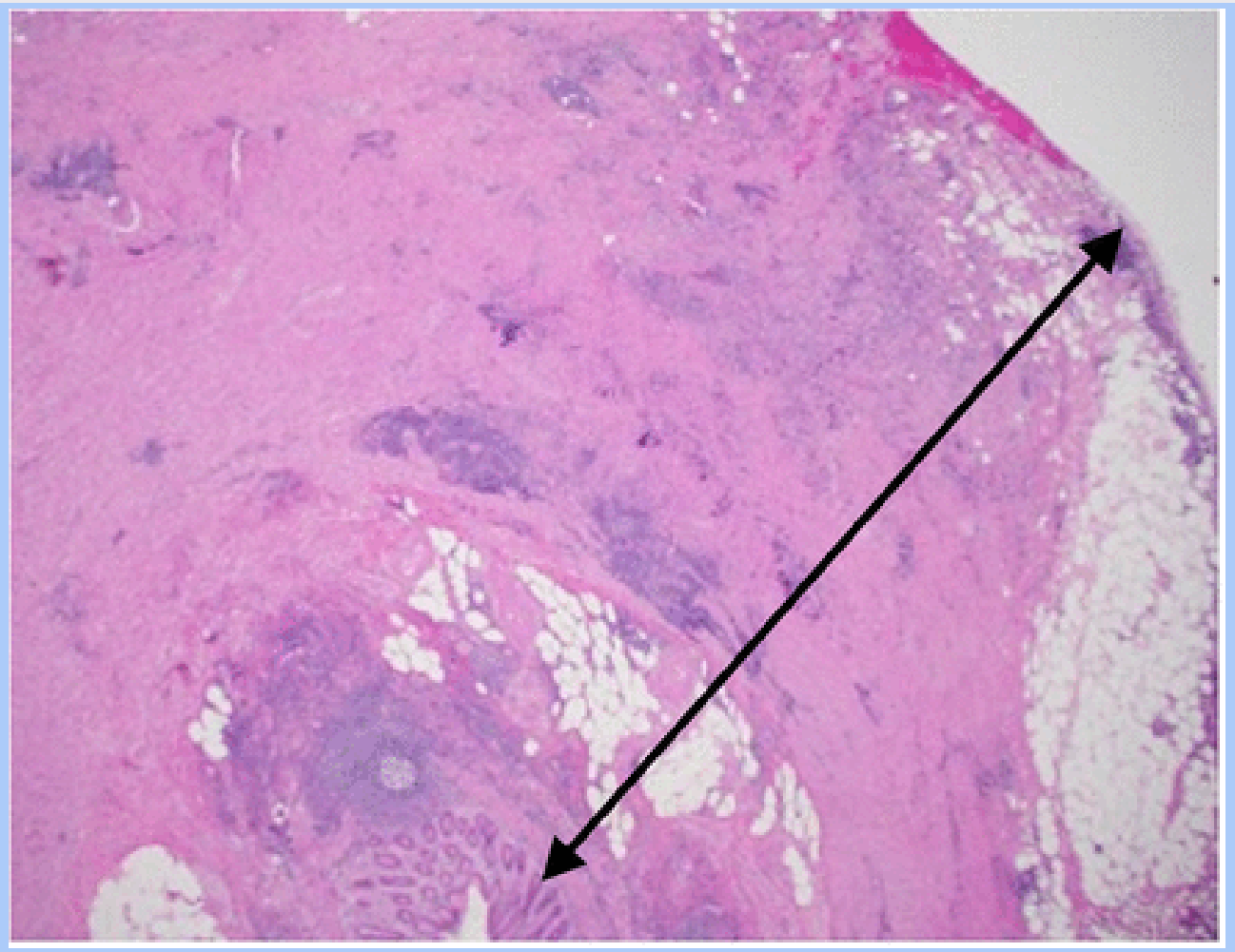


Accumulation of content



Hydrops of the appendix

Chronic appendicitis
Histopathology



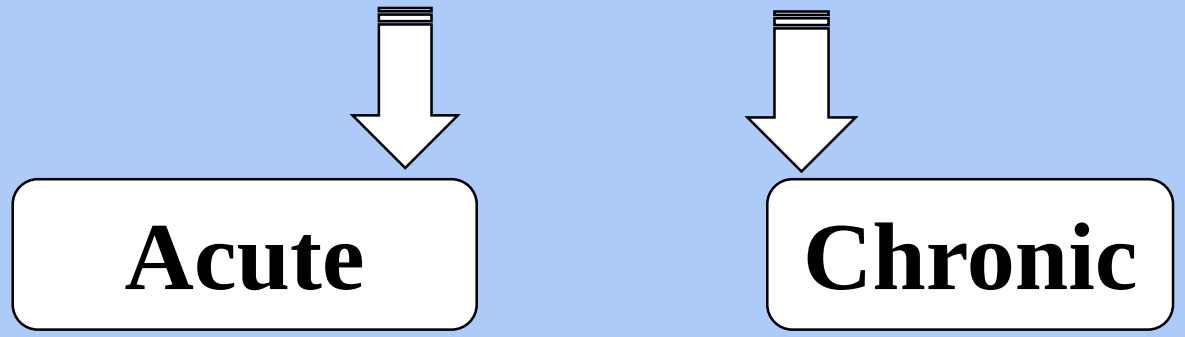
Prominent fibrosis and fatty infiltration of the wall of the appendix.

https://casereports.bmj.com/content/2016/bcr-2015-212485.full?sid=a897b9da-c4f1-46f8-92a7-1fac5ca2ad83

Colitis

- inflammation of the mucosa of large intestine.

According to the clinical course and morphological features



According to the location of inflammatory process:

- **Typhlitis** – inflammation of the caecum
- **Transversitis** – inflammation of the transverse colon
- **Sigmoiditis** – inflammation of the sigmoid colon
- **Proctitis** – inflammation of the rectum
- **Pancolitis** – inflammation of the all parts of large intestine

Acute colitis
Etiology

- **Infectious colitis** – dysentery, Salmonella, staphylococcal, E. coli, typhoid (colotyphus), fungi, parasites, tuberculosis, syphilitic, septic colitis, etc.

- **Toxic colitis** – uremic, gout, medicamentous and mercury chloride (Hg_2Cl) colitis, etc.

- **Toxic-allergic colitis** – alimentary and coprostatic colitis

Acute colitis
Types

- **Catarrhal colitis –** serous, mucous, suppurative and mixed
- **Fibrinous colitis –** croupous and diphtheritic
- **Purulent-phlegmonous colitis**
- **Hemorrhagic colitis**
- **Necrotic colitis –** there is a special type: ***gangrenous colitis***
- **Ulcerative colitis**

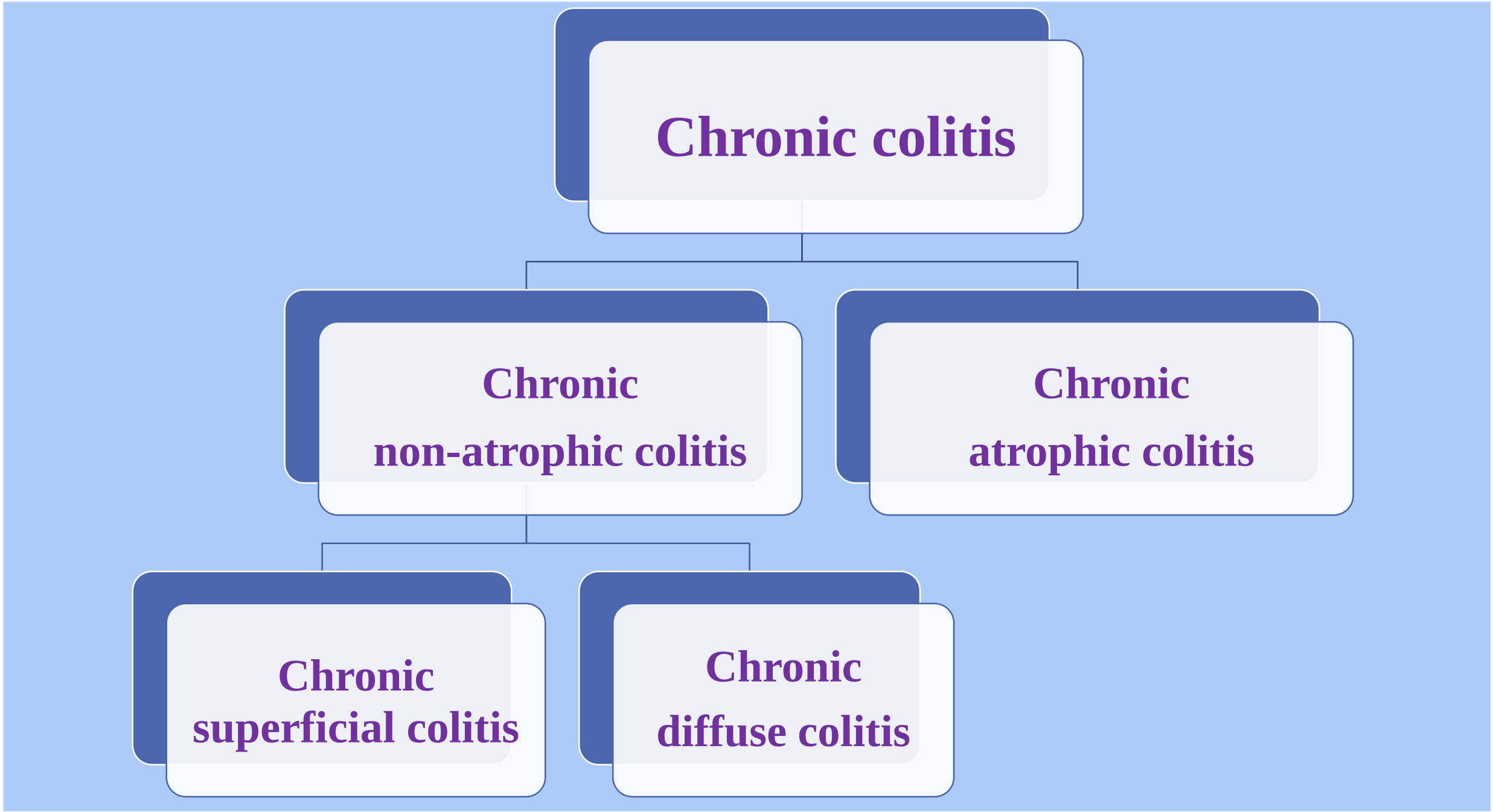
Chronic colitis

Pathogenic agents

- **Chronic colitis** develops as a result of acute colitis factors, but with low intensity and long-term consequences.

Morphology

- Lympho-leukocytic infiltration of the mucosa
- Diffuse sclerotic and sometimes atrophic changes
- Disturbances in regeneration processes


Chronic colitis
Chronic non-atrophic colitis
Chronic atrophic colitis
Chronic superficial colitis
Chronic diffuse colitis

Chronic colitis
Complications

- Sclerosis of large intestine, stenosis
- Spreading of inflammatory process into the periintestinal soft tissue and peritoneum
- Avitaminosis
- Cachexia
- Atrophic chronic colitis is a ***precancerous disease*** of large intestine.

Types of Chronic colitis *(clinical-morphological classification)*

1. **Ulcerative colitis**
2. **Crohn’s disease – granulomatous colitis**
3. **Indeterminate colitis** (between ulcerative colitis and colorectal UC)
4. **Ischemic colitis –** develops due atherosclerosis, diabetes, vascular surgery, systemic vascular diseases (i.e. scleroderma and rheumatoid arthritis), Wegener's granulomatosis, idiopathic lymphocytic phlebitis, amyloidosis, as a complication of birth control pill use.
5. **Obstructive colitis** - occurs mainly during adenocarcinomas.
6. **Other types of colitis:**

– **Nonspecific bacterial colitis** *(acute infectious-type colitis)*

– **Allergic colitis and proctitis –** are related to foods (particularly to cows’ milk) and are seen more commonly in infants and children.

– **Microscopic colitis:**

◦ ***Collagenous colitis*** **–** usually present clinically in middle-aged women as chronic watery diarrhea.

◦ ***Lymphocytic colitis***

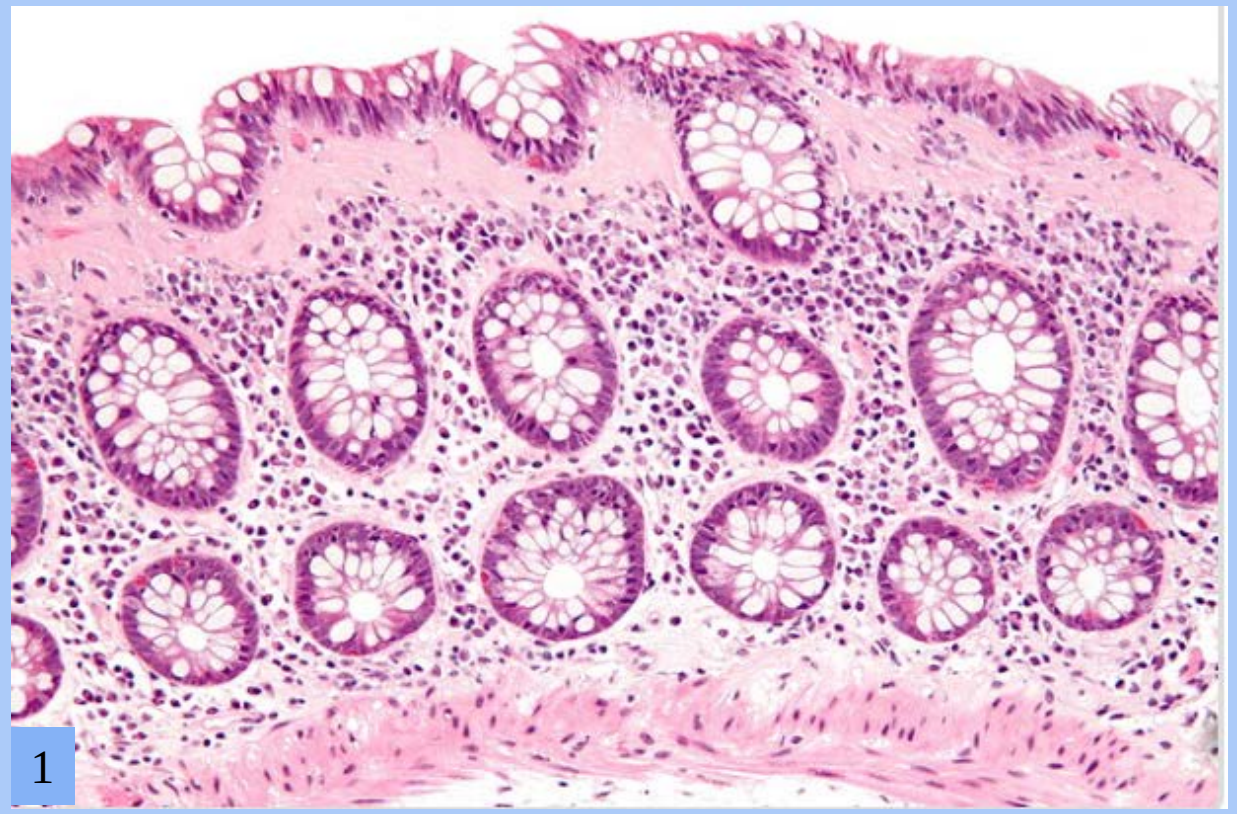
– **Focal active colitis**

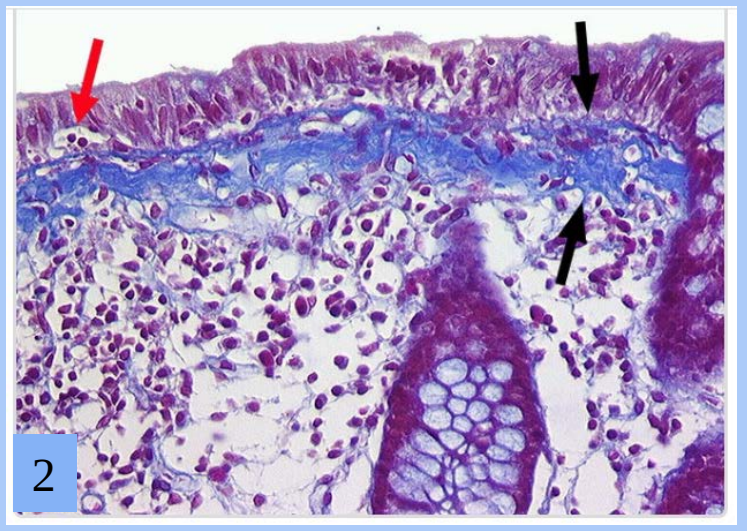
– **Pseudomembranous colitis -** mainly caused by *Clostridium difficile*.

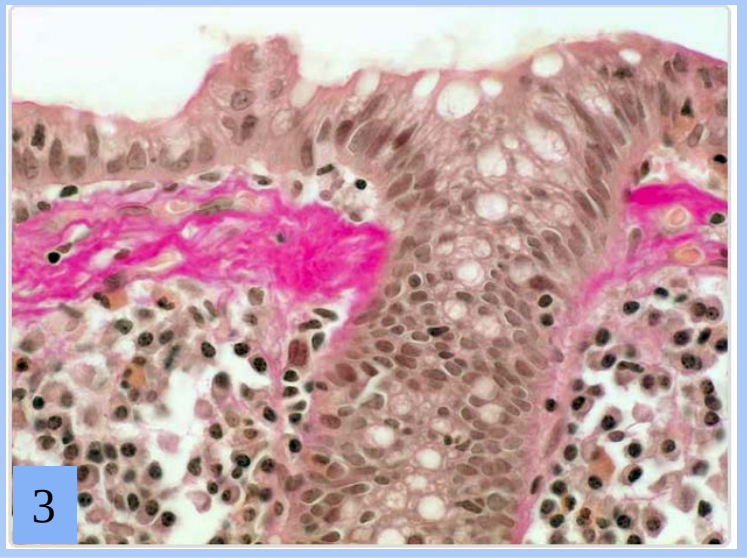
– **Amebic colitis** etc.

Rosai and Ackerman's Surgical Pathology

Collagenous colitis
Histopathology





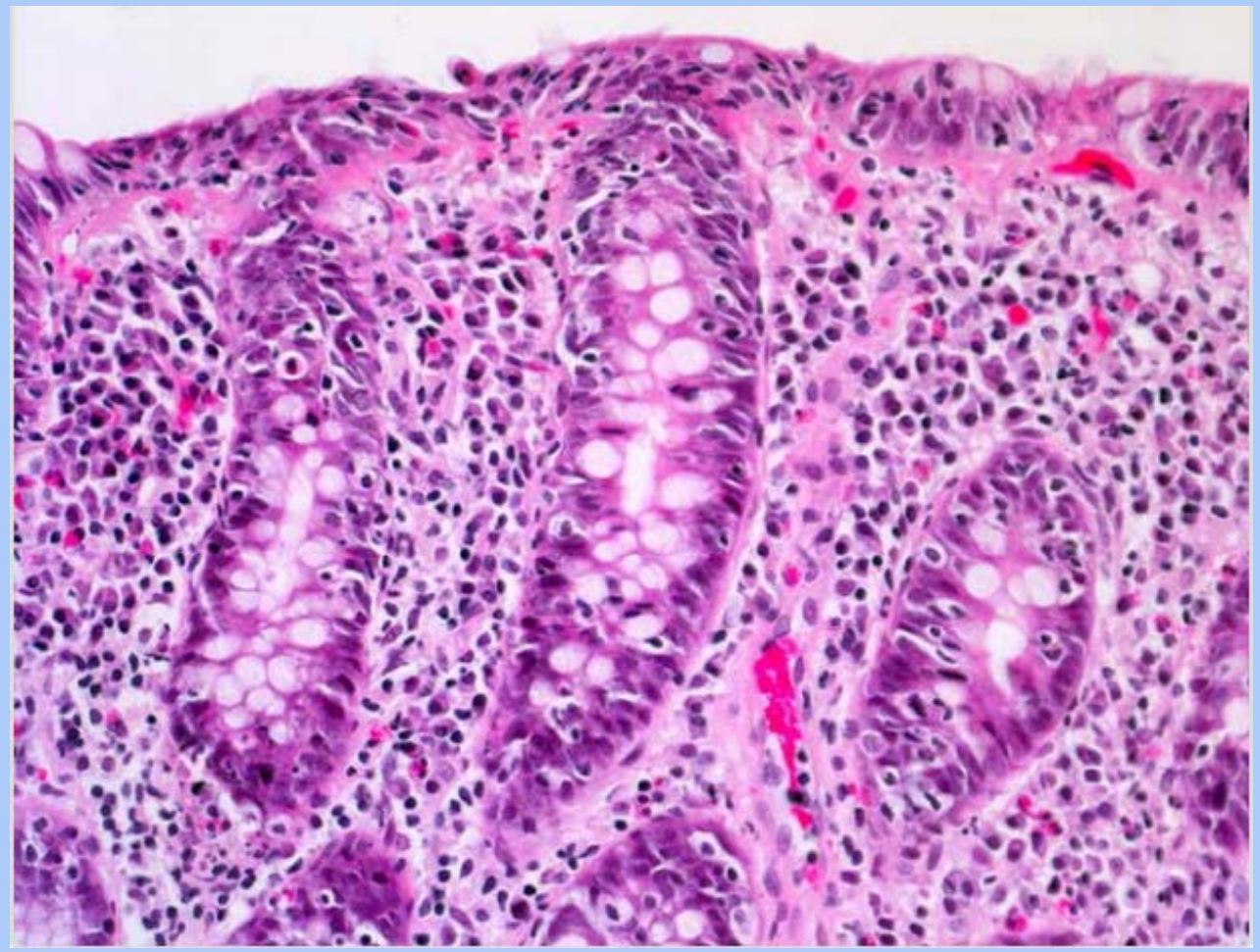


1 – H&E
2 – Trichrome stain
3 – Van Gieson stain

https://www.webpathology.com/image.asp?n=12&Case=1038

Lymphocytic colitis
Histopathology

- Surface epithelial damage
- Increased intraepithelial lymphocytes
- No increase in the thickness of subepithelial collagen
- Normal crypt architecture



https://www.webpathology.com/image.asp?case=1038&n=12

Ulcerative Colitis (UC)

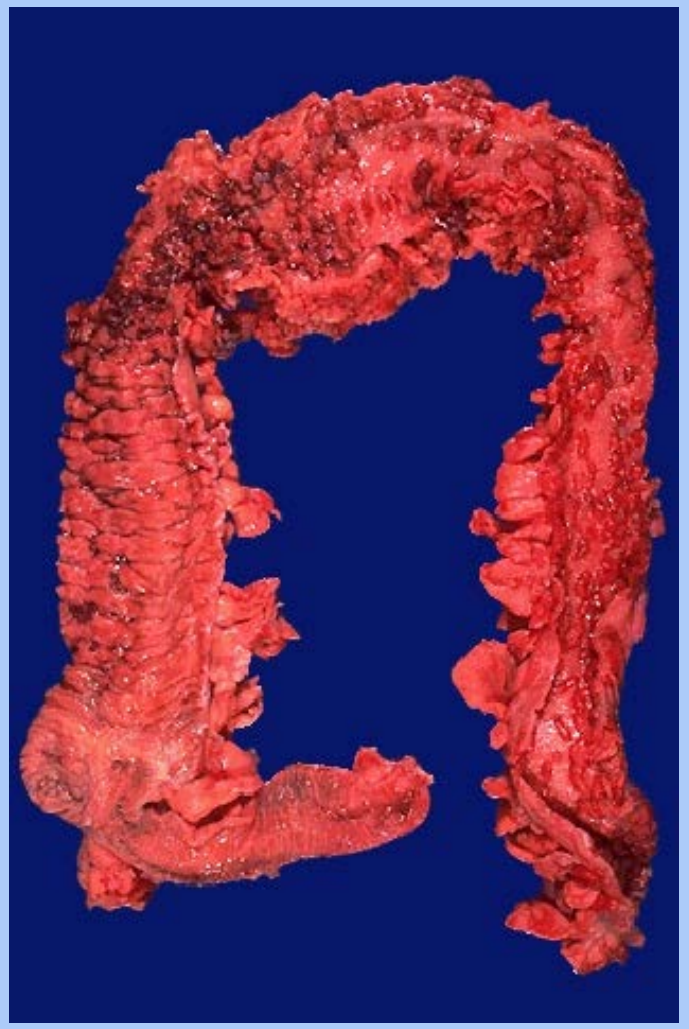
- **Synonyms:** *idiopathic ulcerative colitis, hemorrhagic colitis or ulcerative proctocolitis.*
- Chronic inflammatory disease of the colon and rectum with involvement of the intestinal mucosa and submucosa and ulcer formation.
- UC is more common in persons of Caucasian race, in women and in young persons.
- ***In active phase*** the suppurative, hemorrhagic and ulcerative colitis develop.
- ***In remission*** the sclerosis develop in this regions.
- As a result the large intestine undergoing of diffuse cirrhosis.
- By etiopathogenesis the **autoimmune disease** is considered.

Ulcerative Colitis (UC)

- ***Grossly:*** in the colon the typical pattern of *"**pseudopolyps**"* from severe inflammation and mucosal erosion are seen.
- In the acute form, the mucosal surface is wet and glaring from blood and mucus with numerous ***petechial hemorrhages***.
- ***Ulcers*** of various sizes can appear, they may be small, rounded and superficial or more irregular and somewhat geographic in configuration.
- The intramural nerve plexuses are damaged, the innervation of intestine is disordered, the trophical lesions starts – ***ulcerative pancolitis***.
- The wall of large intestine is thickened as a result of ***sclerosis***.

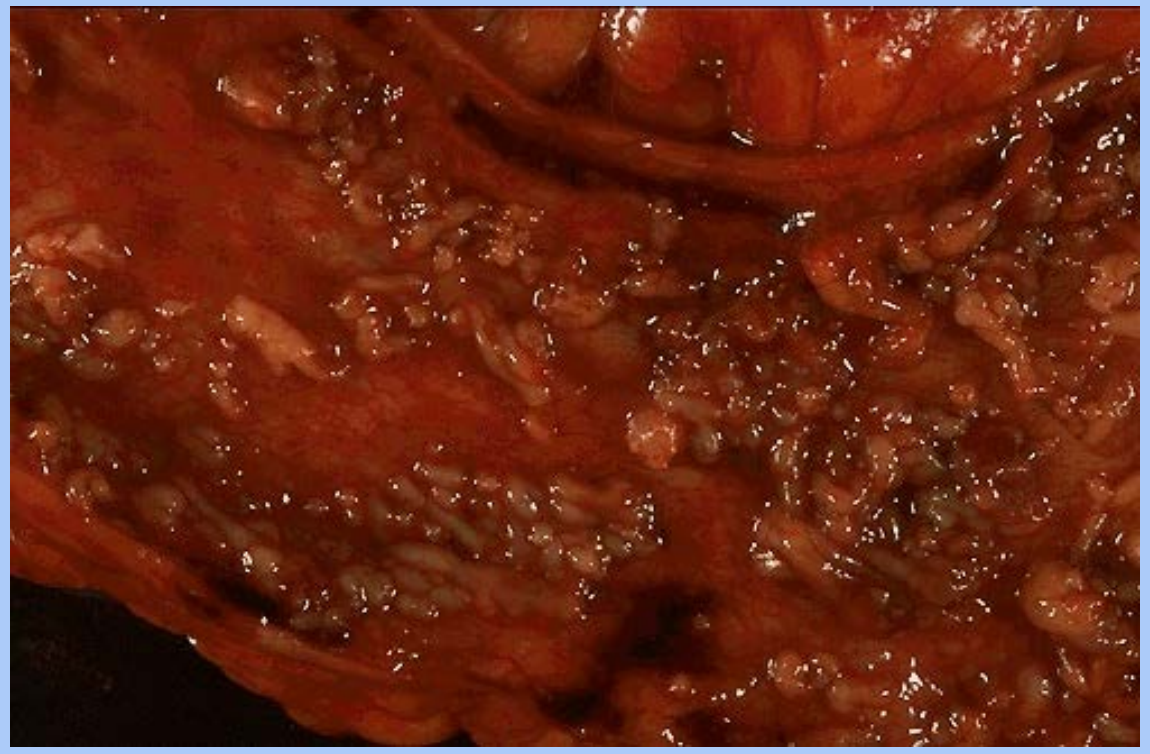
Ulcerative Colitis
Gross Pathology

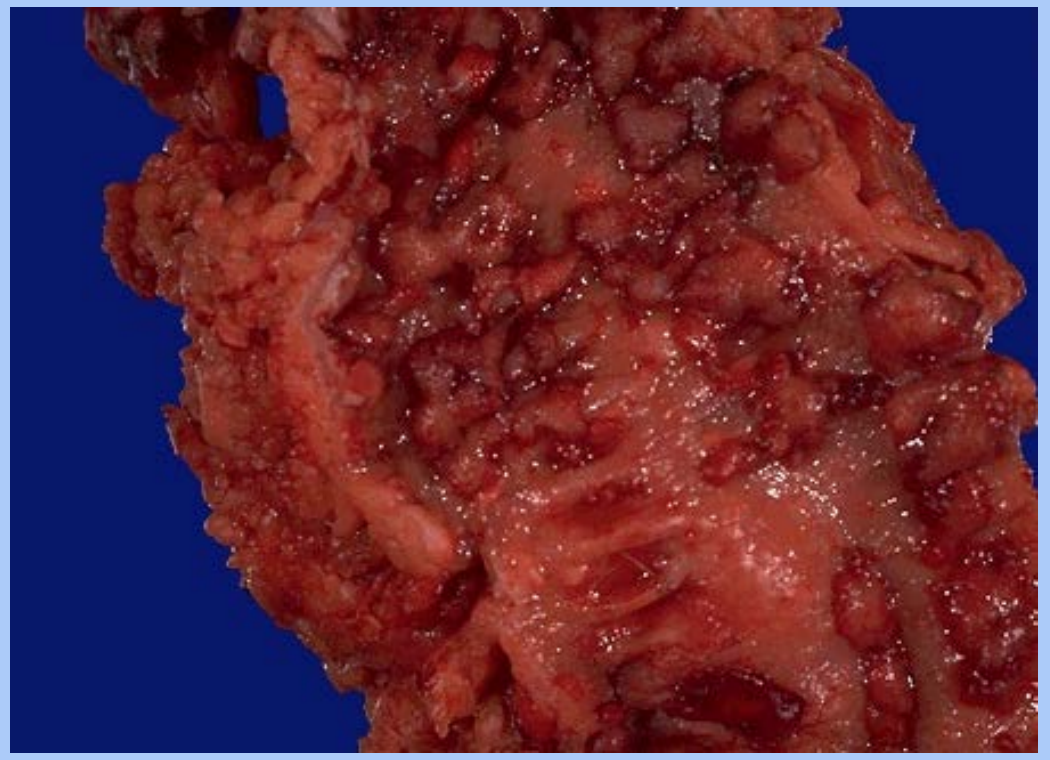
- The most intense inflammation begins at the lower right in the sigmoid colon and extends upward and around to the ascending colon.
- At the lower left is the **ileocecal valve** with a portion of terminal ileum that is *not involved*.
- Inflammation with ulcerative colitis tends to be continuous along the mucosal surface and tends to begin in the rectum.



https://webpath.med.utah.edu/GIHTML/GI071.html

Ulcerative Colitis
Pseudopolyps



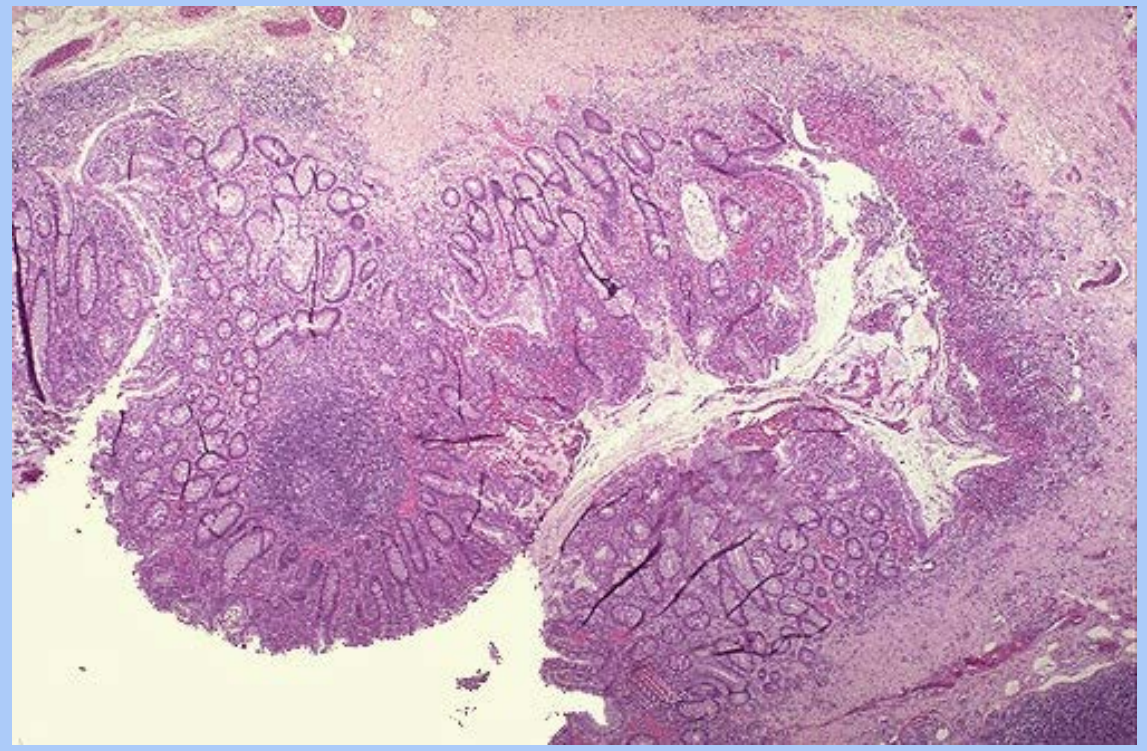


The pseudopolyps can be seen clearly as raised red islands of inflamed mucosa. Between the pseudopolyps is only remaining muscularis.

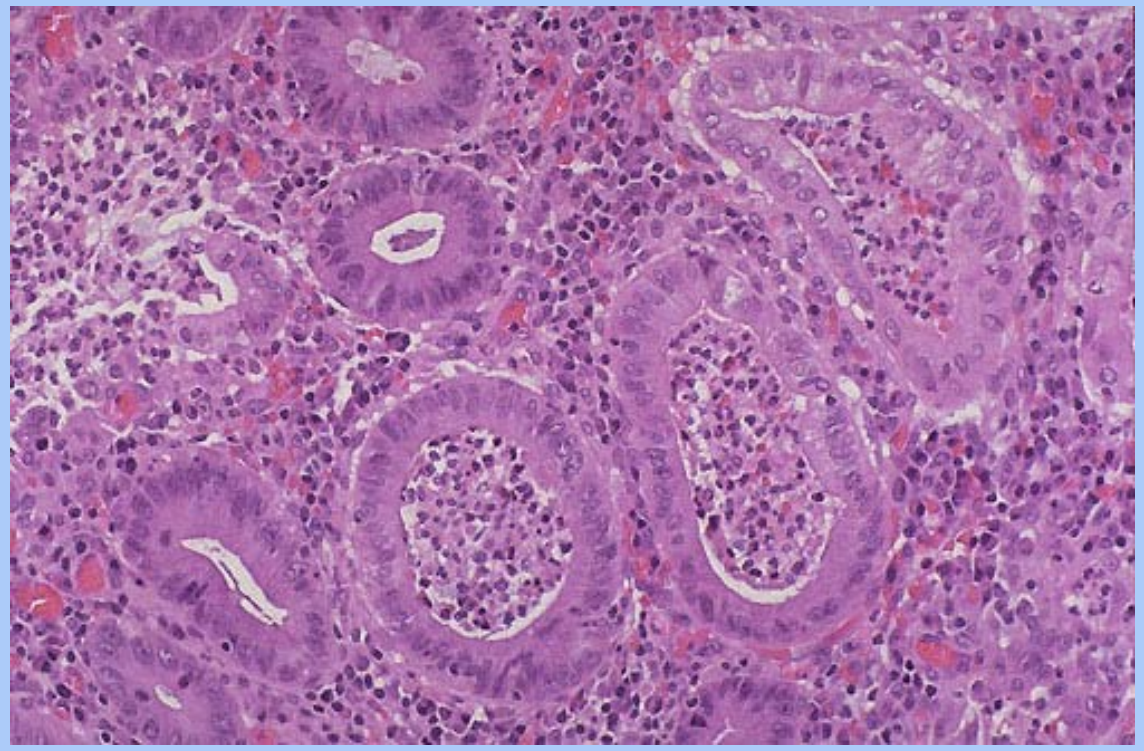
https://webpath.med.utah.edu/GIHTML/GI072.html

https://webpath.med.utah.edu/GIHTML/GI070.html

Ulcerative Colitis
Histopathology



The inflammation of ulcerative colitis is confined primarily to the mucosa.
Here, the mucosa is eroded by an inflammatory process with ulceration that undermines surrounding mucosa.
The resulting **ulceration** often has a flask shape.



Crypt abscesses are a histologic finding more typical with ulcerative colitis.

https://webpath.med.utah.edu/GIHTML/GI073.html
https://webpath.med.utah.edu/GIHTML/GI183.html

Crohn’s disease

Etiology

- Etiology is *unknown*.
- Possible role of *pre-inflammatory cytokines* in the pathogenesis may cause Crohn’s disease.
- Possible association with *Mycobacterium paratuberculosis, measles and mumps infections*.
- **Associated environmental factors**: infection, smocking, consumption of refined sugar, high fiber.
- Most common in *distal ileum and colon*.

Epidemiology

- Inflammatory bowel disease affects *all race and both sexes.*
- The incidence is generally higher in developed countries, especially in *Northern Europe.*
- *Lack of dietary fiber, environmental and genetic factors* are infusing the disease progression.

Crohn’s disease

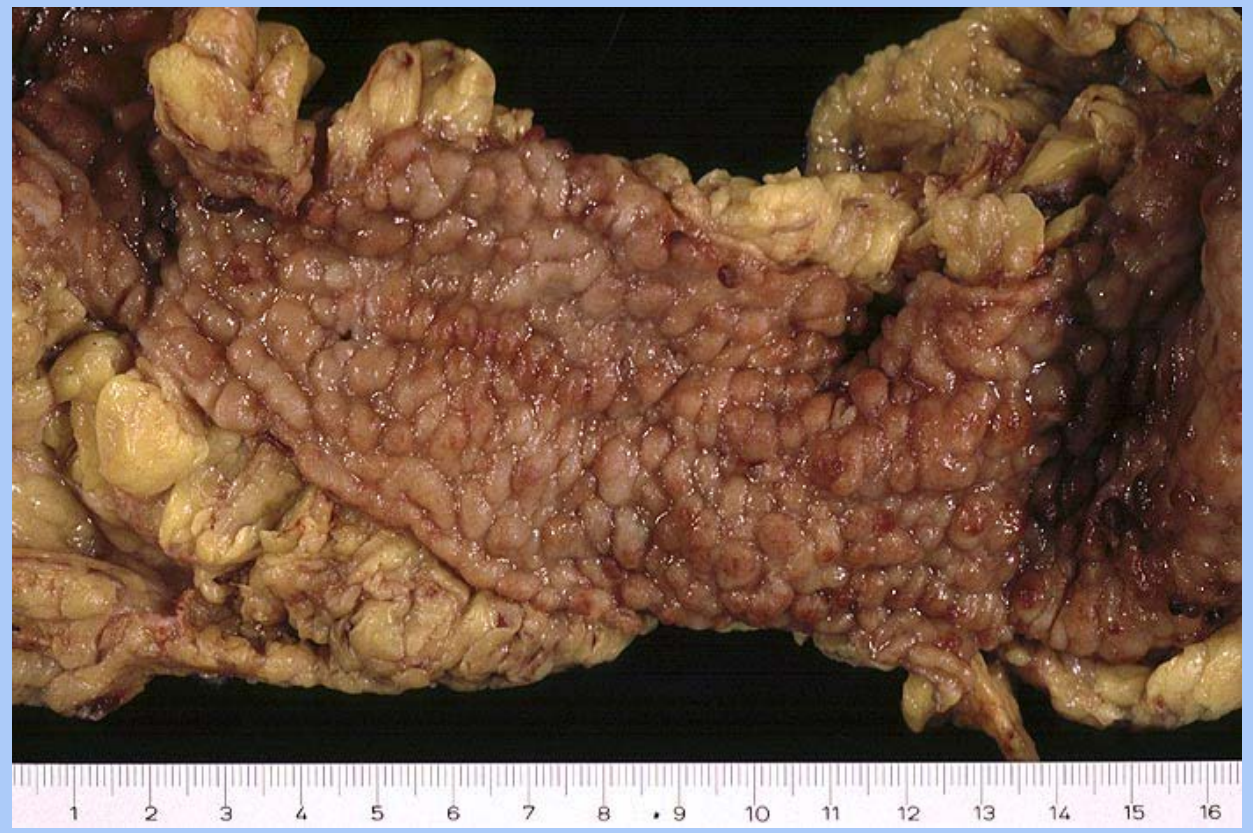
Grossly:

- Typical transmural lesion can produce anything from a small ulcer over a lymphoid follicle ***(aphthoid ulcer)*** to a deep ***fissuring ulcer*** to transmural scarring and chronic inflammation.

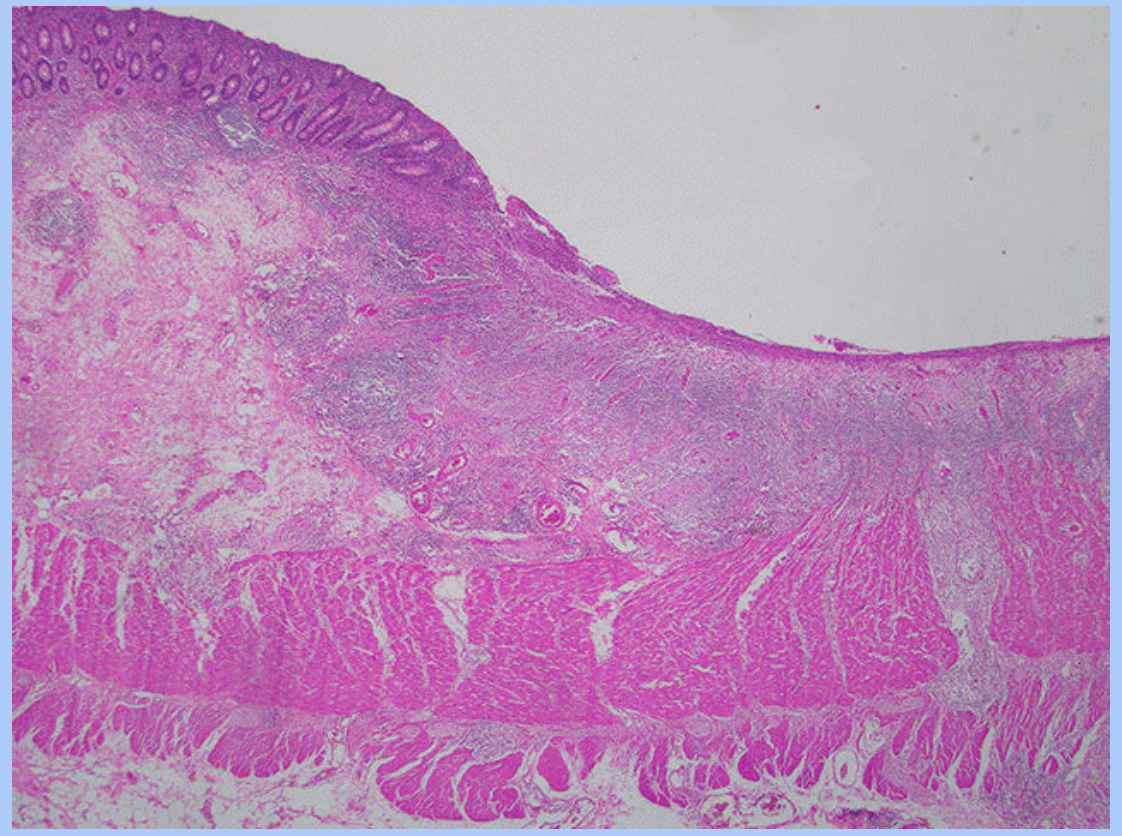
Microscopically:

- **Transmural inflammation** – involvement the full thickness of the wall from the mucosa to the serosa.
- 1/3 of cases have **granulomas.**
- *Extracolonic sites* such as lymph nodes, liver and joints may also have granulomas.
- Deep ulcers may penetrate through the bowel wall to initiate **abscesses** or **fistulae**.
- **Inflammation** is typically **segmental** with uninvolved bowel separating areas of involved bowel.

Crohn's disease
Pathology



Cobblestone-like mucosal relief.

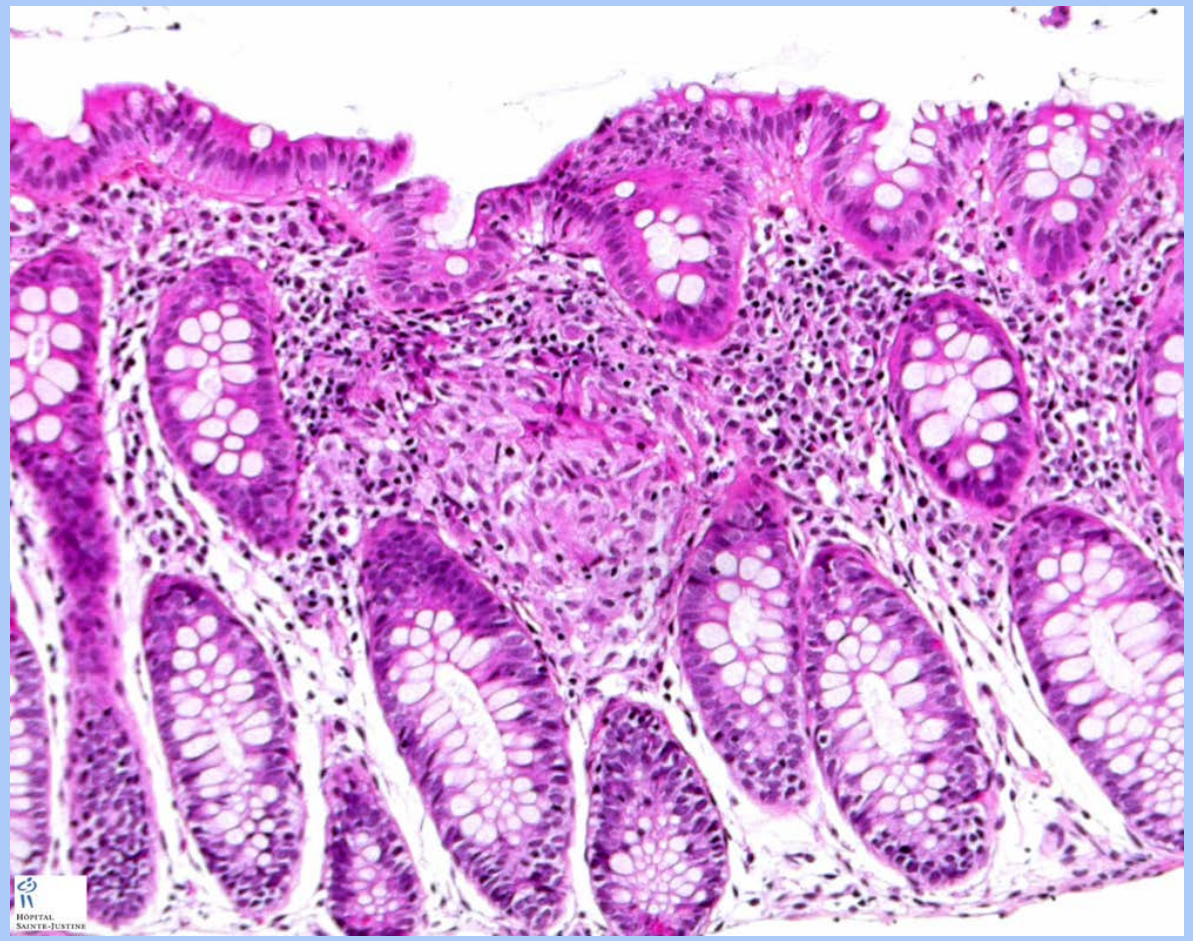


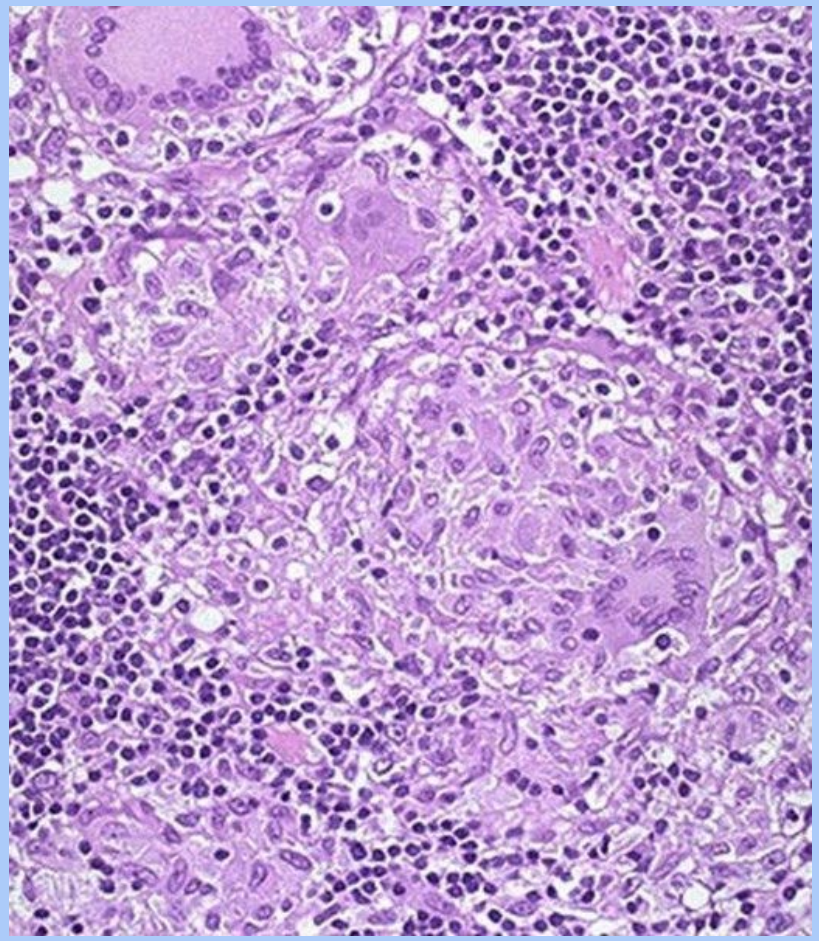
There is a mucosal ulcer accompanied by transmural inflammation. Epithelioid granulomas with giant cells are present in all layers of the bowel. Note submucosal fibrosis.

http://oac.med.jhmi.edu/Pathology/GI/Colon/177A_Full.html

http://translate.google.com/translate?u=http://alf3.urz.unibas.ch/pathopic/e/getpic-fra.cfm?id=004472

Crohn's disease
Granulomas





https://www.pathologyoutlines.com/topic/coloncrohns.html

http://www.humpath.com/spip.php?article4403#documents_portfolio

Crohn's disease
Complications

- Serosal involvement – adhesions to other loops of bowel, bladder, abdominal wall
- Deep fissure ulcers – fistulae and sinuses
- Stricture formation
- Fibrous adhesions
- Perforation of the bowel
- Perianal fistulae, fissures and abscesses
- Increased incidence of bowel cancer
- Sometimes significant bleeding from ulcers
- Systemic complications (similar to UC)
  - Skin, eye, joints, and liver