DISEASE OF THE ORAL CAVITY AND ESOPHAGUS

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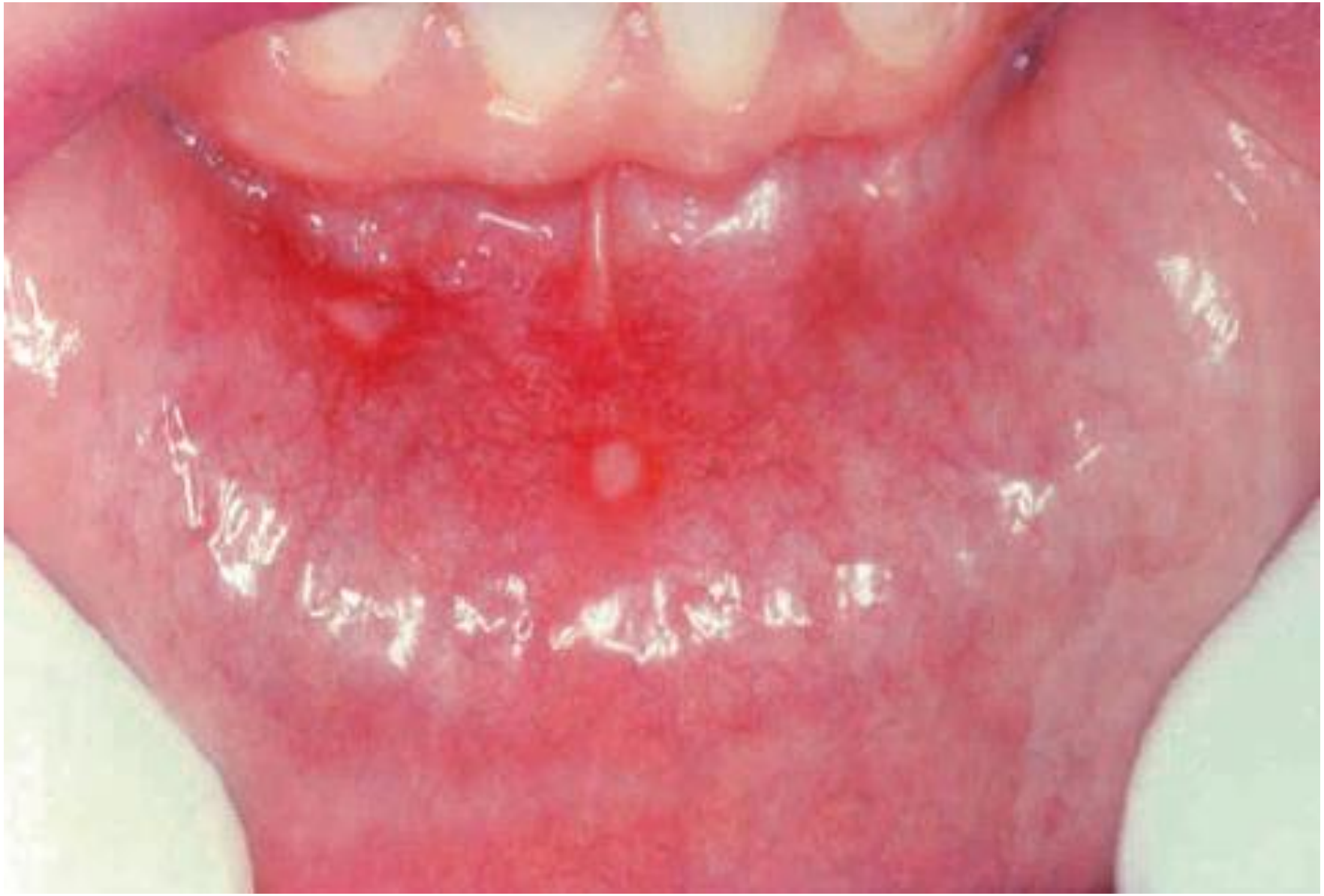
Oral Cavity Pathologies

1. Teeth and their support structure
2. Oral mucosa
3. Salivary glands
4. Jaws

Oral inflammatory lesions

Aphthous Ulcers (Canker Sores)

- Superficial mucosal ulcerations
- Common, up to 40% of the population.
- First 2 decades of life
- Extremely painful, Recurrent.
- Idiopathic, familial tendency.
- may be associated with celiac disease, inflammatory bowel disease, and Behçet disease.
- Solitary or multiple
- Shallow, with a hyperemic base covered by a thin exudate and rimmed by a narrow zone of erythema.
- resolve spontaneously in 7 to 10 days.



Oral inflammatory lesions

Herpes Simplex Virus Infections

- self-limited primary infection that can be reactivated when there is a compromise in host resistance.
- Most orofacial herpetic infections are caused by herpes simplex virus type 1 (HSV-1), with the remainder being caused by HSV-2 (genital herpes).
- Primary infections in children, often asymptomatic.
- 10% to 20% of primary infections manifests as acute herpetic gingivostomatitis, with vesicles and ulcerations.
- Most adults harbor latent HSV-1, and the virus can be reactivated, "cold sore" or recurrent herpetic stomatitis.

Oral inflammatory lesions

Herpes Simplex Virus Infections

- Factors associated with HSV reactivation:
  - trauma, allergies, exposure to ultraviolet light and extremes of temperature, upper-respiratory tract infections, pregnancy, menstruation, and immunosuppression.
- **Recurrent lesions:** groups of small vesicles. The lips (herpes labialis), nasal orifices, buccal mucosa, gingiva, and hard palate are the most common locations.
- lesions resolve within 7 to 10 days, can persist in immunocompromised patients, may require systemic anti-viral therapy.
- **Morphologically,** the lesions resemble those seen in esophageal herpes and genital herpes. The infected cells become ballooned and have large eosinophilic intranuclear inclusions. Adjacent cells commonly fuse to form large multinucleated polykaryons

Oral Candidiasis (Thrush)

- **The most common fungal infection of the oral cavity.**
- Candida albicans is a normal component of the oral flora and only produces disease under unusual circumstances.
- **Predisposing factors**: Immunosuppression, specific strain of C. albicans, composition of the oral microbial flora (microbiota), broad-spectrum antibiotics that alter the normal microbiota can promote oral candidiasis.

Oral Candidiasis (Thrush)

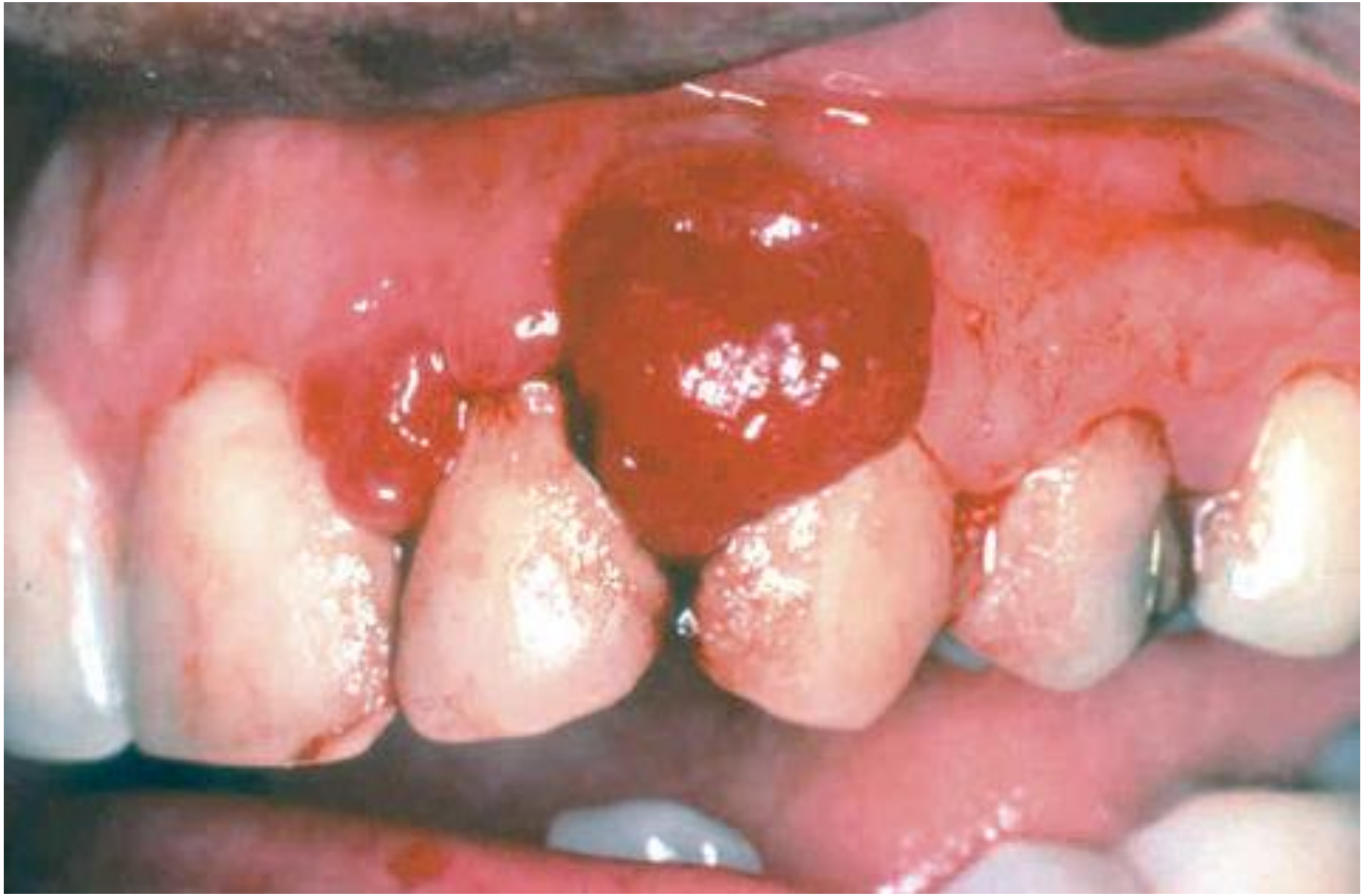
- **The three major clinical forms of oral candidiasis**

1. Pseudomembranous (thrush), most common,
2. Erythematous
3. hyperplastic.

- Thrush is characterized by a superficial, curd like, gray to white inflammatory membrane composed of matted organisms enmeshed in a fibrinosuppurative exudate that can be readily scraped off to reveal an underlying erythematous base.
- In mildly immunosuppressed, such as diabetics, the infection usually remains superficial, but it may spread to deep sites in association with more severe immunosuppression, that may be seen in organ or hematopoietic stem cell transplant recipients, and in patients with neutropenia, chemotherapy-induced immunosuppression, or AIDS.

proliferative and neoplastic lesions of the oral cavity

- ***Pyogenic granuloma:*** is an inflammatory lesion typically found on the gingiva of children, young adults, and pregnant women (pregnancy tumor).
- richly vascular and ulcerated, which gives them a red to purple color.
- growth can be rapid suspicious of a malignant neoplasm.
- histologic examination: proliferation of immature vessels similar to that seen in granulation tissue.
- May regress, mature into dense fibrous masses, or develop into a peripheral ossifying fibroma.
- Complete surgical excision is definitive treatment.

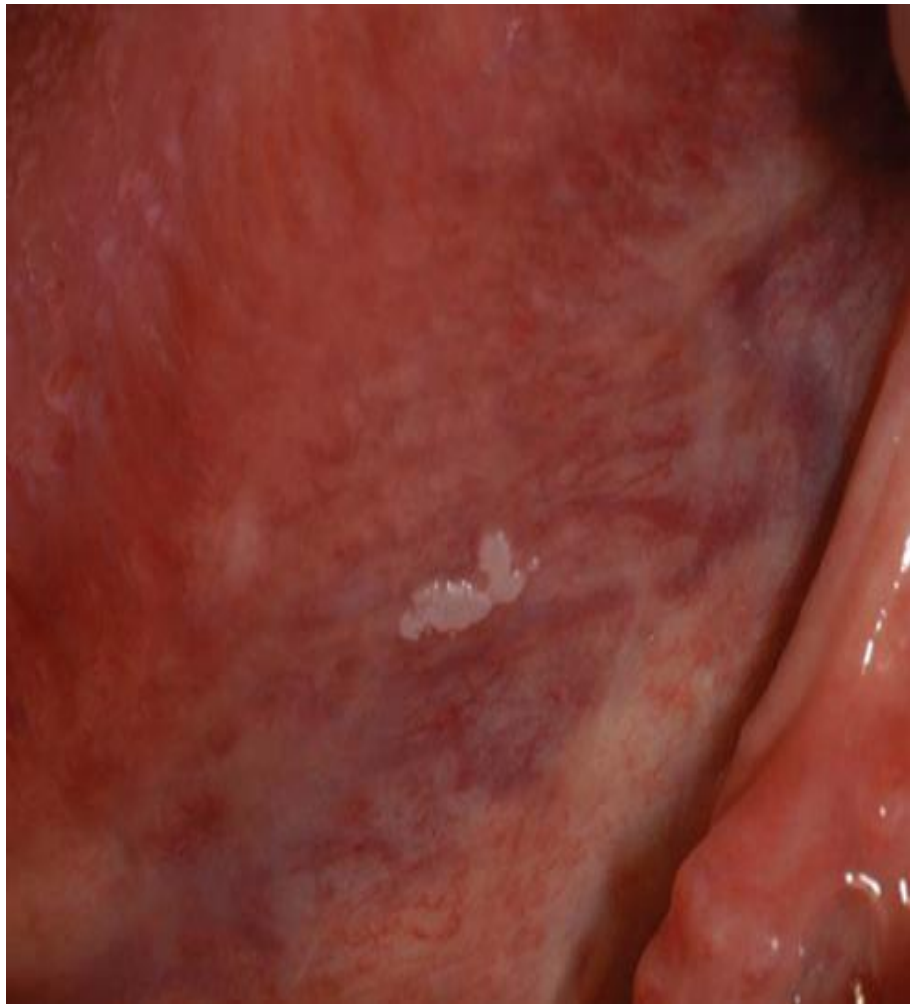


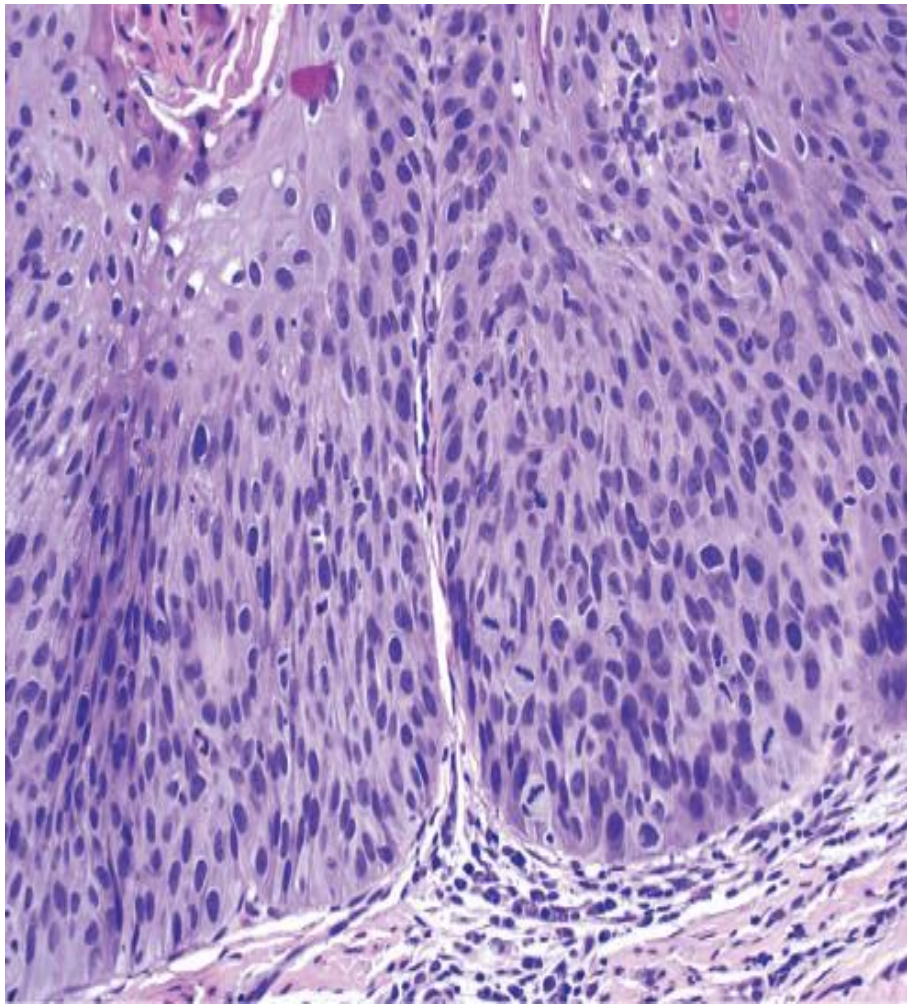
Leukoplakia and Erythroplakia

- **Leukoplakia:** is defined by the WHO as “a white patch or plaque that cannot be scraped off and cannot be characterized clinically or pathologically as any other disease.”
- This description is reserved for lesions that arise in the oral cavity in the absence of any known cause. white patches caused by obvious irritation or entities such as lichen planus and candidiasis are not considered leukoplakia.
- 3% of population has leukoplakic lesions, of which 5% to 25% are dsyplastic and at risk for progression to squamous cell carcinoma.
- all leukoplakias must be considered precancerous until otherwise proven by histology.
- **Erythroplakia***:* is a red, velvety, eroded lesion flat or slightly depressed relative to the surrounding mucosa. Less common, much greater risk for malignant transformation than leukoplakia.
- both typically affect adults between 40 and 70 years of age, with a 2:1 male predominance.
- etiology is multifactorial, tobacco use (cigarettes, pipes, cigars, and chewing tobacco) is the most common risk factor for leukoplakia and erythroplakia.

Leukoplakia and Erythroplakia

- **histologic examination**: leukoplakia and erythroplakia show a spectrum of epithelial changes ranging from hyperkeratosis overlying a thickened, acanthotic but orderly mucosal epithelium to lesions with markedly dysplastic changes sometimes merging into carcinoma in situ.
- The most severe dysplastic changes are associated with erythroplakia, and more than 50% of these cases undergo malignant transformation. With increasing dysplasia and anaplasia, a subjacent inflammatory cell infiltrate of lymphocytes and macrophages is often present.





Squamous Cell Carcinoma

- Cancers of the oral cavity

1. 95% squamous cell carcinomas (SCC)
2. 5 % adenocarcinomas of salivary glands.

- Squamous cell carcinoma:

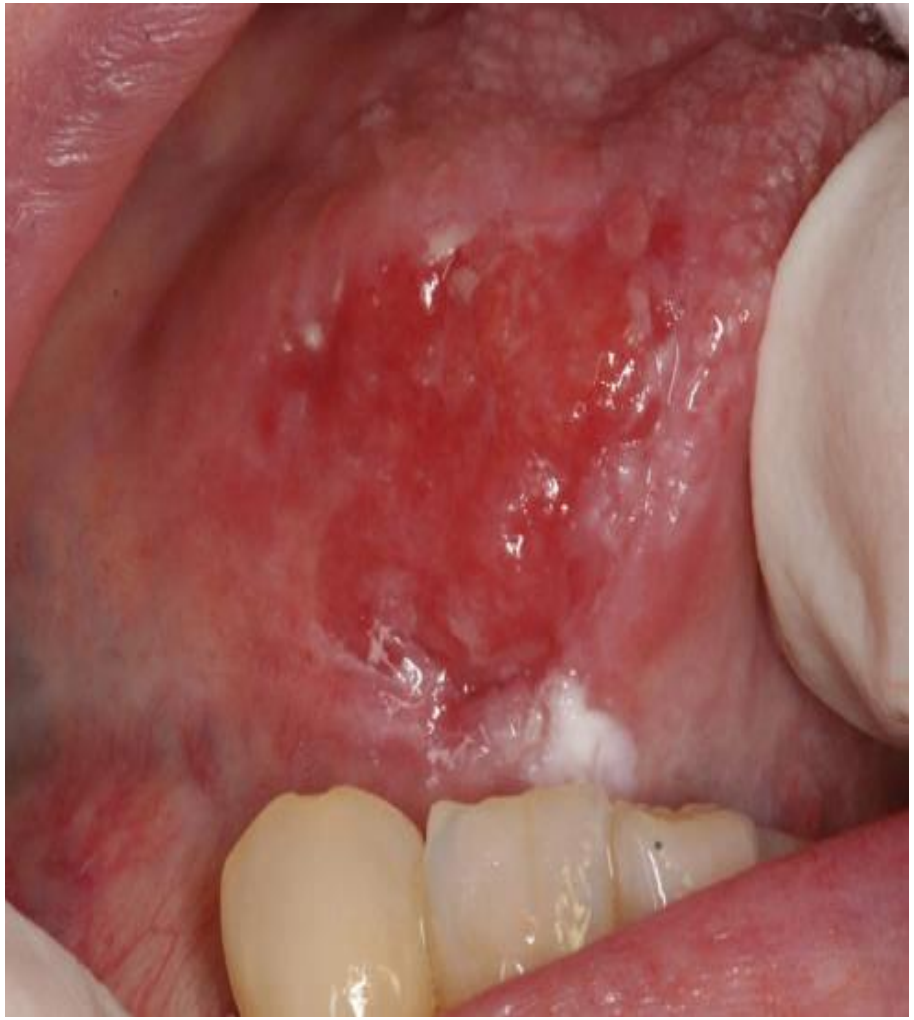
aggressive epithelial, sixth most common world wide overall survival rate less than 50%.

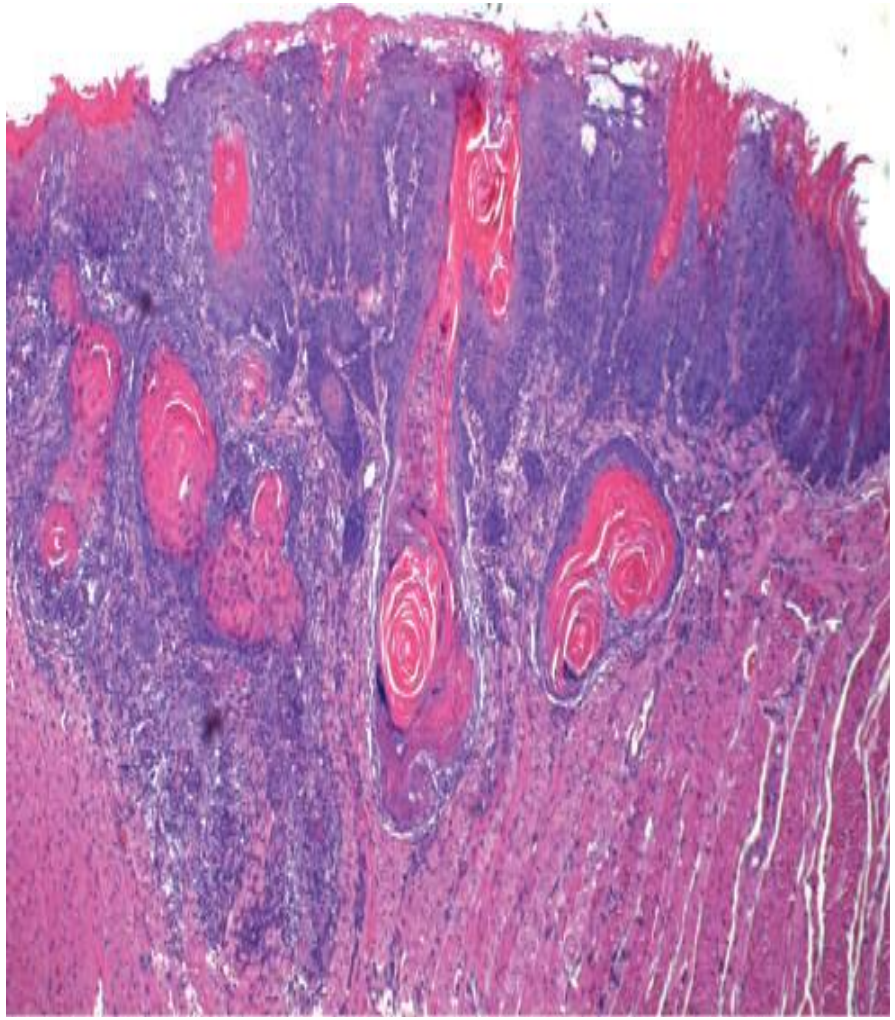
Pathogenesis

- **Squamous cancers of the oropharynx arise through two distinct pathogenic pathways, one involving exposure to carcinogens, and the other related to infection with high risk variants of human papilloma virus (HPV).** Carcinogen exposure mainly stems from chronic alcohol and tobacco (both smoked and chewed) use.
- These mutations *TP53* and genes that regulate cell proliferation, such as *RAS.* The HPV-related tumors tend to occur in the tonsillar crypts or the base of the tongue and harbor oncogenic “high-risk” subtypes, particularly HPV-16. These tumors carry far fewer mutations than those associated with tobacco exposure and often overexpress p16.

Pathogenesis

- The prognosis for patients with HPV-positive tumors is better than for those with HPV-negative tumors.
- The HPV vaccine, which is protective against cervical cancer, offers hope to limit the increasing frequency of HPV-associated oropharyngeal SCC.
- The incidence of oral cavity SCC (particularly in the tongue) has been on the rise in individuals younger than 40 years of age who have no known risk factors. The pathogenesis in this group of patients, who are nonsmokers and are not infected with HPV, is unknown





diseases of salivary glands

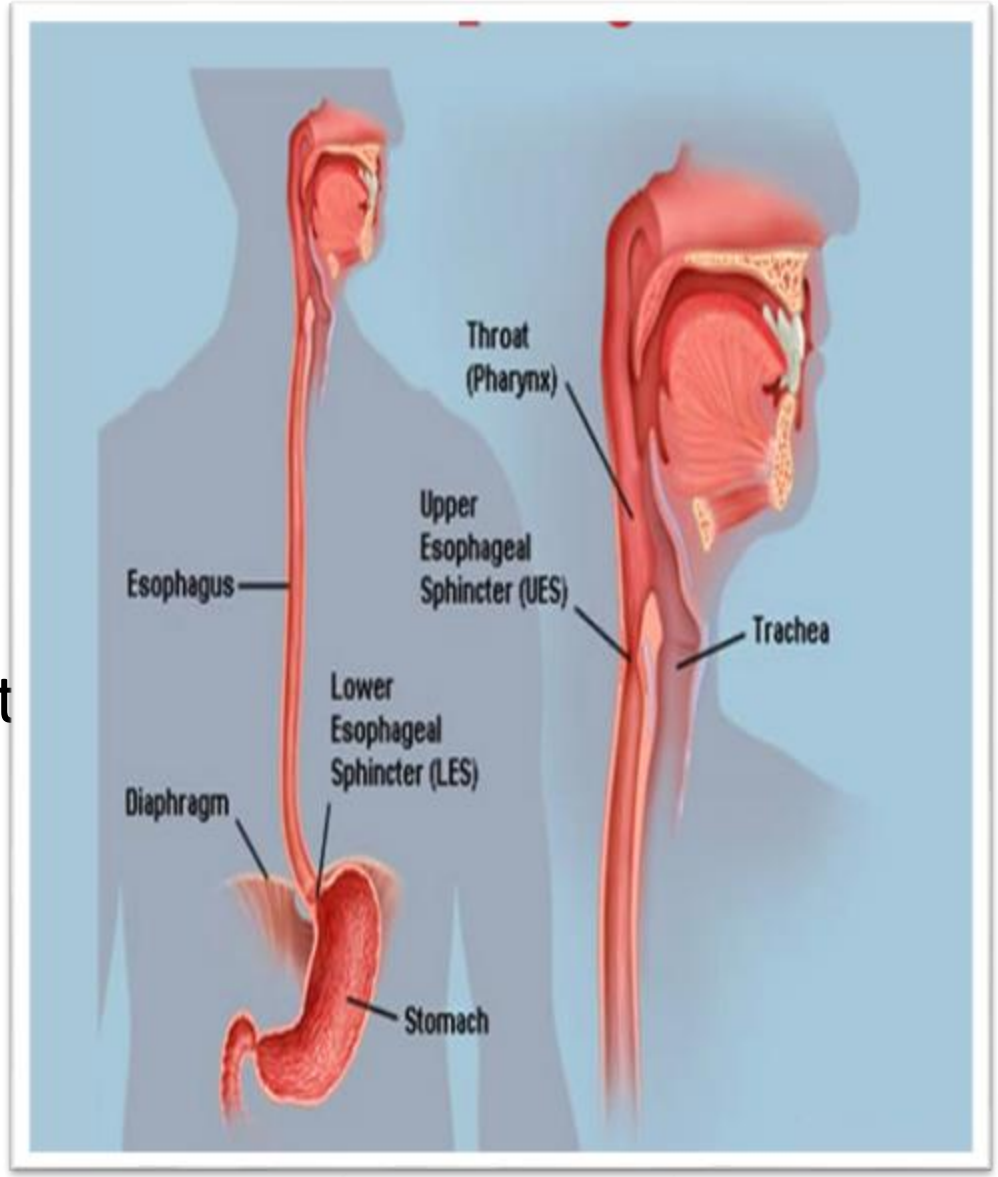
- **Sialadenitis** (inflammation of the salivary glands) can be caused by trauma, infection (such as mumps), or an autoimmune reaction.
- **Pleomorphic adenoma** is a slow-growing neoplasm composed of a heterogeneous mixture of epithelial and mesenchymal cells. It is typically benign.
- **Mucoepidermoid carcinoma** is a malignant neoplasm of variable biologic aggressiveness that is composed of a mixture of squamous and mucous cells.

Table 15.1 Histopathologic Classification and Prevalence of the Most Common Benign and Malignant Salivary Gland Tumors

Benign	Malignant
Pleomorphic adenoma (50%)	Mucoepidermoid carcinoma (15%)
Warthin tumor (5%)	Acinic cell carcinoma (6%)
Oncocytoma (2%)	Adenocarcinoma NOS (6%)
Cystadenoma (2%)	Adenoid cystic carcinoma (4%)
Basal cell adenoma (2%)	Malignant mixed tumor (3%)

Esophagus

- The esophagus develops from the cranial portion of the foregut.
- hollow, highly distensible muscular tube extends from the epiglottis to the GEJ, located just above the diaphragm



Diseases that affect the esophagus

- 1. Obstruction: mechanical or functional.
- 2. vascular diseases: varices.
- 3. Inflammation: esophagitis.
- 4. Tumours.

Mechanical Obstruction

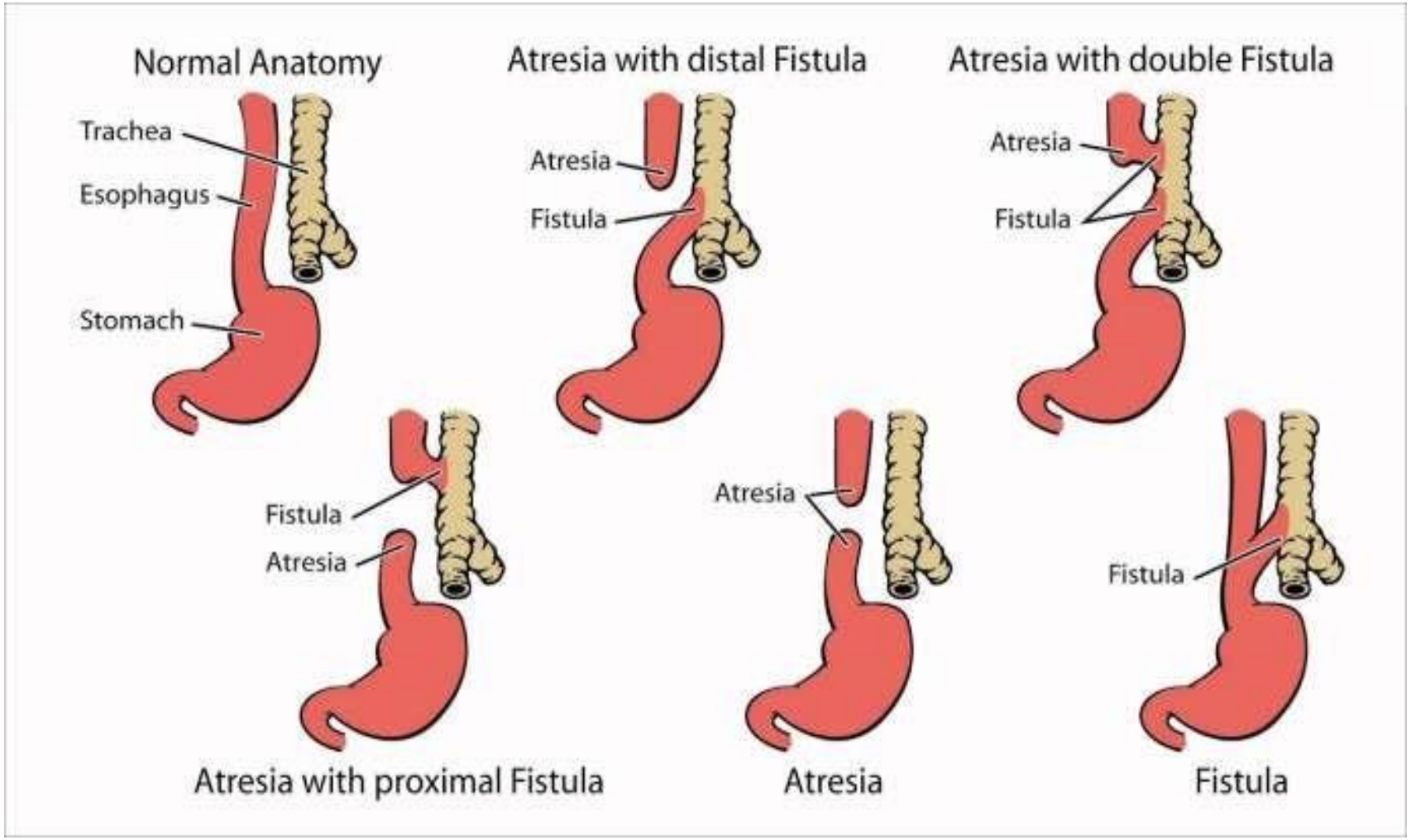
- Congenital or acquired.

- Examples:
- Atresia
- Fistulas
- Duplications
- Agenesis (very rare)
- Stenosis.

may occur in any part of the gastrointestinal tract. When they involve the esophagus, they are discovered shortly after birth, usually because of regurgitation during feeding. Prompt surgical repair is required.

Atresia

- Thin, noncanalized cord replaces a segment of esophagus.
- Most common location: at or near the tracheal bifurcation
- + fistula (upper or lower esophageal pouches to a bronchus or trachea).


Normal Anatomy
Trachea
Esophagus
Stomach
Atresia with distal Fistula
Atresia
Fistula
Atresia with double Fistula
Atresia
Fistula
Fistula
Atresia
Atresia with proximal Fistula
Atresia
Atresia
Fistula
Fistula

Clinical presentation:

- Shortly after birth: regurgitation during feeding
- Needs prompt surgical correction (rejoin).

- Complications if w/ fistula:
- Aspiration
- Suffocation
- Pneumonia
- Severe fluid and electrolyte imbalances.

Esophageal stenosis

- Acquired>>>Congenital.
- Fibrous thickening of the submucosa & atrophy of the muscularis propria.
- Due to infammation and scarring

- Causes:
- Chronic GERD.
- Irradiation
- Ingestion of caustic agents

Clinical presentation

- Progressive dysphagia
- Difficulty eating solids that progresses to problems with liquids.

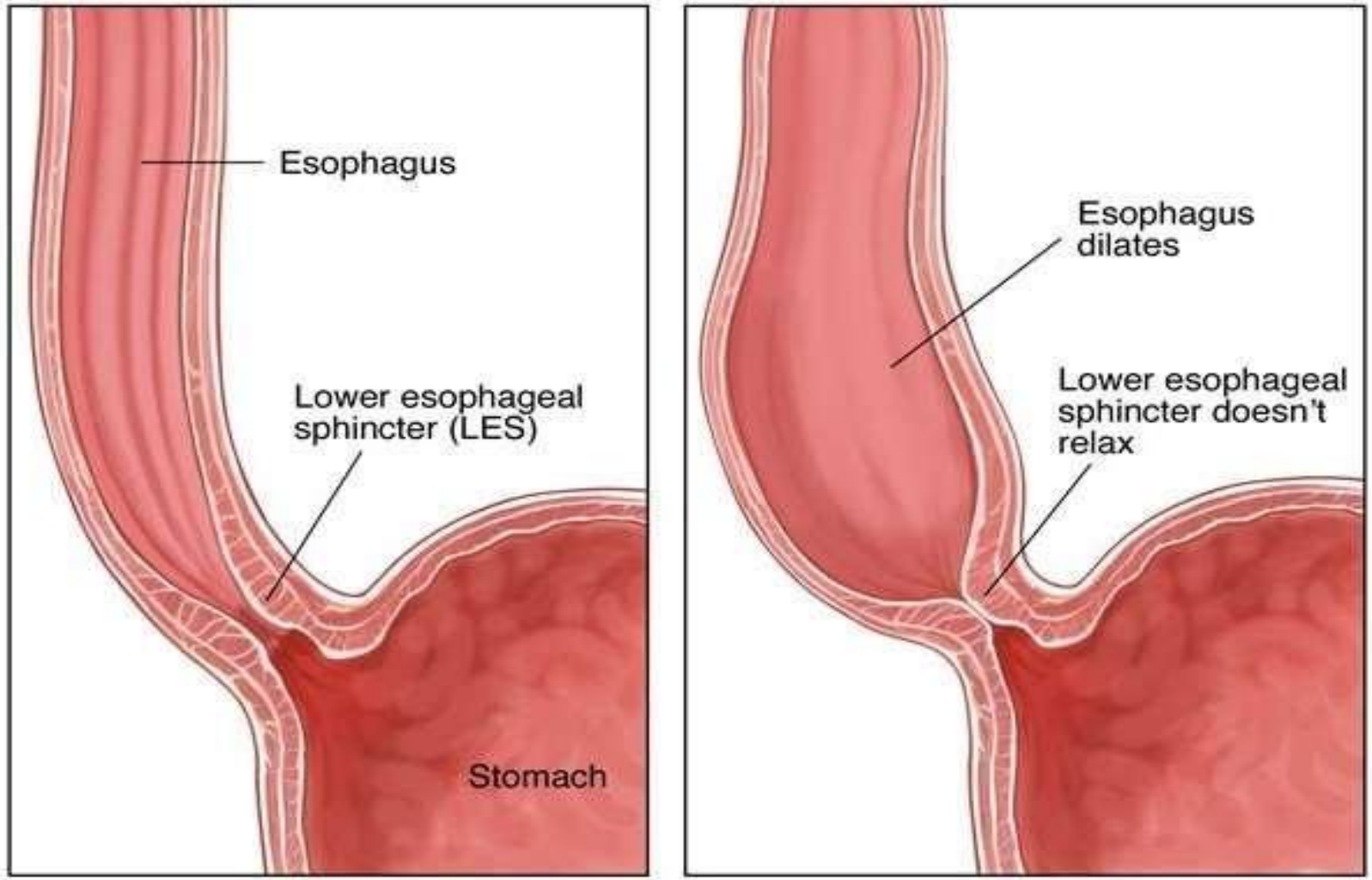
Functional Obstruction

- Efficient delivery of food and fluids to the stomach requires coordinated waves of peristaltic contractions.
- Esophageal dysmotility: discoordinated peristalsis or spasm of the muscularis.
- Achalasia: the most important cause.

Achalasia

- Triad:
- Incomplete LES relaxation
- Increased LES tone
- Esophageal aperistalsis.

- Primary >>>secondary.



Normal **Achalasia**

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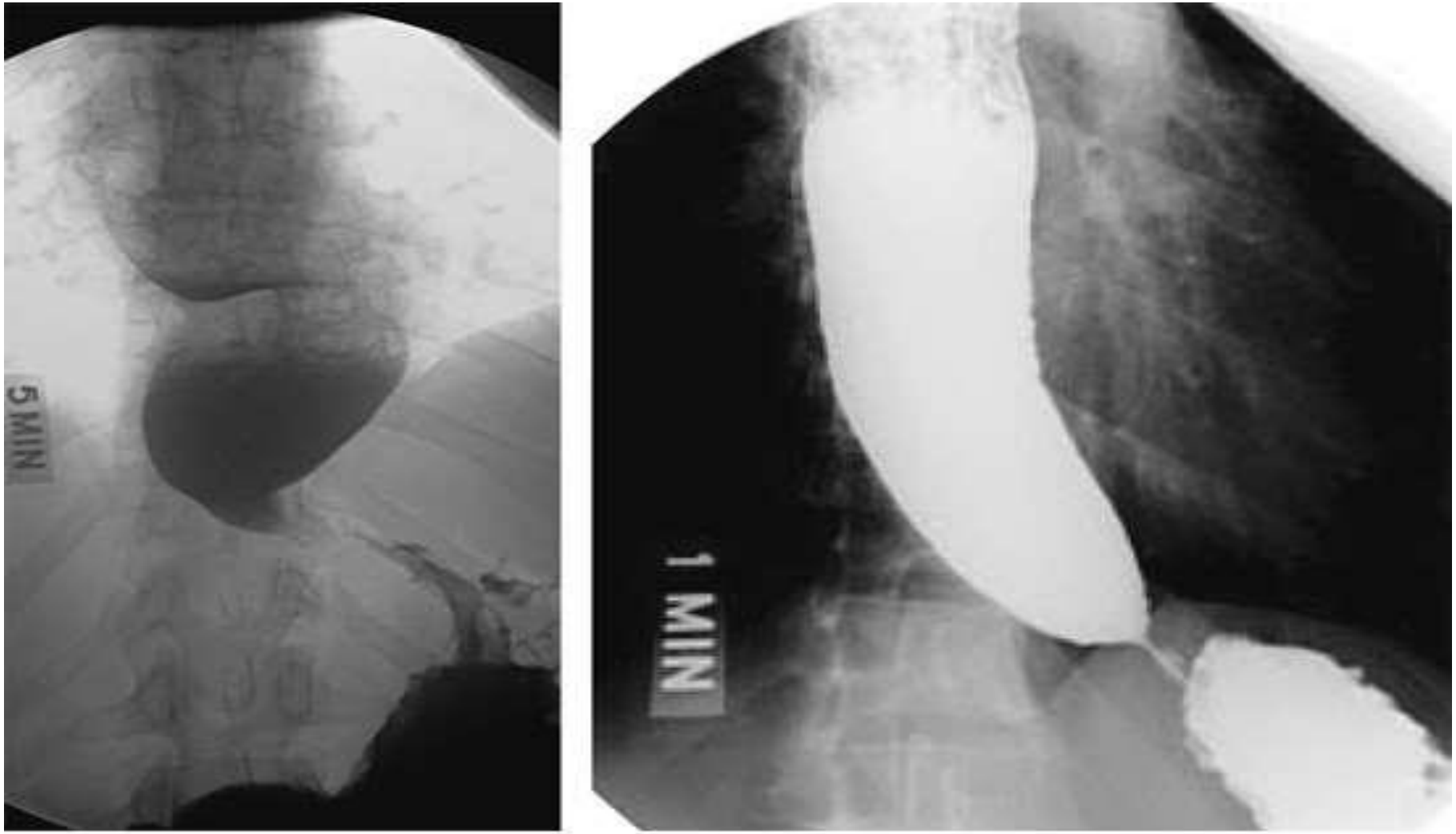
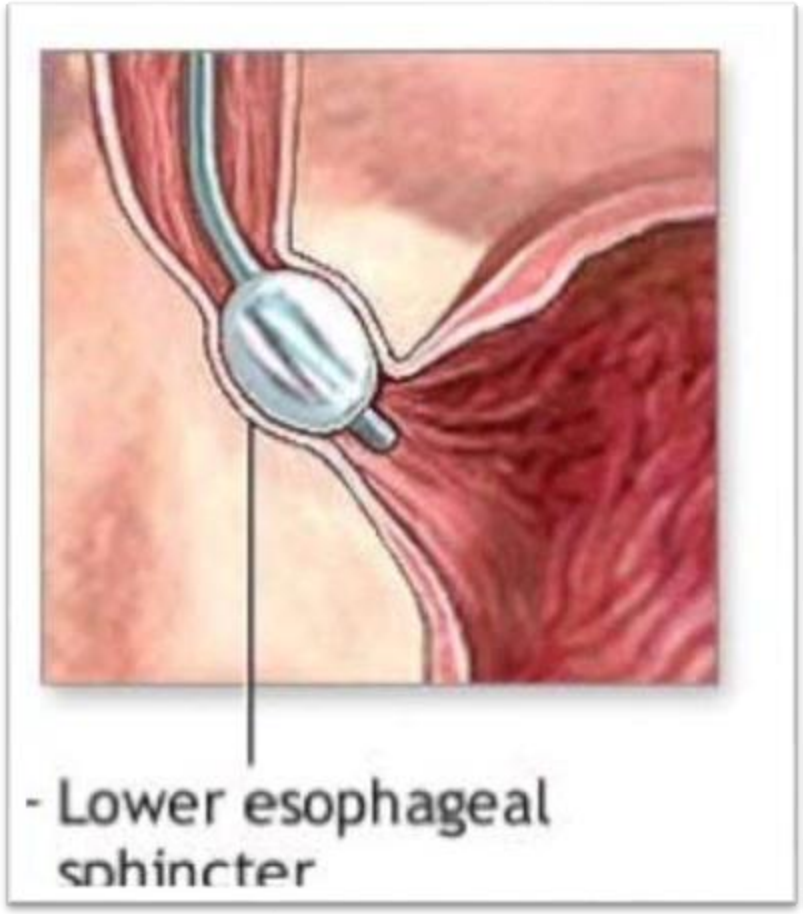
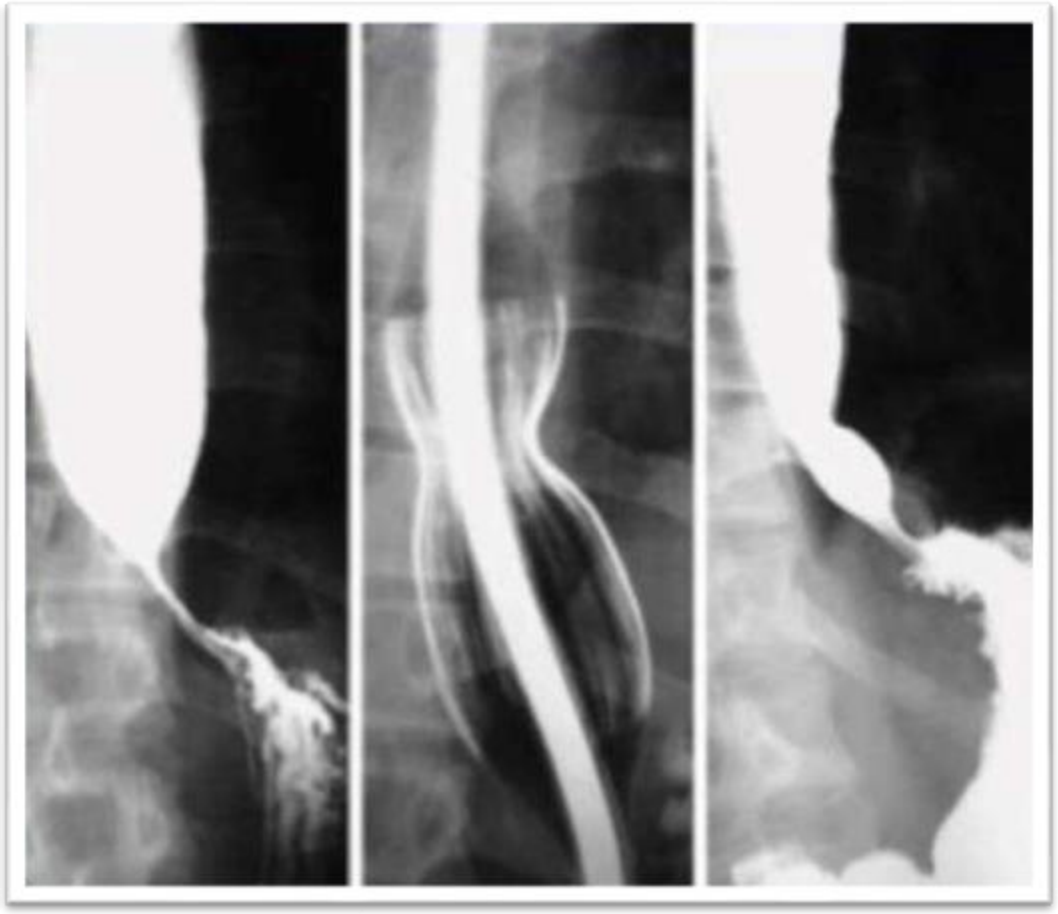


Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

Pneumatic balloon dilatation of the LES





Primary achalasia

- Failure of distal esophageal inhibitory neurons.
- Idiopathic
- Most common

Secondary achalasia

- Degenerative changes in neural innervation

- Intrinsic
- Vagus nerve
- Dorsal motor nucleus of vagus

- **Chagas disease**, Trypanosoma cruzi infection>>destruction of the myenteric plexus>> failure of LES relaxation>> esophageal dilatation.

Clinical presentation

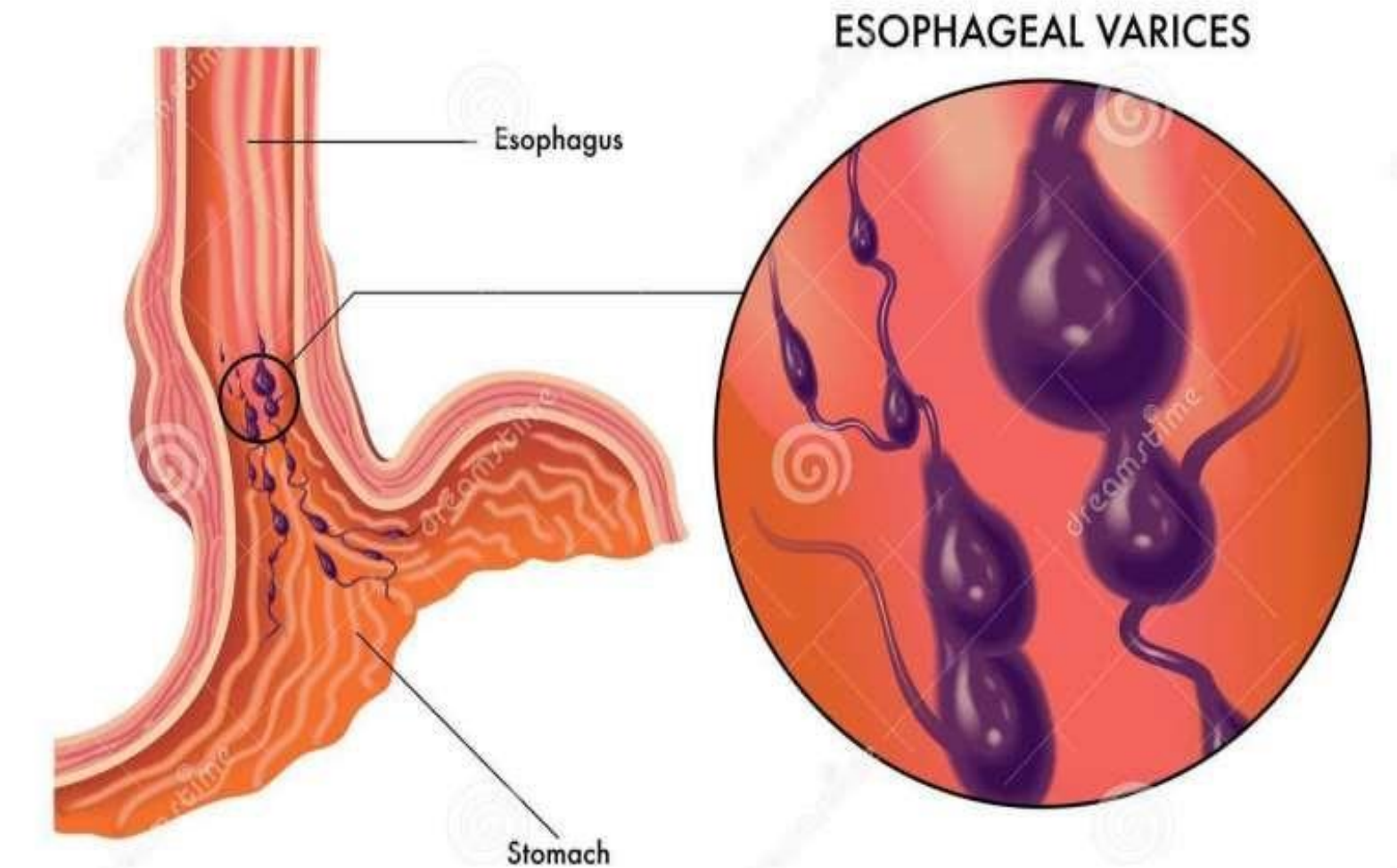
- Difficulty in swallowing
- Regurgitation
- Sometimes chest pain.

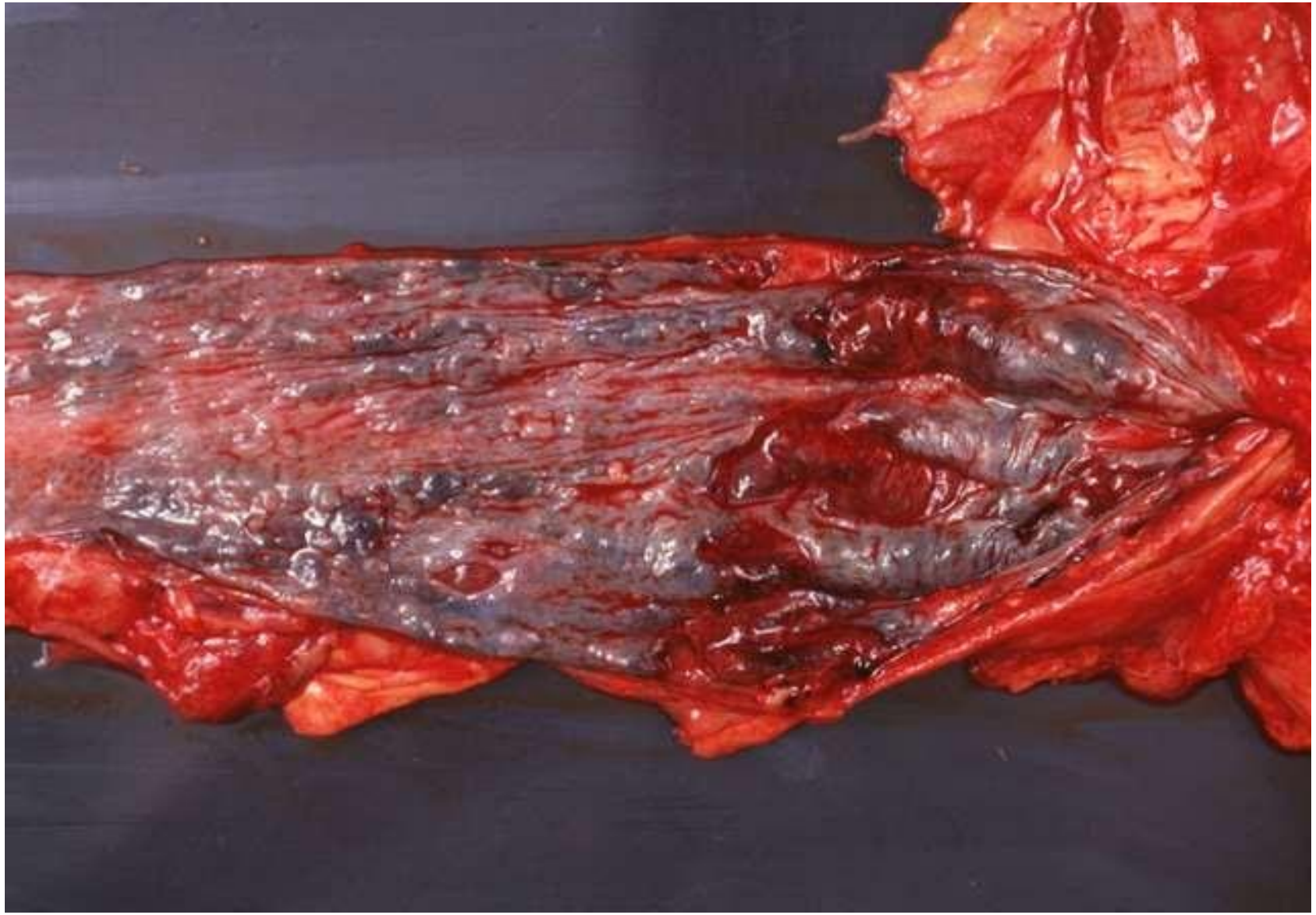
Achalasia-like disease

- Diabetic autonomic neuropathy
- Infiltrative disorders (malignancy, amyloidosis, or sarcoidosis)
- Dorsal motor nuclei lesions (produced by polio or surgical ablation).

Vascular diseases: Esophageal Varices

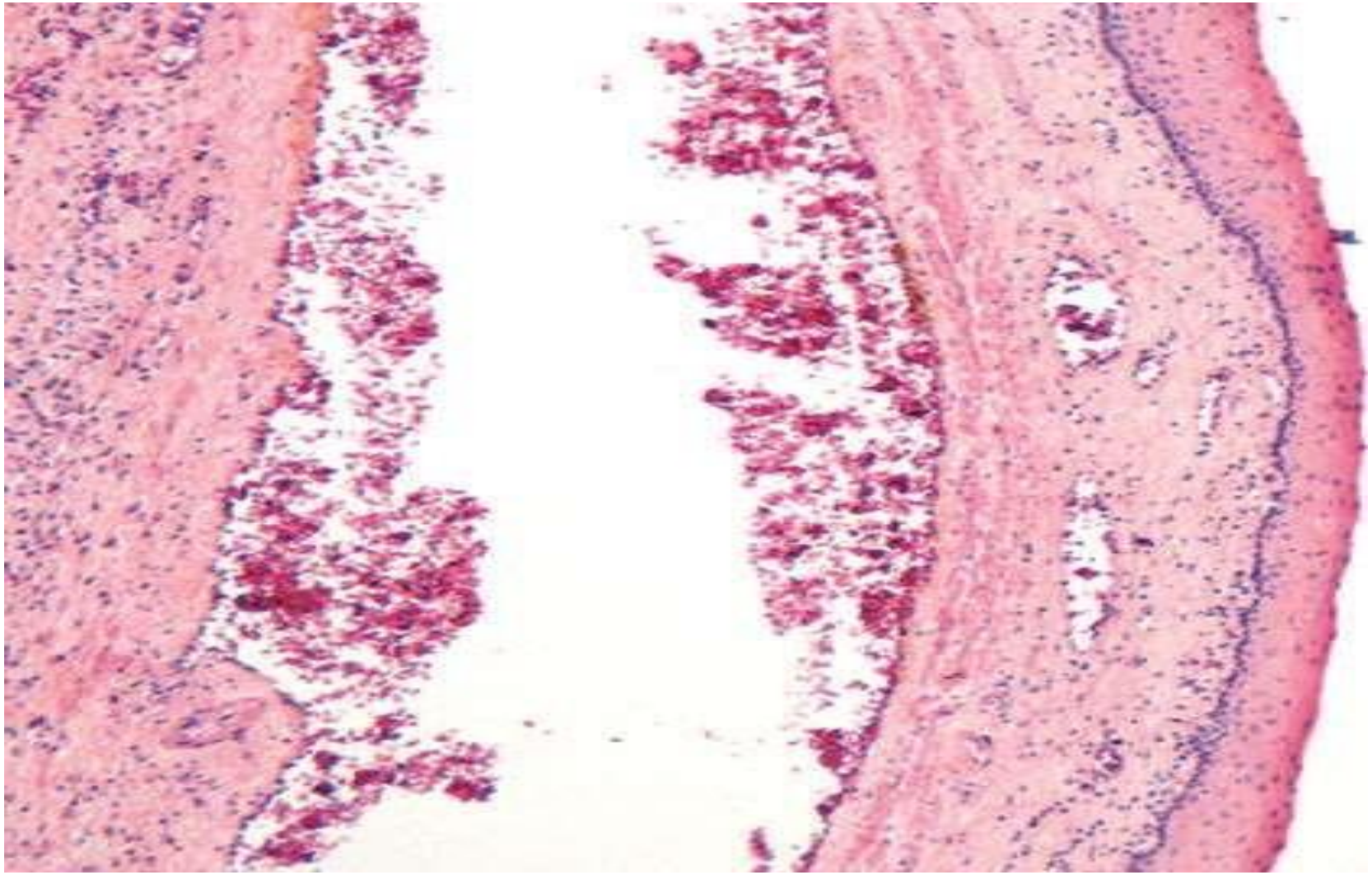
- Tortuous dilated veins within the submucosa of the distal esophagus and proximal stomach.
- Diagnosis by: endoscopy or angiography.





Medpics - UCSD School of Medicine

Dilated varices beneath intact squamous mucosa



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Pathogenesis:

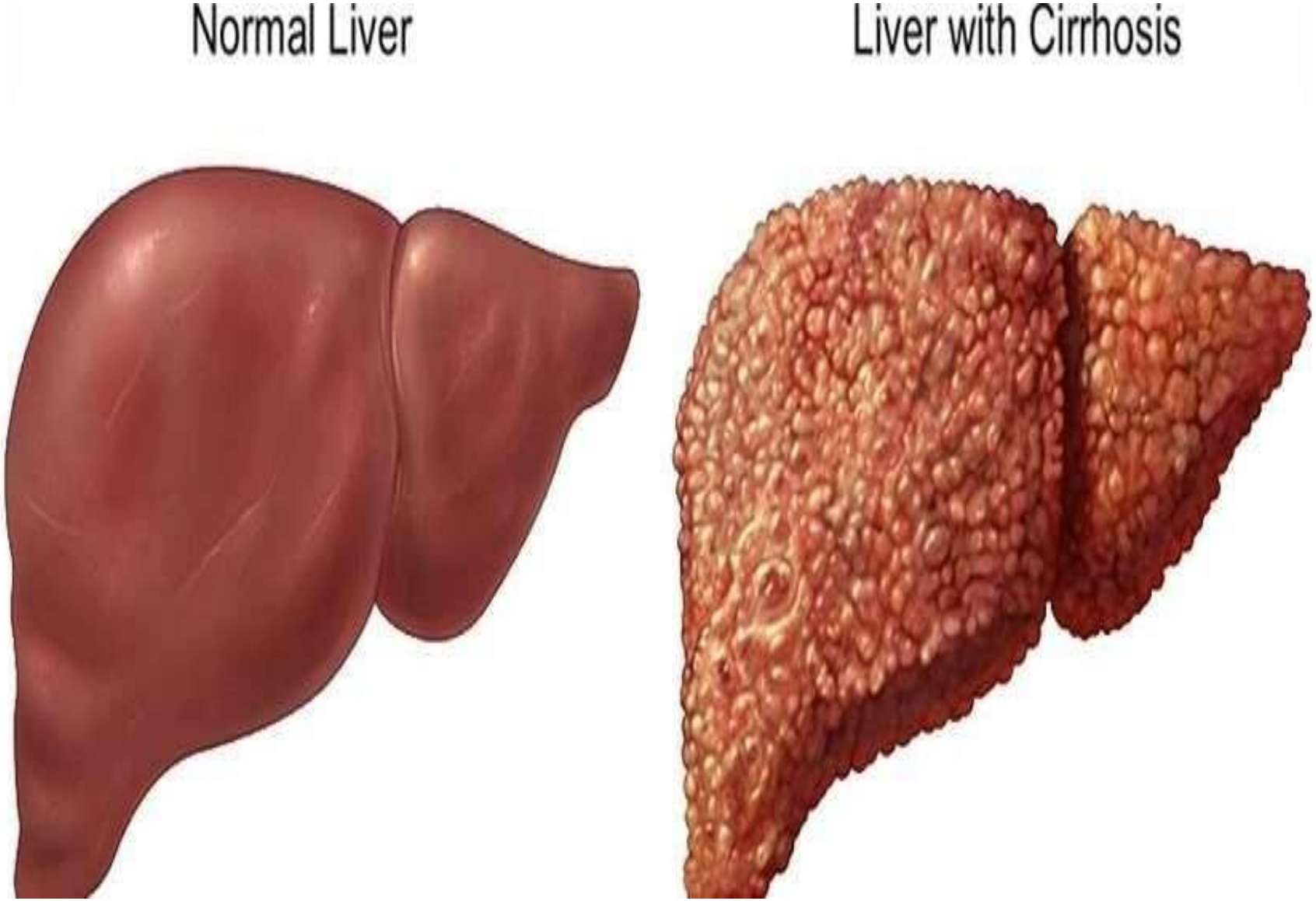
- **Portal circulation**: blood from GIT>>portal vein>>liver (detoxification)>>inferior vena cava.
- Diseases that impede portal blood flow >> portal hypertension >>esophageal varices.
- Distal esophagus : site of Porto-systemic anastomosis.
- **Portal hypertension**>>collateral channels in distal esophagus>>shunt of blood from portal to systemic circulation>>dilated collaterals in distal esophagus>>varices

Causes of portal hypertension

- Cirrhosis is most common

  Alcoholic liver disease.

- Hepatic schistosomiasis 2nd most common worldwide.



http://www.researchintoasthma.com/7-random-facts-about-liver-cirrhosis.html

Clinical Features

- Often asymptomatic.
- Rupture leads to massive hematemesis and death.
- 50% of patients die from the first bleed despite interventions.
- Death due to: hemorrhage, hepatic come, and hypovolemic shock
- Rebleeding in 20%.

Esophagitis

- Esophageal Lacerations.
- Mucosal Injury
- Infections
- Reflux Esophagitis
- Eosinophilic Esophagitis

Esophageal Lacerations

- Mallory weiss tears are most common
- Due to: severe retching or prolonged vomiting
- Present with hematemesis.
- Failure of gastroesophageal musculature to relax prior to antiperistaltic contraction associated w/ vomiting>>stretching>>>tear.

- Linear lacerations
- longitudinally oriented
- Cross the GEJ.
- Superficial
- Heal quickly , no surgical intervention

Health Jade

Chemical Esophagitis

- Damage to esophageal mucosa by irritants
- Alcohol,
- Corrosive acids or alkalis
- Excessively hot fluids
- Heavy smoking
- Medicinal pills (doxycycline and bisphosphonates)
- Iatragenic (chemotx, radiotx , GVHD)

Clinical symptoms & morphology

- Ulceration and acute inflammation.
- Only self-limited pain, odynophagia (pain with swallowing).
- Hemorrhage, stricture, or perforation in severe cases

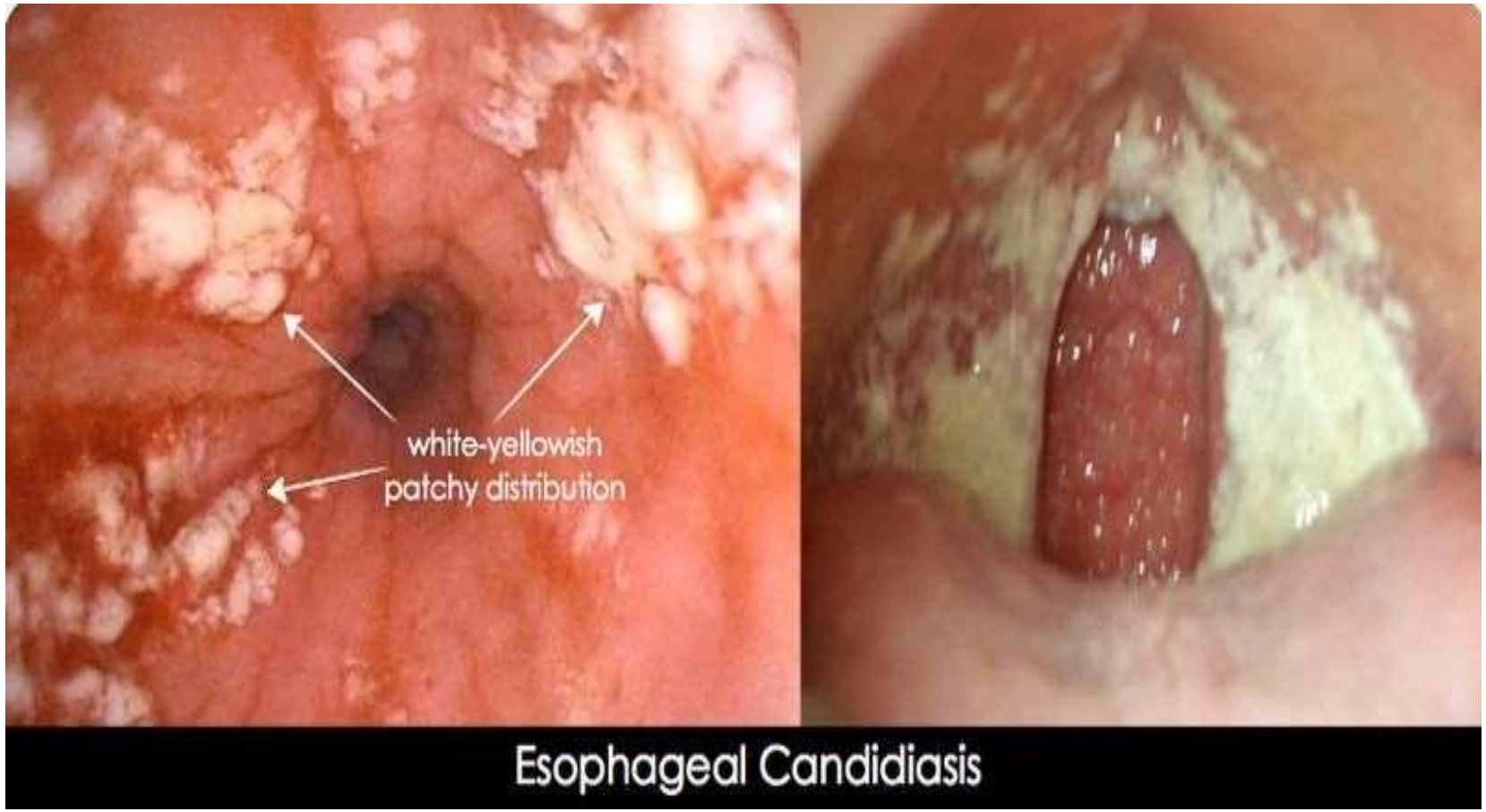
Infectious esophagitis

- Mostly in immunosuppressed.

- Viral (HSV, CMV)
- Fungal (candida >>> mucormycosis & aspergillosis)
- Bacterial: 10%.

- Candidiasis :

- Adherent.
- Gray-white pseudomembranes
- Composed of matted fungal hyphae and inflammatory cells



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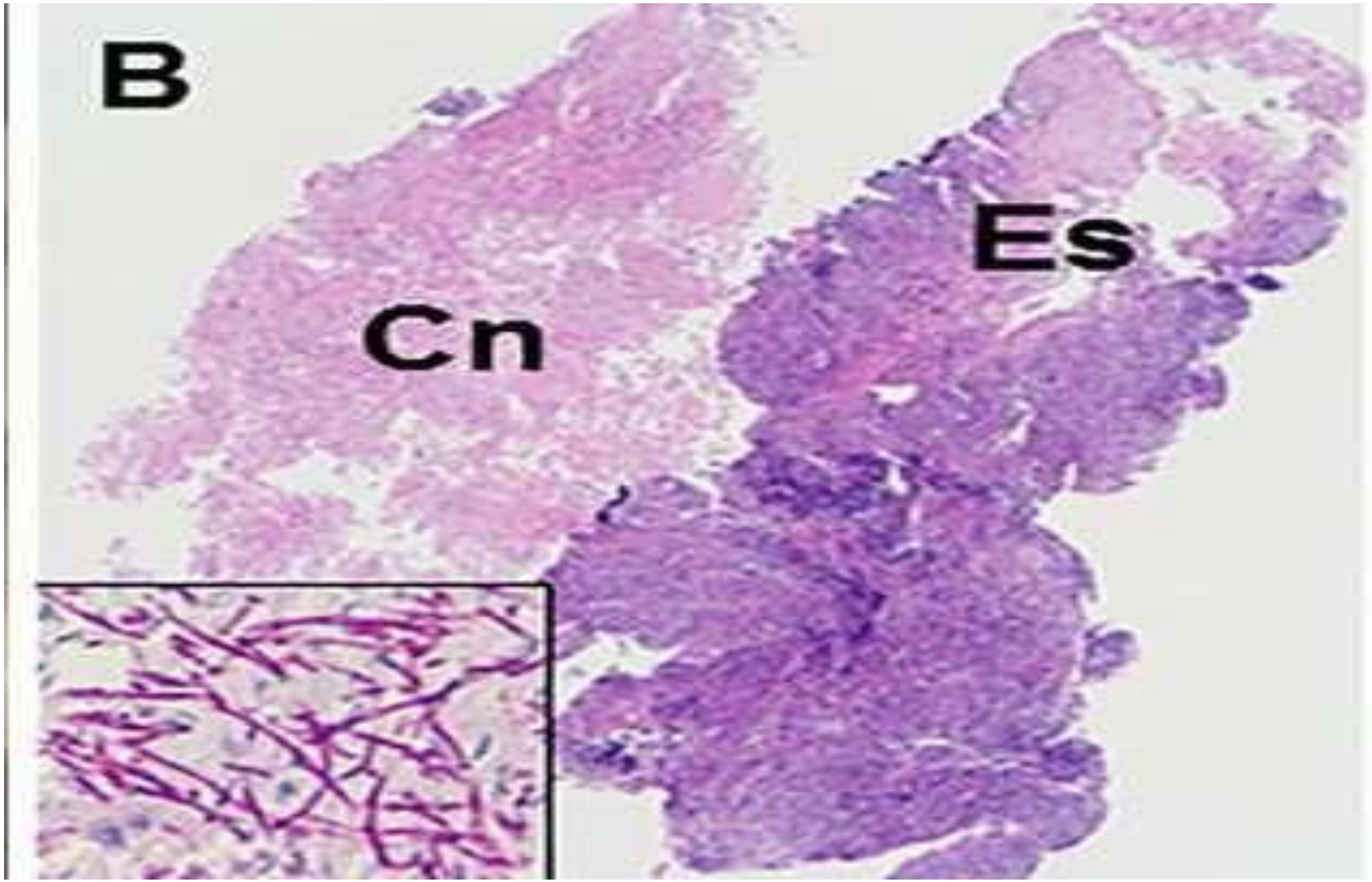
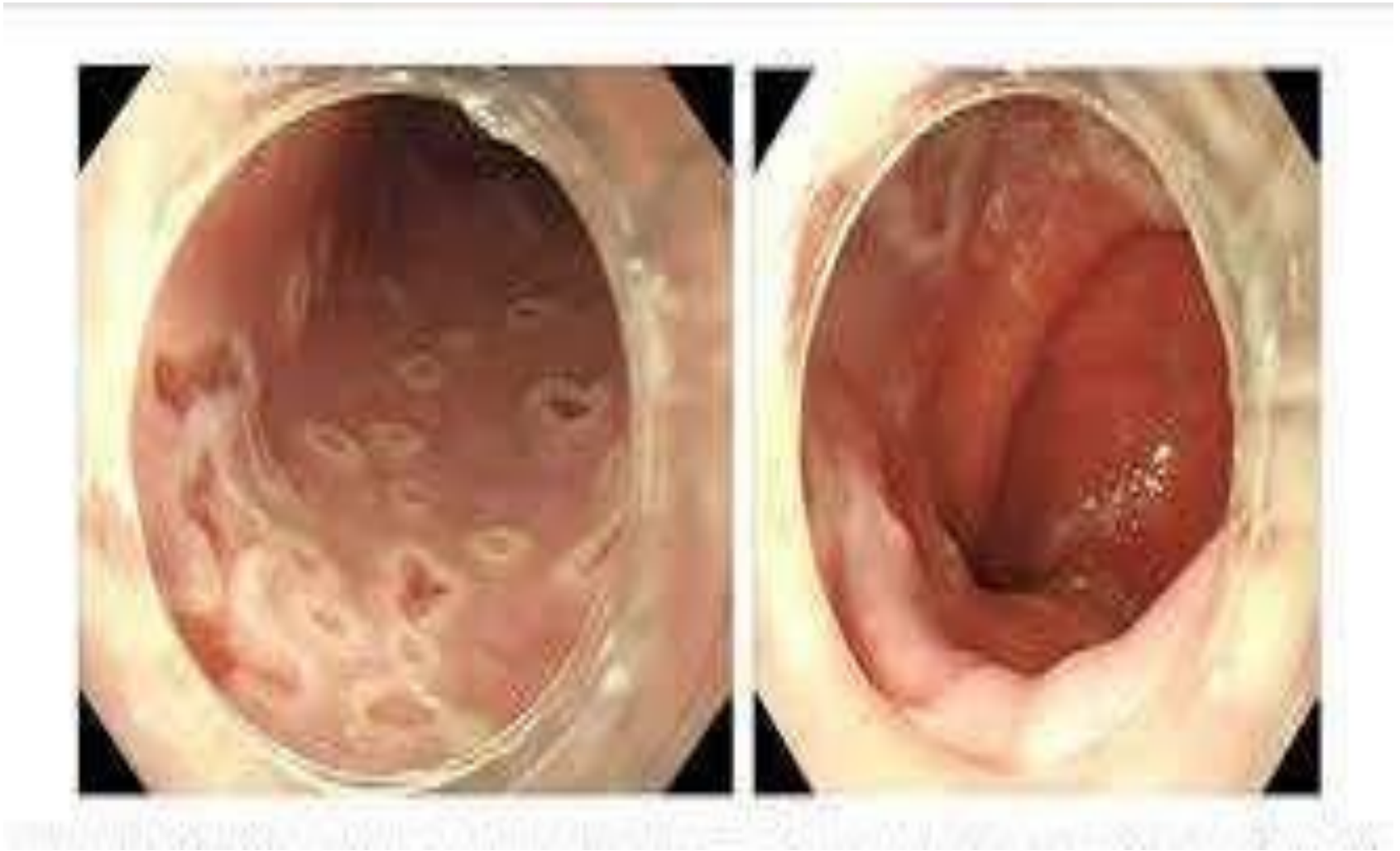
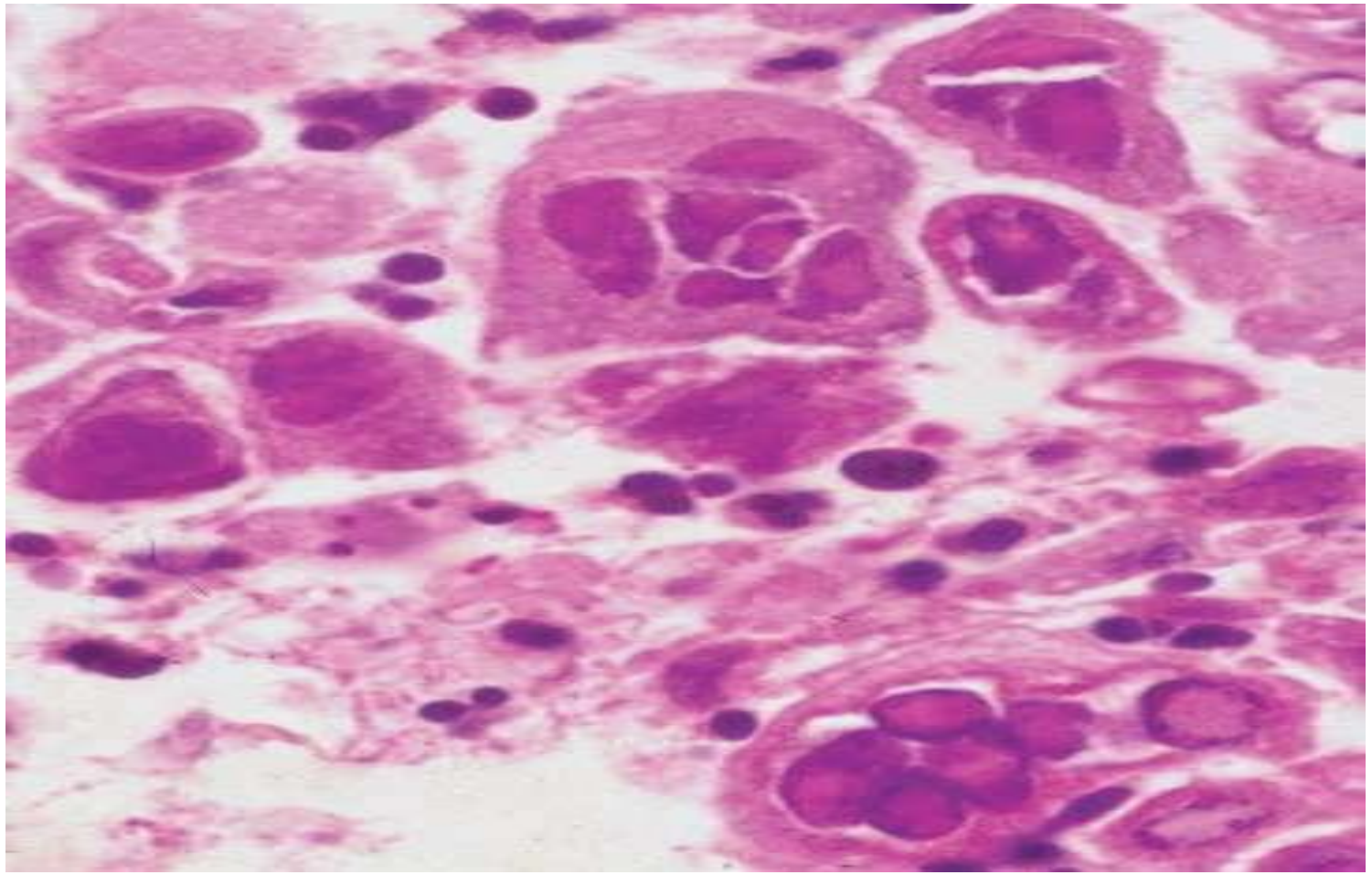


www.researchgate.net/publication/285369734_Esophageal_Candidiasis_as_the_Initial_Manifestation_of_Acute_Myeloid_Leukemia

- Herpes viruses
- Punched-out ulcers
- Histopathologic:
- Nuclear viral inclusions
- Degenerating epithelial cells ulcer edge
- Multinucleated epithelial cells.



Semantic Scholar



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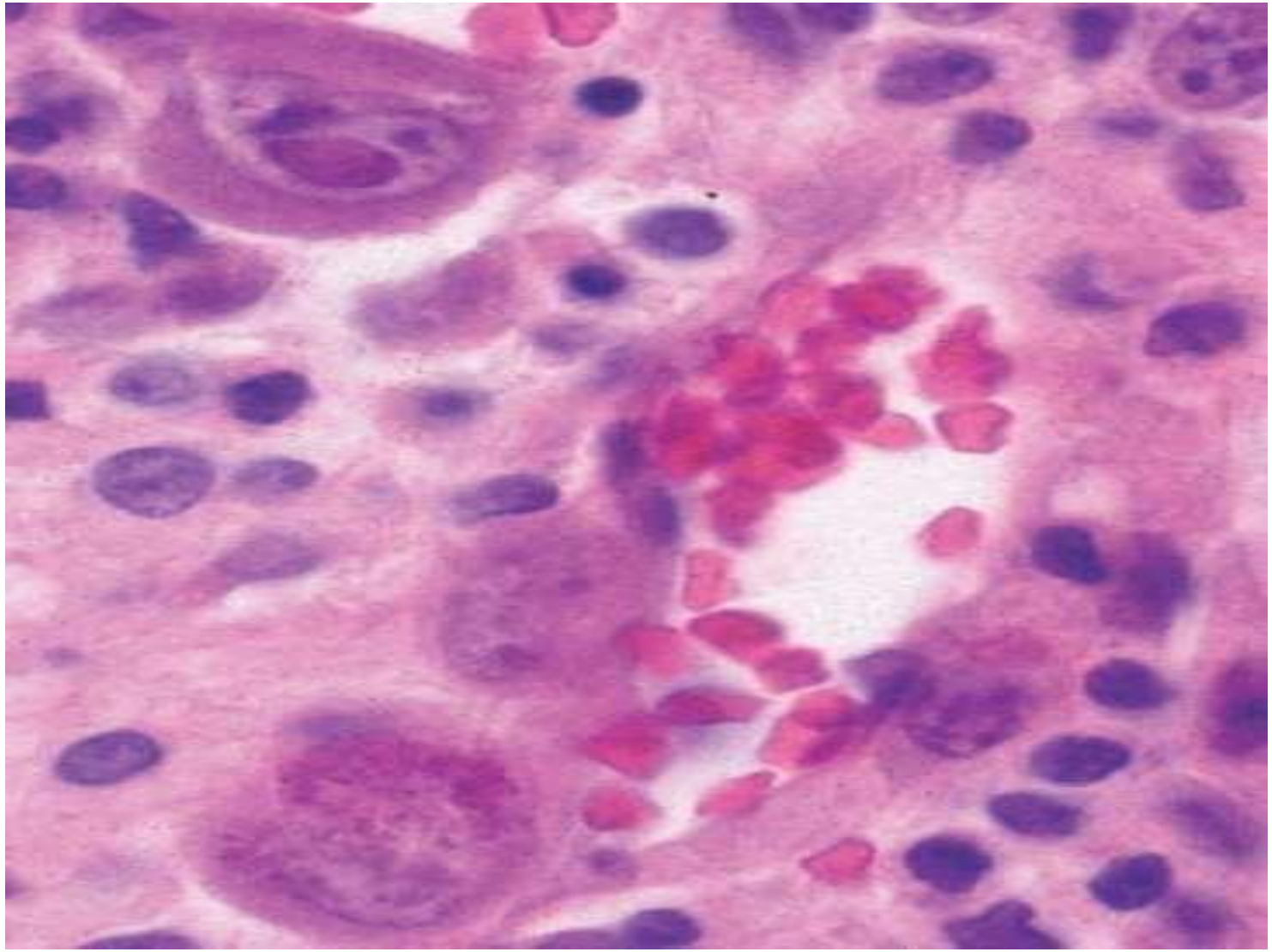
- CMV :
- Shallower ulcerations.
- Biopsy: nuclear and cytoplasmic inclusions in capillary endothelium and stromal cells



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Reflux Esophagitis

- Reflux of gastric contents into the lower esophagus
- Most frequent cause of esophagitis
- Squamous epithelium is sensitive to acids
- Protective forces: mucin and bicarbonate, high LES tone

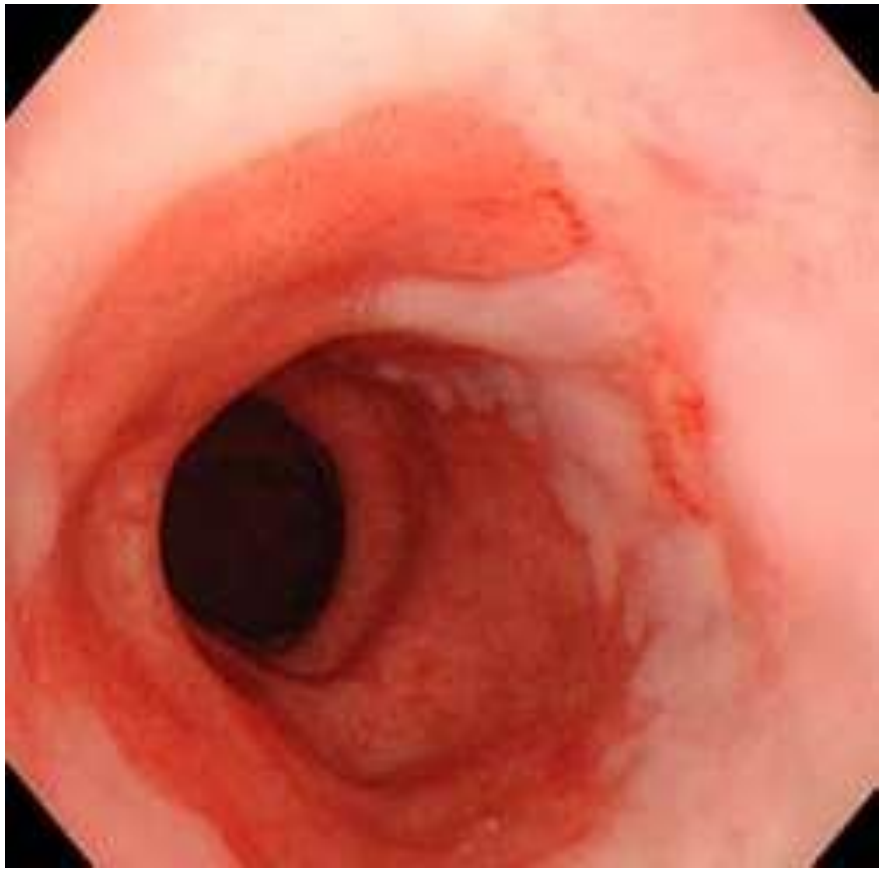
Pathogenesis

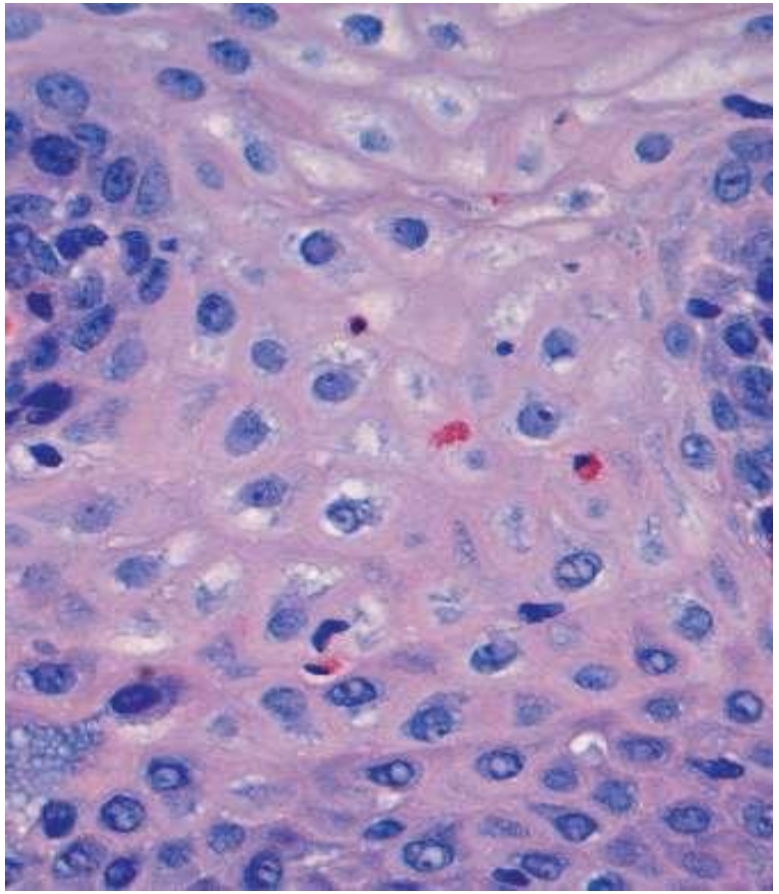
- Decreased lower esophageal sphincter tone
- (alcohol, tobacco, CNS depressants)
- Increase abdominal pressure
  - (obesity, pregnancy, hiatal hernia, delayed gastric emptying, and increased gastric volume)
- Idiopathic!!

Morphology

- Macroscopy (endoscopy)
- Depends on severity (Unremarkable, Simple hyperemia (red)

- Microscopic:
- Eosinophils infiltration
- Followed by neutrophils (more severe).
- Basal zone hyperplasia
- Elongation of lamina propria papillae





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Clinical Features

- Most common over 40 years.
- May occur in infants and children
- Heartburn , dysphagia,
- Regurgitation of sour-tasting gastric contents
- Rarely: Severe chest pain, mistaken for heart disease

- Tx: proton pump inhibitors

Complications

- Esophageal ulceration
- Hematemesis
- Melena
- Strictures
- Barrett esophagus (precursor of Ca.)

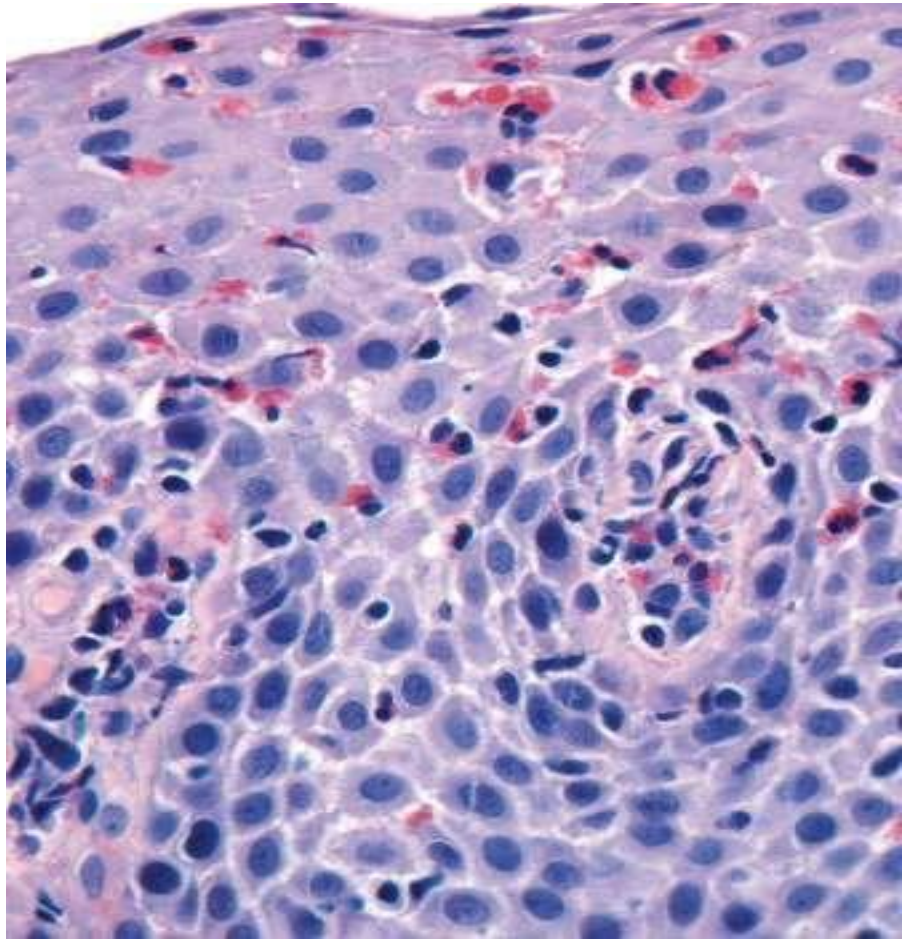
Eosinophilic Esophagitis

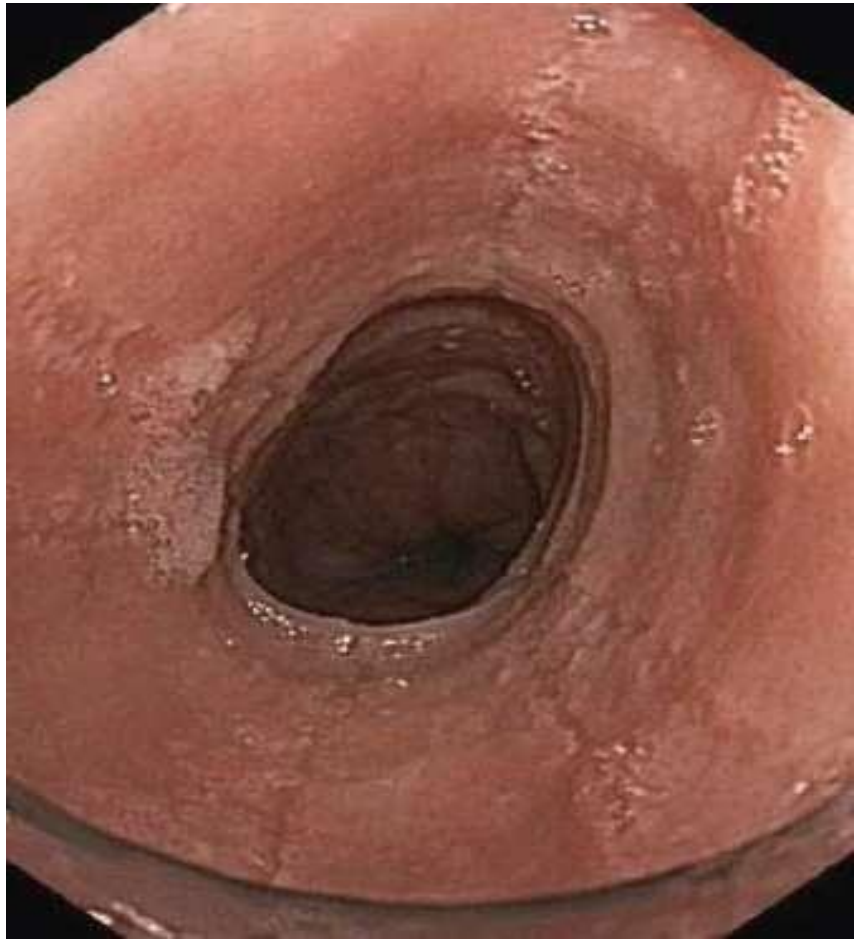
- Chronic immune mediated disorder

- Symptoms:
- Food impaction and dysphagia in adults
- Feeding intolerance or GERD-like symptoms in children

- Endoscopy:
- Rings in the upper and mid esophagus.

- Microscopic:
- Numerous eosinophils w/n epithelium
- Far from the GEJ.





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- Most patients are: atopic (atopic dermatitis, allergic rhinitis, asthma) or modest peripheral eosinophilia.

- Treatment:
- Dietary restrictions(cow milk and soy products)
- Topical or systemic corticosteroids.
- Refractory to PPIs.

Barrett Esophagus

- Complication of chronic GERD
- Intestinal metaplasia within the esophageal squamous mucosa.
- 10% of individuals with symptomatic GERD
- Males>>females, 40-60 yrs
- **Direct precursor of esophageal adenocarcinoma**
- **Metaplasia >> 0.2-1% /year >>dysplasia>>**
- **adenocarcinoma**.

Morphology

- Endoscopy:
- Red tongues extending upward from the GEJ.

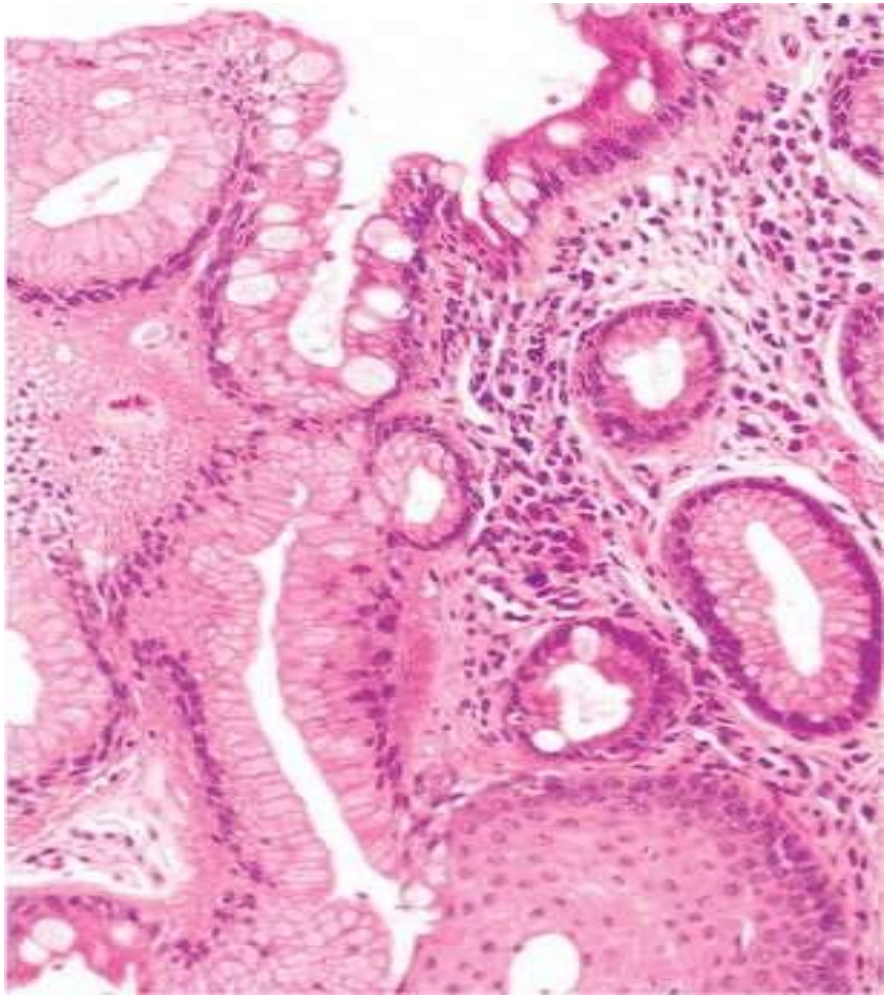
- Histology:
- Gastric or intestinal metaplasia
- Presence of goblet cells
- +-Dysplasia : low-grade or high-grade
- Intramucosal carcinoma: invasion into the lamina propria.

Robert Riddell

- Dr. Riddell has over 230 publications which are largely in gastrointestinal pathology. Many of them are in inflammatory bowel disease. **In 1983, Dr. Riddell was lead author on the paper defining and grading dysplasia** in inflammatory bowel disease, a system that is not only still in use but has been extended to other part of the gastrointestinal tract.
- He has edited or written 5 books, which **include a two volume "bible" on gastrointestinal pathology** and its clinical implications with Drs. Klaus Lewin and Wilfred Weinstein at UCLA.

  This book is currently being re-written. He is also the lead author of the AFIP Fascicle on tumors of the intestines. Dr. Riddell directs an annual week long gastrointestinal pathology course that has now been running for almost 30 years. He is a frequent speaker and talks about intestinal disease in both the upper and lower gastrointestinal tract both nationally and internationally. He has numerous on-going projects including gastroesophageal reflux disease, indeterminate colitis, drug-associated colitis, and molecular changes in dysplasia in ulcerative colitis and the pathology of motility disorder

Gastroenterology Consultants of San Antonio



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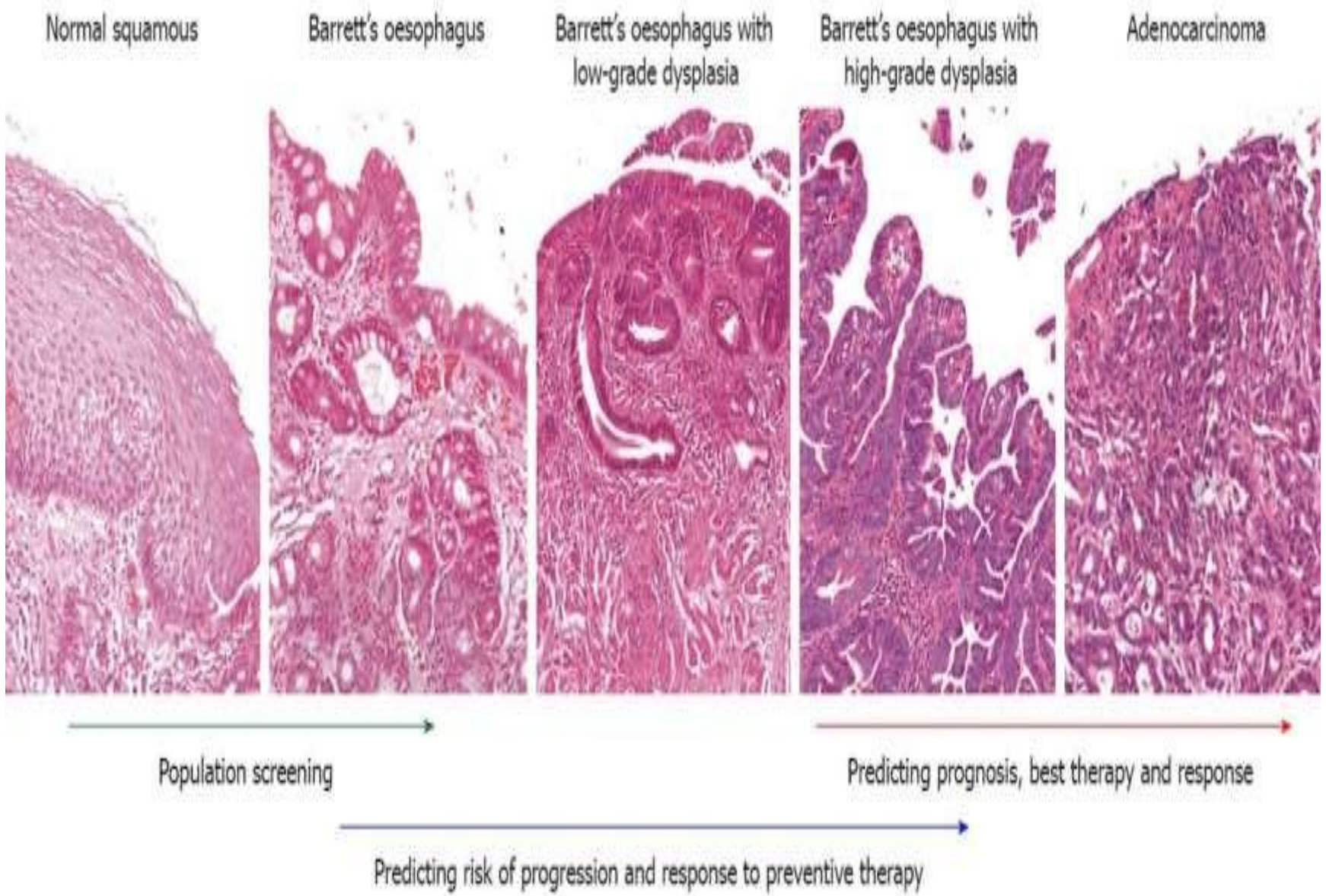


Management of Barrett

- Periodic surveillance endoscopy with biopsy to screen for dysplasia.
- High grade dysplasia & intramucosal carcinoma needs interventions.

Esophageal tumors

- Squamous cell carcinoma (most common worldwide)
- Adenocarcinoma (on the rise, half of cases)

Adenocarcinoma

- Background of Barrett esophagus and long-standing GERD.
  - Risk factors: dysplasia associated Barrett, smoking, obesity, radioTx.
  - Male : female (7:1)
  - Geographic & racial variation (devloped countries)

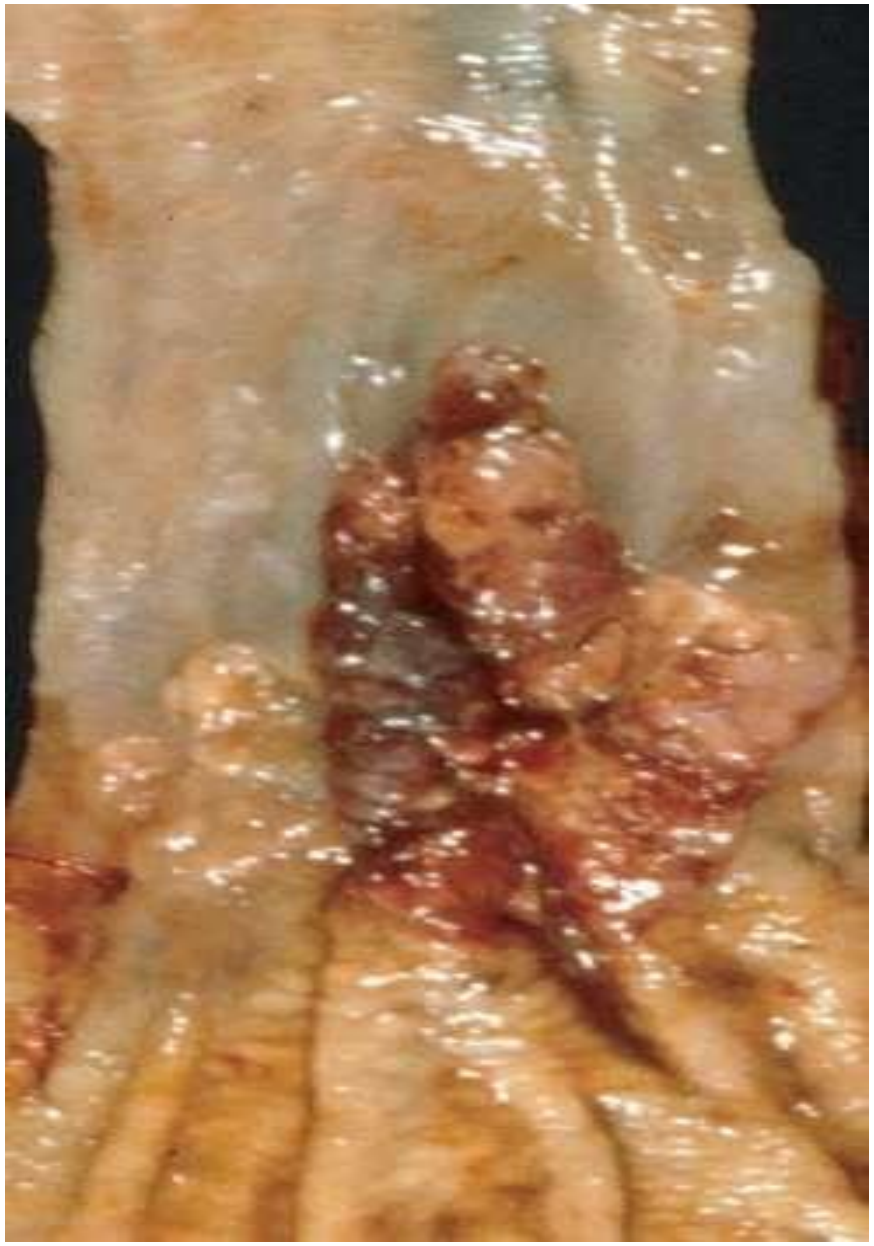
Pathogenesis

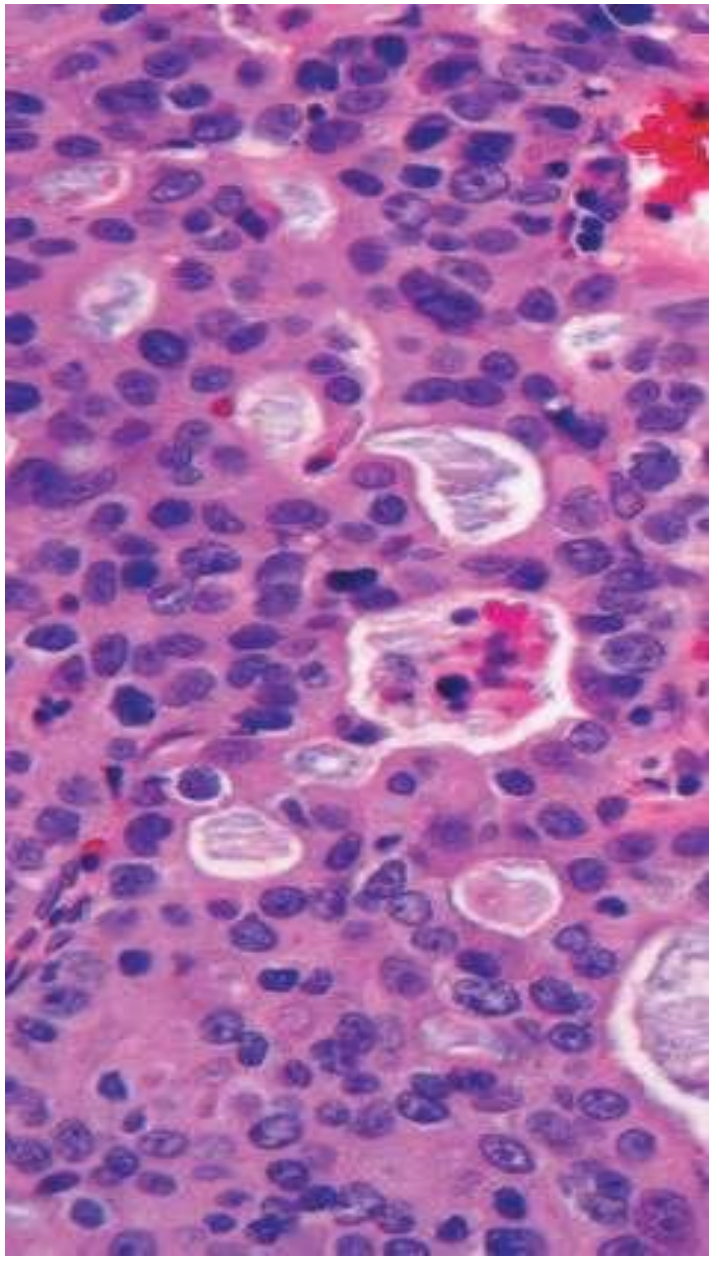
- From Barrett>>dysplasia>>adenocarcinoma
- Chromosomal abnormalities and TP53 mutation.

Morphology

- Distal third.
- Early: flat or raised patches
- Later: exophytic infiltrative masses

- Microscopy:
- Forms glands and mucin.





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Clinical Features

- Pain or difficulty swallowing
- Progressive weight loss
- Chest pain
- Vomiting.
- Advanced stage at diagnosis: 5-year survival <25%.
- Early stage: 5-year survival 80%

Squamous Cell Carcinoma

- Male : female (4:1)
- Underdeveloped countries.

- **Risk factors:**
- Alcohol
- Tobacco use
- Poverty
- Caustic injury
- Achalasia .
- Plummer-Vinson syndrome
- Frequent consumption of very hot beverages
- Previous radiation Tx.

Pathogenesis

- In western : alcohol and tobacco use.
- Other areas: polycyclic hydrocarbons, nitrosamines, fungus-contaminated foods
- HPV infection implemented in high risk regions.

Morphology

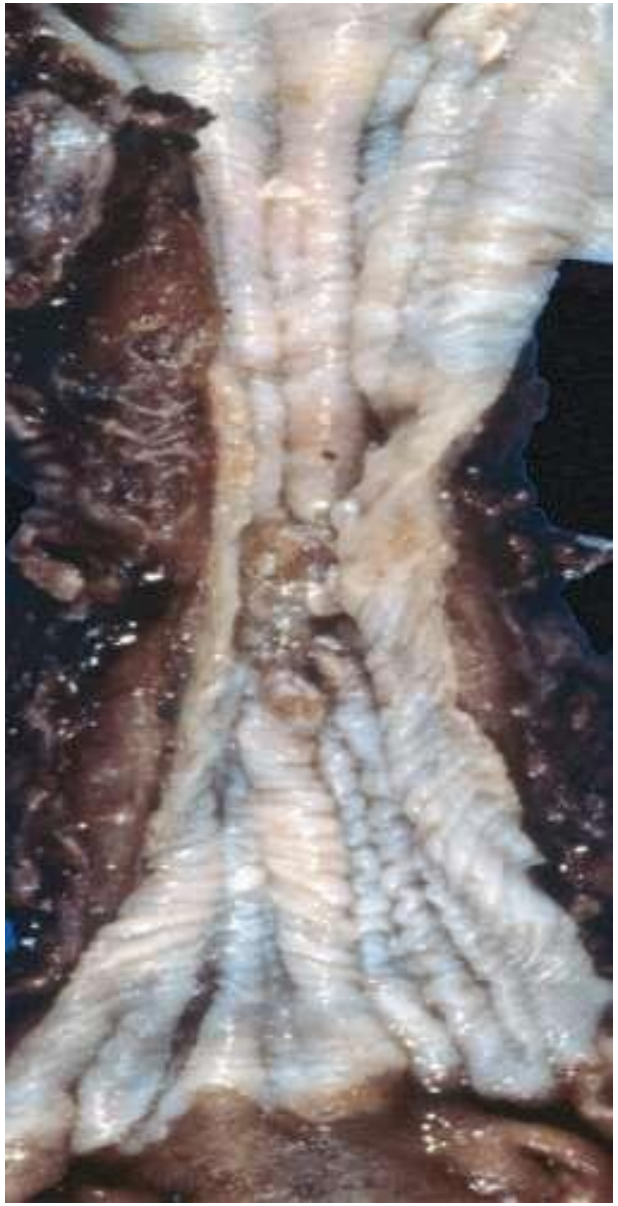
- Middle third (50% of cases)
- Polypoid, ulcerated, or infiltrative.
- Wall thickening, lumen narrowing
- Invade surrounding structures (bronchi, mediastinum, pericardium, aorta).

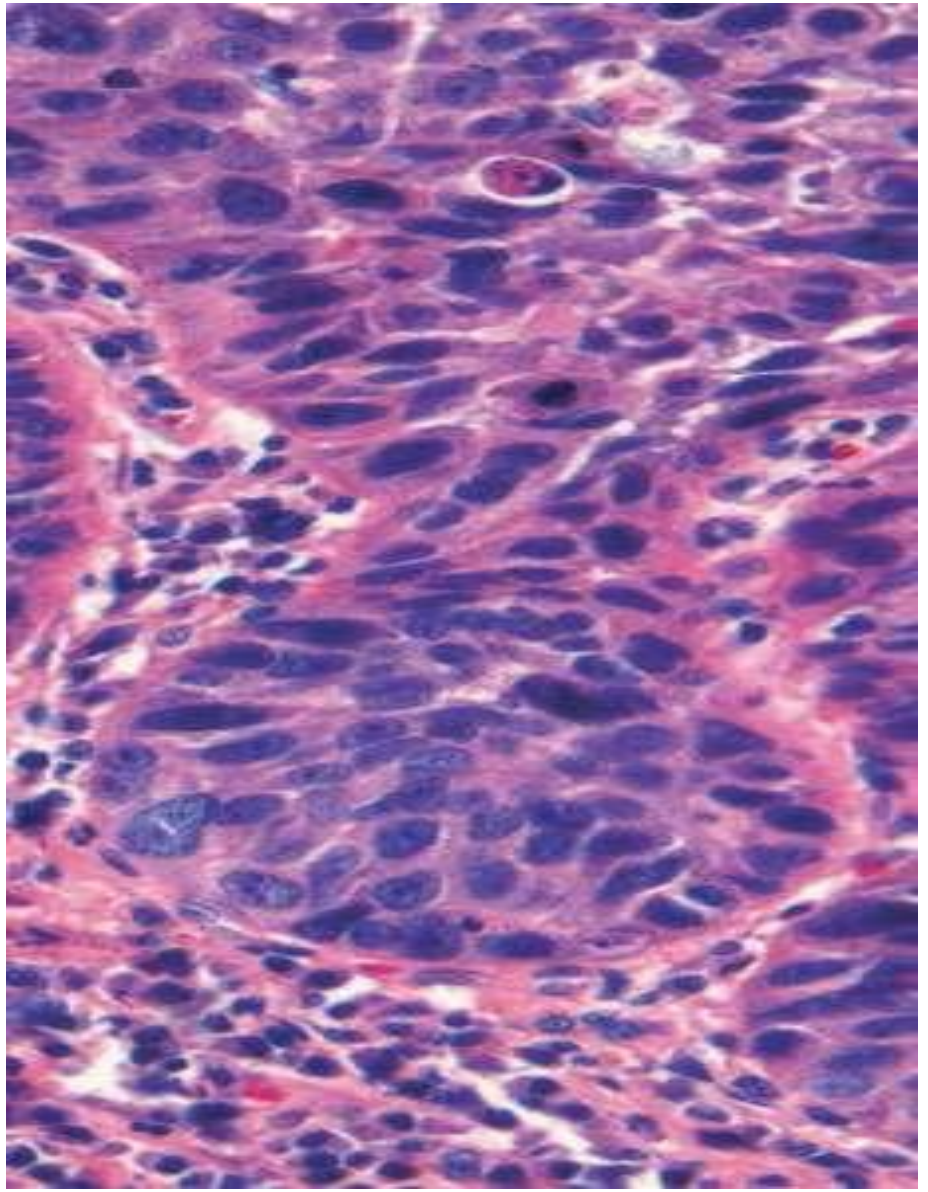
Microscopy:

- Pre-invasive: Squamous dysplasia & CIS.
- Well to moderately differentiated invasive SCC.
- Intramural tumor nodules
- Lymph node metastases :
- Upper 1/3: cervical LNs
- Middle 1/3: mediastinalparatracheal, and tracheobronchial LNs.
- Lower 1/3: gastric and celiac LNs.

Clinical Features

- Dysphagia
- Odynophagia
- Obstruction
- Weight loss and debilitation
- Impaired nutrition & tumor associated cachexia
- Hemorrhage and sepsis if ulcerated.
- Aspiration via a tracheoesophageal fistula
- Dismal Px: 5 year survival <9%





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