

DISEASE OF THE ORAL CAVITY AND ESOPHAGUS

Dr. Omar Hamdan

Gastrointestinal and liver pathologist
Mutah University
School of Medicine-Pathology Department
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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^{حمر} Ulcers (Canker Sores)

- Superficial mucosal ulcerations
- Common, up to 40%^x 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.
اضطراب آبة صغوية
- Solitary or multiple
- Shallow, with a hyperemic base^{↑ blood} covered by a thin exudate and rimmed by a narrow zone of erythema.
- resolve spontaneously in 7 to 10 days.

x



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.
التهاب الفم
- 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.

وصف
لدا

Oral Candidiasis (Thrush)

↳ yeast ^{بِزَجَل}
spore
hyphae ^{صَي}

- 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:** ¹ Immunosuppression, ² specific strain of *C. albicans*, ³ composition of the oral microbial flora (microbiota), ¹ 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, ^{لبين} 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.

ام اثني

↳ ↓↓ neutrophils

Leukoplakia and Erythroplakia

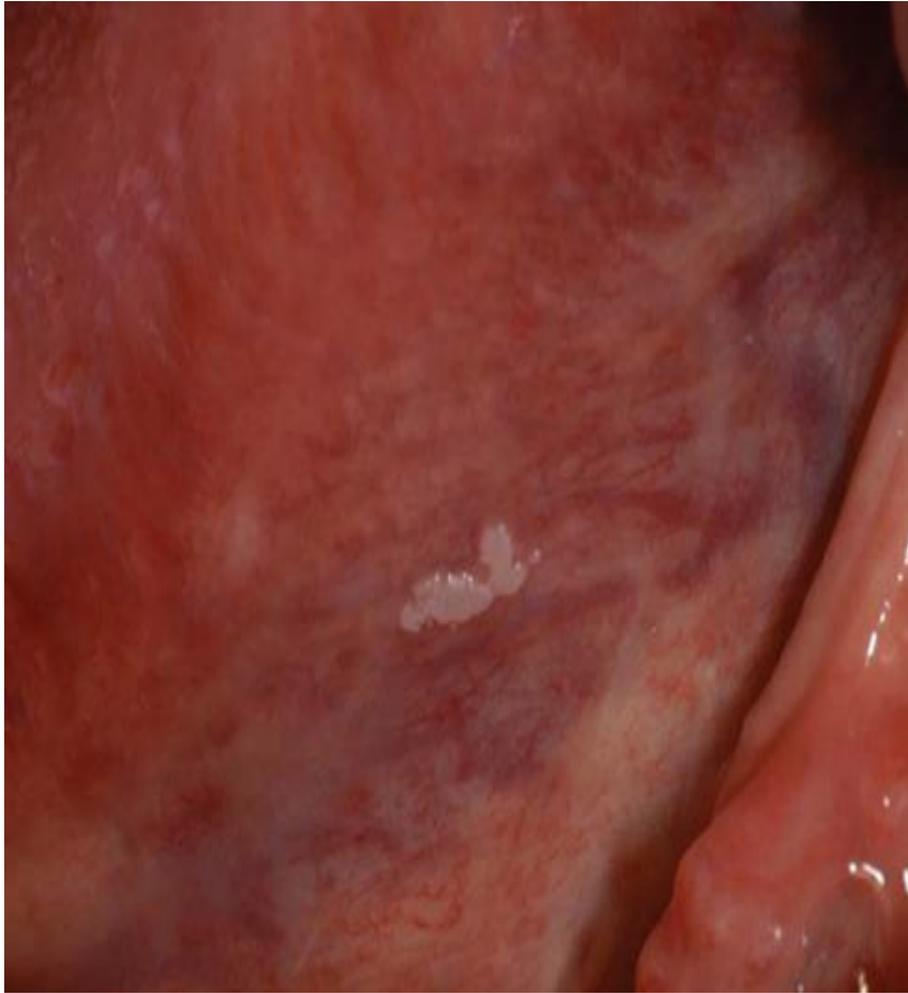
- **Leukoplakia:** is defined by the WHO as “a white patch or plaque that cannot be scraped off and cannot be characterized clinically or pathologically as any other disease.”
قائمتل على مرض مزمن
- This description is reserved for lesions that arise in the oral cavity in the absence of any known cause. 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.
ulcerated
- 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.
↑ thickening of s. spinosum
- 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.



dysplasia / leukoplakia



SCC



basement membrane

Squamous Cell Carcinoma

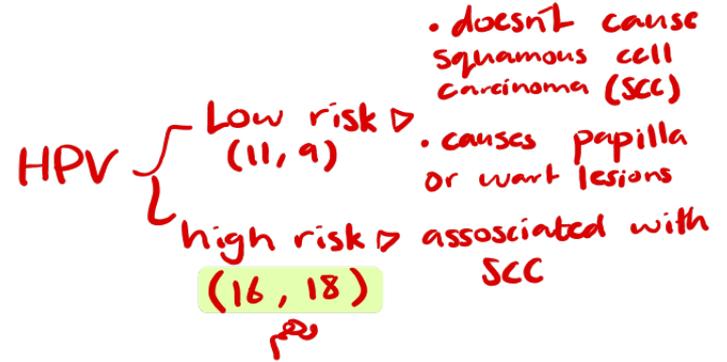
- Cancers of the oral cavity

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

- Squamous cell carcinoma:

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

Pathogenesis

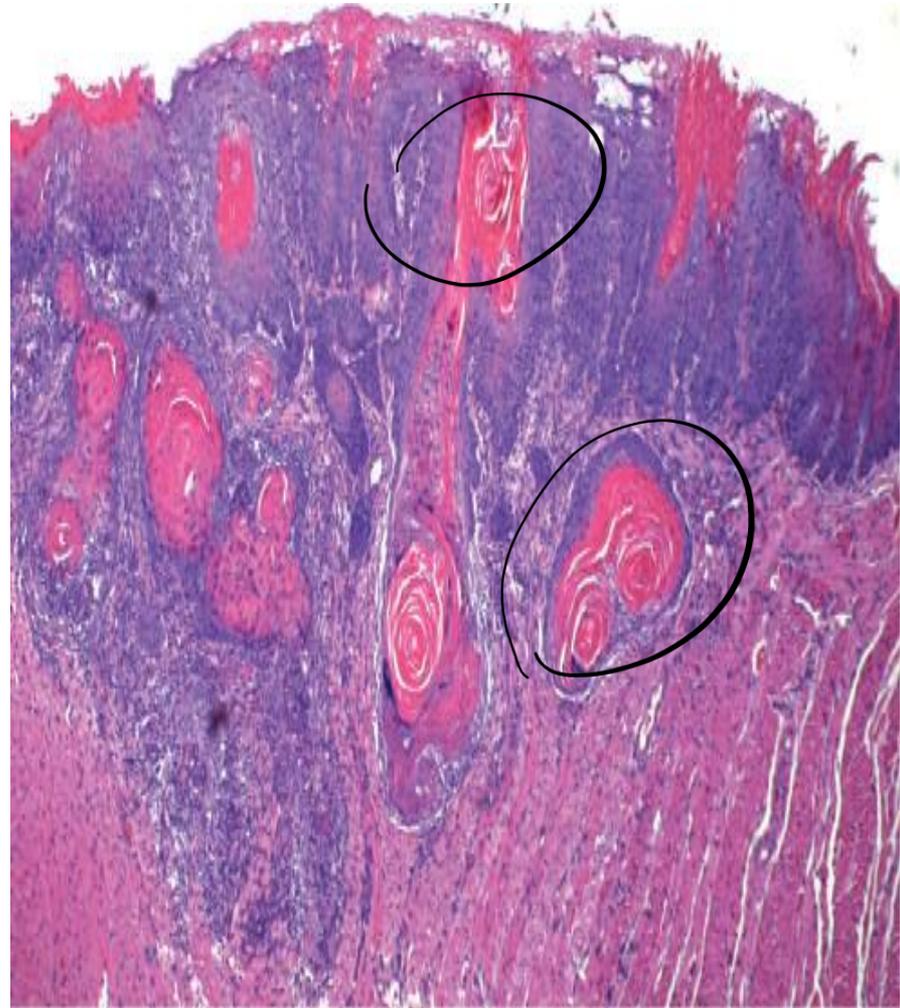
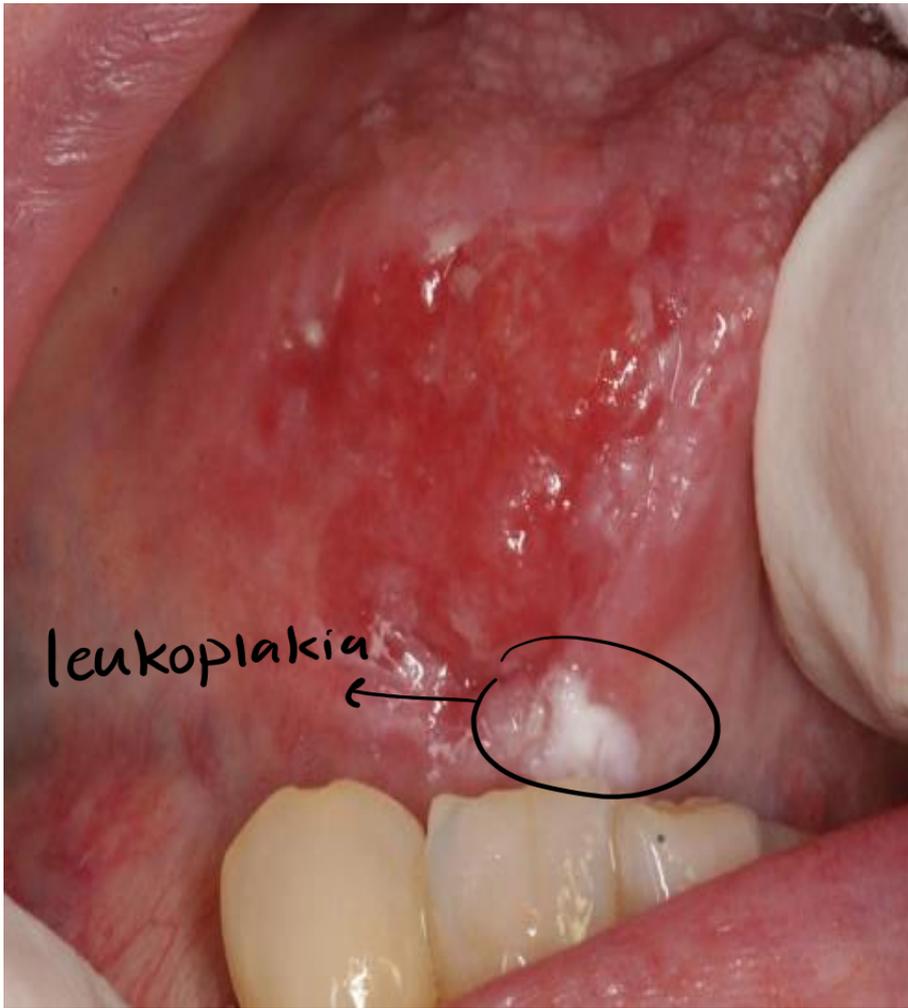


- Squamous cancers of the oropharynx arise through two distinct pathogenic pathways, one involving exposure to carcinogens, and the other related to infection with high risk variants of human papilloma virus (HPV). Carcinogen exposure mainly stems from chronic alcohol and tobacco (both smoked and chewed) use.
 ← good prognosis
- 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.
 → poor prognosis

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.

مسألة



scc

Well-diff. SCC
لأنه مبين Keratin (الوالبس)
ال cells نازلين ومتن ممانطين على مكانهم (invasion)

diseases of salivary glands

- **Sialadenitis** (inflammation of the salivary glands) can be caused by trauma, infection (such as mumps), or an autoimmune reaction.
التهاب

- **Pleomorphic adenoma** is a slow-growing neoplasm composed of a heterogeneous **mixture of epithelial and mesenchymal cells**. It is typically benign.
MC benign

- **Mucoepidermoid carcinoma** is a malignant neoplasm of variable biologic aggressiveness that is composed of a **mixture of squamous and mucous cells**.
MC malignant

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%)

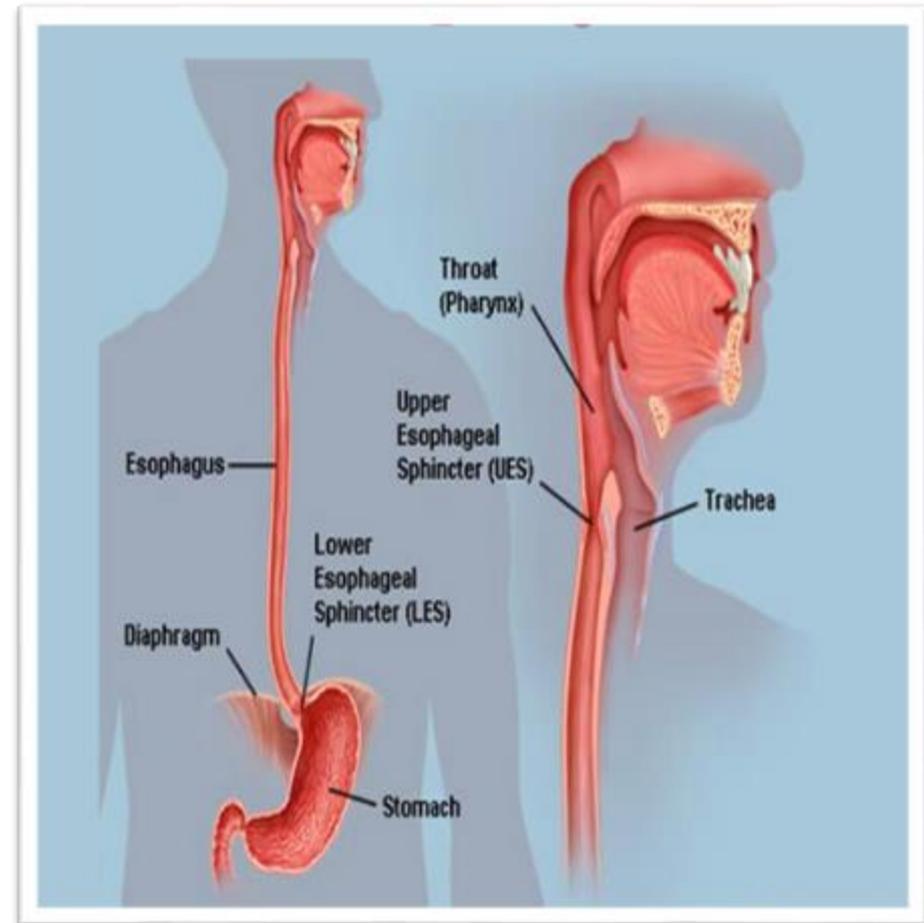
MC ← only

MC

* بدون نسبة
 * الأرقام إذا كانت
 بالعبارة فقط
 الرضا
 * إلا إذا ركز رقم
 معين

Diseases that affect the esophagus

1. Obstruction: mechanical or functional.
2. vascular diseases: varices. دوالي
3. Inflammation: esophagitis.
4. Tumors.



Mechanical Obstruction

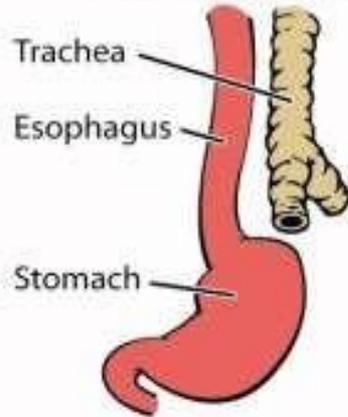
- Congenital or acquired.
- Examples:
- Atresia
- Fistulas
- Duplications 2 esoph.
- Agenesis (very rare) no esoph.
- Stenosis. تضيق

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.

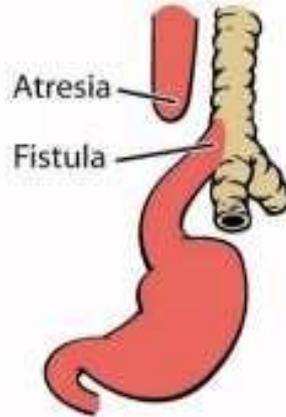
Atresia

- ▮ **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).
→ more common

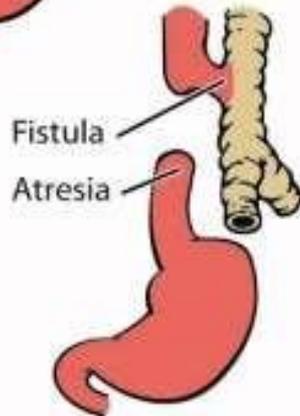
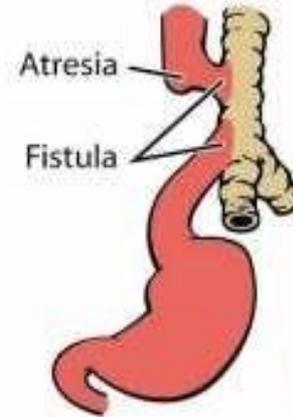
Normal Anatomy



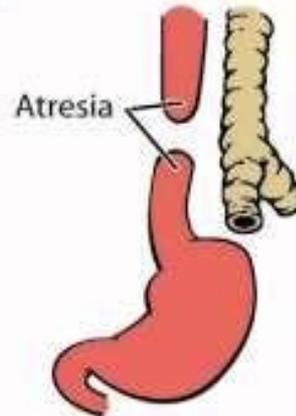
Atresia with distal Fistula



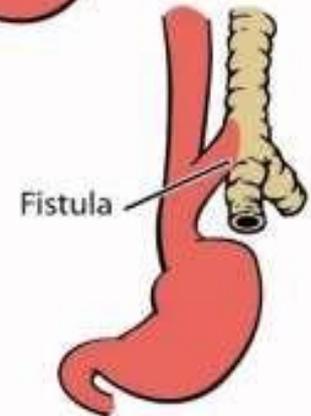
Atresia with double Fistula



Atresia with proximal Fistula



Atresia



Fistula

كلمة نفس الأعراس

Clinical presentation:

- ▮ Shortly after birth: regurgitation during feeding
- ▮ Needs ^{quick} prompt surgical correction (rejoin).

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

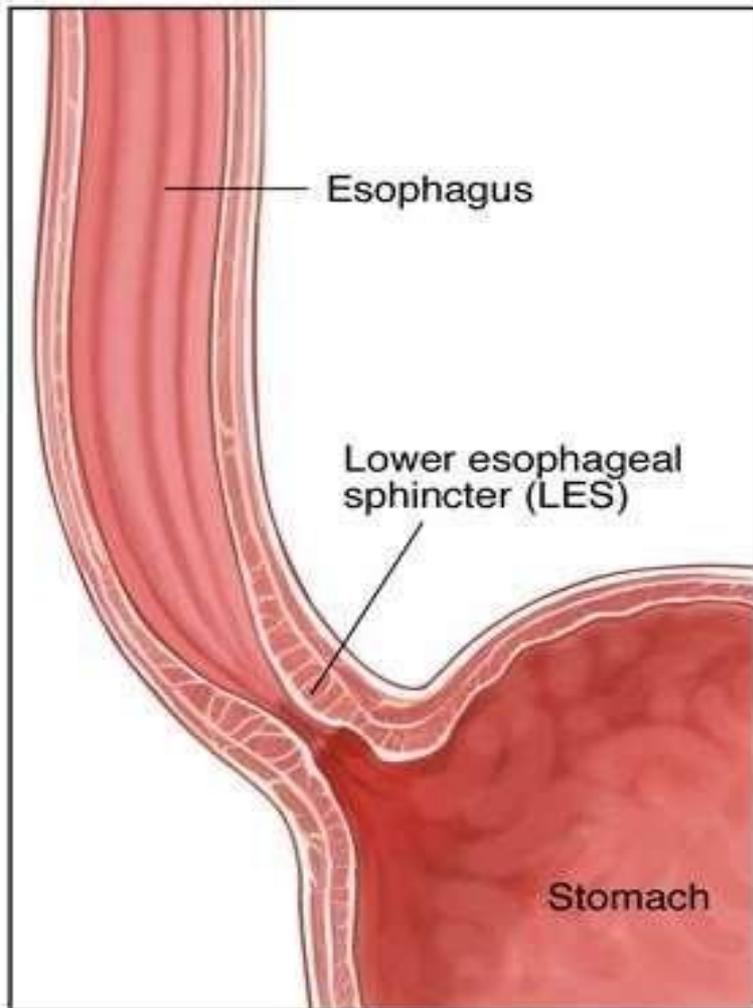
Functional Obstruction

- ▮ 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.**

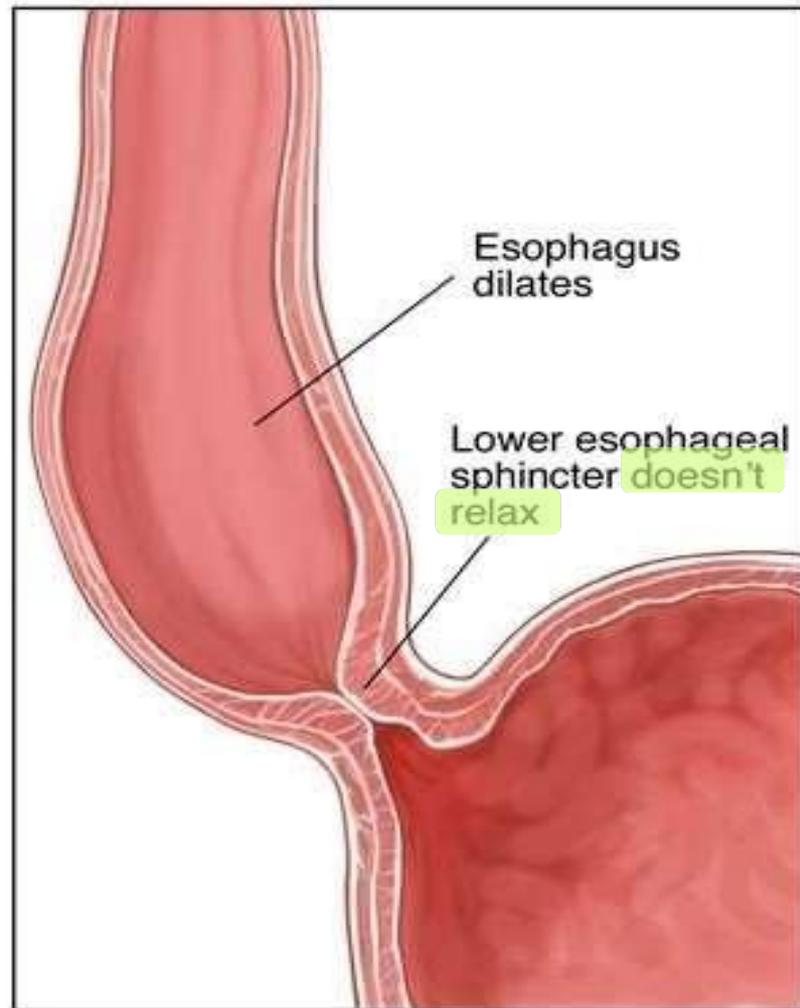
Achalasia

- ▮ *ثلاثية* Triad: *lower esophageal sphincter*
- ▮ Incomplete LES relaxation
- ▮ Increased LES tone
- ▮ Esophageal aperistalsis.

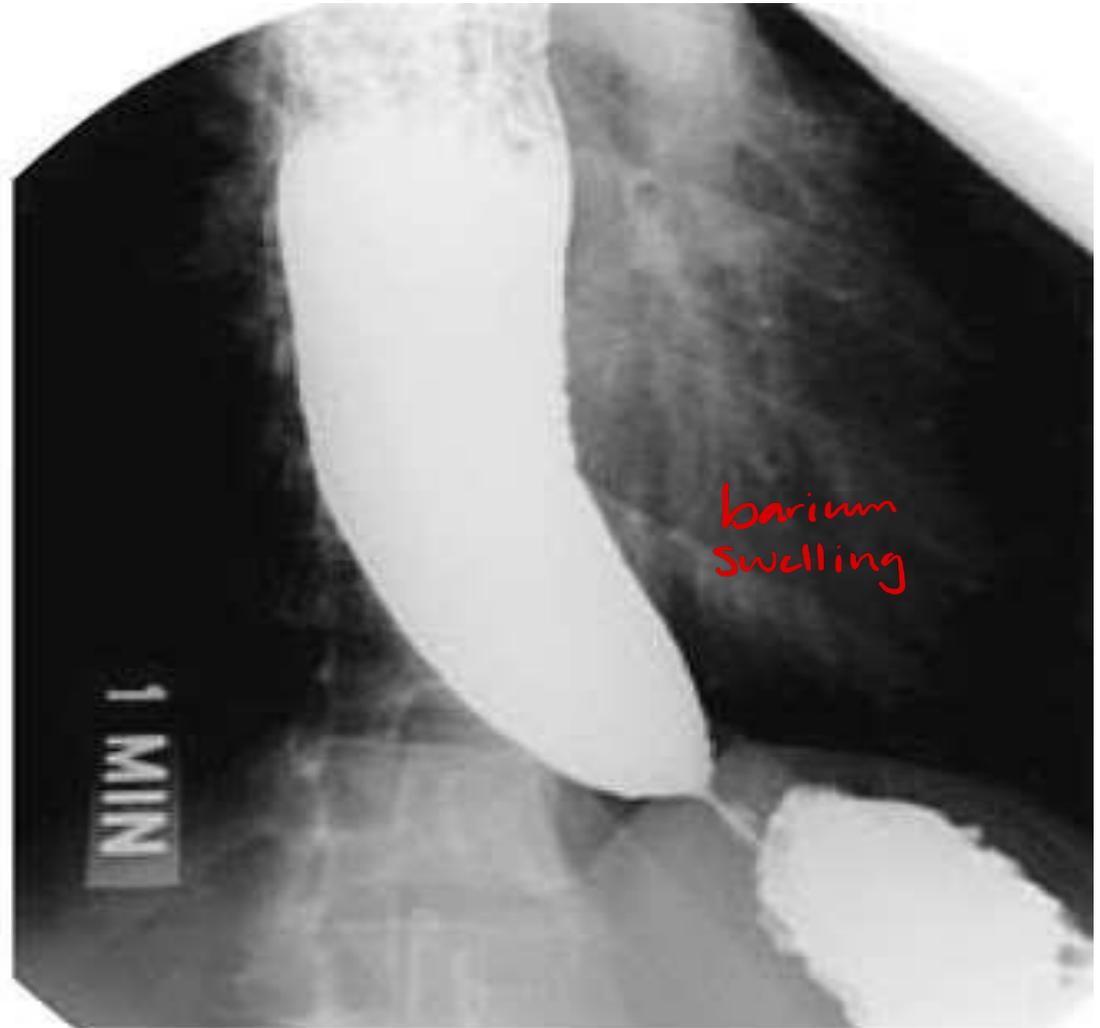
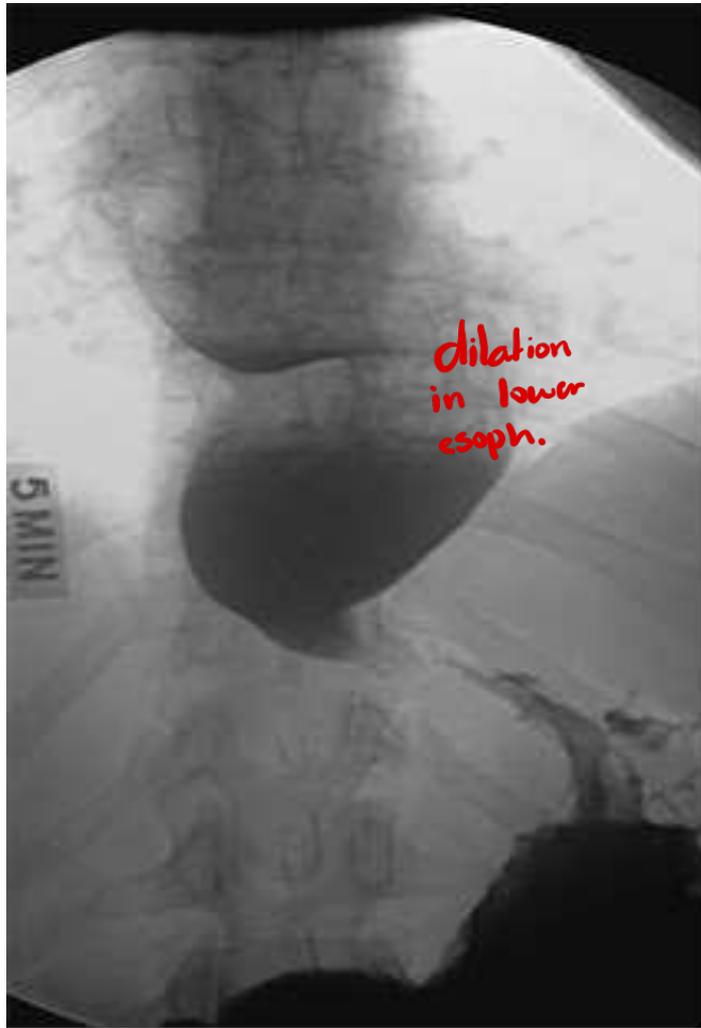
- ▮ Primary *More common* >>> secondary.



Normal



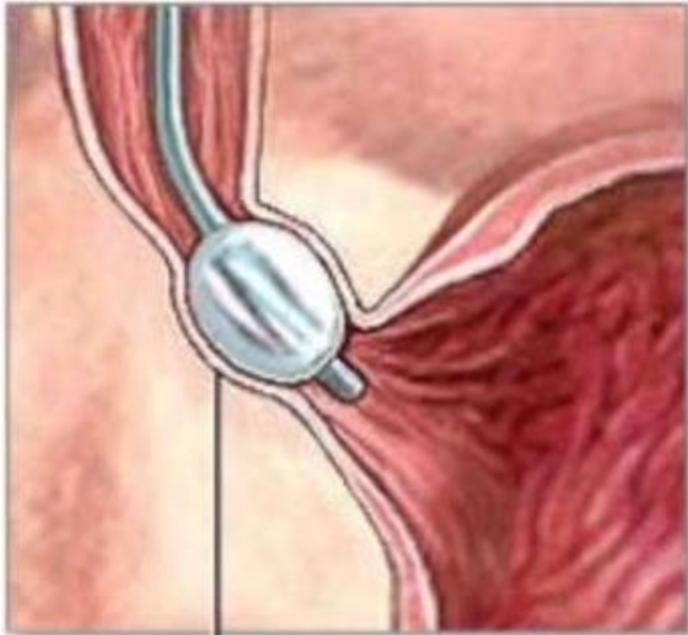
Achalasia



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

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Pneumatic balloon dilatation of the LES



Treatment:

- Lower esophageal sphincter



Primary achalasia

- cause : 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.

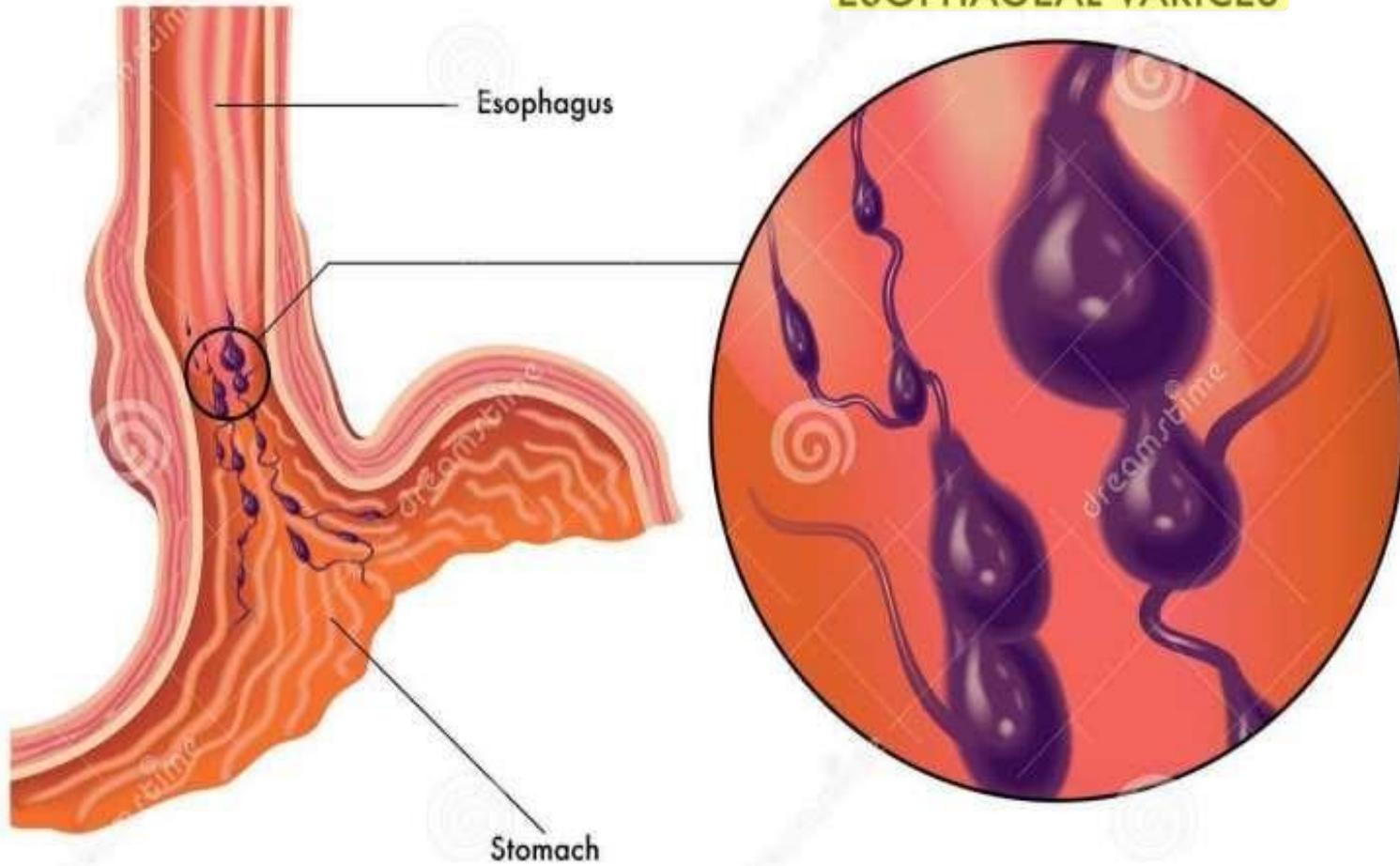
ما ج
تكون
جواب
سؤال

Vascular diseases: Esophageal Varices

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

*type of x-ray
used for BVs.*

ESOPHAGEAL VARICES



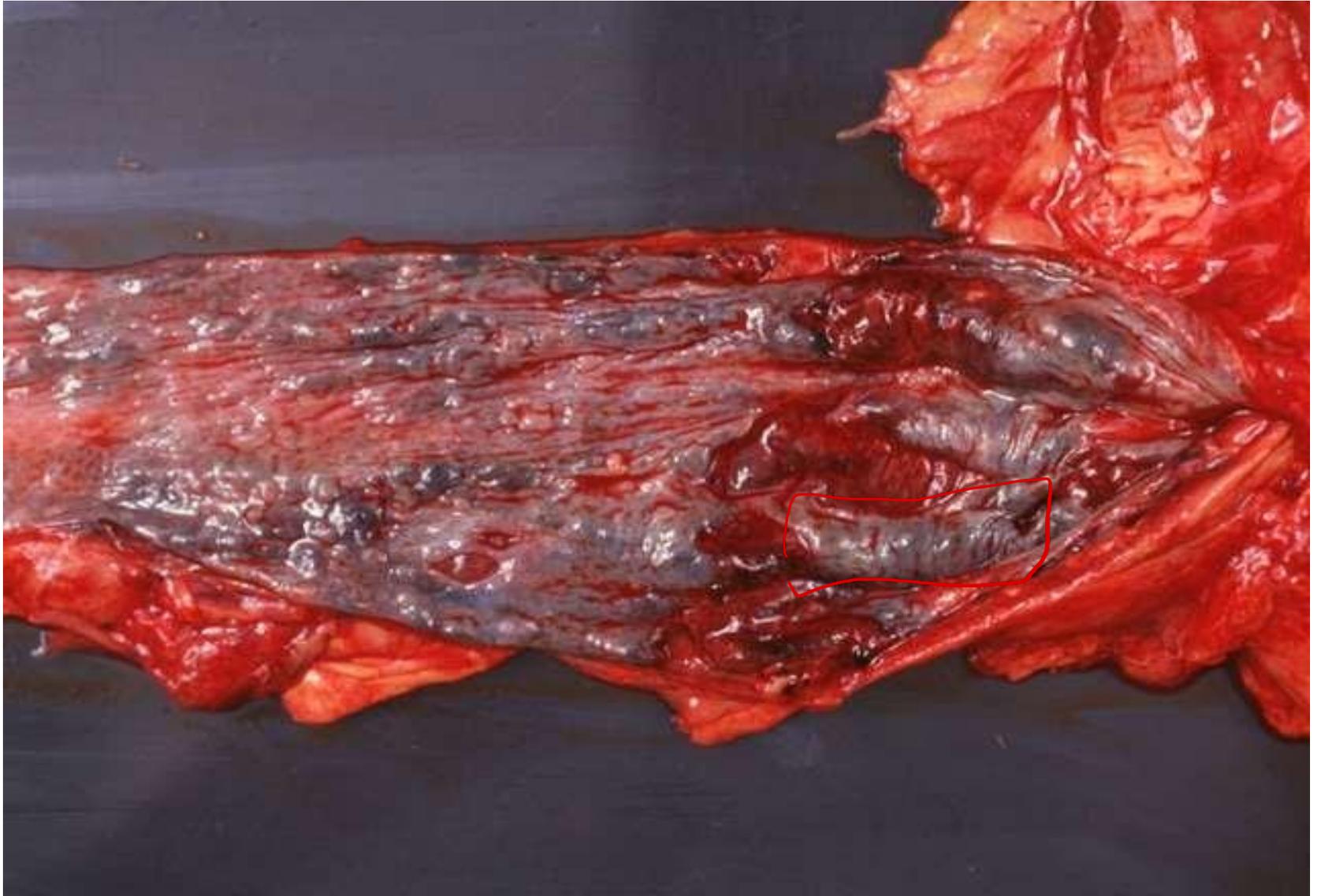
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دوالي
المریء

Dilated varices beneath intact squamous mucosa



Pathogenesis:

المشكلة
المتطلب

* 1

MC cause

Hypertension

- **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

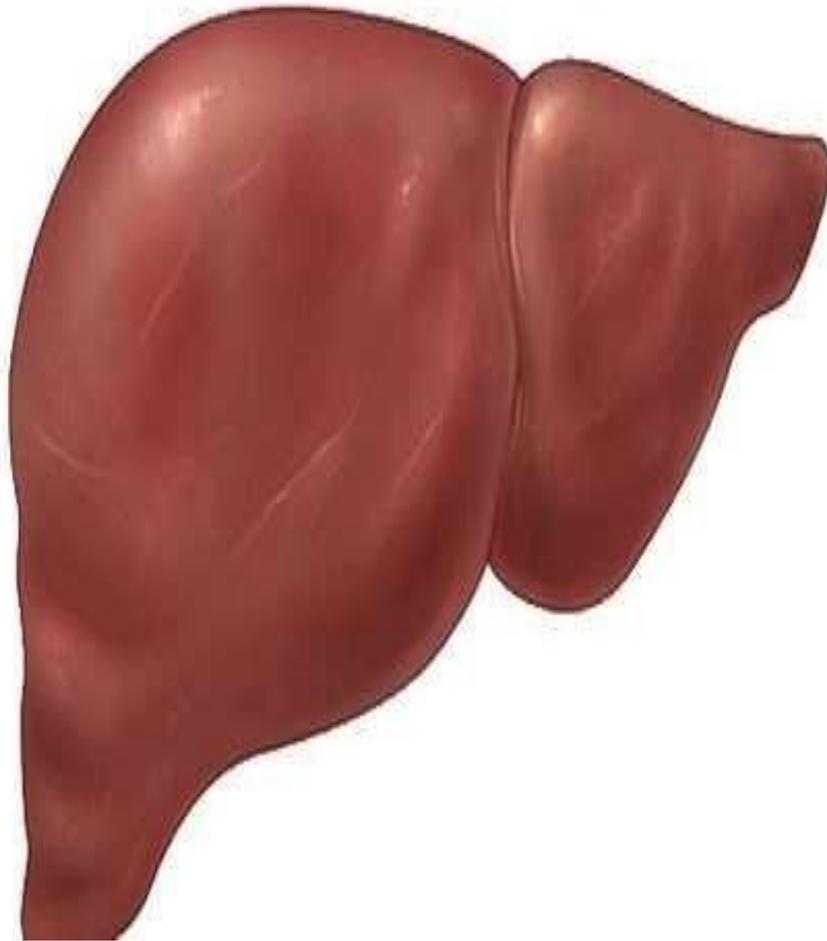
Causes of portal hypertension

*2

- ▮ Cirrhosis is most common
 - a. Alcoholic liver disease.
 - b.
- ▮ Hepatic schistosomiasis 2nd most common worldwide.

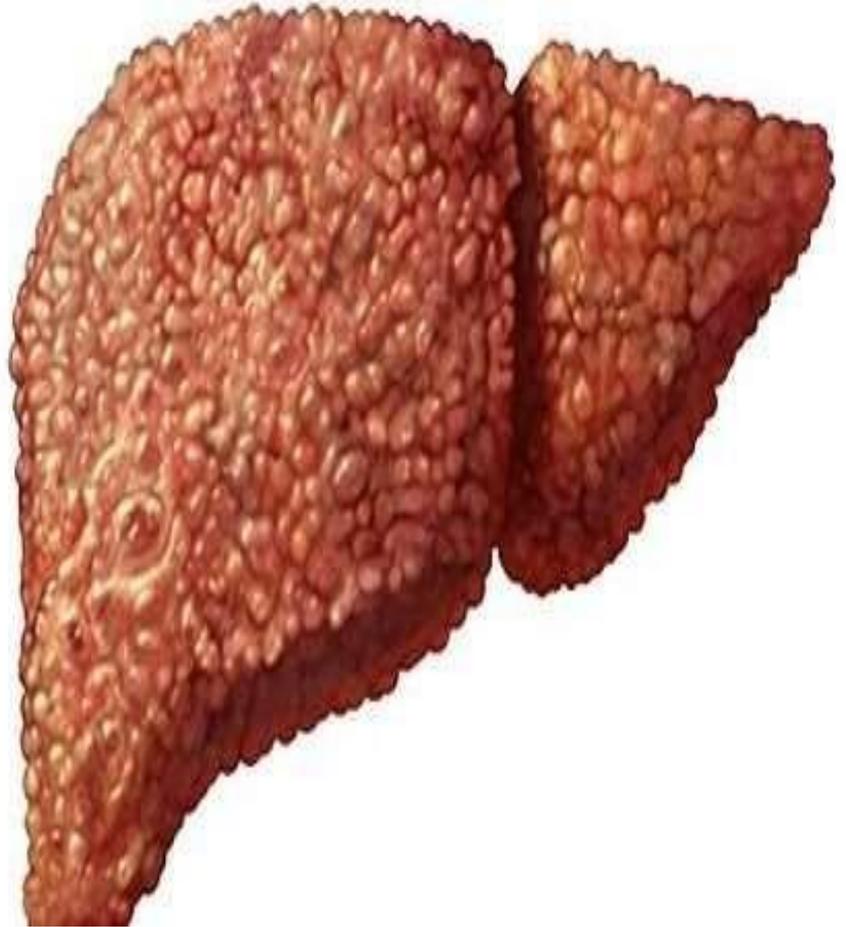
esoph. varices $\xrightarrow{\text{by (MC)}}$ portal hypertension $\xrightarrow{\text{by (MC)}}$ liver cirrhosis (by) $\left\{ \begin{array}{l} \text{alcohol} \\ \text{schistosomiasis} \end{array} \right.$

Normal Liver



Liver with Cirrhosis

↳ by fibrosis



"ما تركزوا عليه كثير"
1* مهم نعرفوا
2*

Clinical Features

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

Hepatic encephalopathy (HE) is an altered level of consciousness as a result of liver failure. Its onset may be gradual or sudden. Other symptoms may include movement problems, changes in mood, or changes in personality. In the advanced stages it can result in a coma.

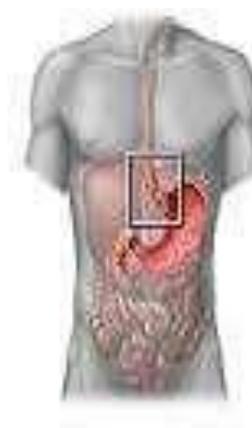
Esophagitis

- ▮ Esophageal Lacerations. ✖
- ▮ Mucosal Injury
- ▮ Infections ✖
- ▮ Reflux Esophagitis اورنادريني MC cause
- ▮ Eosinophilic Esophagitis allergy

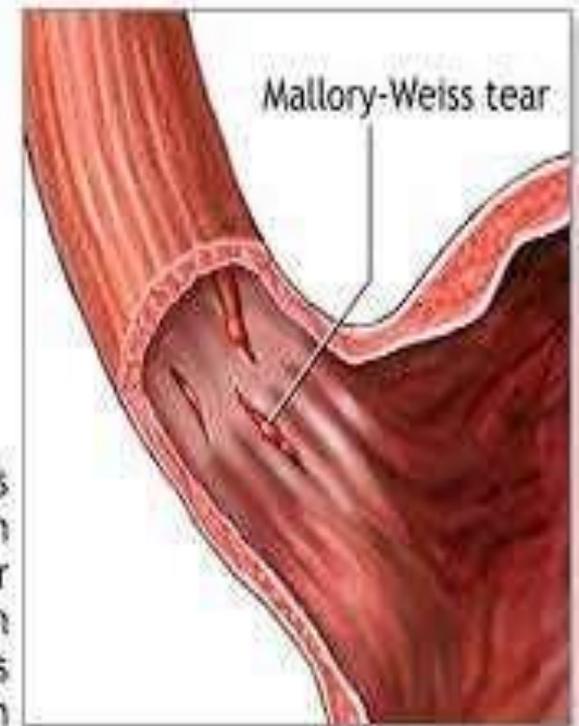
1 Esophageal Lacerations

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

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



Mallory-Weiss tear is a tear in the mucosal layer at the junction of the esophagus and stomach



2 Chemical Esophagitis

- ▮ Damage to esophageal mucosa by irritants
- ▮ Alcohol,
- ▮ ^{بجمل تاكس} Corrosive acids or alkalis
- ▮ Excessively hot fluids
- ▮ Heavy smoking
- ▮ Medicinal pills (doxycycline and bisphosphonates)
- ▮ Iatrogenic (chemotx, radiotx , GVHD)

للي بجا ولوا يستجروا

للي بجا ولوا
transplantation
(Graft vs Host disease)

Clinical symptoms & morphology

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

3 Infectious esophagitis

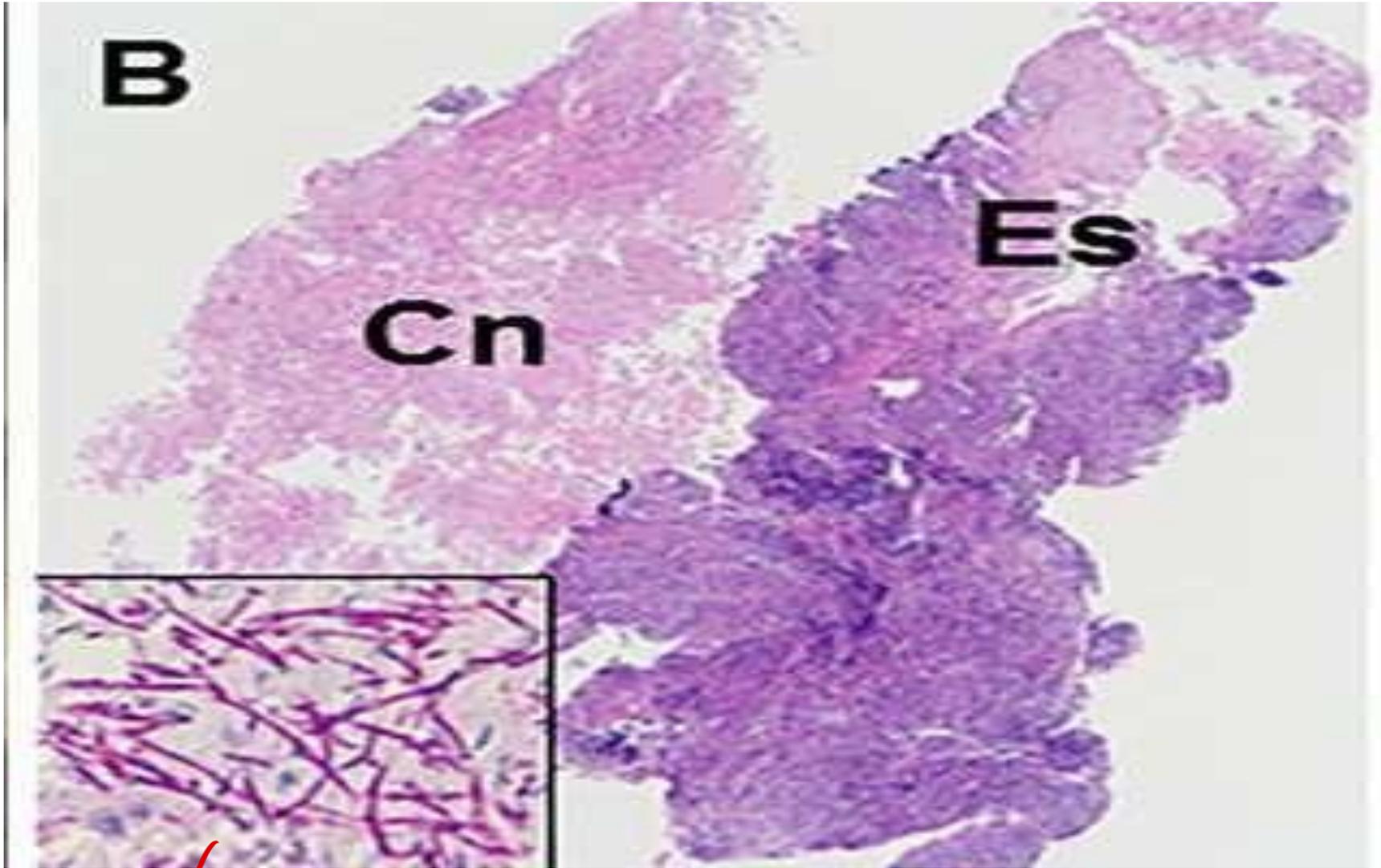
Mostly in immunosuppressed.

- Viral (HSV, CMV)
 - giant cell
 - intranuclear
 - eosinophilic
 - inclusion + تَشَكُّلَات
 - intranuclear cytoplasmic
- Fungal (candida >>> mucormycosis & aspergillosis)
 - yeast
- Bacterial: 10%.
 - less common

- ▮ Candidiasis :
hyphae w/ spores
- ▮ Adherent.
- ▮ Gray-white pseudomembranes
- ▮ Composed of matted fungal hyphae and inflammatory cells



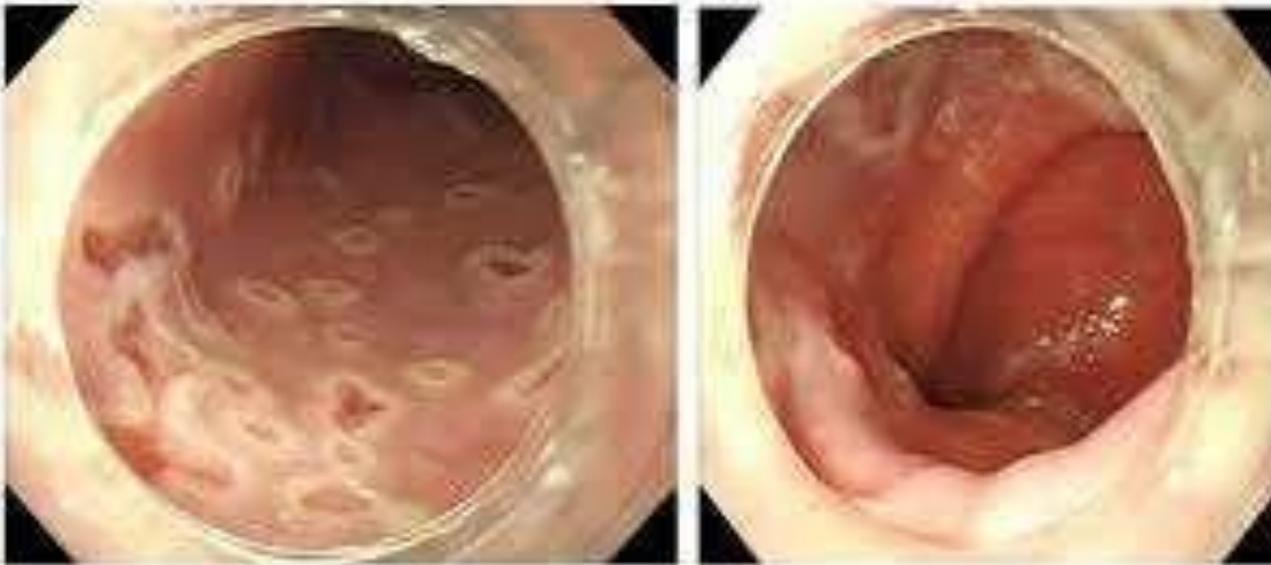
Esophageal Candidiasis

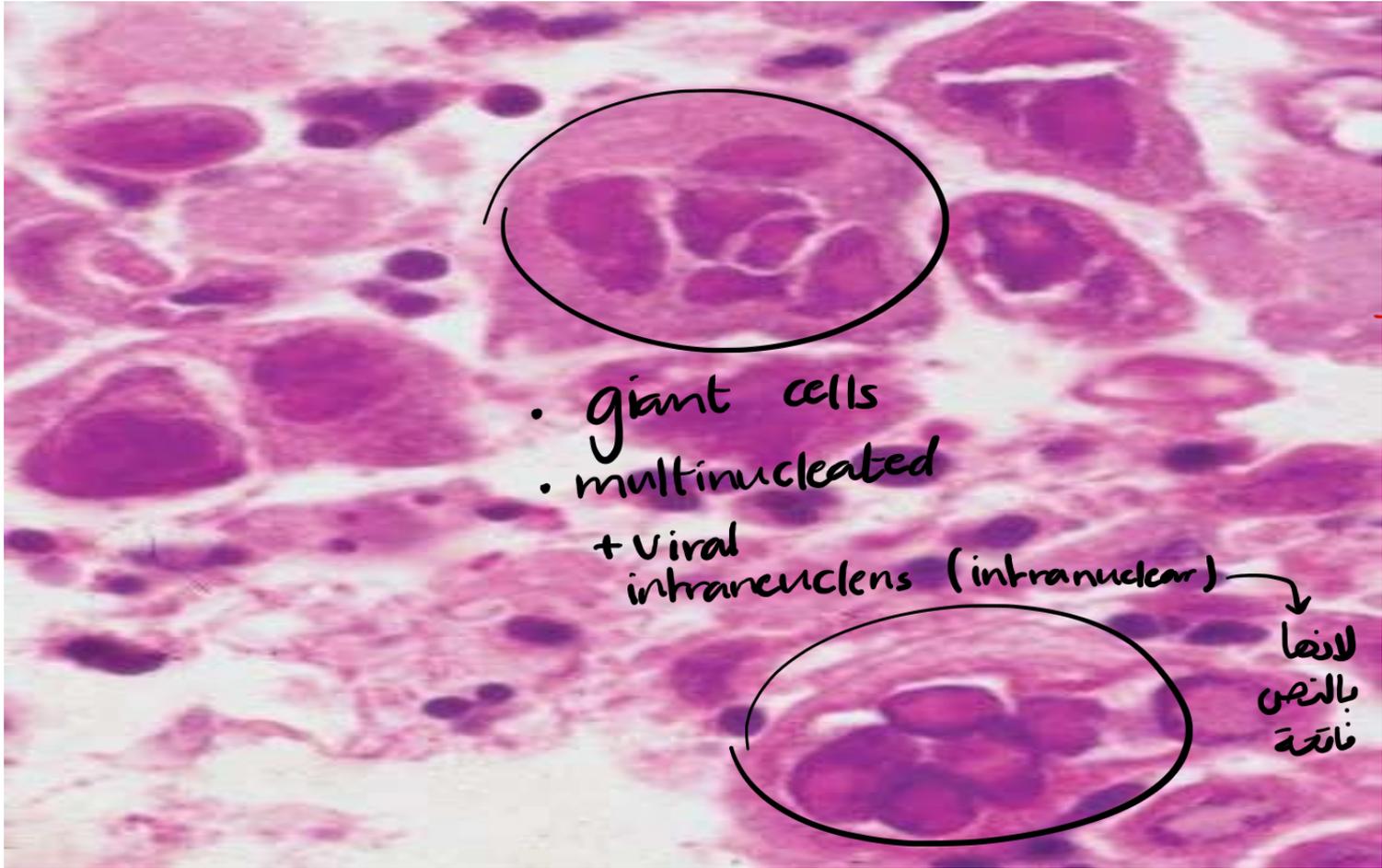


↳ hyphae
جوانا ال inf.
ب GMS stain +ve black

www.researchgate.net/publication/285369734_Esophageal_Candidiasis_as_the_Initial_Manifestation_of_Acute_Myeloid_Leukemia

- Herpes viruses
- Punched-out ulcers / deep center
- Histopathologic:
- Nuclear viral inclusions *لونها فاتح بالنص*
- Degenerating epithelial cells ulcer edge (*بتتوسع*)
- Multinucleated epithelial cells.
+ ulcer with active inf.





- giant cells
- multinucleated

+ Viral inclusions (intranuclear)

لازما
بالنوى
ناتجة

infectious
esophagitis
↓
by
HSV

CMV :

Shallower ulcerations.
كيس باؤسج جوا

basophilic غامقة

Biopsy: nuclear and cytoplasmic inclusions in capillary endothelium and stromal cells



4 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
- * lymphocytis not eosinocytic

Pathogenesis

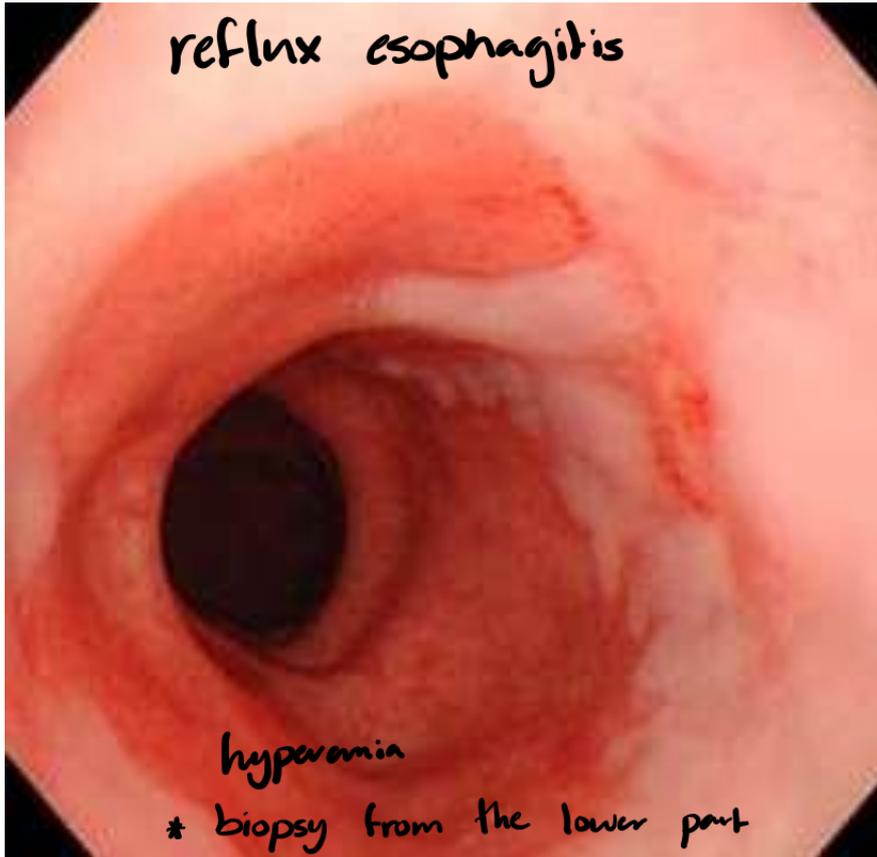
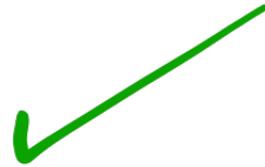
- □ Decreased lower esophageal sphincter tone
 - (alcohol, tobacco, CNS depressants)
- □ Increase abdominal pressure
 - (obesity, pregnancy, hiatal hernia, delayed gastric emptying, and increased gastric volume)
- □^{or} Idiopathic!!

Morphology

- ▮ **Macroscopy (endoscopy)**
- ▮ Depends on severity (Unremarkable, Simple hyperemia (red))
- ▮ **Microscopic:**
- ▮ Eosinophils¹ infiltration *but MC → lymphocytes³*
- ▮ Followed by neutrophils² (more severe).
- ▮ Basal zone hyperplasia
- ▮ Elongation of lamina propria papillae

lymphocytic esophagitis & eosinophilic esophagitis *كيف نفرق بين*

by biopsy: *issue in the lower part of esoph. due to reflux* *↓* *in the proximal part*



reflux esophagitis

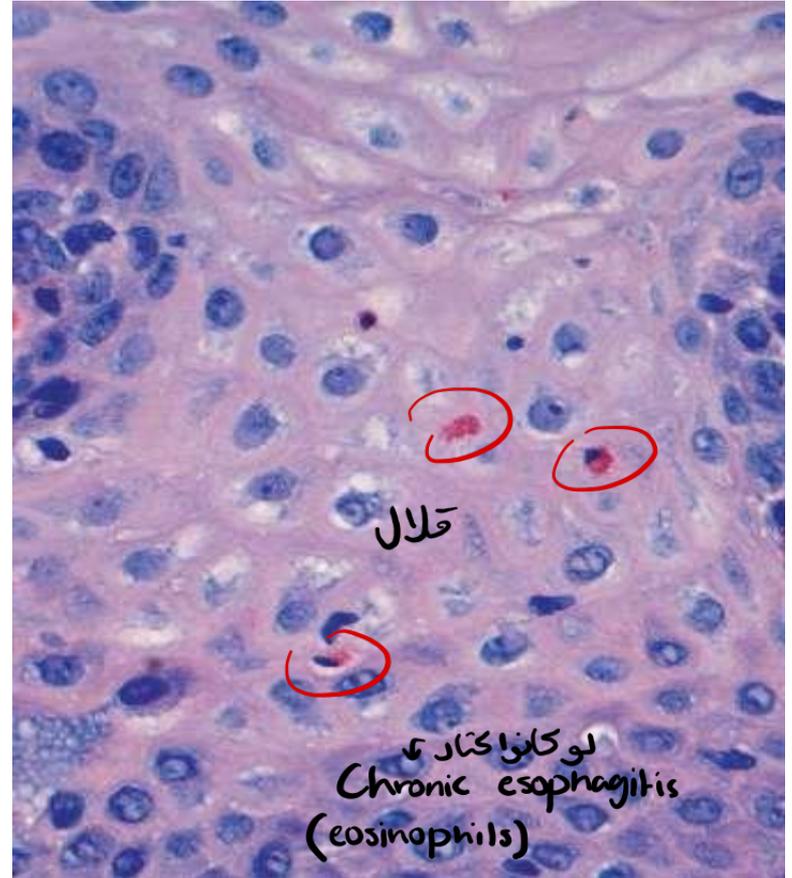
hyperemia

* biopsy from the lower part

ب ال upper
normal

nature.com

ring like



قلال

لوكانز اكلتار
Chronic esophagitis
(eosinophils)

acute

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 Melena refers to black, tarry stools that occur due to the presence of digested blood in the stool. It usually indicates bleeding in the upper gastrointestinal tract, such as the stomach or the first part of the small intestine. Melena is a concerning symptom that requires medical evaluation to determine the underlying cause, which could range from ulcers to more serious conditions like gastrointestinal bleeding.

▮ Strictures

▮ Barrett esophagus (precursor of Ca.)

↳ due to acute inf. changes

Eosinophilic Esophagitis

- **Chronic** ^{auto} immune mediated disorder
 - ↳ Tx: steroids
 - PPI من
- **Symptoms:**
- Food impaction ^{انخسار} and dysphagia ^{عسر البلع} 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.
 - ↳ proximal / upper



* ring or trachea-like

Robbins Basic Pathology 10th edition
GERD-like symptoms → eosinophilic esophagitis

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

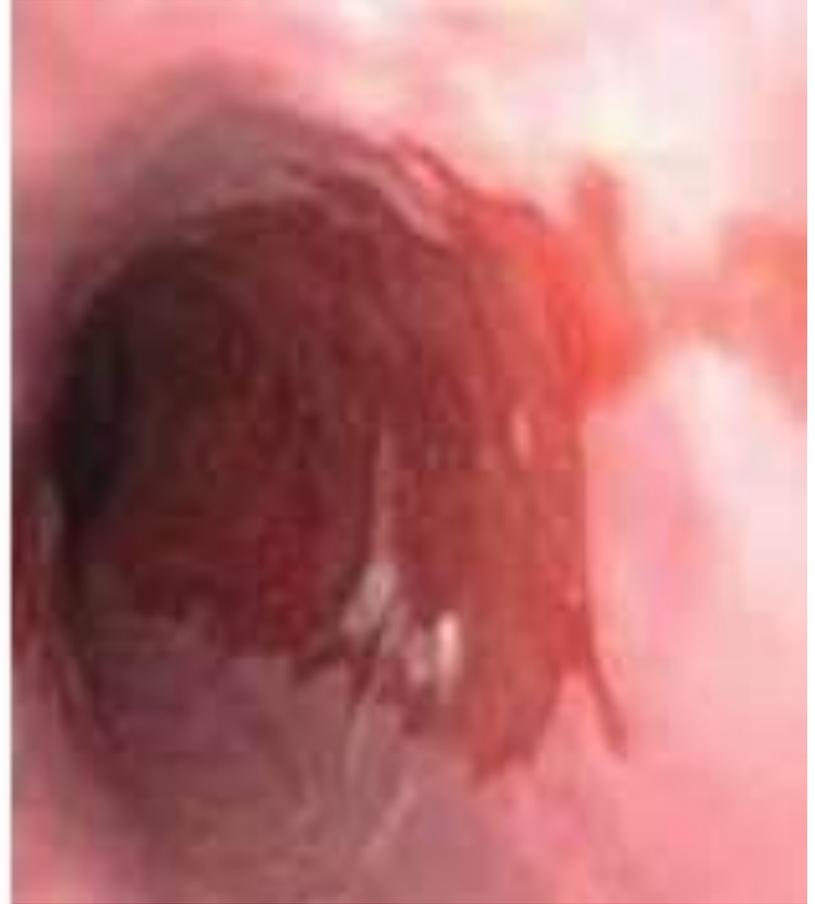
- Treatment:
- Dietary restrictions(^{منع} cow milk and soy products)
- Topical or systemic corticosteroids.
- Refractory to PPIs.

Barrett Esophagus

- □ **Complication of chronic GERD**
 - □ **Intestinal metaplasia within the esophageal squamous mucosa.**
 - □ **10% of individuals with symptomatic GERD**
كل اللي في المتأثرة
 - □ **Males >> females, 40-60 yrs**
 - □ **Direct precursor of esophageal adenocarcinoma**
 - □ **Metaplasia >> 0.2-1% /year >> dysplasia >>**
adenocarcinoma.
- Squamous → cuboidal / columnar / goblet cell*

Morphology

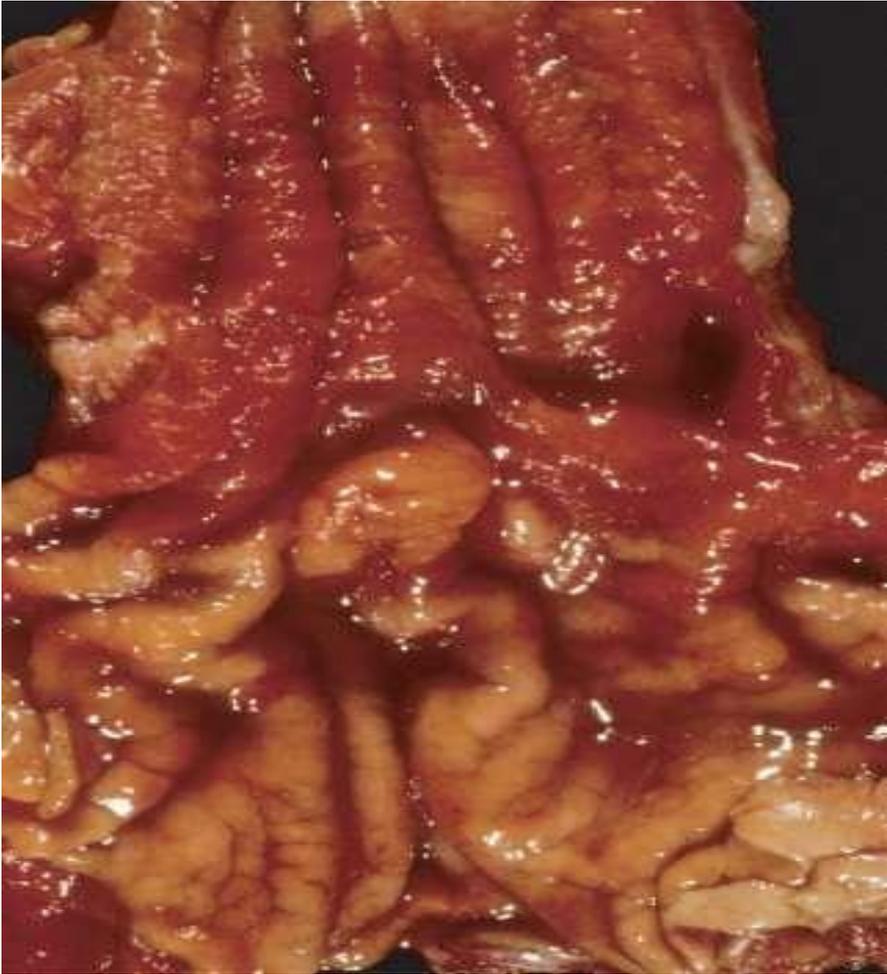
- ▮ **Endoscopy:**
- ▮ **Red tongues** extending upward from the GEJ.
- ▮ **Histology:**
- ▮ Gastric or intestinal metaplasia
- ▮ Presence of **goblet cells**
- ▮ +-Dysplasia : low-grade or high-grade
- ▮ Intramucosal carcinoma: invasion into the lamina propria.



Red tongues extending upwards from GEJ
→ Barrett esoph.

[Gastroenterology Consultants of San Antonio](#)

Benign gland
mucin - like
goblet cell





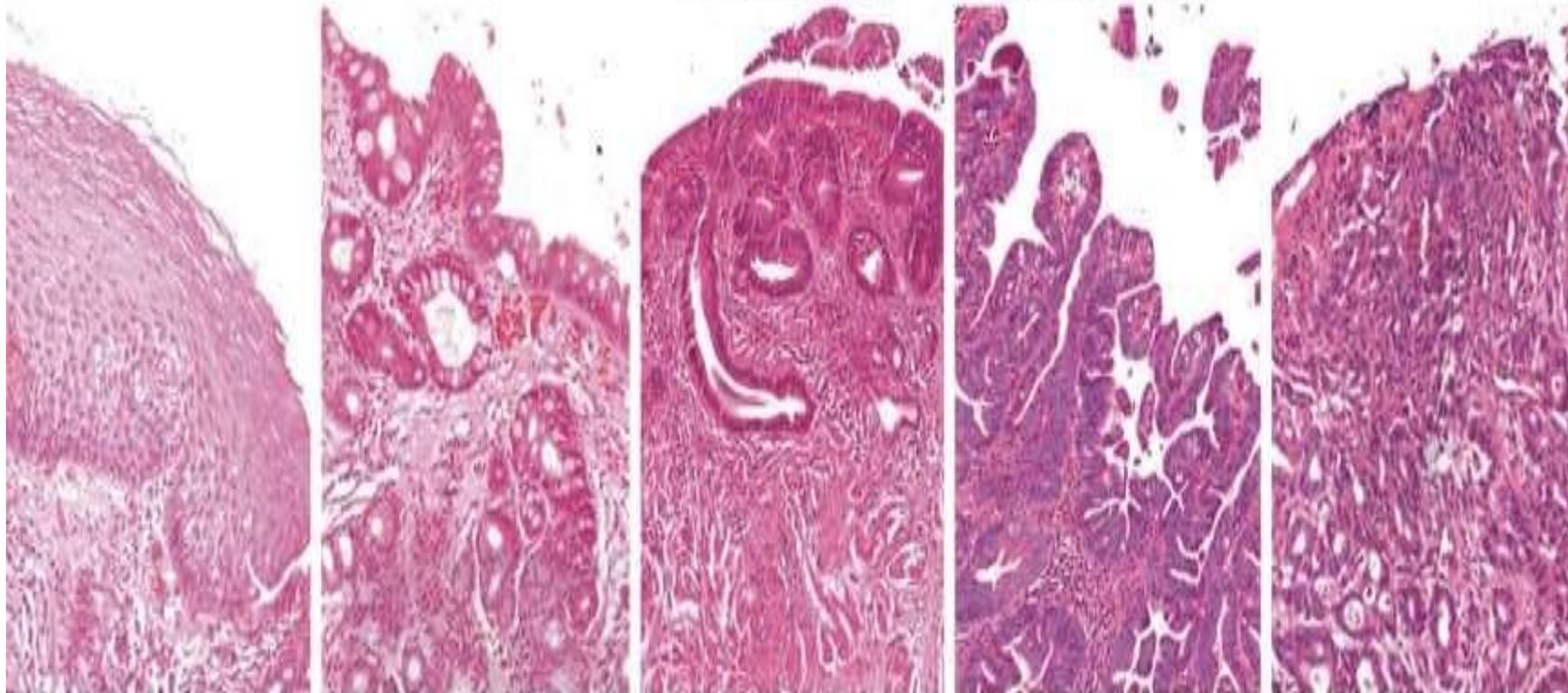
Normal squamous

Barrett's oesophagus

Barrett's oesophagus with low-grade dysplasia

Barrett's oesophagus with high-grade dysplasia

Adenocarcinoma



Population screening

Predicting prognosis, best therapy and response

Predicting risk of progression and response to preventive therapy

Management of Barrett

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

Esophageal tumors

- Squamous cell carcinoma (most common worldwide)
- Adenocarcinoma (on the rise, half of cases)
2nd MC

Adenocarcinoma

- ▮ Background of Barrett esophagus and long-standing GERD.
- ▮ Risk factors: dysplasia associated Barrett, smoking, obesity, radioTx.
- ▮ Male :female (7:1)
- ▮ Geographic & racial variation (developed countries)
- ▮ From Barrett >> dysplasia >> adenocarcinoma
- ▮ Chromosomal abnormalities and TP53 mutation.

Morphology

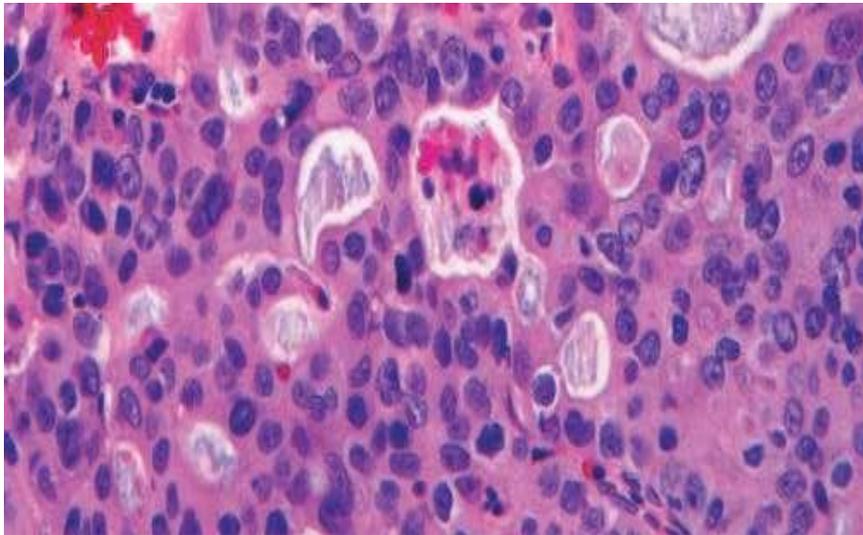
Distal third.

Early: flat or raised patches

: tending to grow outward beyond the surface epithelium from which it originates.

Later: exophytic infiltrative masses

Microscopy: Forms glands and mucin.



adenocarcinoma



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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 ^{كأوية}
- 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 ^{بالخضار}
- HPV infection implemented in high risk regions.
↳ SCC good prognosis

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

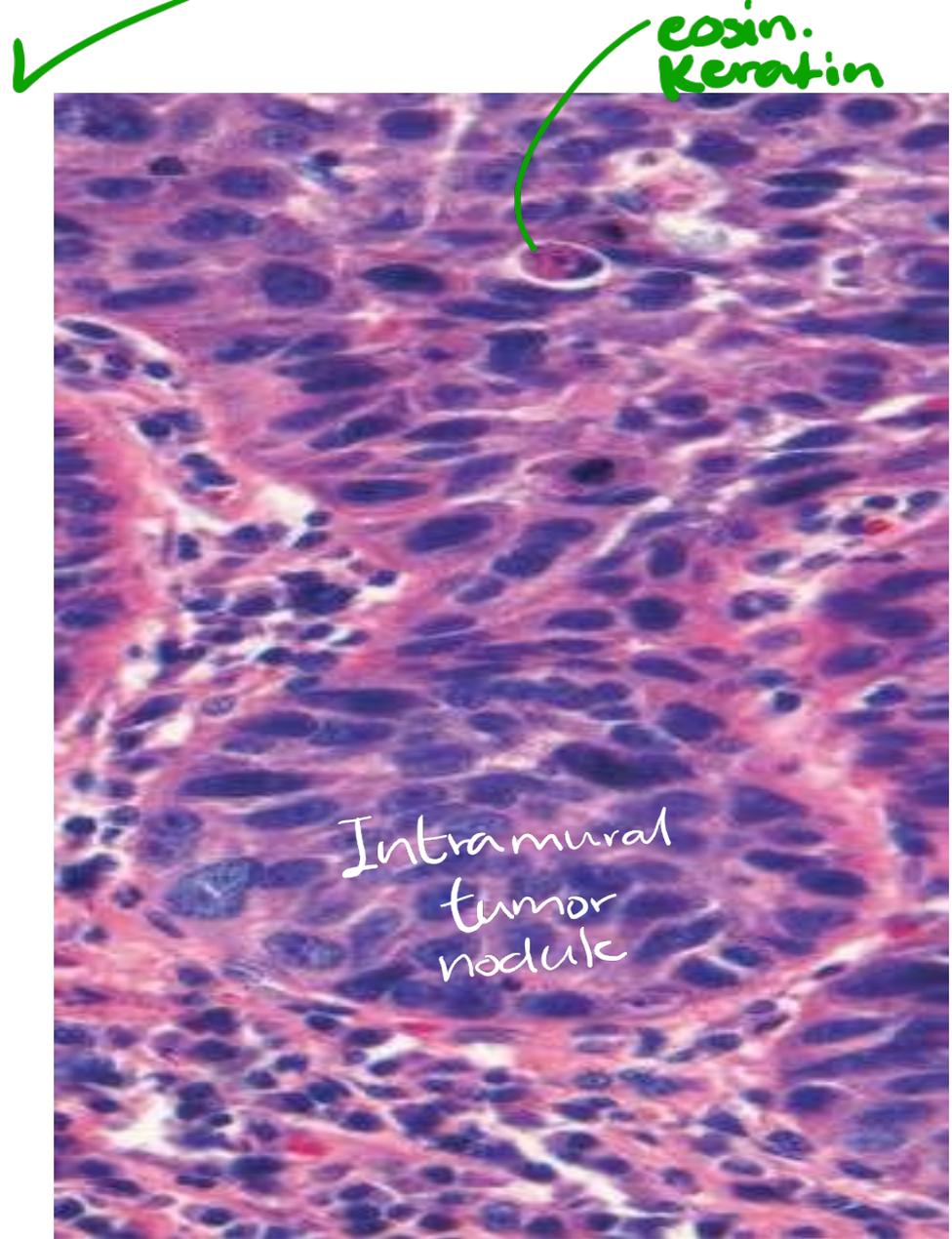
Lymph node metastases :

- ▮ 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%

poor prognosis



neoplastic cells

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* signs & symptoms are the same