GI | esophageal pathology | ملخص شامل للمحاضرتين الأولى والثانية
Done by: Ola Alahdab

-The esophagus is lined by stratified non-keratinized squamous epithelium, & contains four layer the mucosa, submucosa, muscular layer, and connective tissue layer. It extends from the **epiglottis** to the **gastroesophageal junction** (GEJ), This junction represents a physiological sphincter; by preventing food backflow into the esophagus.

Esophagus Diseases:

1. Obstruction:
- Mechanical obstruction: seen with naked eyes like atresia, stenosis, or tumors.
- Functional obstruction: abnormality in the innervation affecting its motility: achalasia.

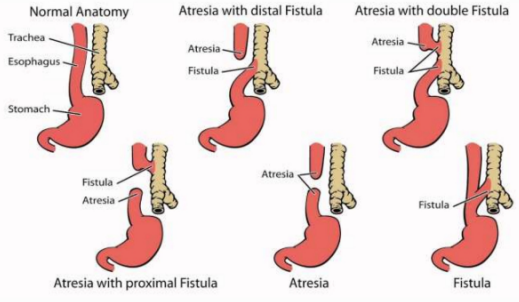
2. vascular diseases: varices.

3. Inflammation: esophagitis.

■ Mechanical Obstruction: (congenital or acquired)

A. Atresia انسداد خلقي / رتق
B. fistulas (connection between two hollow spaces)ناسور / اتصال غير طبيعي-ممر بين فراغين أجوفين
C. stenosis (mostly acquired) تضيق
D. agenesis (esophagus is absent) عدم التخلق / فشل عضو في التطور أثناء نمو الجنين
E. duplications (double-lumen esophagus, rare)

A. Atresia:



- A thin, noncanalized cord replaces a segment of esophagus, so no formation of a continuous esophageal tube.
- Whatever passes through the esophagus would result in an obstruction.
- occurs mostly at or near the **tracheal bifurcation**.
- Usually associated with **B. Fistula** (connecting the upper or lower esophageal pouches to a bronchus or trachea).
- The tracheoesophageal fistula (TEF) can lead to breathing problems (aspiration pneumonia) if saliva from the mouth or stomach contents enter the trachea and lungs.
- Neonates with TEF or esophageal atresia are unable to feed properly, prompt surgery is required.

■ **Clinical presentation:**

› Shortly after birth: regurgitation تقيؤ during feeding (because milk cannot pass).
Complications of TEF: Aspiration (breathing foreign objects into airways, usually food, saliva or stomach contents), Suffocation, Pneumonia, Severe fluid and electrolyte imbalances.

C. stenosis: (Mostly acquired)

- Narrowing of the esophageal lumen.
- Caused by fibrous thickening of the submucosa (mucosa is intact) and atrophy of the muscularis propria.
- Mostly it is secondary to a previous inflammatory insult and scarring caused by chronic gastroesophageal reflux (stomach acid and other irritants damage the lining of the esophagus over time, This leads to inflammation and scar tissue, which causes the esophagus to narrow).

- **Causes**:

1. Chronic GERD (gastroesophageal reflux disease).
2. Irradiation (in cancer patients treated with radiotherapy).
3. Ingestion of caustic agents مواد حارقة (chemicals, alkaline or acidic material).

- **Clinical presentation**:

- The main symptom is dysphagia (difficulty in swallowing).
- Difficulty eating solids, occurs long before liquids problems.

■ Functional obstruction:

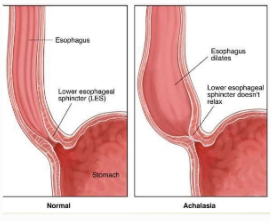
- problem in innervation, the GIT has its own "within-wall" nervous system: intrinsic (enteric) nervous sys which has two intrinsic nervous plexuses: the submucosal plexus and the myenteric plexus.
- Efficient delivery of food and fluids to the stomach requires coordinated waves of peristaltic contractions, & Discoordinated peristalsis or spasm of the muscularis causes Esophageal dysmotility.

Impaired peristaltic movements➡️ no propelling of food➡️ Functional obstruction

Achalasia: the most important cause of functional obstruction.

- **Characterized by a triad**:

1. Incomplete LES relaxation (the sphincter takes longer duration to relax).
2. Increased LES tone (in the resting state, when there is no food, increased tone of the sphincter).
3. Esophageal aperistalsis (no peristaltic waves, when food enters the esophagus it passes under the effect of gravity only).



Food entrance ➡️ accumulation ➡️ dilatation of the esophagus.

- **Primary achalasia** (most common):

- Idiopathic.
- Caused by failure of distal esophageal inhibitory neurons.

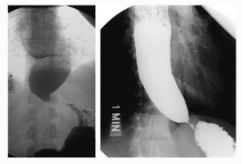
- **Secondary achalasia**:

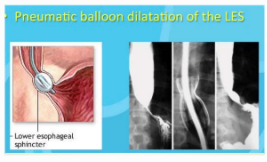
- Degenerative changes in neural innervation, either intrinsic to the esophagus or within the extraesophageal vagus nerve or the dorsal motor nucleus of the vagus, may lead to secondary achalasia.

› This occurs in Chagas disease, in which **Trypanosoma Cruzi** infection causes **destruction of myenteric plexus**, failure of LES relaxation, and esophageal dilatation.

extra

- **Diagnosis**:
1. Manometric study: measures **pressure** and **muscle tone** across the gastroesophageal sphincter.
2. barium swallow: a test that determine the cause of dysphagia, hematemesis, ..
› **Sulfate** is a metallic compound that shows up on X-ray and is used to help see abnormalities in the esophagus and stomach. When taking the test, the patient drinks a preparation containingthis solution. The X-rays track its path through the digestive system.
- **under x-ray:**





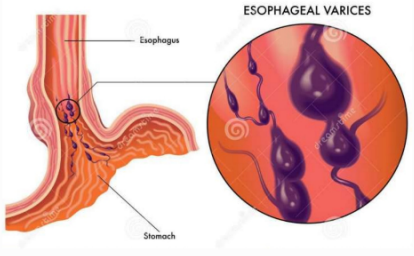
1. No normal peristatic movement.
2. LES and the GEJ are narrowed, producing "bird's beak" appearance.
3. Esophagus dilatation (enlarged above the narrowing).
- **Treatment**: (focus on relaxing LES)
Endoscopic balloon dilatation of LES (pneumatic dilation), disturb muscle fibers of LES in order to decrease pressure. A specially designed balloon is inserted through the LES and inflates it.
- **Clinical presentation**: Difficulty in swallowing, regurgitation and sometimes chest pain.

- Achalasia-like disease:

- If one of the triad arms is absent.
- The most common cause is **Diabetic autonomic neuropathy**.
- **Other causes**:
› Infiltrative disorders like malignancy, amyloidosis, or sarcoidosis.
› Dorsal motor nuclei lesions (caused by polio or surgical ablation استئصال).

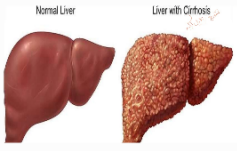
■ Vascular diseases:

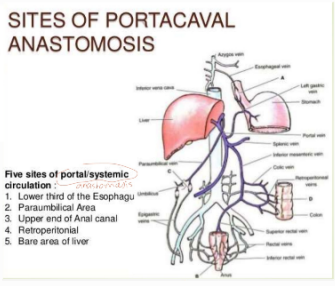
Varices:



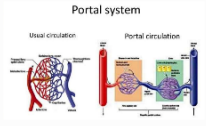
- Venous blood from GIT empty into the hepatic portal vein, which carries the blood to the liver before entering the general circulation. After passing through the portal circulation, the venous blood from the digestive system empties into the vena cava and returns to the heart to be distributed throughout the body.
- **Pathogenesis**:
› Diseases that impede portal blood flow cause **portal hypertension,** which can lead to esophageal varices (dilated, tortuous veins within the submucosa of the distal esophagus and proximal stomach (gastroesophageal junction) beneath intact mucosa).
› **Why distal esophagus?** There is a specific type of anastomosis between the veins of portal circulation and those of the systemic circulation called **Porto-systemic anastomosis**, the distal end of esophagus and the superior part of rectum are potential sites of a harmful anastomosis because these anastomoses become congested and form venous dilatations, such dilatation can lead to **esophageal varices, anorectal varices (hemorrhoids)**, and at the level of **umbilicus (caput medusae)**.
- Esophageal varices form when blood flow to the liver is blocked. The blood flow begins to back up, increasing pressure within the portal veins. This increased pressure (Portal

hypertension) forces the blood to seek other pathways through smaller veins (collateral channels) that allow portal blood to shunt into the caval system through the porto-systemic anastomosis. However, these thin-walled channels are not designed to carry large volumes of blood, thus, the veins balloon with the added blood and leak or even rapture, resulting in a life threating bleeding.

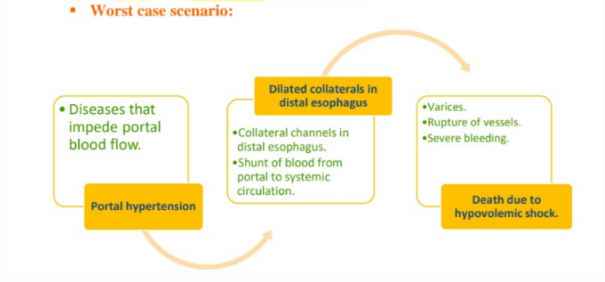




- **Causes**:
› Cirrhosis (most common): a number of liver diseases including hepatitis infection and alcoholic liver disease.
› Parasitic infection: **Hepatic schistosomiasis** is the 2nd most common cause of esophageal varices.
- **Complication**:
› The most serious one is **severe bleeding** which can be fetal and often responsible of **hypovolemic shock**.



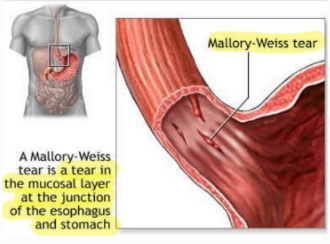
- **Clinical features**:
› Usually there is NO signs and symptoms unless their is a bleeding. variceal rupture can lead to massive hematemesis & death (it is a medical emergency).
› Despite intervention, half of patients die from the first bleeding episode due to: **hemorrhage, hepatic coma, and hypovolemic shock**.
› Once the first bleeding occurs the risk of another bleeding episode greatly increases.
- Among those who survive, additional episodes of hemorrhage, each potentially fetal, occur in as many as 20% of cases.
- **Diagnosis**: endoscopy or angiography.



■ Inflammatory diseases:

ESOPHAGITIS:

- Inflammation or irritation of the esophagus.
- **causes**:
Esophageal Lacerations تمزقات | Mucosal Injury | Infections (viral, fungal, & rarely bacterial) | Reflux Esophagitis | Eosinophilic Esophagitis.
- **Esophageal Lacerations**:
☆ **Mallory-Weiss syndrome**: **bleeding** from a laceration in the mucosa at gastroesophageal junction. caused by severe/violent vomiting and retching, **tearing** is due to failure of gastroesophageal musculature to relax prior to antiperistaltic contraction associated with vomiting. (Gastric contents cause the esophageal wall to stretch and tear).



-The lacerations are **roughly linear** and **longitudinal, crossing the gastroesophageal junction.**
› Patients usually present with **hematemesis** (vomiting up blood).
› Vomited blood is usually **fresh** (bright red blood) which indicates acute esophagitis, **in contrast to coffee-ground vomiting** that is associated with blood exposure to gastric acid. (This reaction causes the vomitus to look like ground coffee).
› Sperficial tears generally heal quickly (self-limited).

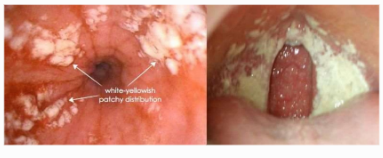
- **Chemical Esophagitis**:
- The stratified squamous mucosa of the esophagus may be damaged by:
Alcohol | **Corrosive acids or alkalis** | **Excessively hot fluids** | **Heavy smoking** | **Medicinal pills** (doxycycline and bisphosphonates), these pills may adhere to the esophageal lining and dissolve in the esophagus rather than passing immediately into the stomach, resulting in **pill-induced esophagitis** | **Iatrogenic** (illness caused by medical treatment):
1. Chemotherapy 2. Radiotherapy 3. GVHD (graft-versus-host-disease).
- **Symptoms and morphology**:
- The morphologic changes consist of **ulceration and acute inflammation**.
› Esophagitis due to chemical injury generally causes only self-limited pain, particularly **odynophagia** (pain with swallowing).
› **Hemorrhage, stricture, or perforation** (in severe cases).

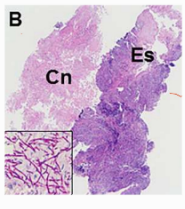
INFECTIOUS ESOPHAGITIS:

- In debilitated or immunosuppressed patients (mostly).
- caused by infectious pathogens, such as:
1. **Fungus**: Candida (mostly), Mucormycosis, & Aspergillosis.
2. **Virus**: HSV (herpes simplex virus), CMV (cytomegalovirus).
3. **Bacteria**: 10% only.
- Immunohistochemistry stains can detect HSV or CMV.
- viruses mostly affects immunocompromised patients.

1. Candidiasis:

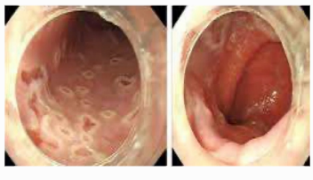
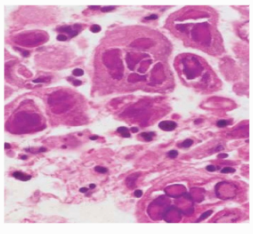
- **oral thrush in oral cavity that spread down** to esophagus.
- **typical/macroscopic appearance** (In endoscopy): **grayish-white adherent pseudomembranes** on esophagus.
- **Histologically/microscopic** (biopsy): inflammation, ulceration, & **candida hyphae**
- **Symptoms**: **dysphagia & odynophagia**.
- **Treatment**: Antifungals.





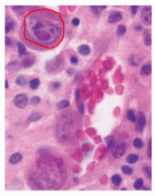
2. Herpetic esophagitis: (by HSV)

- **punched-out ulcers (deep, heated-up rounded edges).**
- infects the squamous (epithelial) cells.
- **Histologically**: viral cytopathic effect:
- Multi-nucleated giant cells.
- Intra-nuclear inclusion within the nucleus.
- Ground-glass appearance of the nucleus

**(normally the color of chromatin should be blue in the nucleus, but in HSV the chromatin appears faint (whitish) in the center and the bluish chromatin is at the edges of nucleus).

3. CMV (cytomegalovirus):



- very superficial, shallow ulcers.
- enlarged cells.
- infects stromal fibroblasts & endothelial cells lining mucosal capillaries.
- Biopsy:nuclear & cytoplasmic inclusions in capillary endothelium & stromal cells.

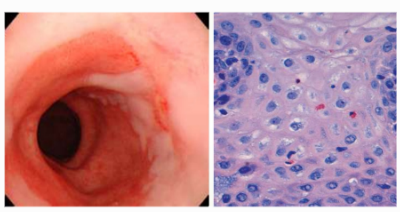
REFLUX ESOPHAGITIS: (The most common cause of esophagitis)

- Heartburn حرقة/حموضة المعدة in epigastric area or the central chest is the most frequent symptom.
- The gastroesophageal sphincter is relaxed when it should be closed, which called **GASTROESOPHAGEAL REFLUX DISEASE (GERD)**.
- squamous epithelium is sensitive to acids, so it has protective factors like mucous and bicarbonate (from submucosal glands). When there is an always recurrent reflux, this protection will decrease. Another protection is the closed sphincter, anything that causes the sphincter to relax will cause symptoms.
- Pathogenesis:

1. **CNS depressants, alcohol, and smoking:** decrease lower esophageal sphincter tone (cause sphincter relaxation).
2. **obesity, hiatal hernia, delayed gastric emptying & increased gastric volume, tumors, ascites**استسقاء بطني **& gases** (irritable bowel syndrome), **& pregnancy**: Increase abdominal pressure causing reflux of gastric content into the lower esophagus. In pregnancy, the enlarged uterus causes pressure on stomach, thus raising gastric acidic secretions.
3. Idiopathic causes (relaxed sphincter with unknown cause).

- Macroscopically (endoscopy):
- Hyperemia (Redness), because it is an inflammation, it depends on severity (mild symptoms have simple hyperemia).
- Histologically:

1. Earliest features: squamous epithelium infiltration by eosinophils.
2. In severe cases, it is followed by neutrophils.
3. Basal zone hyperplasia.
4. Elongation of lamina propria papillae.

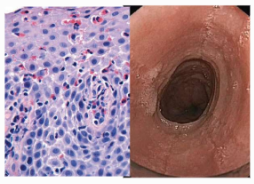


- Symptoms:
- Heartburn حرقة/حموضة المعدة in epigastric area or the central chest, is the most frequent symptom.
- Dysphasia (difficulty in swallowing), in more severe cases.
- Regurgitation of sour-tasting gastric contents (it reaches the mouth).
- Rarely, Severe chest pain (can be mistaken with a heart disease).

- in reflux patients, the symptoms are present **at night** because the patient is in a supine position.
- In adults >40 years, but any one can be affected (including infants and children).
- **symptoms in infants**: crying (from pain of heart burn), regurgitation, vomiting, and **failure to thrive** فشل النمو (no increase in weight).
- **Treatment**: proton pump inhibitors (PPIs).
- **Complecations:**
1. **Ulceration**.
2. **Hematemesis**: blood vomiting.
3. **Melena**: black colored stool due to **upper** GI bleeding, due to the effect of acids and enzymes (if it was lower GI bleeding, the stool would have fresh colored blood).
4. **Strictures, dysphagia.**
5. **Barrett esophagus**: metaplasia, can progress to dysplasia, then **carcinoma**.

EOSINOPHILIC ESOPHAGITIS: (chronic, allergic, atopic)

- Inflammation of the esophagus.
- **Chronic** immune-mediated disorder.
- Mostly **allergic,** due to food that contain soy products.
- Most patients are **atopic** (atopy = genetic tendency to develop allergic diseases) or have modest peripheral eosinophilia.
- Can happen in infants due to an allergy to milk.
- **Symptoms**:
- In children: **GERD-like symptoms** (vomiting, reflux and sometimes heartburns), **BUT they don't respond to PPI's because the problem here is not acidity.**
- In adults: **dysphagia and food impaction** (feeling that food is stuck in esophagus)
- **Macroscopically** (endoscopy): **constricted rings** in the **upper & middle esophagus.**
- **Histologically:** numerous eosinophils within epithelium, far from the GEJ (Gastroesophageal junction).
- **Treatment**: topical or systemic **corticosteroids,** dietary restrictions (because it is an allergy; cow milk and soy products).



Reflux esophagitis ➡ Lower esophagus ➡ near the GEJ
Eosinophilic esophagitis ➡ upper & middle esophagus ➡ far from the GEJ

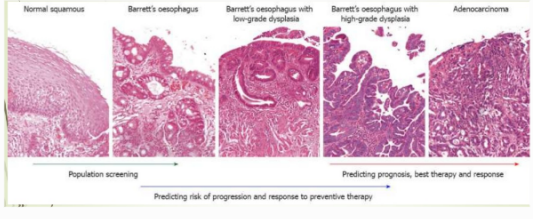
BARRETT ESOPHAGUS :

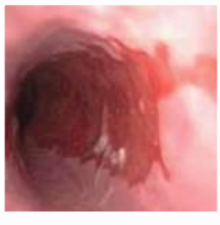
- A complication of chronic GERD.
- A **metaplasia** (squamous epithelium transforms into columnar epithelium that is more resistant to acid, forming a glandular epithelium).

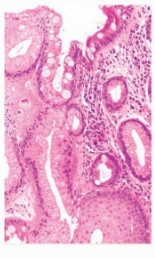
- The glandular epithelium can be gastric type or intestinal type (Higher risk) epithelium. **(defining feature is goblet cells in intestinal type).**

Goblet cells = Barrett

- Only **10%** of GERD patients develop Barrett.
- It is **reversible**, but dysplasia and carcinoma aren't.
- More in males.
- Between **40-60 years** of age.
- The patient must have reflux for years to be able to develop Barrett.
- **metaplasia (first) ➡️ low grade dysplasia ➡️ high grade dysplasia ➡️ carcinoma**
- It is **a Direct precursor of esophageal adenocarcinoma**.
- Only 0.2-1% of people with Barrett esophagus progress to dysplasia and adenocarcinoma.
- **Macroscopically** (endoscopy): **red tongues** extending upward from GEJ.
- **Histologically:**
- Gastric/intestinal **metaplasia** (with goblet cells in the intestinal type).
- +-Dysplasia.
- Intramucosal carcinoma: invasion into lamina propria.
- **Management**: endoscopy with biopsy to screen for dysplasia.





ESOPHAGEAL TUMORS:

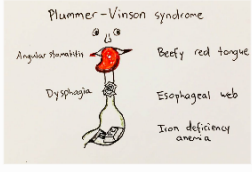
1. Squamous cell carcinoma (SCC): (most common).

- Malignant.
- Not associated with Barrett.
- Comes from squamous epithelial cells.
- Male:Female (4:1).
- More in developing countries.
- In **middle esophagus** (50%), & can occur in the lower esophagus.
- **Risk factors:**

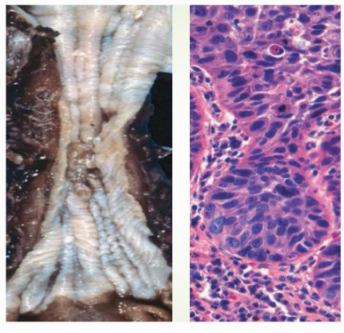
1. alcohol & smoking (mostly).
2. **Achalasia**.
3. **Plummer-Vinson syndrome**: associated with iron deficiency & anemia.
4. Frequent consumption of **very hot beverages** المشروبات الساخنة.
5. Caustic injury.

6. Poverty.
7. Previous radiation therapy.
- **Histologically:**
- Polypoid, ulcerated or infiltrative.
- Wall thickening, lumen narrowing.
- **Intramural** tumor nodules.
- keratin, inter-cellular bridges, no gland formation, & it looks like squamous epithelium.
- starts as squamous **dysplasia**, then turn into well to moderately differentiated squamous cell insitu (carcinoma in situ), then invasive squamous cell carcinoma (to mediastinum, bronchi, pericardium, aorta).
- **Pathogenesis**:
- In western countries: alcohol and tobacco.
- Other areas: polycyclic hydrocarbons, nitrosamines, fungus-contaminated food.
- HPV infection.

***CARCINOMAS USUALLY METASTASIZE TO Lymphatics:**



- Upper 1/3 (tumor location): cervical lymph nodes.
- Middle 1/3: mediastinal, paratracheal and tracheobronchial lymph nodes.
- Lower 1/3: gastric and celiac lymph nodes.



- **Clinical features:**
- **D**ysphagia | **O**dynophagia | **O**bstruction | **D**ebilitation
- **Weightloss** (very important in cancers).
- Impaired nutrition & tumor associated **cachexia**.
- **Hemorrhage and sepsis** (if ulcerated).
- **Aspiration** via a tracheoesophageal fistula.
- **5-year survival** <9% (bad prognosis).

2. Adenocarcinoma:

- malignant.
- Arises from Barrett.
- In the **distal third** of esophagus.
- **Risk factors:** dysplasia-associated Barrett (causal relationship), smoking, obesity, radiotherapy.
- Male:Female (7:1).
- Affected by geographic & racial variation.
- more in developed countries.
- **Pathogenesis**:
Barrett —> dysplasia —> adenocarcinoma.
- Acquisition of **genetic and epigenetic changes**.
- Chromosomal abnormalities and **TP53 mutation** (mutations accumulation causes **irreversible** disease).

- **Macroscopically** (endoscopy):
Rarely, flat or raised patches.
Lately, exophytic infiltration masses.
- **Histologically:** glands and mucin.
- **Clinical features:**
- Pain or difficulty swallowing.
- Progressive **weightloss** **(ALARMING SYMPTOM).**
- **Chest pain**.
- Vomiting.
- **5-year survival percentage:**
- Advanced stage diagnosis: <25% (bad prognosis).
- Early diagnosis: 80%.