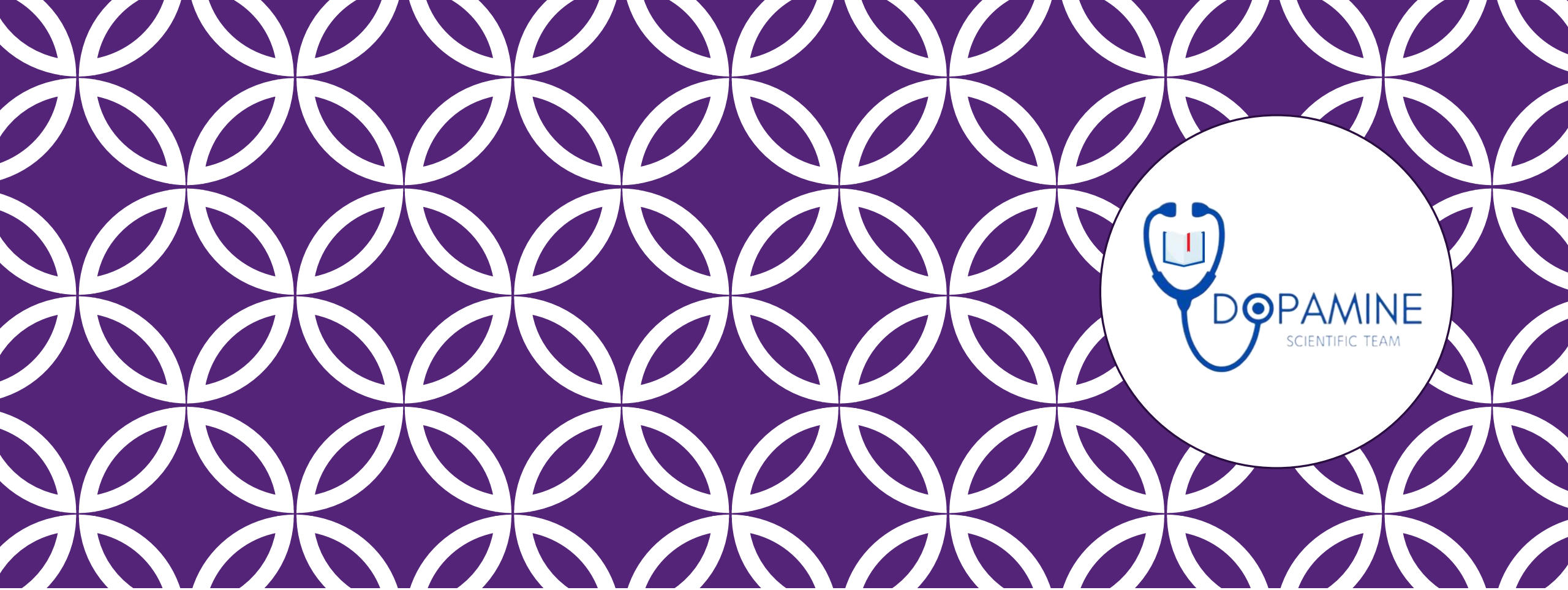

ESOPHAGEAL DISEASES | LEC 1 & 2

ESOPHAGEAL ANATOMY & PHYSIOLOGY

- The esophagus is a muscular tube extending from the epiglottis to the GEJ.
- It is lined by non-keratinized stratified squamous epithelium.
- The normal esophageal mucosa has a tan to pale pink color normally.
- The LES is a physiologic sphincter responsible for emptying of food into the stomach.
- Any abnormality (increase or decrease) in the LES tone can cause problems.
- The lower esophagus drains into tributaries of the portal vein and contains portosystemic anastomoses, which is vital in the pathogenesis of some diseases.
- Mucin and bicarbonate secretions, especially in lower esophagus are protective from GERD.

Abbreviations:

GEJ: Gastroesophageal Junction; **LES**: Lower Esophageal Sphincter; **GERD**: Gastroesophageal reflux Disease

CIS: Carcinoma in situ; **SCC**: Squamous Cell Carcinoma; **LN**: Lymph Node; **5-year**: 5-year survival rate

LECTURE 1: ESOPHAGEAL DISEASES (PART 1)

Contents (each title below is in a separate slide):

1. Mechanical Obstruction
2. Functional Obstruction
3. Vascular diseases
4. Esophagitis

MECHANICAL OBSTRUCTION

Disease & Description	Location	Pathogenesis	Cause/Treatment	Clinical Presentation
Atresia: Thin, non-canalized cord replaces a segment of esophagus. **Fistula:** upper or lower esophageal pouches (caused by atresia) connects to bronchus or trachea.	At or near the tracheal bifurcation.	Many forms: • Atresia without Fistula • Atresia with proximal Fistula • Atresia with distal Fistula • Atresia with double Fistula • Fistula without Atresia	**Cause:** Usually Congenital **Treatment:** Prompt surgical correction	**Atresia:** shortly after birth; regurgitation; incompatible with life. **Fistulas:** 1. Aspiration 2. Suffocation 3. Pneumonia 4. Electrolyte imbalance
Stenosis: Fibrous thickening of the submucosa & atrophy of the muscularis propria.		Inflammation and scarring → thickening.	**Cause:** Usually acquired; 1. Chronic GERD 2. Systemic Sclerosis 3. Irradiation 4. Caustic agents	**Progressive dysphagia:** Difficulty eating solids then liquids as well.
Duplication & Agenesis	Duplication & agenesis are congenital and are listed alongside atresia; agenesis is very rare..			

FUNCTIONAL OBSTRUCTION

Disease	Pathogenesis	Diagnosis	Clinical Presentation
Achalasia (the most important cause of functional obstruction)	**Esophageal dysmotility:** Discoordinated peristalsis or spasm of the muscularis.	**Barium swallow test:** • Barium accumulates in the esophagus • LES appears as a string	• **Triad:** 1. Incomplete LES relaxation 2. Increased LES tone 3. Esophageal aperistalsis • This causes accumulation of food in the esophagus. • Difficulty in swallowing • Regurgitation • Chest pain (sometimes)

Types of Achalasia	Epidemiology	Etiology & Pathogenesis
Primary Achalasia	More common	**Idiopathic;** degeneration of distal esophageal inhibitory neurons.
Secondary Achalasia	Less common	Loss of neural innervation due to damage to: • Esophagus • Vagus nerve • Dorsal motor nucleus of vagus nerve Chagas disease by *Trypanosoma cruzi*, causing destruction of myenteric plexus

VASCULAR DISEASES

Disease	Causes	Diagnosis
Esophageal Varices (the most important vascular disease of the esophagus)	**Portal Hypertension,** which can be caused by: • Alcoholic liver disease & Cirrhosis (most common) • Hepatic schistosomiasis (2nd most common)	• **Endoscopy** • **Angiography**

Description & Pathogenesis	Clinical Presentation
• Tortuous dilation of veins within the submucosa of the distal esophagus and proximal stomach. • Portal hypertension causes blood shunting into sites of portosystemic anastomosis, such as the collateral channels in distal esophagus.	• Often asymptomatic. • Rupture leads to massive hematemesis and death. • 20% of patients die from the first bleed despite interventions. • Death due to hemorrhage, hepatic coma, and hypovolemic shock. • Rebleeding in 60% of patients. Patients with liver cirrhosis should undergo monitoring for developing varices.

ESOPHAGITIS

Esophageal Lacerations	**Clinical Presentation**
• Severe retching and forceful prolonged vomiting causes esophageal distention and tearing of the mucosa, causing severe bleeding and hematemesis. • It usually heals quickly and spontaneously.	Mallory Weiss tears (most common) • Linear, longitudinal lacerations crossing the GEJ • Superficial (only mucosa); fresh-colored blood in vomitus

Chemical Esophagitis	**Clinical Presentation**
Damage to esophageal mucosa by **irritants**: • Alcohol & Heavy smoking • Corrosive acids or alkalis & Excessively hot fluids • Medicinal pills (doxycycline and bisphosphonates) • Iatrogenic (chemotherapy, radiotherapy, GVHD) *GVHD: Graft-versus-host disease*	• Ulceration and acute inflammation. • Self-limited pain & odynophagia • Hemorrhage, stricture, or perforation in severe cases.

Infectious Esophagitis; mostly in immunocompromised	**Clinical Presentation**
Fungal: *Candida*; mucormycosis; aspergillosis (most common is *Candida)* **Viral**: Herpes Simplex (HSV); Cytomegalovirus (CMV) **Bacterial**: less common; can occur secondary to others	**Candida**: gray-white pseudomembranes seen by endoscopy and caused by hyphae and inflammatory cells; can extend to oral thrush **HSV**: punched-out ulcers; erythematous; epithelial cytopathology, especially multinucleated cells (specific for HSV infections) **CMV**: shallower ulcers; epithelial, endothelial & stromal cytopathology

LECTURE 2: ESOPHAGEAL DISEASES (PART 2)

Contents (each title below is in a separate slide):

1. GERD & Eosinophilic Esophagitis
2. Barrett's Esophagus & Adenocarcinoma
3. Squamous Cell Carcinoma

GERD & EOSINOPHILIC ESOPHAGITIS

GERD Description & Epidemiology	Pathogenesis & Treatment	Morphology	Clinical Presentation
• Reflux of gastric contents into the lower part of the esophagus. • Most frequent cause of esophagitis. • Most common complaint by patients visiting the outpatients. • Most common over 40 years. • May occur in infants and children	• Can be idiopathic • Decreased lower esophageal sphincter tone (alcohol, tobacco, hiatal hernia, CNS depressants) • Increase abdominal pressure (obesity, pregnancy, delayed gastric emptying, and increased gastric volume) **Treatment**: PPIs	**Macroscopy (endoscopy):** Depends on severity **Microscopy (histology):** • Early on, eosinophils • Later, neutrophils • Basal zone hyperplasia • Elongation of lamina propria papillae	• Heartburn & Dysphagia • Acid regurgitation • Severe chest pain (rarely); mistaken for MI **Complications:** • Esophageal ulceration • Hematemesis • Melena • Strictures • Barrett's esophagus

Eosinophilic Esophagitis	Symptoms & Treatment	Morphology	Other Clinical Manifestations
Chronic, immune-mediated disorder that is similar to GERD but must be differentiated from it for correct management.	• Food impaction & dysphagia • Feeding issues, allergies; GERD-like symptoms in children. **Treatment:** refractory to PPIs Instead, diet without cow's milk or soy products; corticosteroids	• **Rings** in the upper and mid esophagus. • **Numerous** eosinophils in the epithelium far from GEJ, so it is different from GERD.	Most patients are atopic; can have: • Atopic dermatitis • Allergic rhinitis; asthma • Modest peripheral eosinophilia

BARRETT'S ESOPHAGUS & ADENOCARCINOMA

Barrett's Esophagus: intestinal metaplasia defined by the presence of **goblet cells**

Etiology & Epidemiology:
- Complication of chronic GERD.
- Affects 10% of symptomatic, longstanding GERD.
- Common in 40-60 years'-old.
- Common in Males >> Females.

Complications:
- Risk of dysplasia = 0.2-1%/Year
- Dysplasia can vary in grade and is considered the immediate precursor of adenocarcinoma.

- **Endoscopy:** Red tongues extending upwards from the GEJ.

- **Microscopy:** Intestinal metaplasia (**with goblet cells**); +/- dysplasia or intramucosal carcinoma

Management:
- Periodic surveillance for development of dysplasia.
- If high-grade dysplasia or intramucosal carcinoma is present, intervention is needed.

Esophageal Adenocarcinoma: Barrett's → Dysplasia → Adenocarcinoma (genetic & epigenetic changes)

Etiology & Epidemiology:
- More common in developed countries; ½ of esophageal tumors
- Longstanding GERD and Barrett's.
- Increased risk with dysplasia
- Smoking, obesity and radiotherapy.
- Male : Female = 7 : 1
- Geographic and racial variations.

Pathogenesis:
See the sequence above.
- Chromosomal abnormalities.
- TP53 gene mutations.
- Multistep process with environmental factors.

Morphology:
Distal third of esophagus
- Early on, flat or raised patches.
- Later, exophytic infiltrative masses.
- Glandular structures that produce mucin.

Clinical presentation:
- Exophytic obstruction

Dysphagia; odynophagia
- Chest pain; vomiting
- Cachexia; weight loss

Prognosis:
- If early, 5-year ≈ 80%
- If late, 5-year < 25%

SQUAMOUS CELL CARCINOMA

Etiology & Epidemiology:	Pathogenesis:	Morphology:	Clinically:
• Most common esophageal cancer worldwide; ½ of all cases • Male : Female = 4 : 1 • More common in rural, low resource, and developing countries **Risk factors:** • ***Not*** *associated with GERD* • Alcohol; tobacco • Poverty • Caustic agents; very hot beverages • Achalasia • Plummer-Vinson syndrome (iron deficiency Anemia, dysphagia, and esophageal webs) • Previous radiotherapy	1. **In western countries:** alcohol and tobacco use. 2. **Other areas:** nutritional deficiency, exposure to polycyclic hydrocarbons, nitrosamines, fungus-contaminated foods. 3. **HPV infection** has been implicated in squamous cell carcinoma in **high-risk regions**	• 50% of the cases occur in the **middle third** of esophagus • Polypoid, ulcerated, or **infiltrative masses** • **Wall thickening** and luminal narrowing • **Invade** surroundings (bronchi, mediastinum, pericardium, aorta). **Microscopy:** 1. **Pre-invasive:** squamous dysplasia & CIS 2. **Invasive:** Well to moderately differentiated invasive SCC. 3. **Metastasis:** Intramural nodules away from the main tumor even at diagnosis **Upper 1/3:** ➔ cervical LNs **Middle 1/3** ➔ mediastinal, paratracheal, and tracheobronchial LNs. **Lower 1/3** ➔ gastric and celiac LNs.	• Dysphagia • Odynophagia • Obstruction • Cachexia • Weight loss • Debilitation Can involve **ulceration** leading to **hemorrhage** and **sepsis** Tracheoesophageal or tracheobronchial **fistula; aspiration** **Prognosis:** Most present late 5-year ≈ 10%

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