

# Diseases of the esophagus- 2

Manar Hajeer, MD, FRCPath  
University of Jordan, School of medicine  
Modified by: Rani Tachijian

# Diseases that affect the esophagus

- ▶ 1. Obstruction: mechanical or functional.
- ▶ 2. Vascular diseases: varices.
- ▶ 3. Inflammation: esophagitis.
- ▶ 4. Tumors.

# Reflux Esophagitis

## Gastroesophageal reflux disease, GERD

- ▶ Reflux of gastric contents into the lower esophagus
- ▶ Most frequent cause of esophagitis
- ▶ Most common complaint by patients
  
- ▶ Squamous epithelium is sensitive to acids which are carried in the gastric juices to the lower part of the esophagus upon recurrent reflux of these contents.
- ▶ However, there are protective forces: mucin and bicarbonate from submucosal glands, high LES tone, the contraction of which prevents reflux of acidic gastric content.

# Pathogenesis

- ▶ **Decreased lower esophageal sphincter tone**

(alcohol, tobacco, hiatal hernia (it is when part of the stomach herniates through the diaphragm and becomes part of the thoracic cavity), some medications such as CNS depressants)

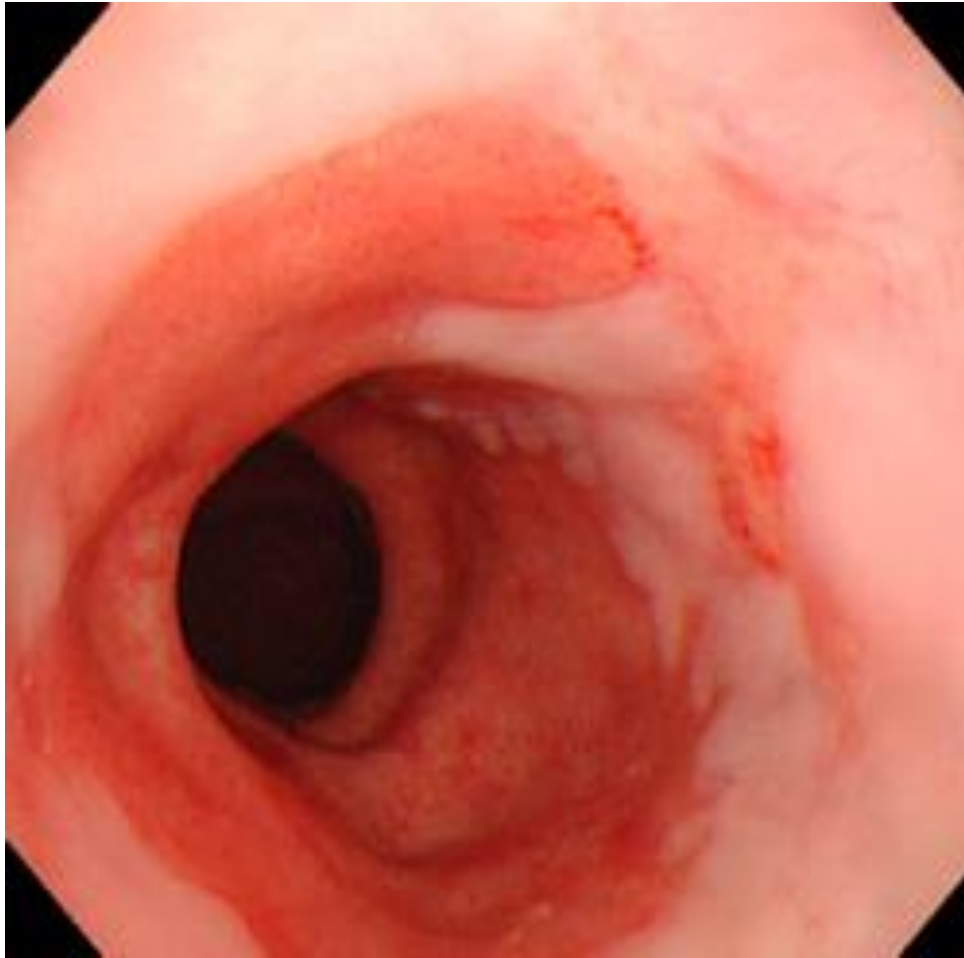
- ▶ **Increase abdominal pressure**

(obesity,, pregnancy, delayed gastric emptying, and increased gastric volume)

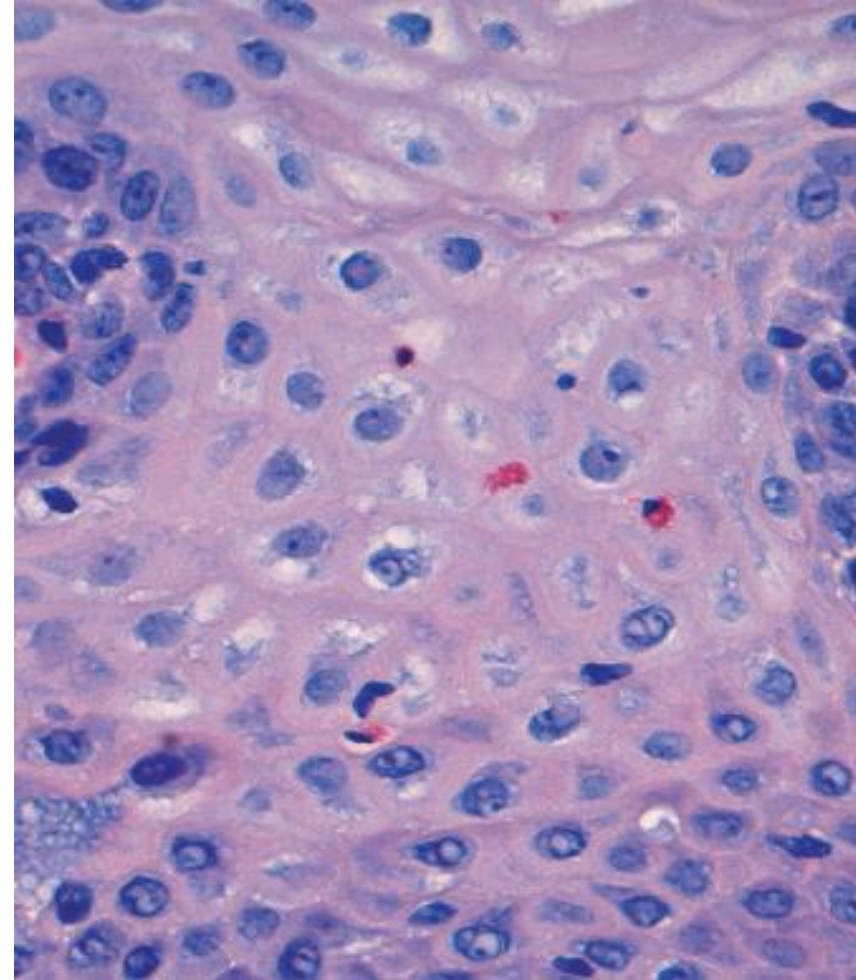
- ▶ **Idiopathic!!**

# MORPHOLOGY

- ▶ **Macroscopy (endoscopy)**
- ▶ Depends on severity of reflux (Unremarkable (no changes), Simple erythema due to inflammation)
- ▶ **Microscopic:**
- ▶ Eosinophils infiltration of squamous epithelium (early)
- ▶ Neutrophils later (more severe).
- ▶ Accompanied with neutrophils is Basal zone hyperplasia of basal squamous epithelia.
- ▶ Elongation of lamina propria papillae
- ▶ If we find 2 out of these findings in an esophageal biopsy microscopically, we can establish diagnosis of reflux esophagitis along with the clinical manifestations.



Erythema and redness of lower esophagus associated with reflux esophagitis



Those cells with granular eosinophilic cytoplasm are the eosinophils

# Clinical Features

- ▶ Most common over 40 years.
- ▶ May occur in infants and children
- ▶ Heartburn. Burning in epigastric region
- ▶ Dysphagia.
- ▶ Regurgitation of sour-tasting gastric contents to the mouth in severe cases
- ▶ Rarely: Severe chest pain, mistaken for heart disease (e.g. MI, because of the chest pain, especially when they present to the ER).
- ▶ Tx: proton pump inhibitors to decrease acid secretion

# Complications

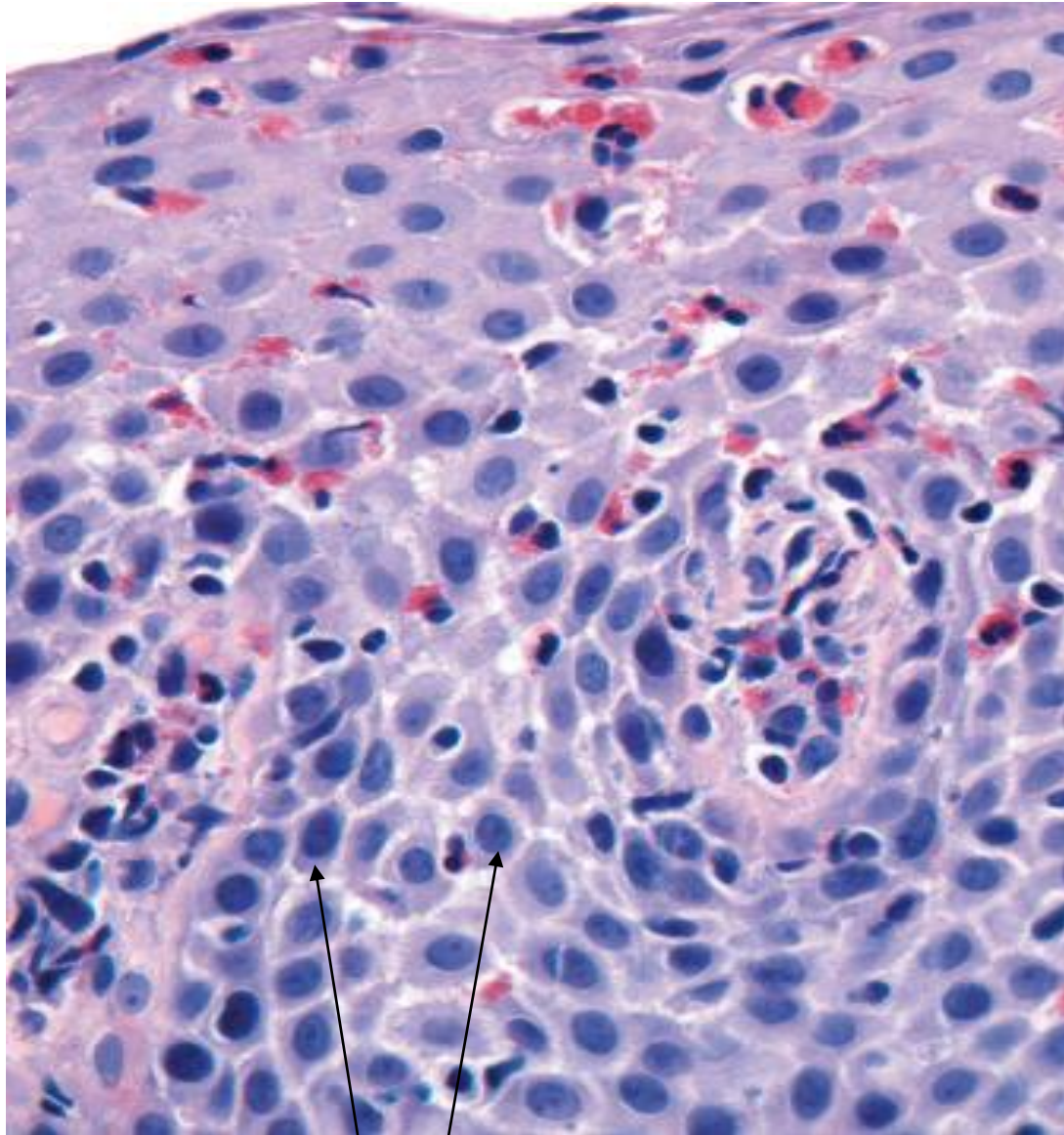
- ▶ Esophageal ulceration causing peptic ulcerations
- ▶ Hematemesis
- ▶ Melena in cases of bleeding which passes through stomach and is altered by the acid which passes in the stool and turns its colour into black.
- ▶ Strictures & stenosis in recurrent/long-standing reflux esophagitis because the repair of the inflammation could be by fibrosis narrowing the lumen of the esophagus.
- ▶ Most feared complication is Barrett esophagus (intestinal metaplasia, could be a precursor of Ca. esophageal adenocarcinoma)



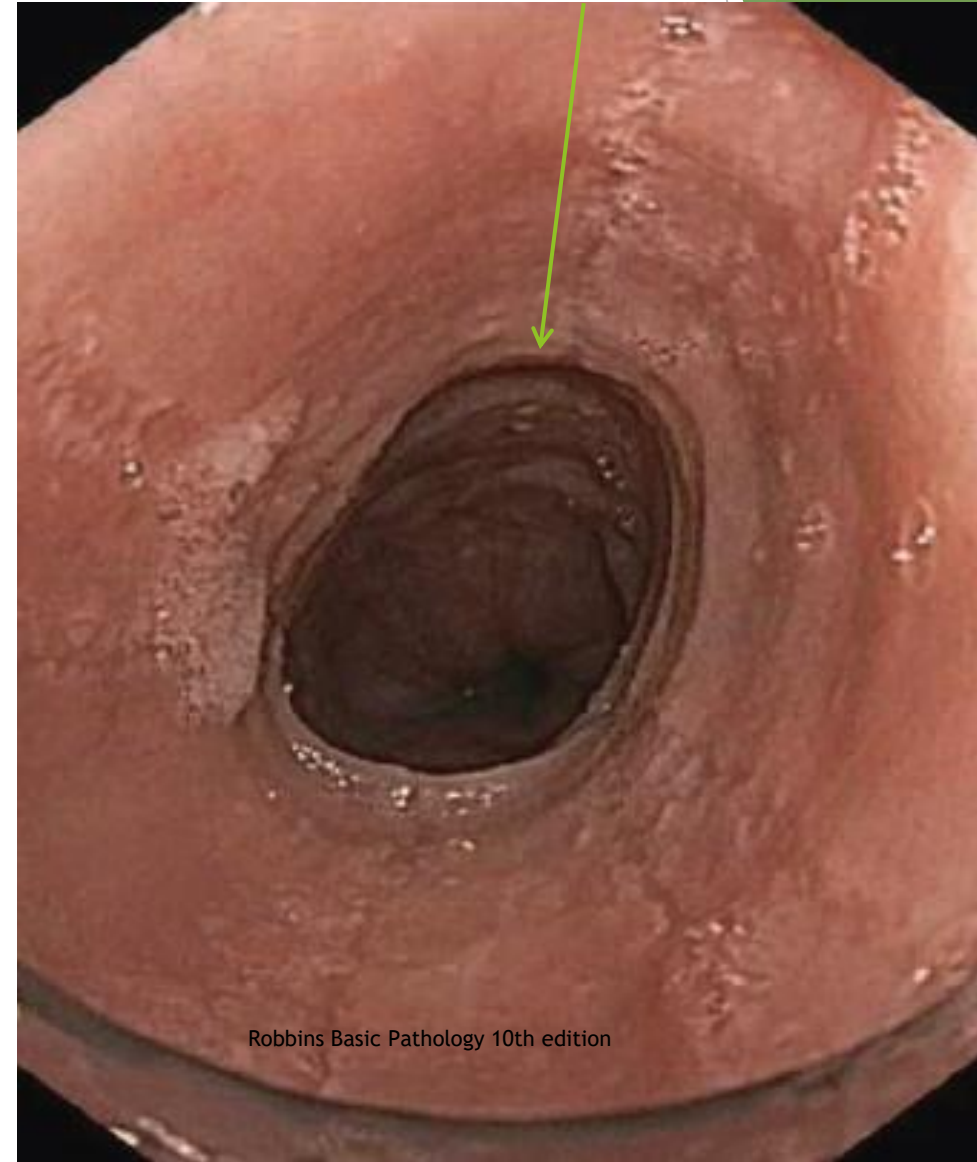
# Eosinophilic Esophagitis

- ▶ Chronic immune mediated disorder
- ▶ **Symptoms: Variable**
- ▶ Food impaction and dysphagia in adults
- ▶ Feeding intolerance or GERD-like symptoms and allergies to certain types of food in children
- ▶ **they will present to the outpatient clinics as irritable children and recurrent vomiting which is when we need to differentiate whether it is GERD or Eosinophilic Esophagitis**
- ▶ **Morphology:**
- ▶ Rings in the upper and mid esophagus. (classical morphology, absent in GERD which affects lower esophagus).
- ▶ Numerous eosinophils in squamous epithelium (difference from GERD: higher number of eosinophils).
- ▶ Far from the GEJ.

Rings causing symptoms such as dysphagia



Numerous eosinophils with eosinophilic granular cytoplasm, infiltrating squamous epithelium



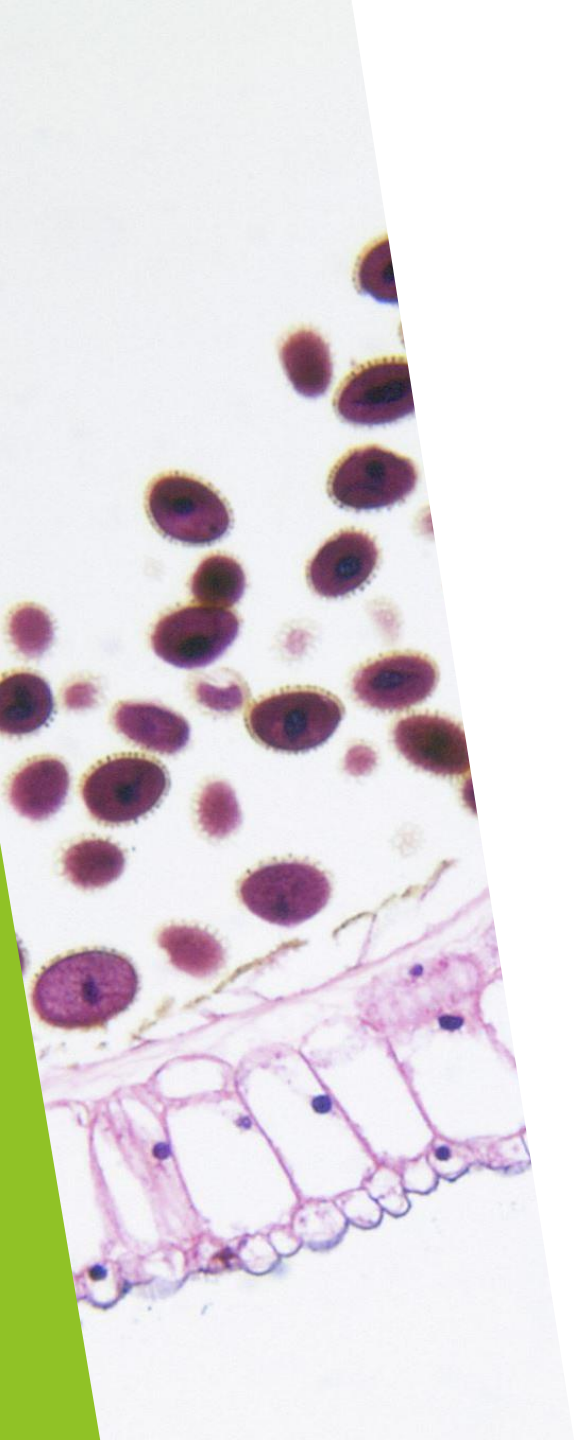
Robbins Basic Pathology 10th edition

# Management:

- ▶ Most patients are atopic (atopic dermatitis, allergic rhinitis, asthma) or modest peripheral eosinophilia (increased number of eosinophils in peripheral blood examinations).
- ▶ Refractory (unresponsive) to PPIs. (that's why we need to differentiate between GERD and EE, it is not straightforward, however).
- ▶ **Treatment:**
- ▶ Dietary restrictions( cow milk (especially in children) and soy products)
- ▶ Topical or systemic corticosteroids.

# 5-Barrett Esophagus

- ▶ Complication of chronic GERD
- ▶ Intestinal metaplasia (presence of goblet cells in esophagus)
- ▶ 10% of individuals with symptomatic GERD
- ▶ Males>>females, 40-60 yrs
- ▶ **Direct precursor of esophageal adenocarcinoma**
- ▶ **0.2-1% /year develop dysplasia (precursor of adenocarcinoma, can be graded as high- or low-grade tumor).**

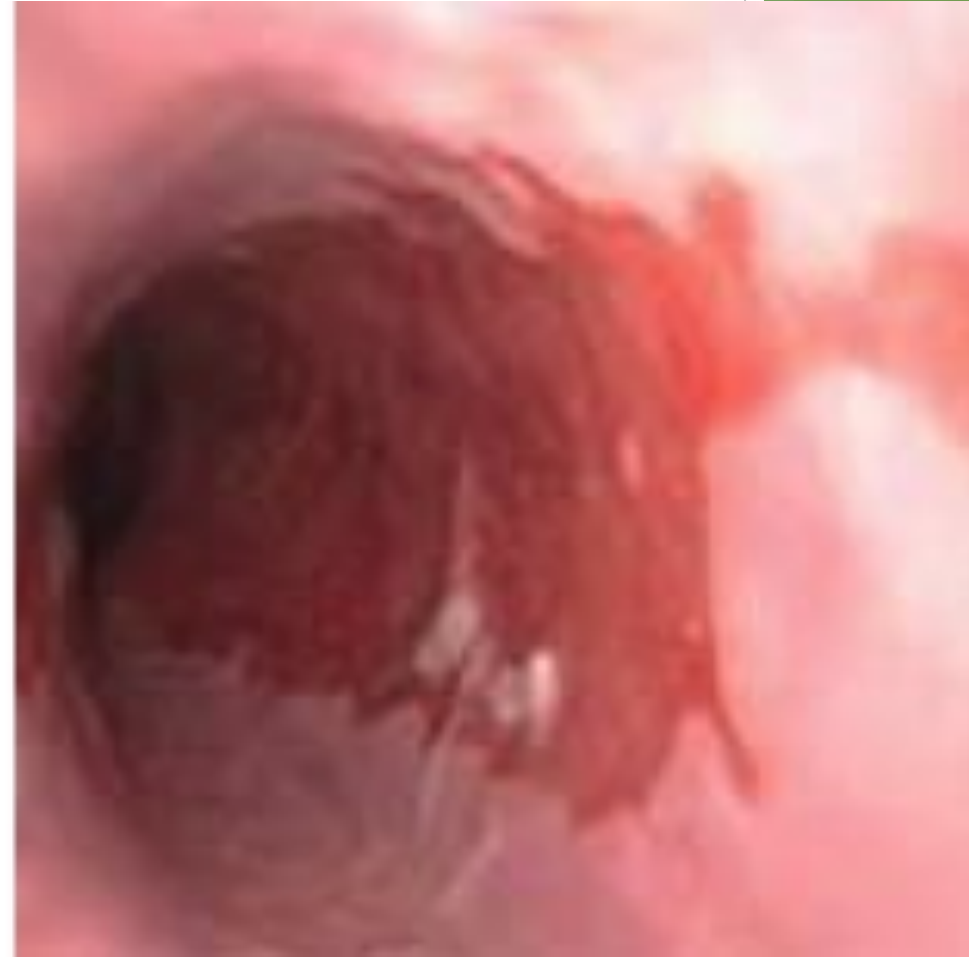


# MORPHOLOGY

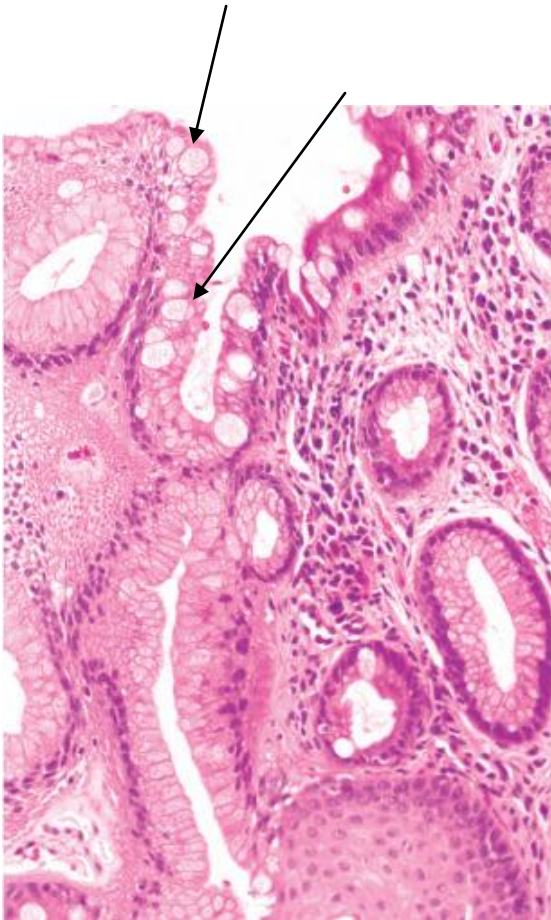
- ▶ **Endoscopy:**
- ▶ Red tongues extending upward from the GEJ.
  
- ▶ **Histology:**
- ▶ **Intestinal metaplasia (defined by Presence of goblet cells) this is mandatory to establish diagnosis and to follow-up the case for regression of metaplasia or development of dysplasia).**
- ▶ +-Dysplasia : low-grade or high-grade
- ▶ Intramucosal carcinoma: invasion into the lamina propria.



Red tongue, from the GEJ upward, biopsy from these tongues will highlight metaplasia and presence of goblet cells

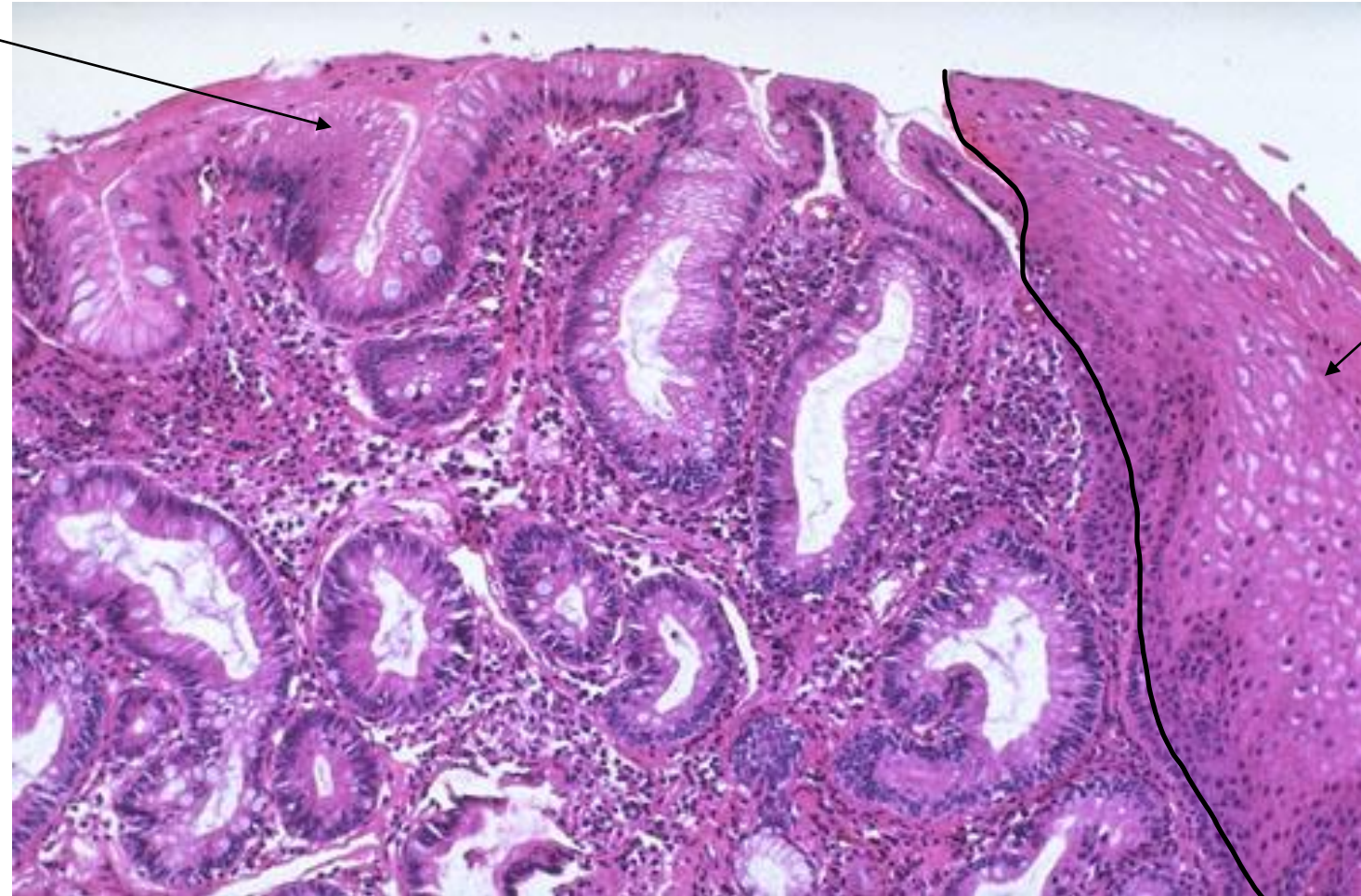


► [Gastroenterology Consultants of San Antonio](#)



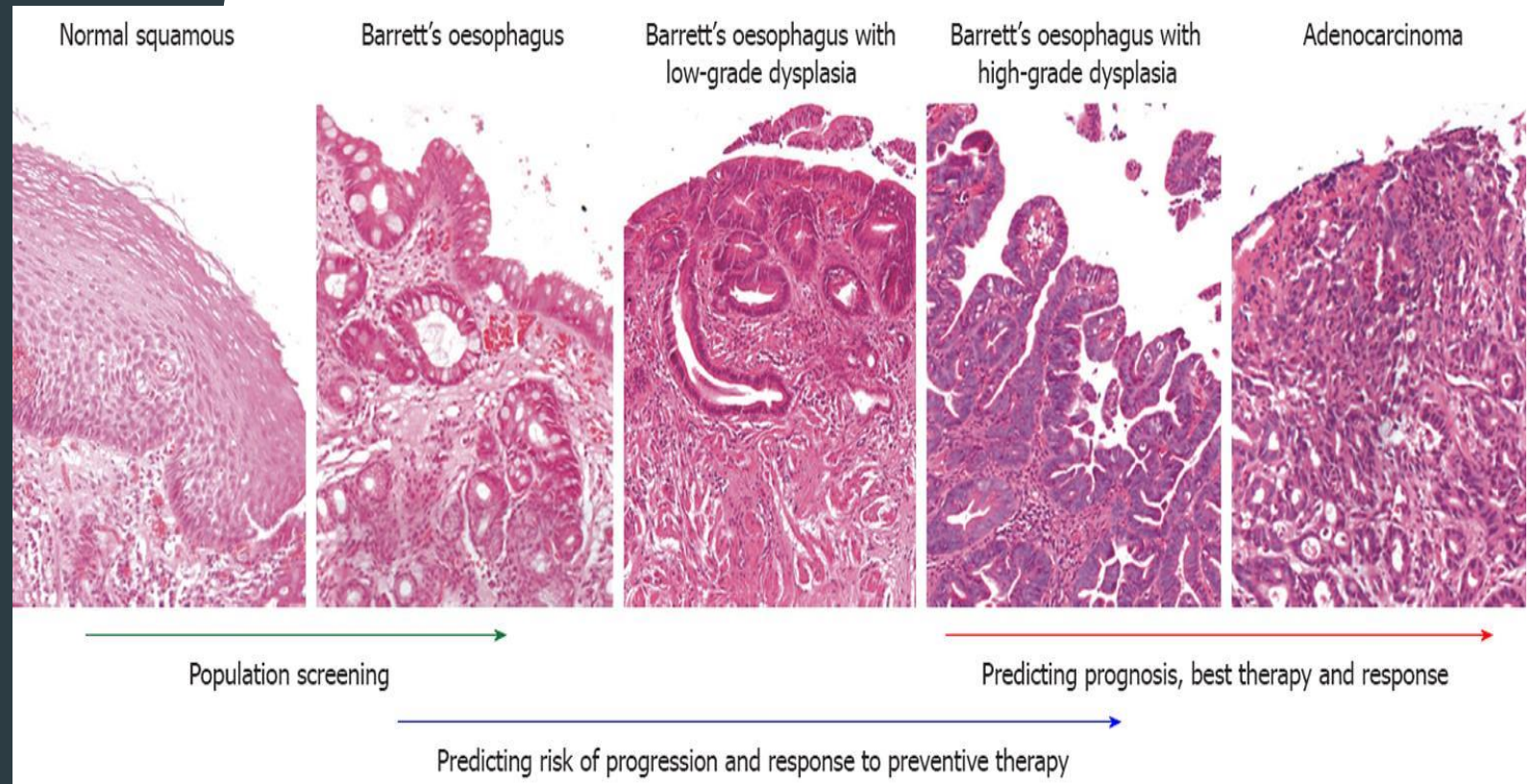
Esophagus is normally tan to light pink in colour but, here, it is red and erythematous. We can see the goblet cells here in the biopsy (black arrows in the left picture).

Goblet cells distended with somehow bluish mucin. Such structures should only be found in the intestine. Elsewhere, it is considered intestinal metaplasia.



Normal squamous epithelium





It is a progression:  
Normal squamous epithelium with chronic GERD → Barrett's esophagus → low-grade dysplasia → high-grade dysplasia → invasive adenocarcinoma.

# Management of Barrett

Periodic surveillance endoscopy with biopsy to screen for dysplasia.



High grade dysplasia & intramucosal carcinoma needs interventions.

# 6-ESOPHAGEAL TUMORS

Squamous cell carcinoma (most common worldwide)

Adenocarcinoma (on the rise,  $\frac{1}{2}$  of cases in developed countries, other half from squamous cell carcinoma)

# Adenocarcinoma

- ▶ Background of Barrett esophagus and long-standing GERD.
- ▶ Risk is greater if: documented dysplasia, smoking, obesity, radioTx.
- ▶ Male : female (7:1)
- ▶ Geographic & racial variation (developed countries, could be associated with obesity and higher incidence of GERD which could cause Barret's esophagus and, then, adenocarcinoma)

# Pathogenesis

- ▶ From Barrett>>dysplasia>>adenocarcinoma.
- ▶ Acquisition of genetic and epigenetic changes.
- ▶ Chromosomal abnormalities and TP53 mutation.
- ▶ Multi-step process, affected by many environmental factors

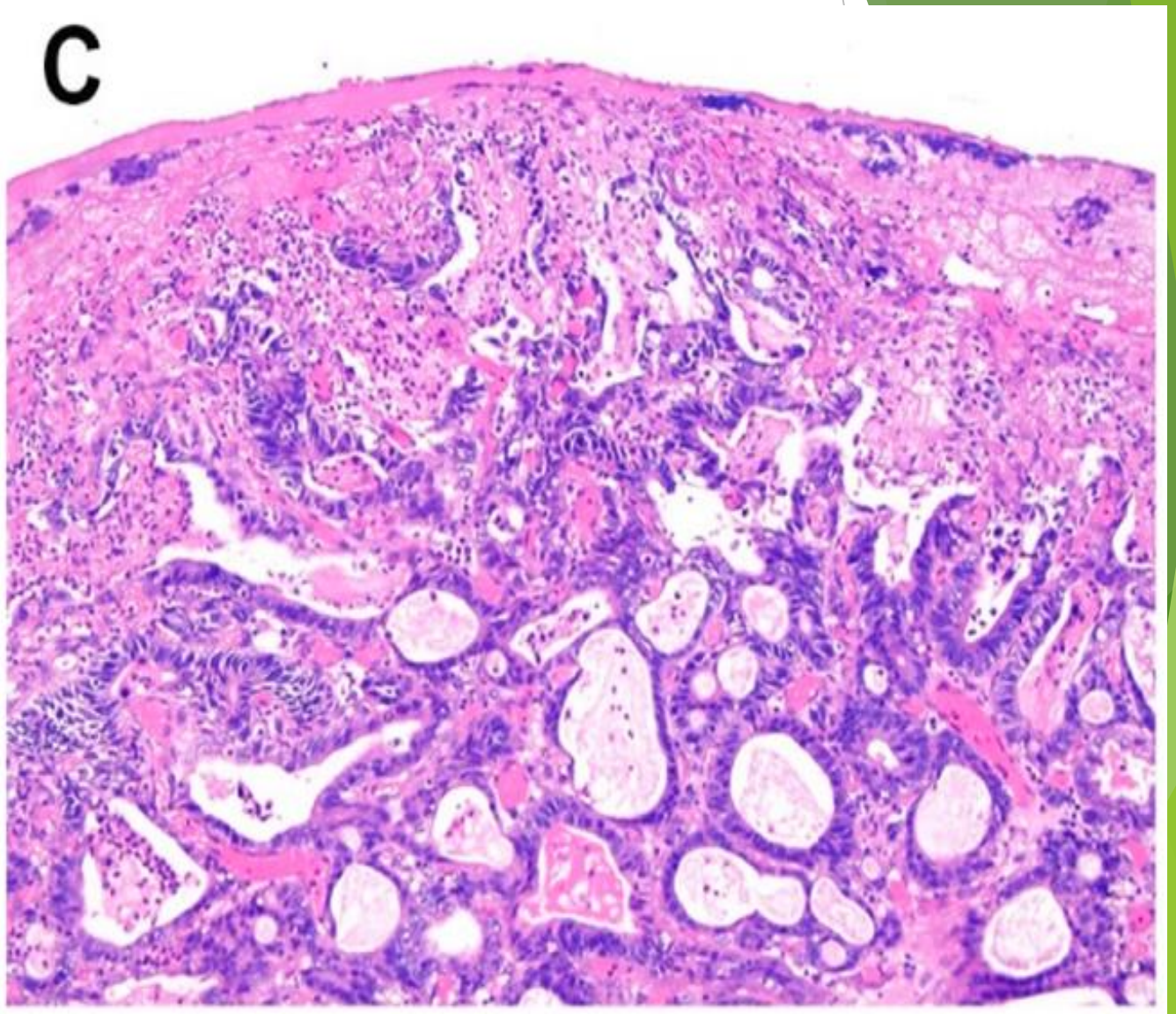
# MORPHOLOGY

- ▶ Distal third of esophagus, same as GERD
- ▶ Early: flat or raised patches
- ▶ Later: exophytic and forms a tumor, infiltrative masses to the lumen which could cause obstruction of esophagus, could infiltrate wall of esophagus upward and downward
  
- ▶ Microscopy:
- ▶ Forms glands and mucin.



Robbins Basic Pathology 10th edition

Exophytic mass just at GEJ



# Clinical Features

- ▶ Pain or difficulty swallowing
- ▶ In advanced cases, Progressive weight loss (tumor causes cachexia -weight loss. Also because of the difficulty in swallowing, patient stops eating).
- ▶ Chest pain
- ▶ Vomiting.
- ▶ Advanced stage at diagnosis: 5-year survival <25%. Most important and unfortunate feature, they present late thinking it is related to reflux
- ▶ Early stage: 5-year survival 80% if discovered from Barret's esophagus or dysplasia and we follow the patient up upon early discovery of invasive adenocarcinoma
- ▶ Time of presentation and time of diagnosis is very important.



# Squamous Cell Carcinoma SCC

- ▶ Male : female (4:1)
- ▶ More in rural, low resource countries.
- ▶ Risk factors: **unrelated to GERD**
- ▶ Alcohol
- ▶ Tobacco use
- ▶ Poverty
- ▶ Caustic injury
- ▶ Achalasia .
- ▶ Plummer-Vinson syndrome (iron deff.anemia, dysphagia, webs **in esophagus**)
- ▶ Frequent consumption of very hot beverages
- ▶ Previous radiation Tx .
- ▶ Remember, these are risk factors, one or a combination of them along with environmental factors could cause the disease.

# Pathogenesis

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

# MORPHOLOGY

- ▶ Middle third (50% of cases) unlike adenocarcinoma which is in lower third
- ▶ Polypoid, ulcerated, or infiltrative.
- ▶ Wall thickening, lumen narrowing (can present with dysphagia)
- ▶ Invade surrounding structures (bronchi, mediastinum, pericardium, aorta).

# Mid esophagus

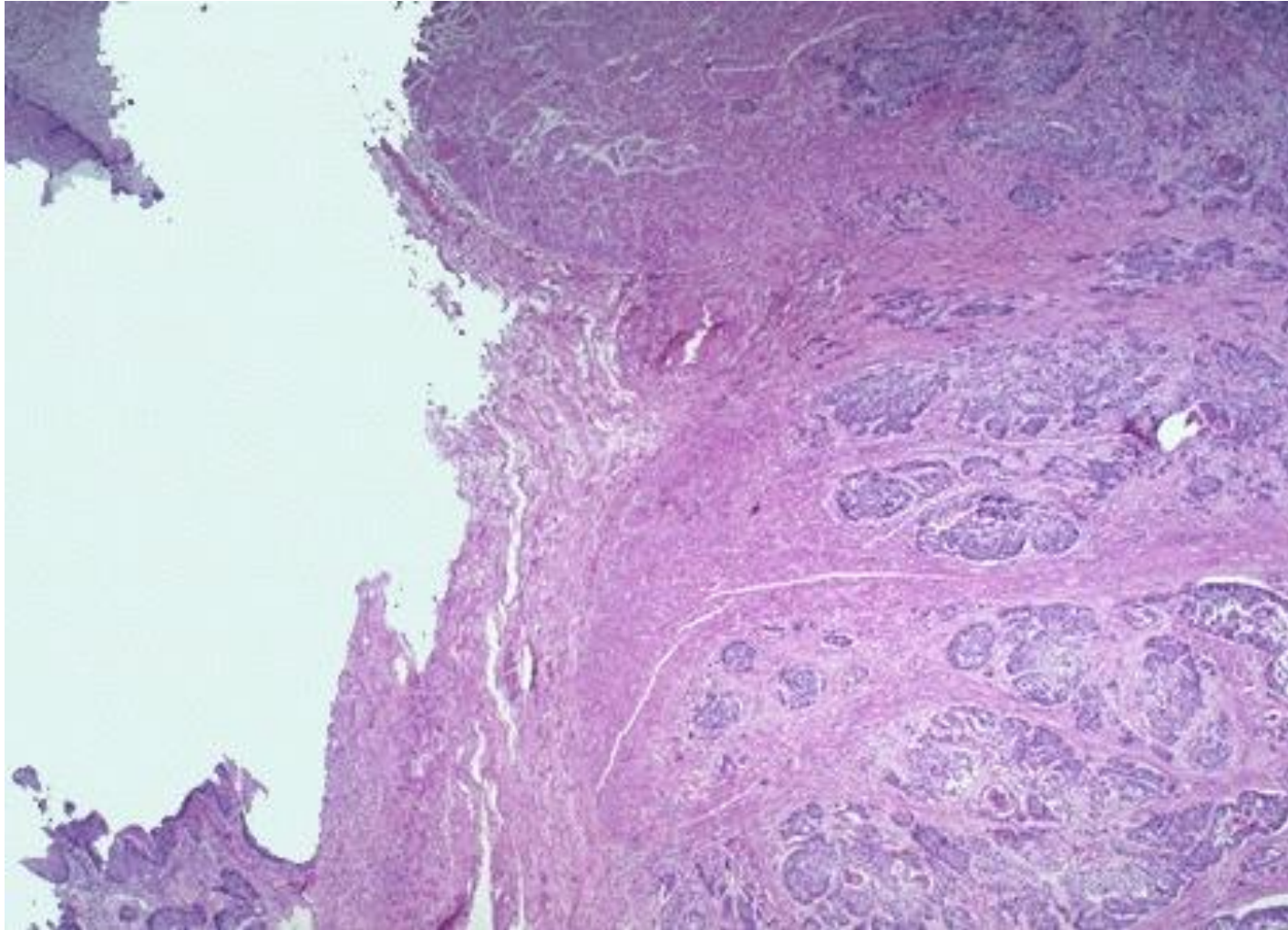


- ▶ Bulging mass in the mid-esophagus

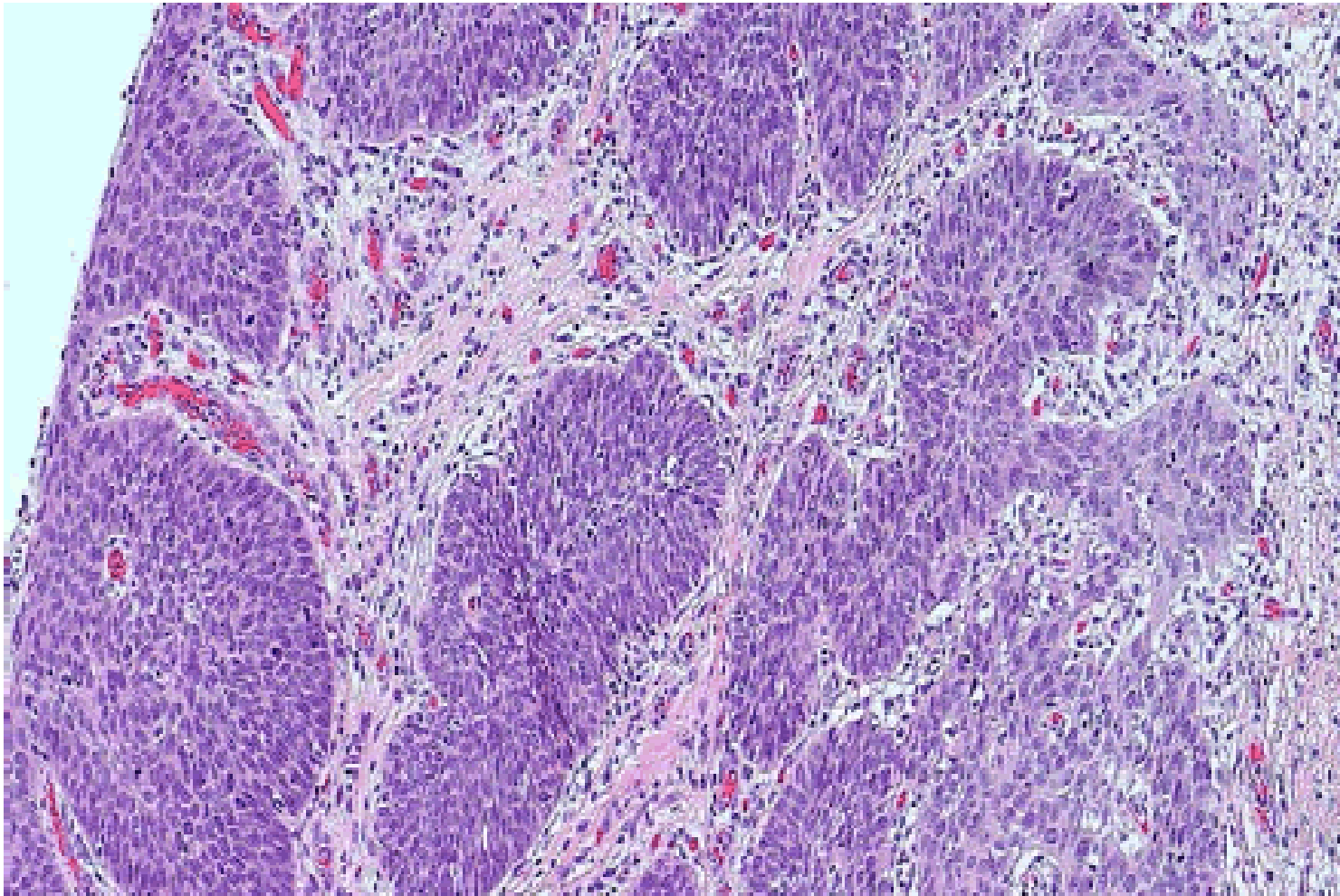
# Microscopy:

- ▶ Pre-invasive: Squamous dysplasia & CIS **carcinoma in-situ**.
- ▶ Well to moderately differentiated invasive SCC.
- ▶ Intramural tumor nodules away from main tumor.
- ▶ Lymph node metastases (**depends on initial tumor location in esophagus**) :
- ▶ Upper 1/3: cervical LNs
- ▶ Middle 1/3: mediastinalparatracheal, and tracheobronchial LNs.
- ▶ Lower 1/3: gastric and celiac LNs.

# Invasive SCC



Invasive SCC  
composed of cells  
of squamous origin  
similar to normal  
lining of the  
esophagus



**Figure 4: Squamous cell carcinoma of the esophagus with focal invasion into the muscularis mucosa and associated desmoplastic response.**

desmoplastic= fibrotic,  
fibrous



# 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 10%



The background features abstract, overlapping geometric shapes in various shades of green, ranging from light lime to dark forest green. The shapes are primarily triangles and polygons, creating a dynamic, layered effect. The central area is white, providing a clean space for the text.

*Good Luck!*