GI

Pathology

LEC no.

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Diseases of the esophagus-2

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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 visiting clinics
- Squamous epithelium is sensitive to acids that are carried in the gastric juices to the lower part of the esophagus upon recurrent reflux of these contents. However, there are some protective forces …
- Protective forces: mucin and bicarbonate from submucosal glands, high LES (lower esophageal sphincter) tone.

Pathogenesis

- **Decreased lower esophageal sphincter tone due to** alcohol, tobacco, hiatal hernia, or some medications such as CNS depressants
- **Increase abdominal pressure**

  (obesity, pregnancy, delayed gastric emptying, and increased gastric volume)
- **Idiopathic!!** **(Unknown cause)**

Note: Hiatal Hernia: when a part of the stomach herniates through the diaphragm and enters the thoracic cavity. This will lead to a decrease in the tone of the LES and reflux of gastric content into the lower esophagus

MORPHOLOGY

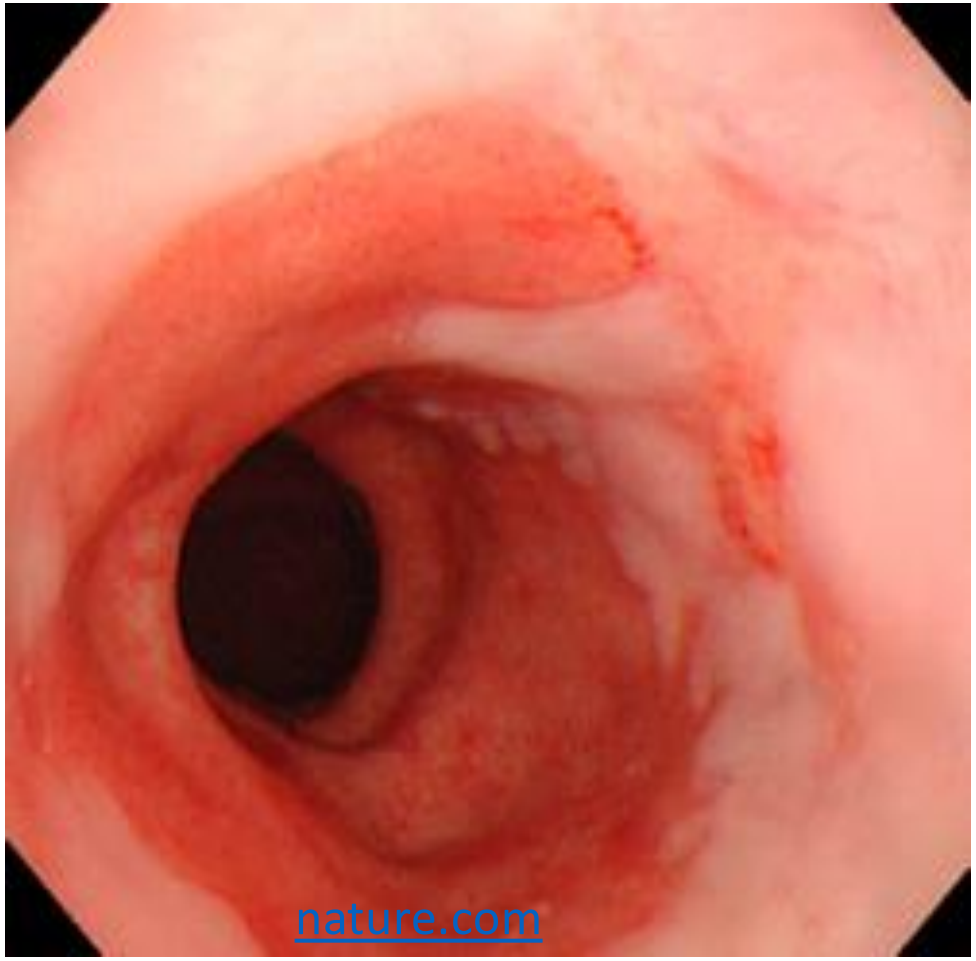
If we see two of these characteristics upon microscopic examination of biopsies taken from the esophagus, we can establish a diagnosis of reflux esophagitis along with the clinical manifestations.

➢ **Macroscopy (endoscopy)**

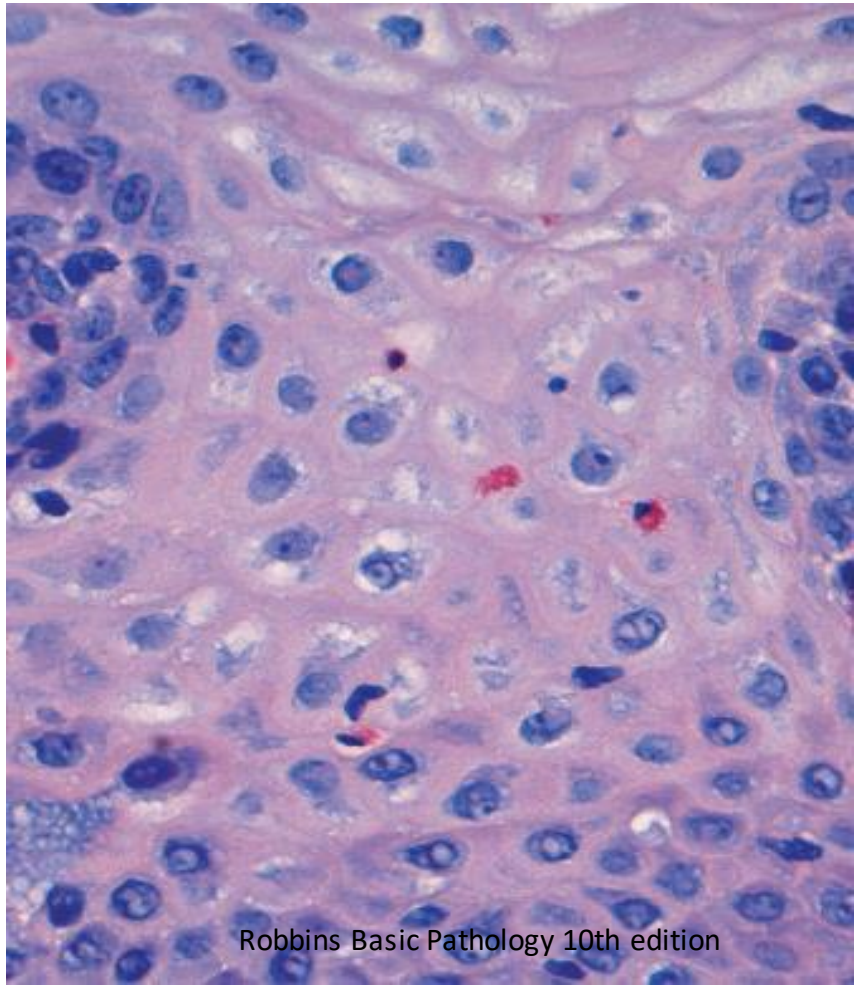
- Depends on the severity of the reflux; Mucosa could be **Unremarkable with no changes** or could have **Simple erythema** and redness due to inflammation

➢ **Microscopic:**

- Eosinophils infiltration (early)
- Neutrophils later (more severe).
- Accompanied by Basal zone hyperplasia of the basal squamous epithelial cells and
- Elongation of lamina propria papillae



This is the erythema of the lower esophagus in patients with reflux esophagitis



Eosinophils with granular eosinophilic cytoplasm

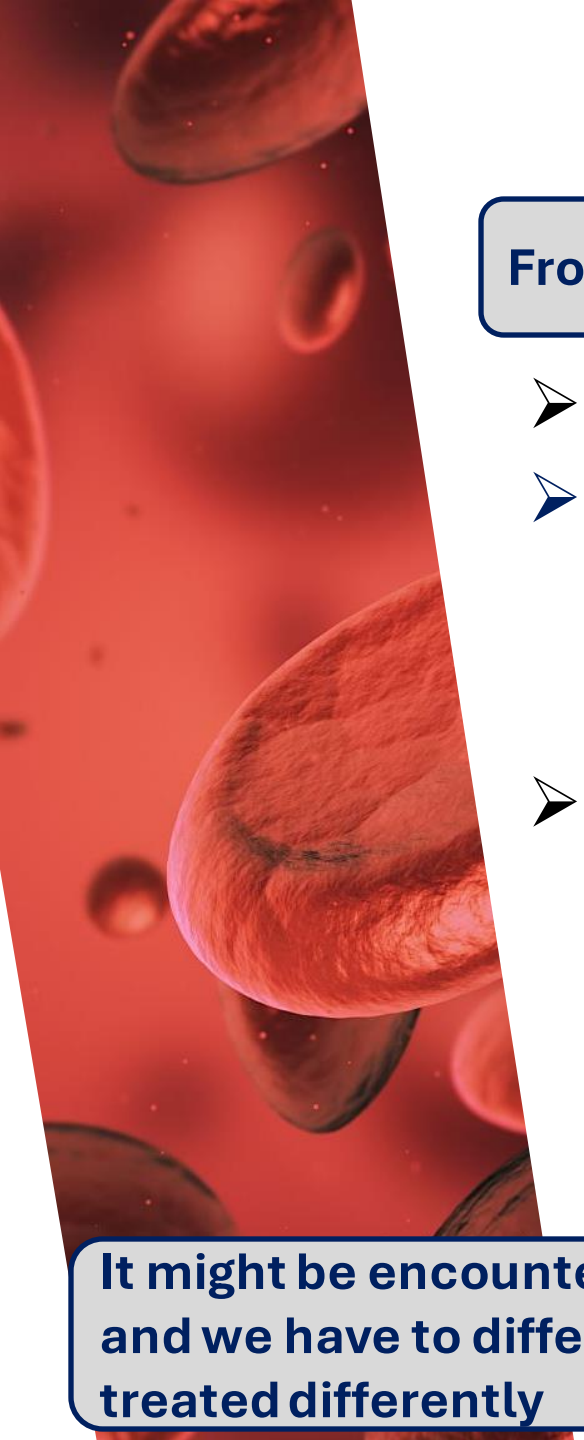
Clinical Features

- Most common in patients over 40 years.
- May occur in infants and children.
- It is presented with:
  - Heartburn (burning sensation in the epigastric area)
  - Dysphagia and difficulty in swallowing.
  - Regurgitation of sour-tasting gastric contents to the mouth in severe cases
  - Rarely: Severe chest pain, mistaken for heart disease especially when they present to the emergency room.

- Treatment: proton pump inhibitors to decrease acid secretion

Complications

- Esophageal ulceration
- Hematemesis (vomiting blood)
- Melena in cases of bleeding that passes through the stomach and altered by its acidity passing in the stool as black blood.
- Strictures and stenosis in patients with recurrent reflux esophagitis because the inflammation is repaired by fibrosis which could lead to narrowing of the lumen of the esophagus.
- Most severe: Barrett esophagus which is an intestinal metaplasia in the esophagus. (It might be a precursor of esophageal carcinoma)

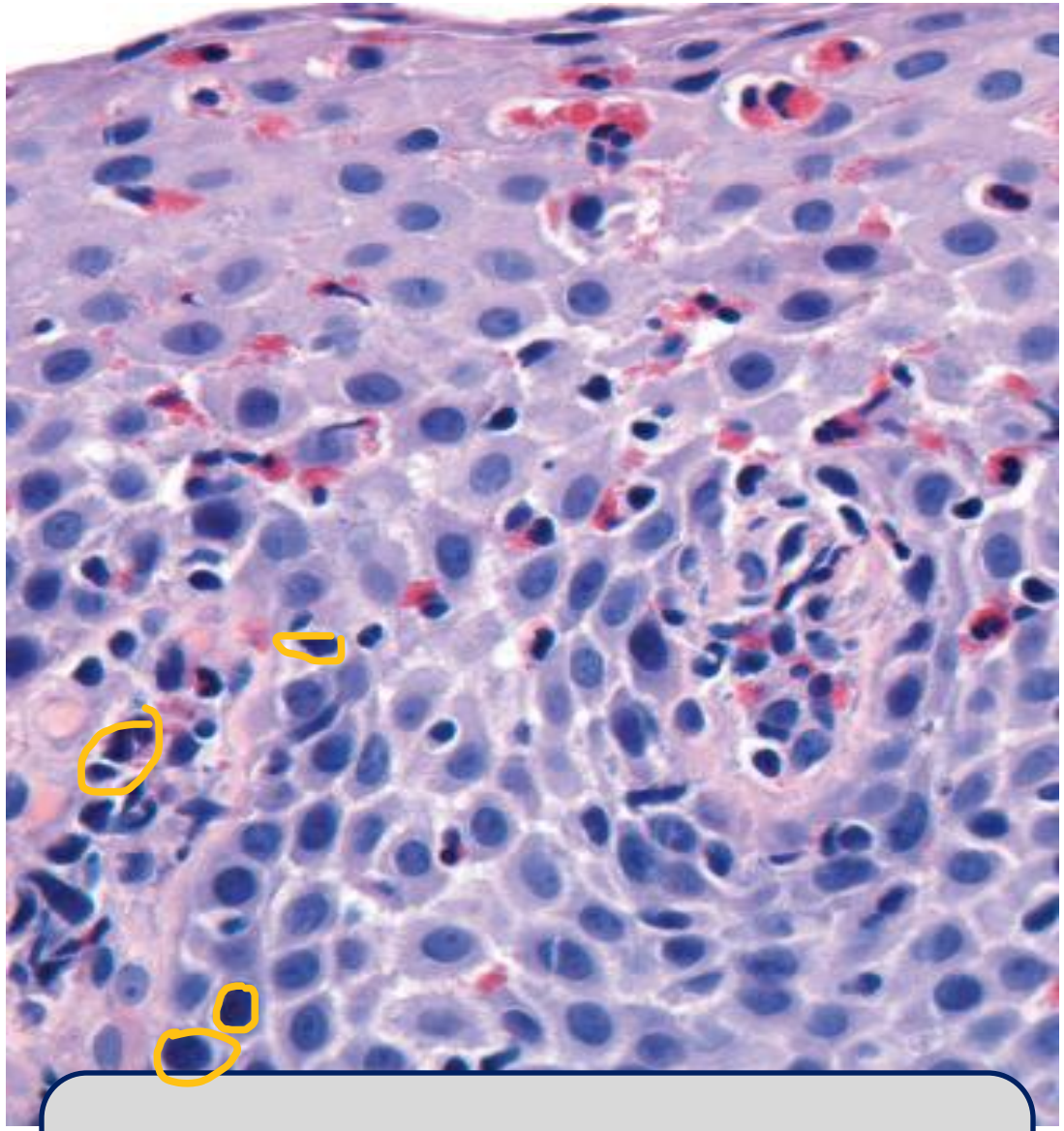


Eosinophilic Esophagitis

From its name it is rich in eosinophilic infiltration of the squamous epithelium

- Chronic immune mediated disorder
- **Variable Symptoms:**
  - Food impaction and dysphagia in adults
  - Feeding intolerance (or allergy to certain foods) or GERD-like symptoms in children
- **Morphology:**
  - Classical: Rings in the upper and mid esophagus (while reflux esophagitis affects lower part of esophagus.
  - Numerous eosinophils in epithelium (much more than the eosinophils we see in reflux esophagitis)
  - Far from the GEJ (gastroesophageal junction)

It might be encountered in children which present to the clinic as irritable with recurrent vomiting and we have to differentiate whether it's is GERD or eosinophilic esophagitis because they are treated differently



Numerous eosinophils infiltrating the squamous epithelium(in yellow)

Endoscopic picture showing rings in the esophagus which can cause dysphagia and food impaction

Atopic = Allergic

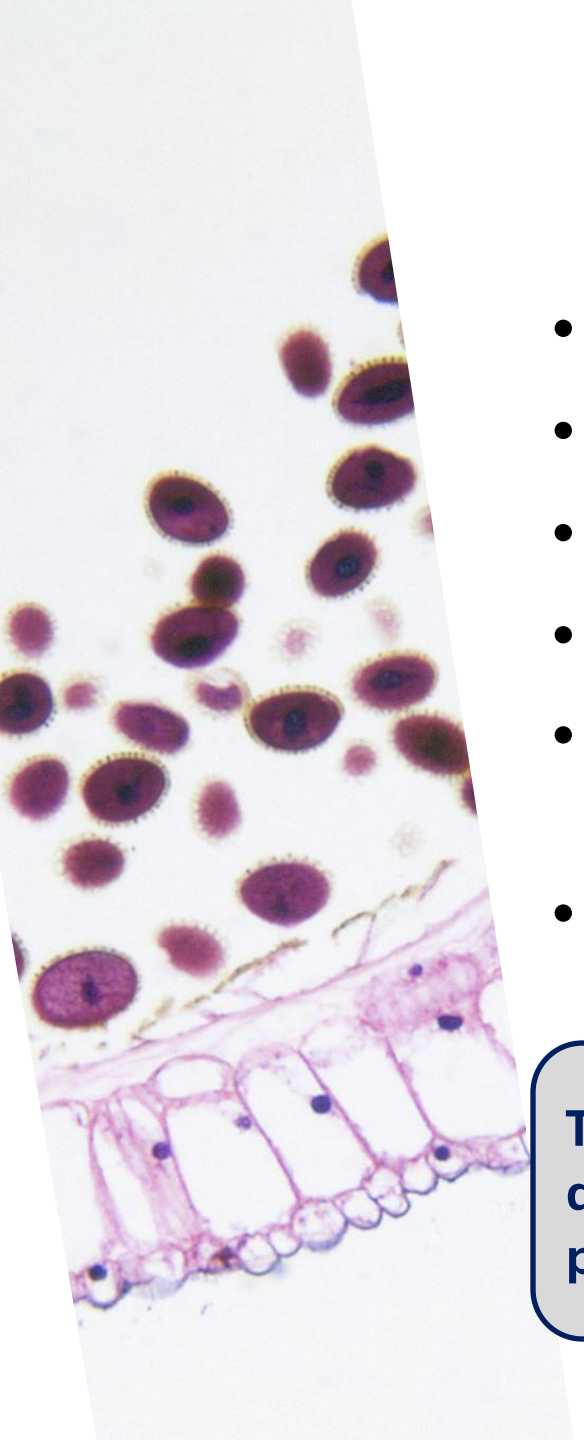
Management

- Most patients are atopic (atopic dermatitis, allergic rhinitis, asthma) or modest peripheral eosinophilia, which is an increased number of eosinophils in peripheral blood examination
- Refractory to PPIs.

They do not respond to proton pump inhibitors. That's why we have to differentiate between reflux and eosinophilic esophagitis

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

5-Barrett Esophagus



- Complication of chronic GERD
- Intestinal metaplasia. (presence of goblet cells)
- 10% of individuals with symptomatic GERD
- Males>>females, 40-60 yrs
- **Direct precursor of esophageal adenocarcinoma** thus diagnosis is very important
- **0.2-1% /year develop dysplasia (precursor of adenocarcinoma)**

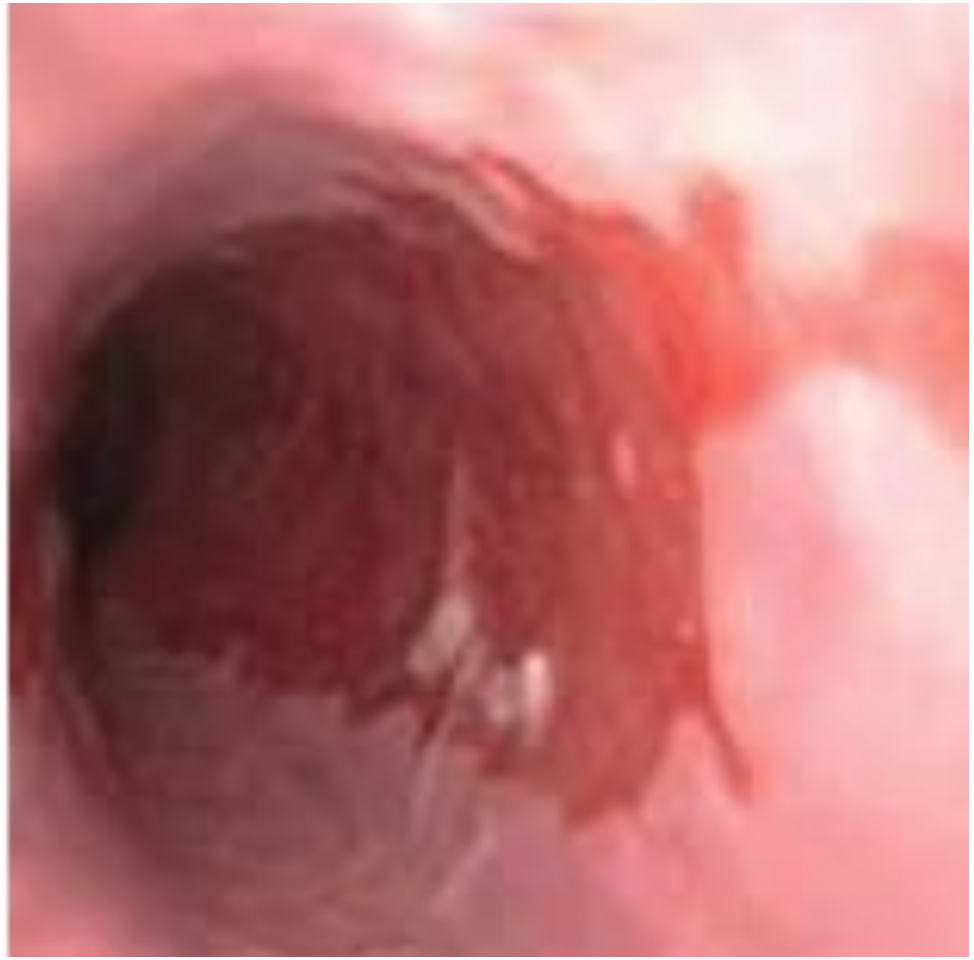
The risk of dysplasia when metaplasia occurs is 0.2 – 1 % per year. And this dysplasia can be graded as low grade or high grade, and it can be a precursor of adenocarcinoma of the esophagus.

MORPHOLOGY

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

- Histology:
- **Intestinal metaplasia (defined by** Presence of goblet cells)
- +-Dysplasia : low-grade or high-grade
- Intramucosal carcinoma: invasion into the lamina propria.

Important: we cannot diagnose Barret esophagus without the presence of intestinal metaplasia, so a biopsy is mandatory to establish a diagnosis and to follow up the case for the regression of metaplasia or the development of dysplasia, or the development, later on, of invasion which we call intramucosal carcinoma, or early carcinoma.



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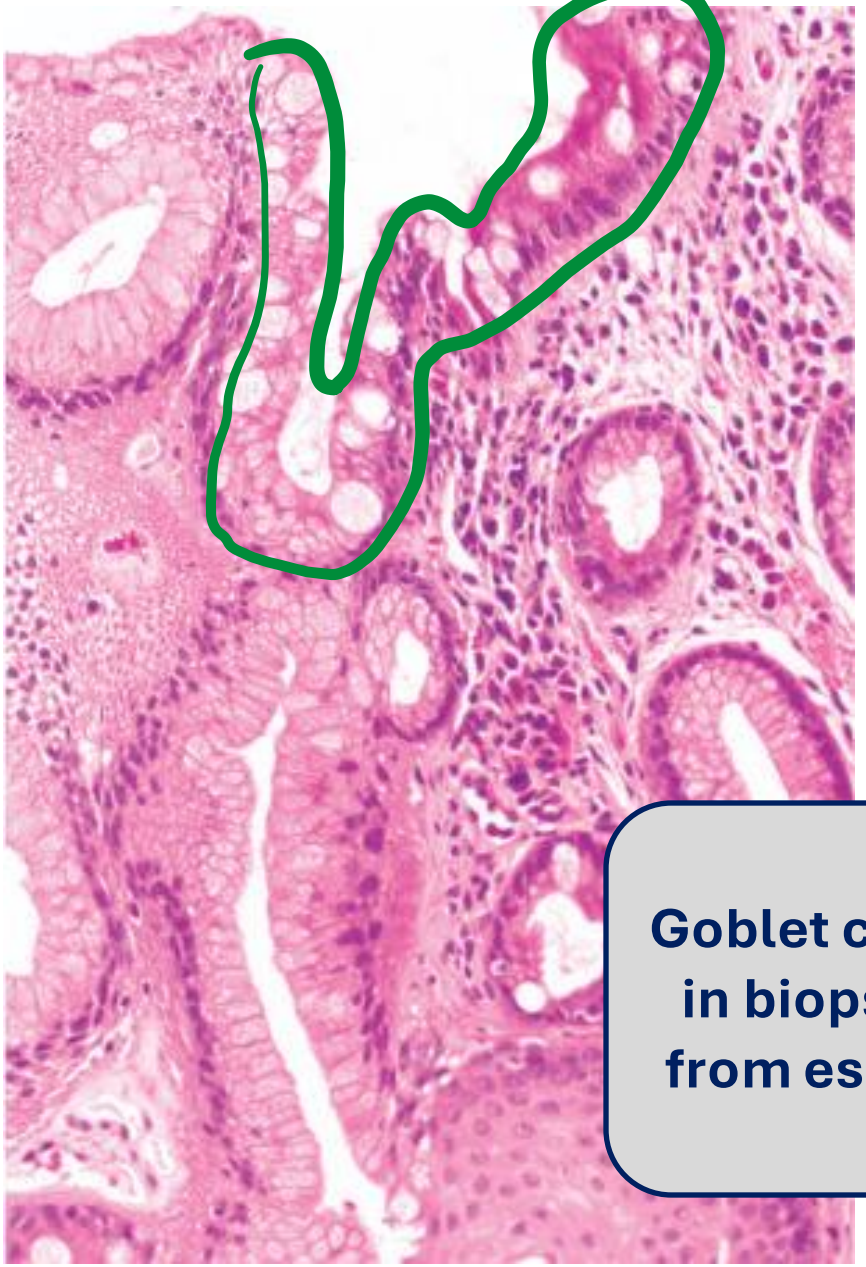
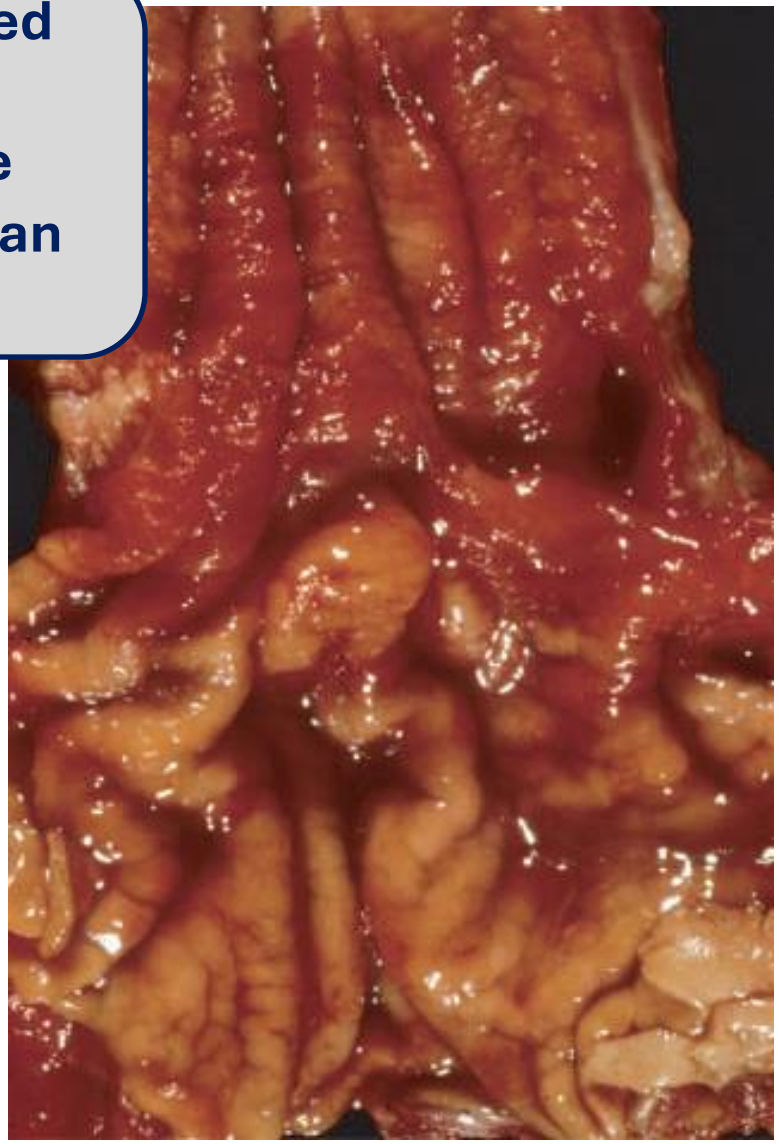
These are the red tongues extending from the GEJ upward

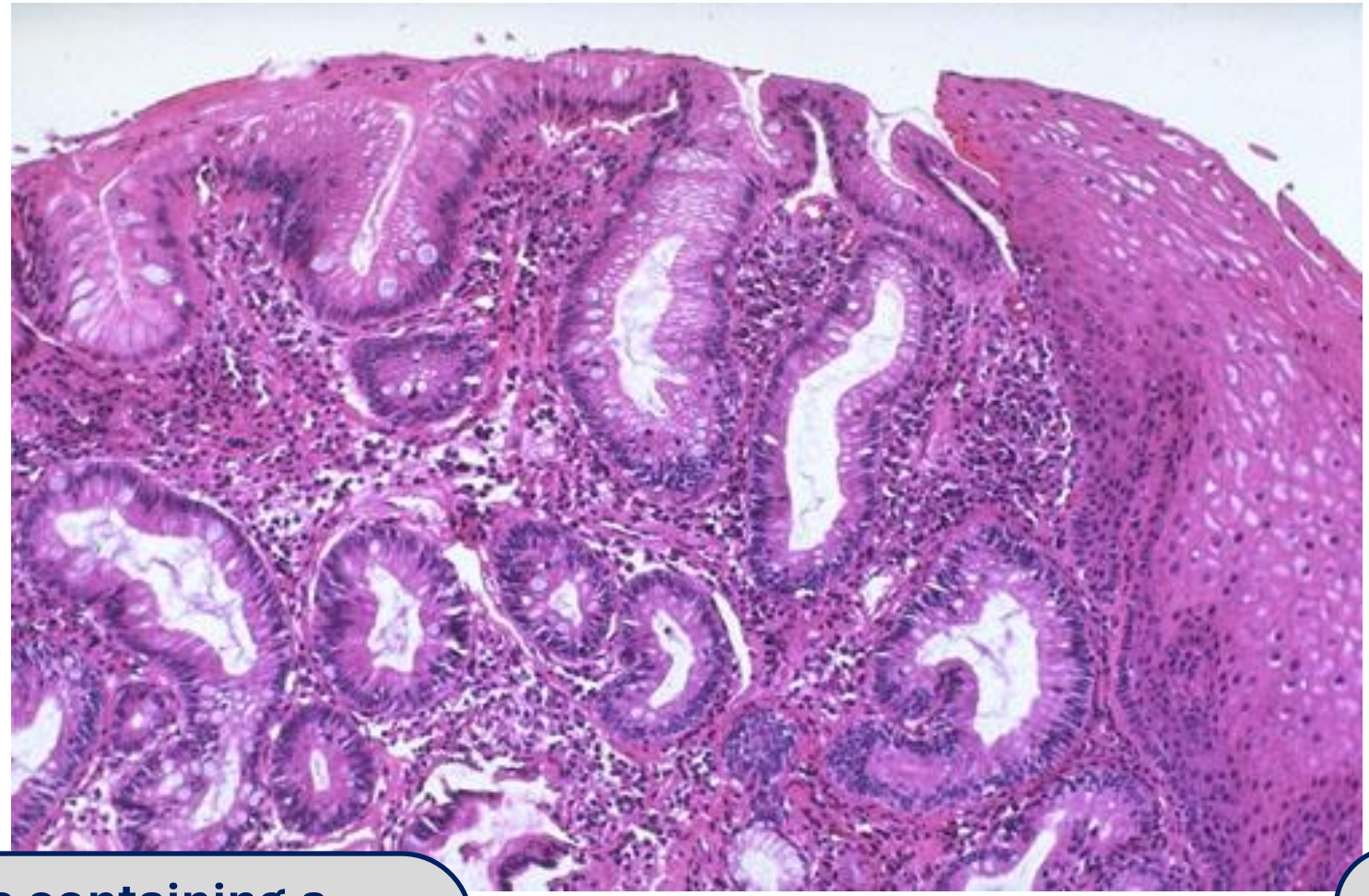


Goblet cells seen in biopsy taken from esophagus

Erythematous red esophagus as opposed to the normal pinkish tan color



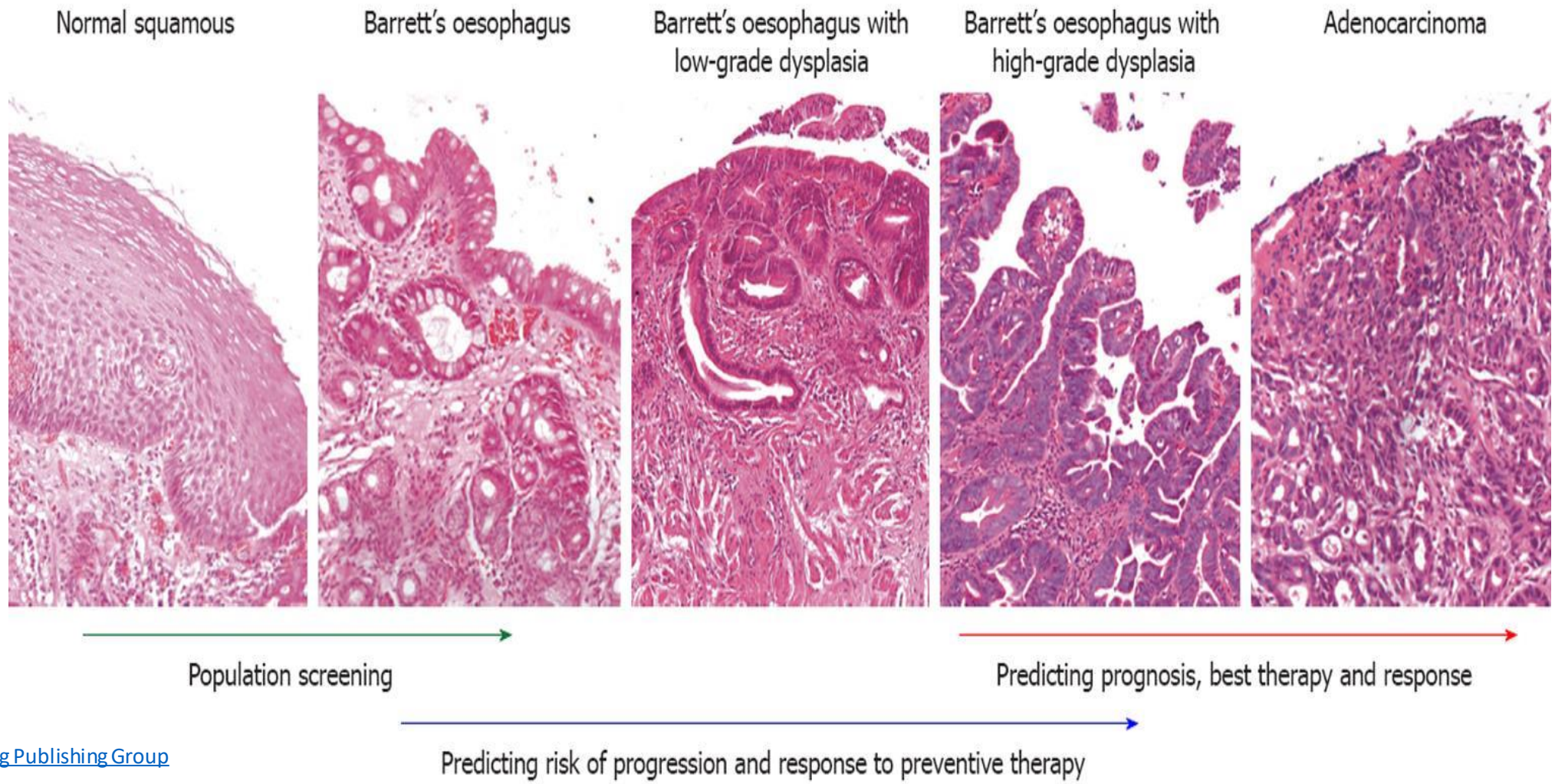
Robbins Basic Pathology 11th edition



Goblet cells containing a somewhat blue stain. These cells should be found in intestines not esophagus, so when they're found, it means there is intestinal metaplasia.

Normal squamous epithelium

Progression of Barrett Esophagus to adenocarcinoma



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Management of Barrett

Periodic surveillance endoscopy with biopsy to screen for dysplasia.

If high grade dysplasia & intramucosal carcinoma then patient needs interventions.

6-ESOPHAGEAL TUMORS

Squamous cell carcinoma (most common worldwide)

Adenocarcinoma (on the rise, ½ of cases in developed countries)

Adenocarcinoma

- Background of Barrett esophagus and long-standing GERD.
- Risk is greater if:
  - documented dysplasia
  - smoking
  - obesity
  - radiotherapy
- Male : female (7:1)
- Geographic & racial variation (more common in developed countries)

Pathogenesis

- From Barrett>>dysplasia>>adenocarcinoma.
- Acquisition of genetic and epigenetic changes.
- Chromosomal abnormalities and TP53 mutation.

The process of pathogenesis is multistep and affected by many factors

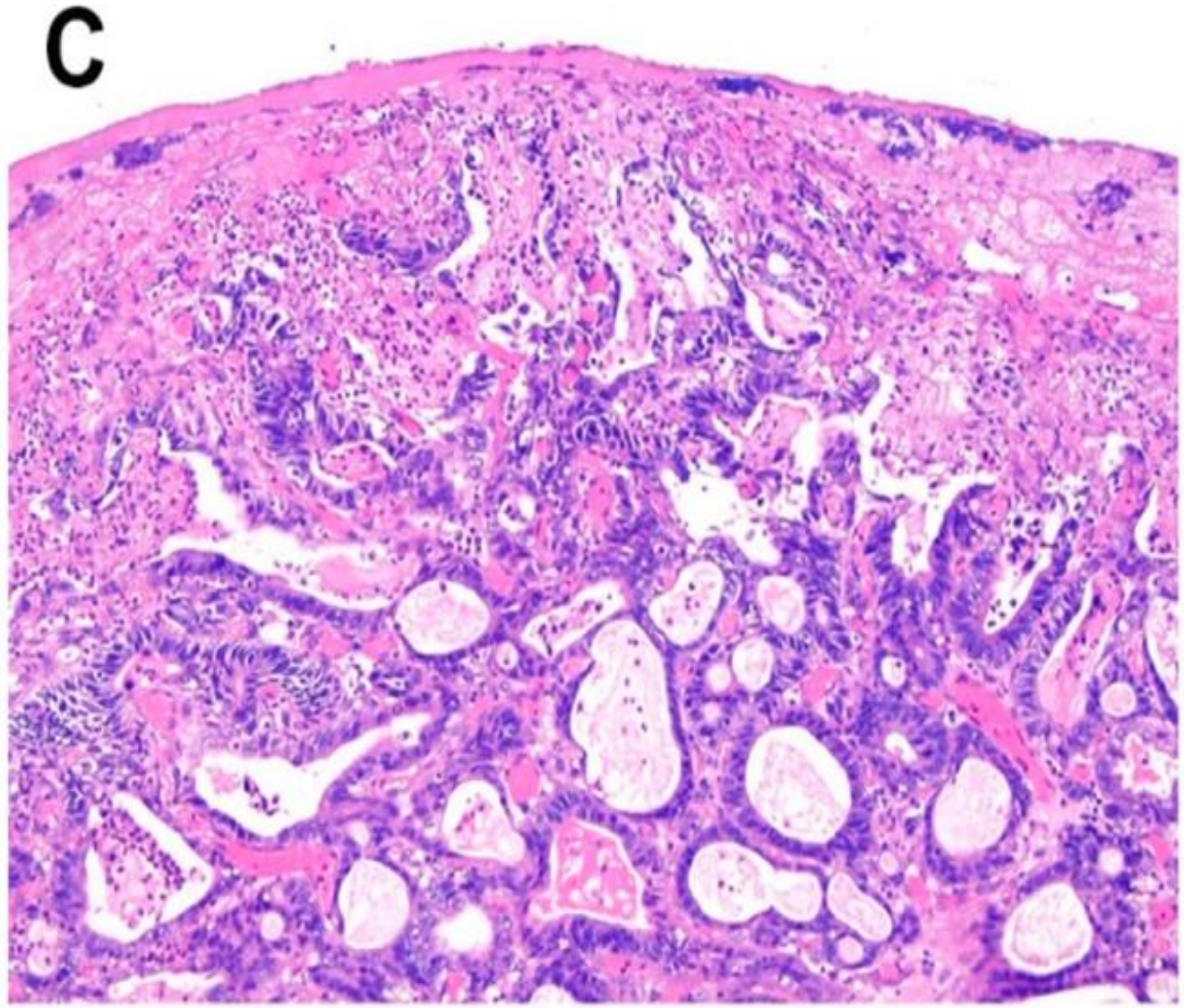
MORPHOLOGY

- Distal third of esophagus which is the site for GERD and reflux esophagitis
- Early: flat or raised patches
- Later: exophytic infiltrative masses, forming tumors projecting into the lumen and causing obstruction

- Microscopy:
- Forms glands and mucin.

Exophytic mass at GEJ

Robbins Basic Pathology 10th edition



Clinical Features

- Pain or difficulty swallowing
- Progressive weight loss in advanced cases due to the tumor itself and due to difficulty in swallowing
- Chest pain
- Vomiting.
- Advanced stage at diagnosis: 5-year survival <25%.
- Early stage: 5-year survival 80%

So, the time of diagnosis is so important!!

Squamous Cell Carcinoma

- Male : female (4:1)
- More in rural, low resource countries.

- **Risk factors: (not related to reflux esophagitis)**
  - 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 .

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 appears in the lower part of the esophagus)
- Polypoid, ulcerated, or infiltrative causing …
- Wall thickening, lumen narrowing
- Invade surrounding structures (bronchi, mediastinum, pericardium, aorta).

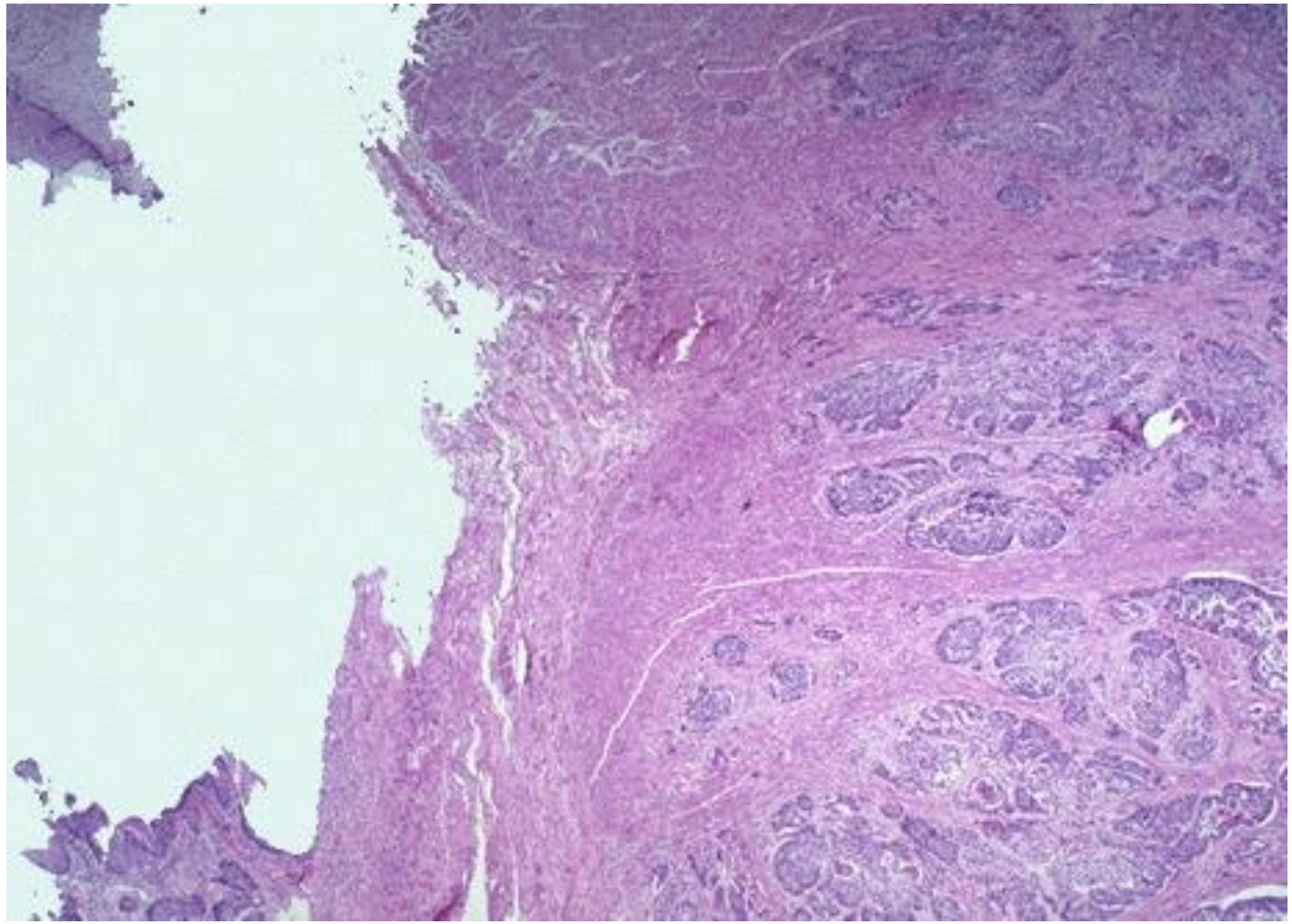
Mid esophagus

Bulging mass in the mid esophagus

Microscopy:

- Pre-invasive: Squamous dysplasia & CIS (Carcinoma in situ)
- Well to moderately differentiated invasive SCC.
- Can present sometimes as intramural tumor nodules away from main tumor. So, the tumor can be carried sometimes by the rich lymphatic supply to other parts of the esophagus.
- Lymph node metastases:
- Upper 1/3: cervical Lymph Nodes (LN)
- 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 the normal lining of the esophagus

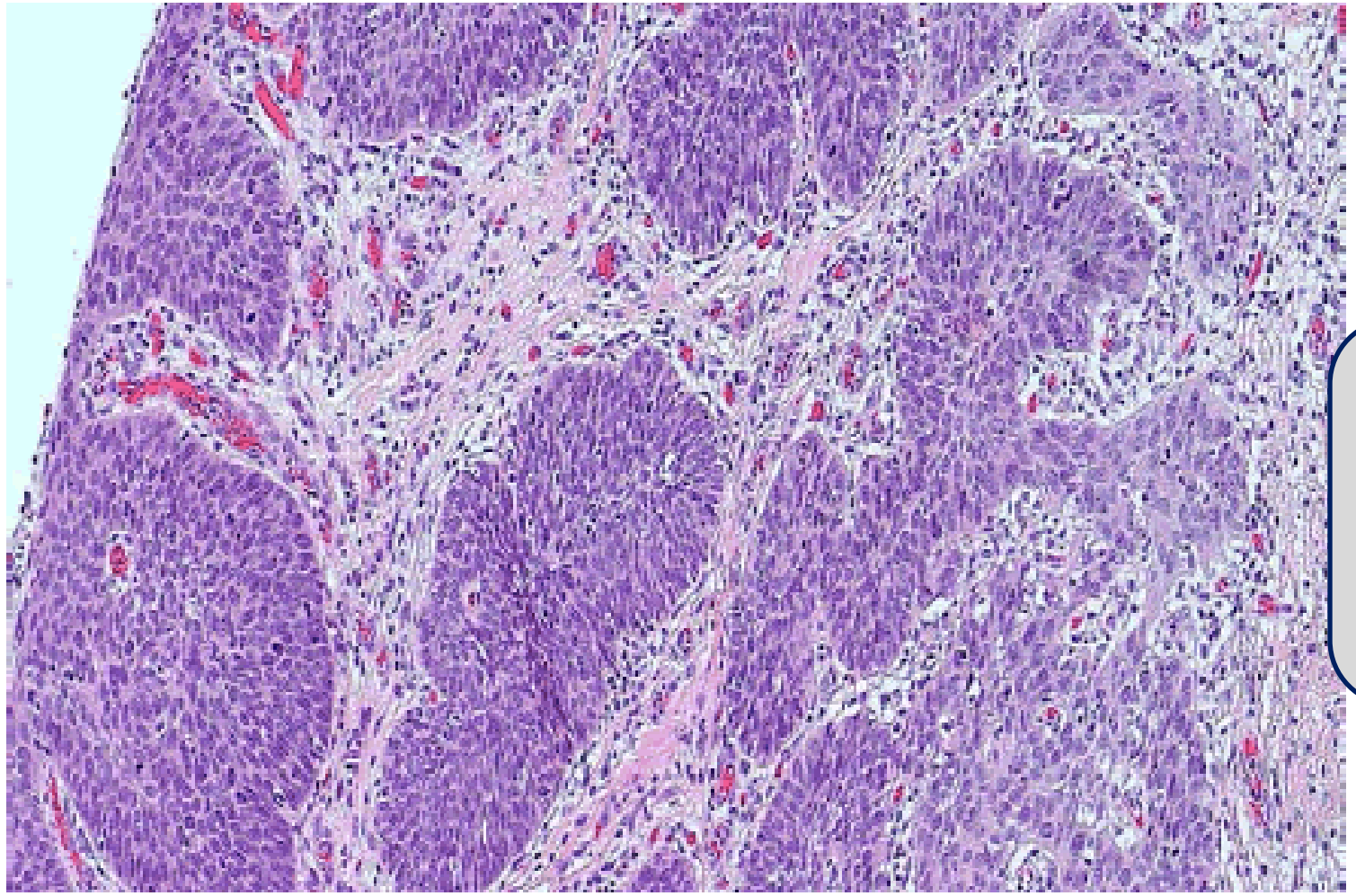


Figure 4: Squamous cell carcinoma of the esophagus with focal invasion into the muscularis mucosa and associated desmoplastic response.

Invasive SCC invading the underlying tissue with associated fibrotic or desmoplastic response around them

Clinical Features

- Dysphagia
- Odynophagia (Pain upon swallowing)
- Obstruction
- Weight loss and debilitation
- Impaired nutrition & tumor associated cachexia
- Hemorrhage and sepsis if ulcerated.
- Aspiration via a tracheoesophageal fistula between the tumor and the trachea of the bronchus
- Dismal Prognosis: 5-year survival 10%. Usually, present late with advanced disease.