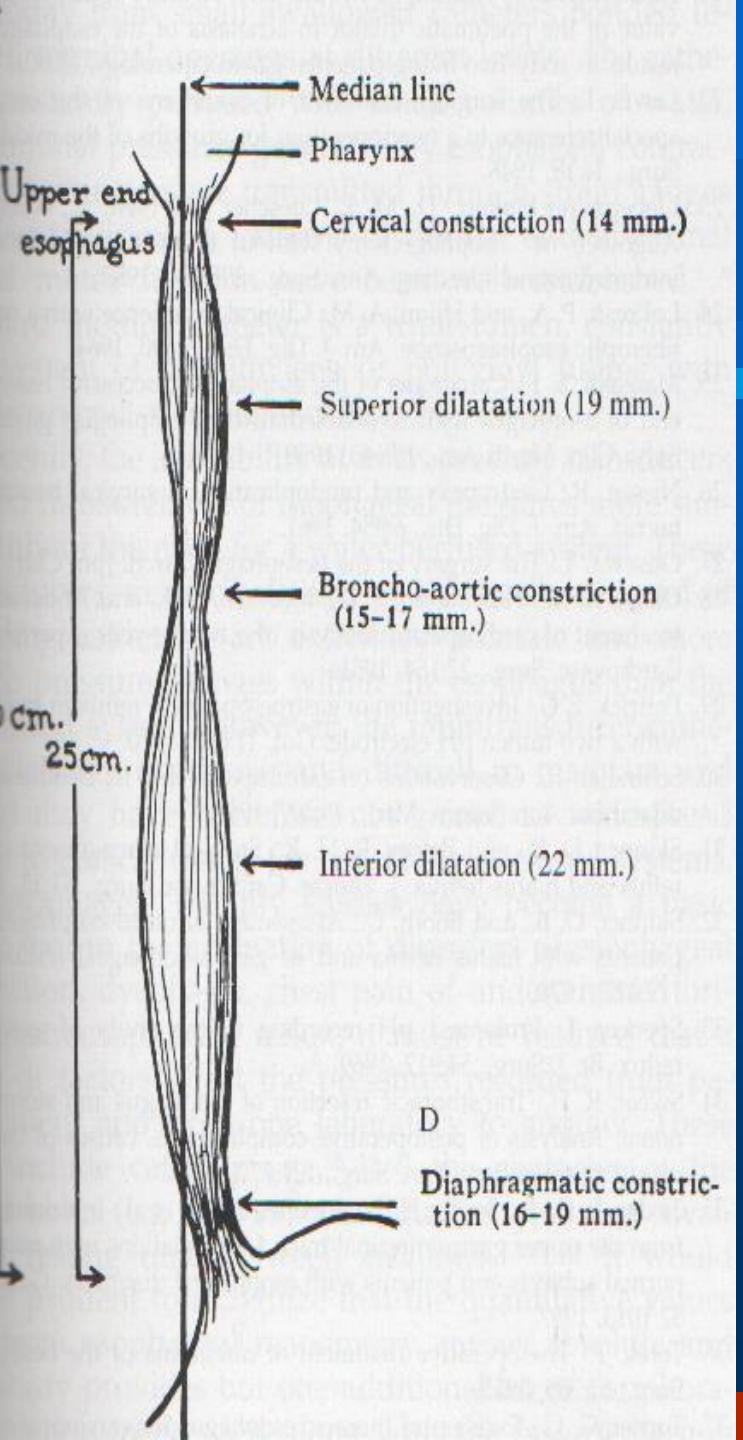
MEDICINSKI FAKULTET
SVEUČILIŠTA U SPLITU

Diseases of the esophagus

Prof. dr. sc. Miroslav Šimunić

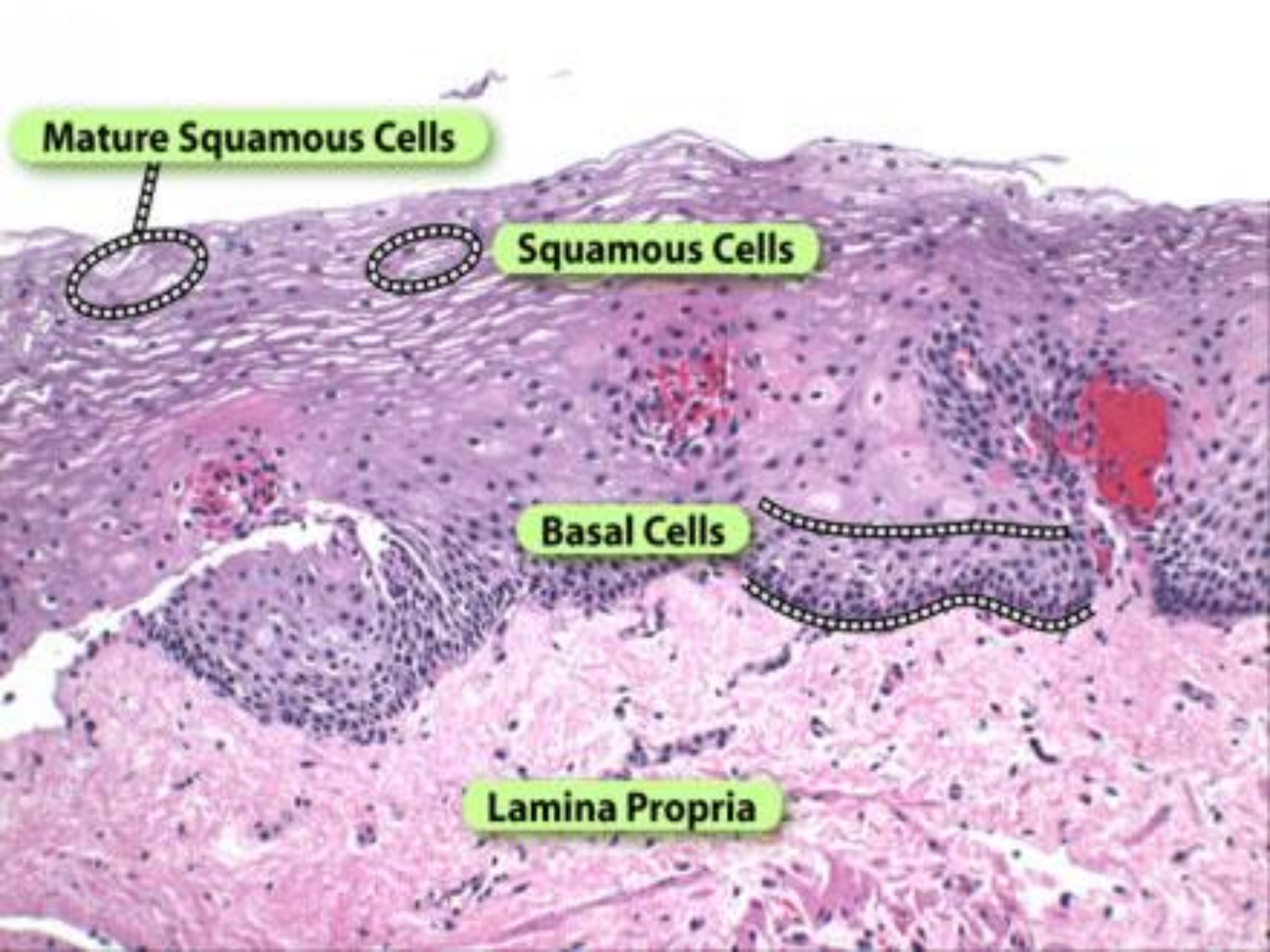
KBC Split

Split, 2015



Esophagus

- Upper 1/3 is skeletal muscle
- Lower 1/3 is smooth muscle
- Middle is combo of both
- Contains two sphincters
- Lined by squamous epithelium
- < 3 cm below diaphragm


Mature Squamous Cells
Squamous Cells
Basal Cells
Lamina Propria

Dysphagia

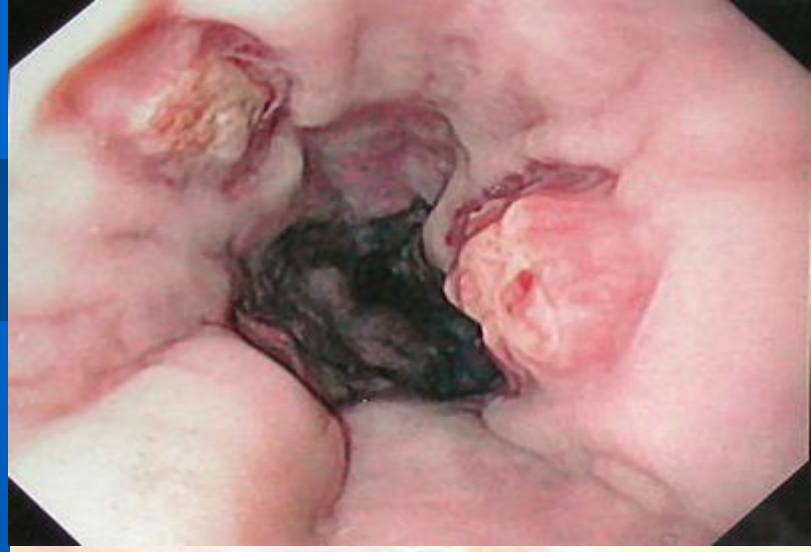
- The act of swallowing is comprised of a series of events requiring intact *central, autonomic, and enteric nervous systems* as well as a set of functional *striated and smooth muscles*
- Interference with these precise mechanisms will result in *dysphagia*

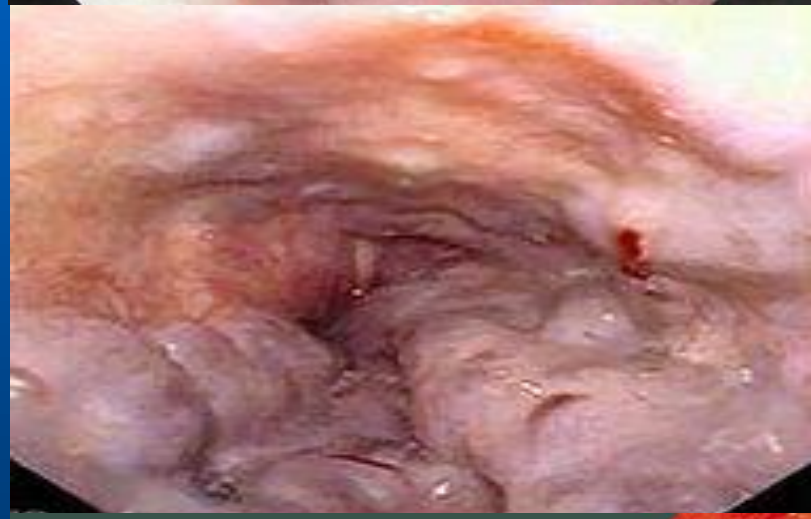
Dysphagia

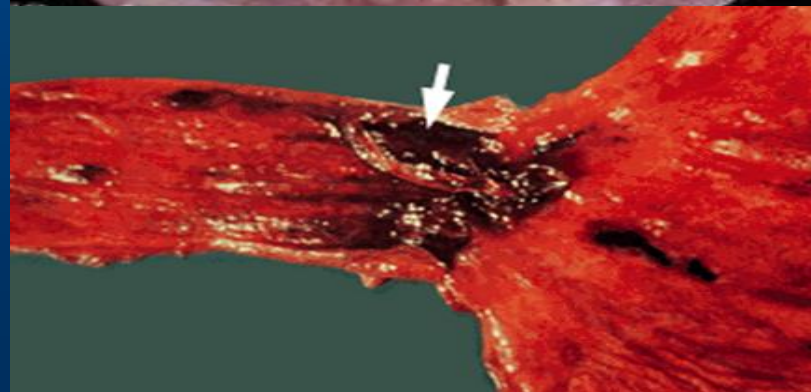
- Lesions of the esophagus run from bland esophagitis to highly lethal cancers.
- All produce *dysphagia* (difficulty in swallowing), which is attributed either to deranged esophageal motor function or to narrowing or obstruction of the lumen.
- Gastroesophageal reflux disease (GERD) - (*heartburn or* retrosternal pain) usually reflects regurgitation of gastric contents into the lower esophagus.

Esophageal varices

- Extremely dilated sub-mucosal veins in the lower esophagus
- *Hematemesis* (vomiting of blood) and *melena* (blood in the stools) are evidence of severe inflammation, ulceration, or laceration of the esophageal mucosa.
- Massive hematemesis may reflect life-threatening rupture of esophageal varices.







Structural abnormalities

- Structural abnormalities of the esophagus can be either congenital or acquired.
- The two most common congenital esophageal abnormalities are
  - Esophageal Atresia (EA) and
  - Tracheoesophageal Fistula (TEF).
- Anatomic disorders encountered infrequently (Table).

Selected Anatomic Disorders Of The Esophagus

Disorder	Clinical Presentation and Anatomy
Stenosis	Adult with progressive dysphagia to solids and eventually to all foods; a lower esophageal narrowing, which is usually the result of chronic inflammatory disease, including GERD
Atresia, fistula	Newborn with aspiration, paroxysmal suffocation, pneumonia; esophageal atresia (absence of a lumen) and tracheoesophageal fistula may occur together
Webs, rings	Episodic dysphagia to solid foods; a (presumably) acquired mucosal web or mucosal and submucosal concentric ring partially occluding the esophagus
Diverticula	Episodic food regurgitation especially nocturnal, sometimes pain is present; an acquired outpouching of the esophageal wall

ANATOMIC AND MOTOR DISORDERS

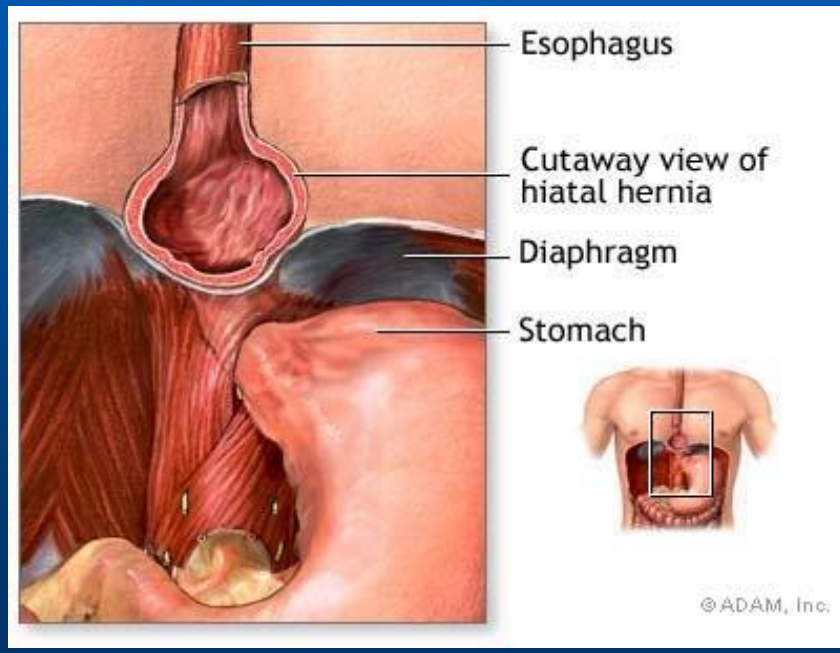
- **Motility Abnormalities**
  - They create difficulty in swallowing, called dysphagia.

- Dysphagia is a symptom of several esophageal motility disorders as well as several obstructive disorders such as esophageal webs or Schatzki ring: narrowing of the lower part of the esophagus that can cause difficulty swallowing.

- The narrowing is caused by a ring of mucosal tissue (which lines the esophagus) or muscular tissue.

ANATOMIC AND MOTOR DISORDERS

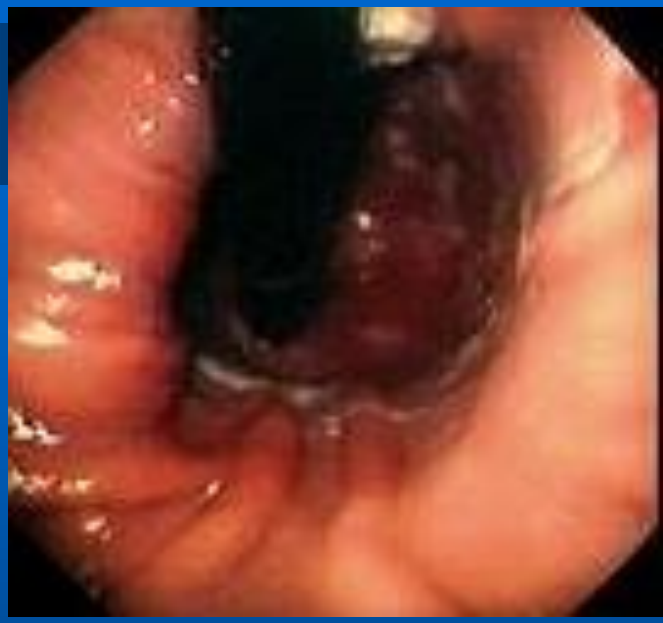
- Esophageal function may be affected secondarily by many esophageal disorders.
- In hiatal hernia, separation of the diaphragmatic crura and widening of the space between the muscular crura and the esophageal wall permits a dilated segment of the stomach to protrude above the diaphragm.

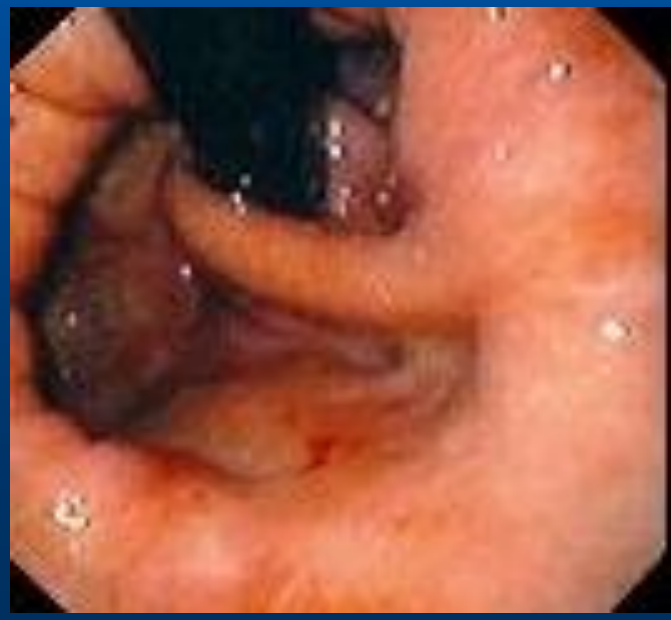


Two anatomic patterns

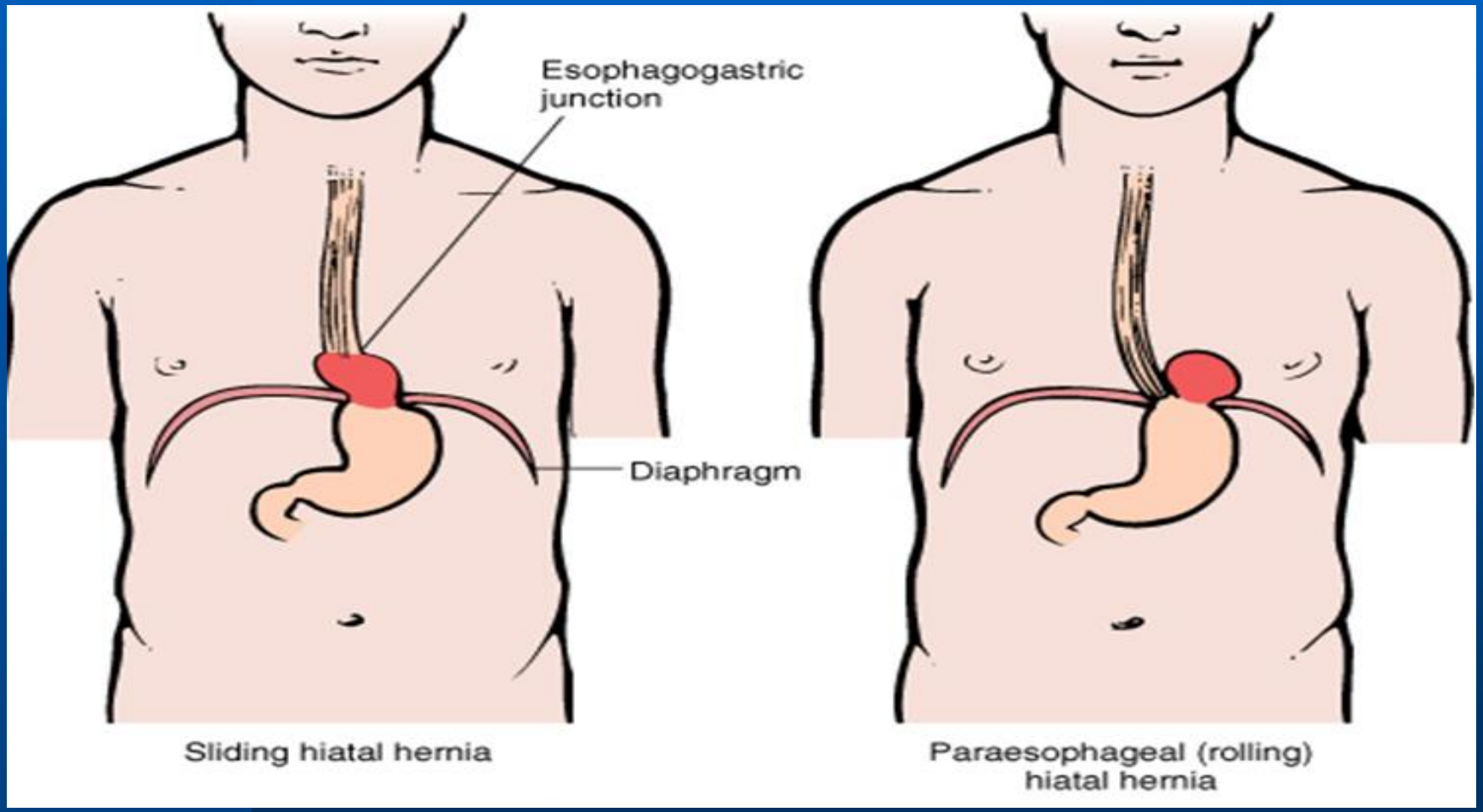
- The sliding hernia (axial) constitutes 95% of cases; protrusion of the stomach above the diaphragm creates a bell-shaped dilation, bounded below by the diaphragmatic narrowing.

- In paraesophageal hernias, a separate portion of the stomach, usually along the greater curvature, enters the thorax through the widened foramen. The cause of this deranged anatomy is obscure.

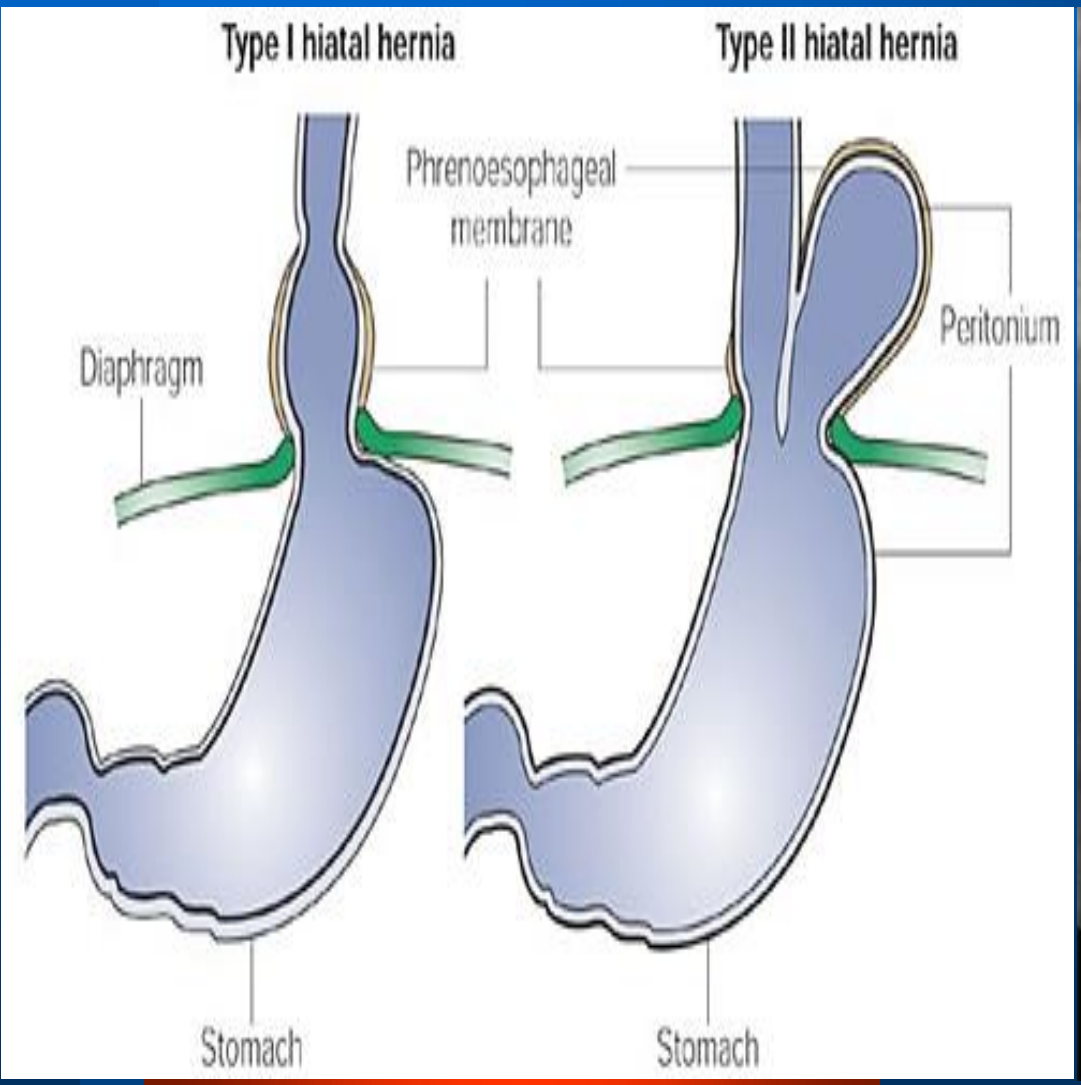


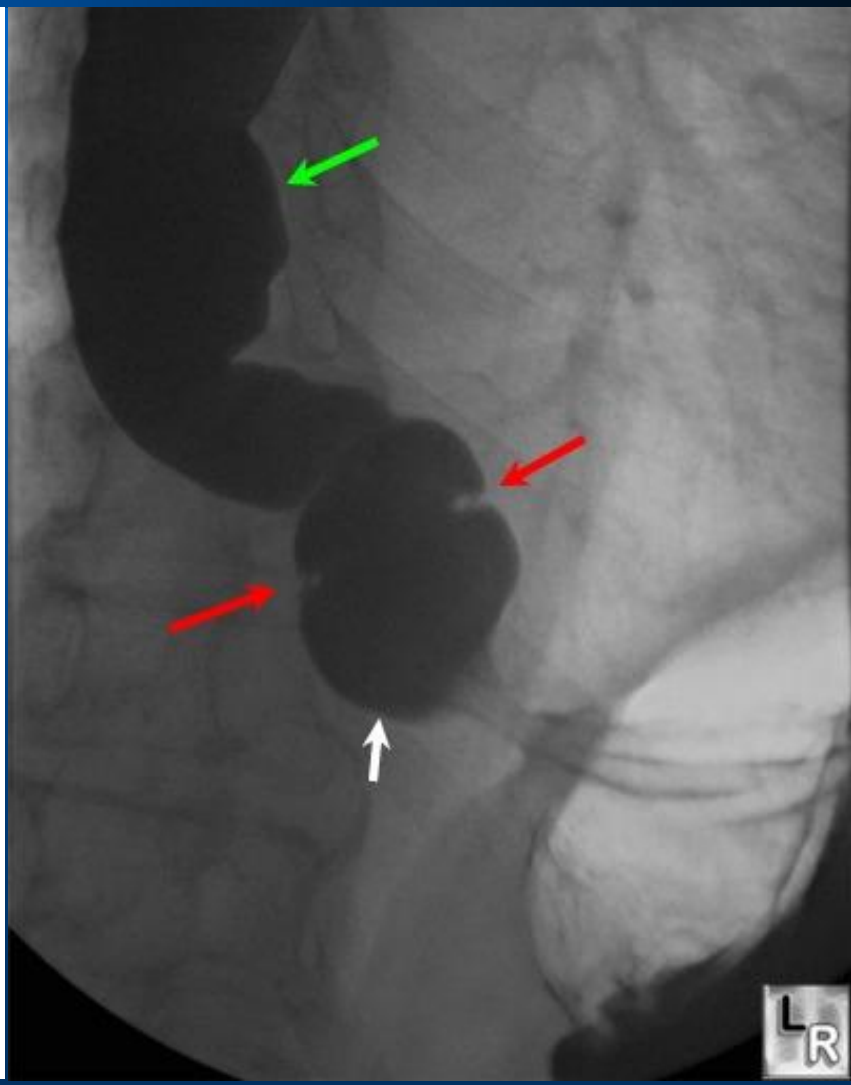


Comparison of the two forms of hernias



Comparison of the two forms of hernias





Comparison of the two forms of hernias

- Only about 9% of these adults, however, suffer from heartburn or regurgitation of gastric juices into the mouth.
- These symptoms more likely result from incompetence of the lower esophageal sphincter than from the hiatal hernia and are accentuated by positions favoring reflux (bending forward, lying supine) and obesity.
- Although most patients with sliding hiatal hernias do not have reflux esophagitis, those with severe reflux esophagitis are likely to have a sliding hiatal hernia.

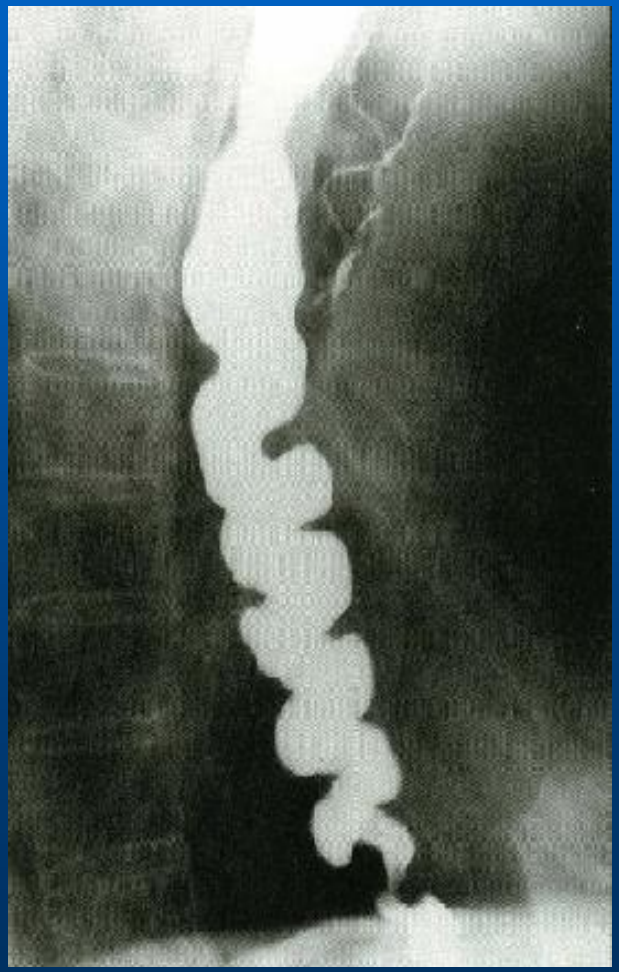
Comparison of the two forms of hernias

- Other complications affecting both types of hiatal hernias include mucosal ulceration, bleeding, and even perforation.
- Paraesophageal hernias rarely induce reflux, but they can become strangulated or obstructed.

Achalasia

- The term *achalasia* means "failure to relax" and in the present context denotes incomplete relaxation of the lower esophageal sphincter in response to swallowing.

- This produces functional obstruction of the esophagus, with consequent dilation of the more proximal esophagus.



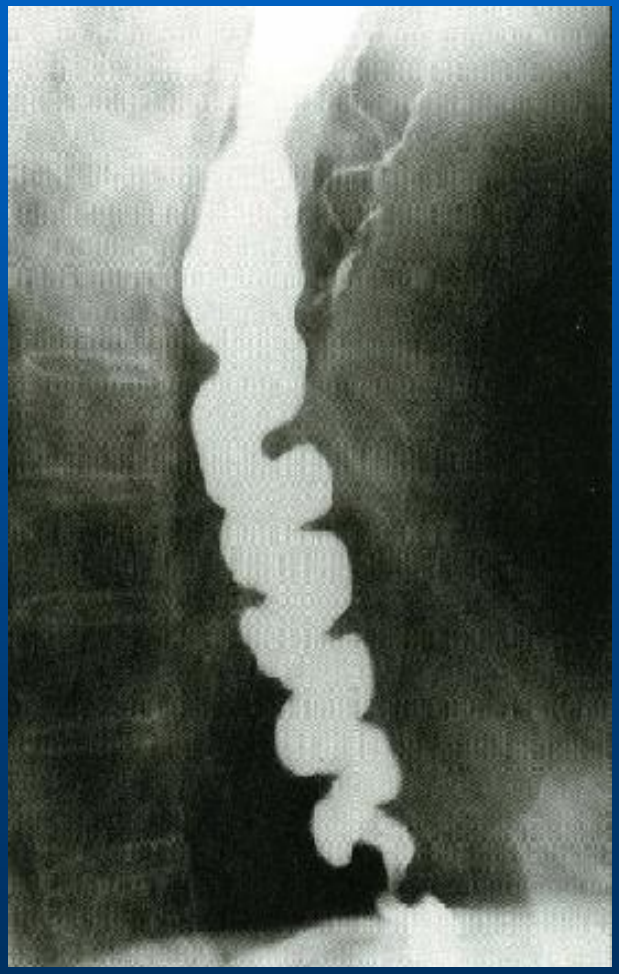
Achalasia

- **There are three major abnormalities :**

(1) Aperistalsis (absence of peristalsis)

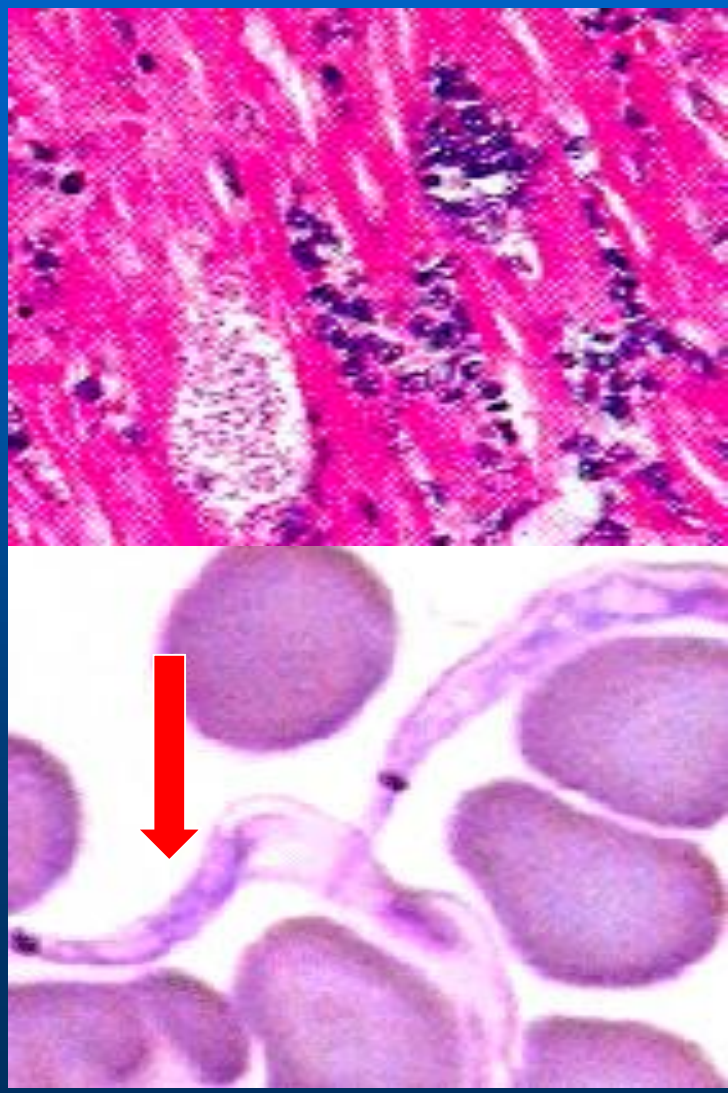
(2) Increased resting tone of the lower esophageal sphincter.

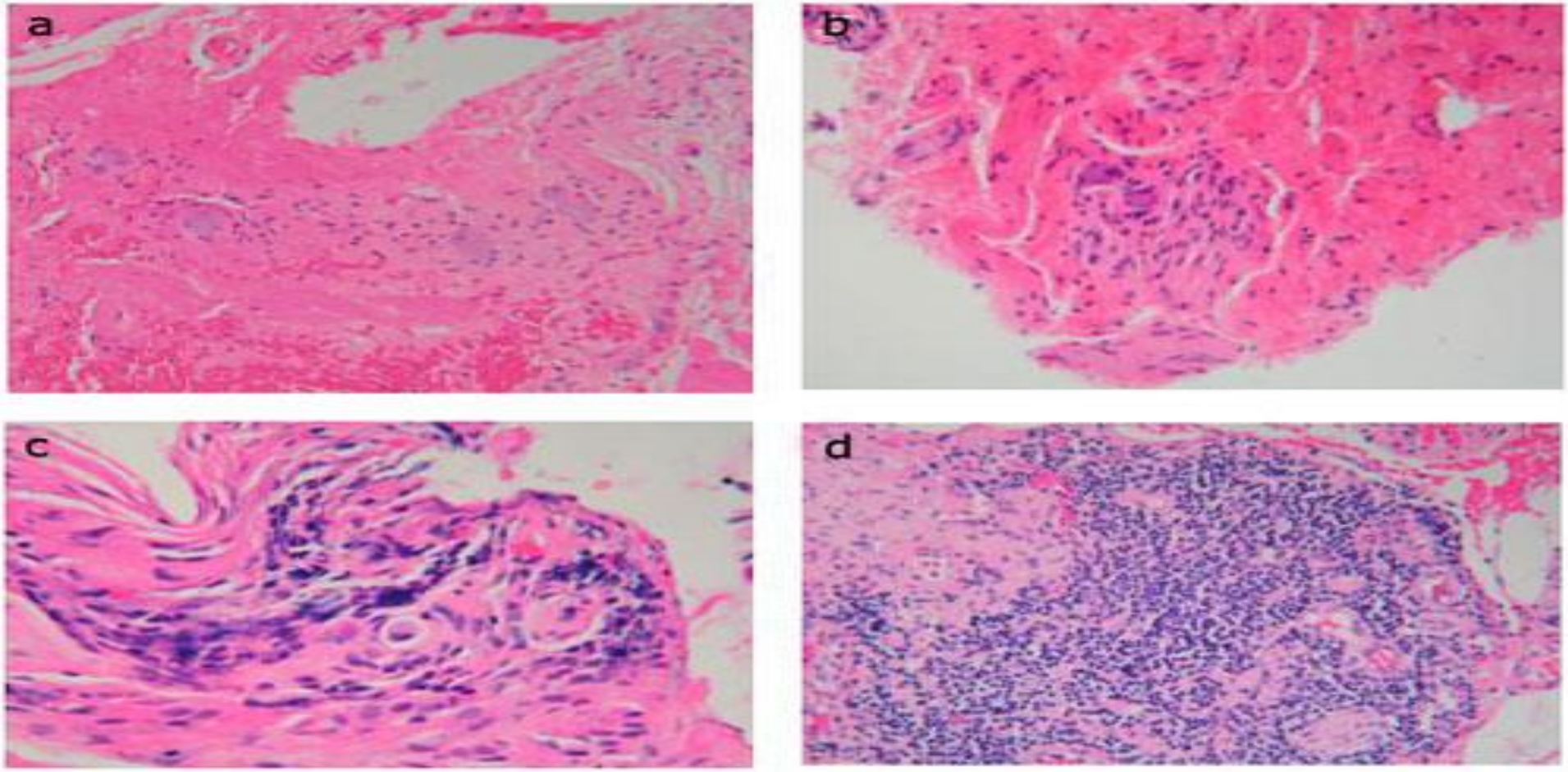
(3) Partial or incomplete relaxation of the LES with swallowing



Achalasia

- **Primary** achalasia:
  - loss of intrinsic **inhibitory innervation** of the lower esophageal sphincter and smooth muscle segment of the esophageal body.
- **Secondary** achalasia
  - may arise from pathologic processes that impair esophageal function.
- **Chagas disease**
  - caused by *Trypanosoma cruzi*, which causes destruction of the **myenteric plexus** of the esophagus, duodenum, colon, and ureter.





a: Normal myenteric plexus demonstrating multiple ganglion cells and minimal lymphocytic infiltration.
b: Mild myenteric inflammation. There is mild lymphocytic inflammation, and ganglion cells can be identified.
c: Moderate myenteric inflammation with lymphocytic infiltrate is present. Ganglion cells are absent.
d: Severe myenteric inflammation with lymphocytes densely clustered within this myenteric plexus. Ganglion cells are absent.

Morphology

- In primary achalasia there is progressive dilation of the esophagus above the level of the lower esophageal sphincter.
- The wall of the esophagus may be normal thickness, thicker than normal because of hypertrophy of the muscularis, or markedly thinned by dilation.

Morphology

- Although not a mucosal disease, stasis of food produce mucosal inflammation and ulceration proximal to LES.
- Those changes cause progressive dysphagia and inability to completely convey food to the stomach.
- Nocturnal regurgitation and aspiration of undigested food usually becomes manifest allready in childhood.
- There is the hazard of developing esophageal squamous cell carcinoma (in about 5% of patients) and typically at an earlier age than in those without achalasia.

Symptoms

- Backflow (regurgitation) of food
- Chest pain, which may increase after eating or may be felt in the back, neck, and arms
- Cough
- Difficulty swallowing liquids and solids
- Heartburn
- Unintentional weight loss

Examination

- Esophageal manometry: is a test used to measure the function of the lower esophageal sphincter by specific tube through oesophagus to stomach
- Esophagogastroduodenoscopy
- Upper GI x-ray

Treatment

- Incurable
- Palliative measures
  - Nonsurgical
  - Surgical
    - Both are directed toward relieving the obstruction caused by the no relaxing LES

Treatment

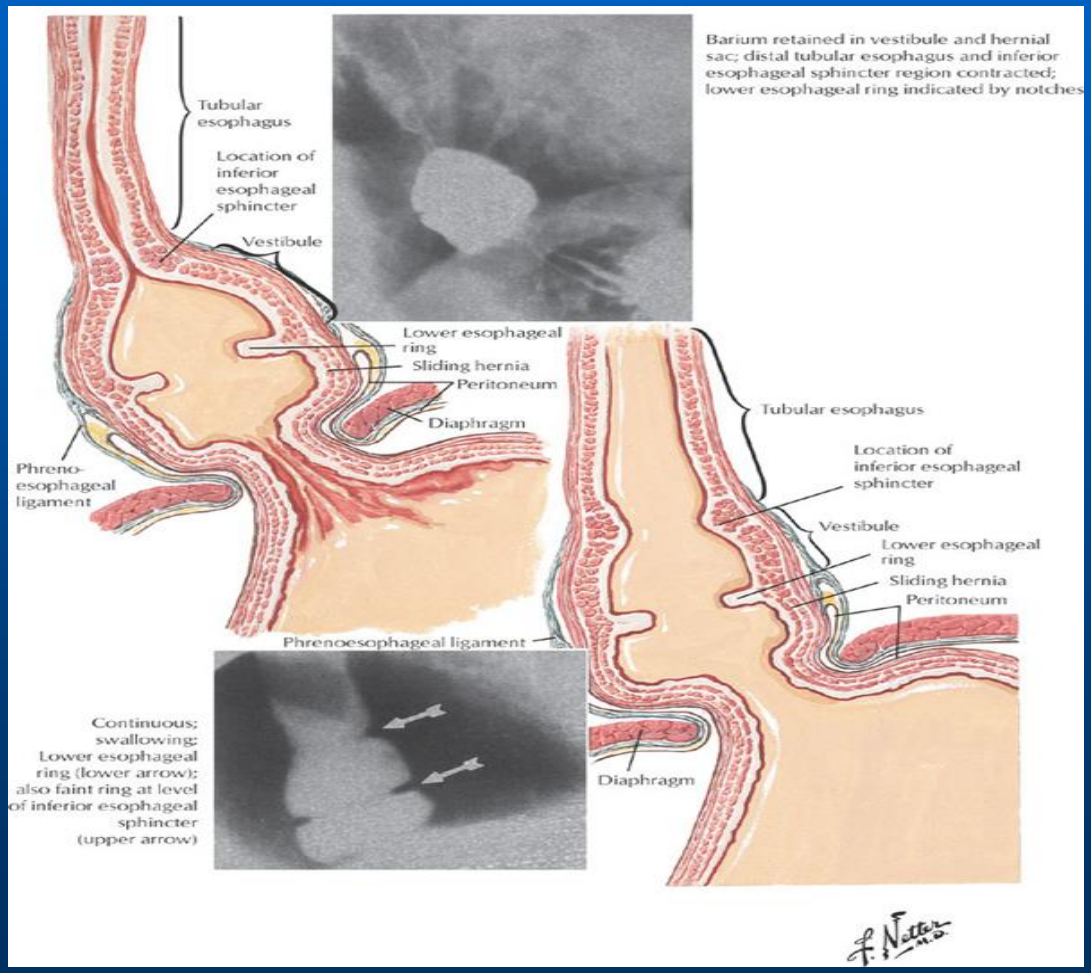
- The basic approach is to reduce the pressure at LES
  - Injection with botulinum toxin (Botox) - relax the sphincter muscles, but any benefit wears off within a matter of weeks or months
  - Medications, such as long-acting nitrates or calcium channel blockers (also relax LES).
- Wideling (balloon dilation) of the narrowed esophagus (done during esophagogastroduodenoscopy).
- Surgery (called an esophagomyotomy)

Diverticula

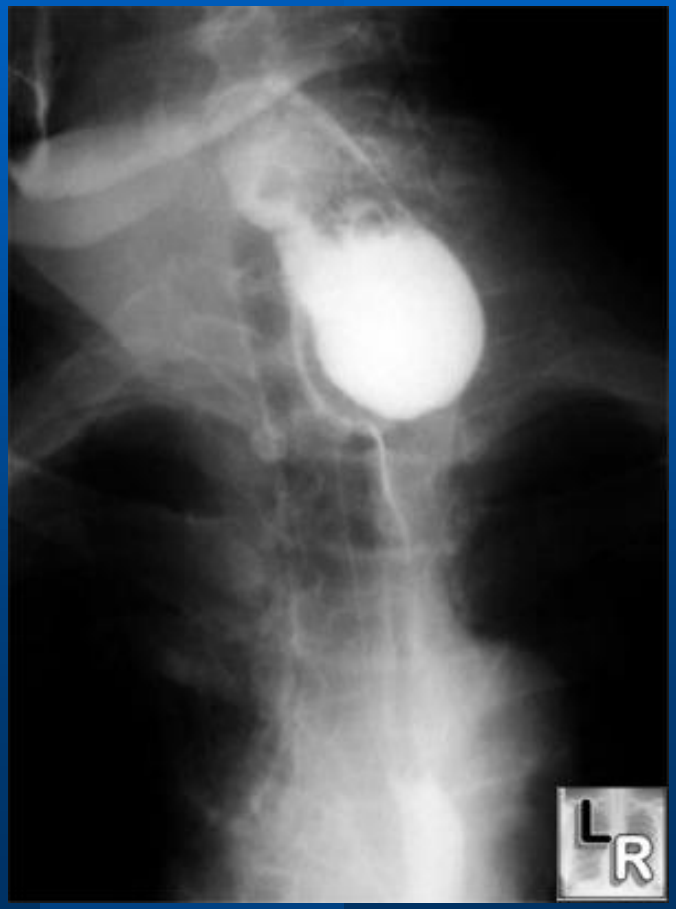
a) "outpouching" of all visceral layers
    1) false – only mucosa and submucosa

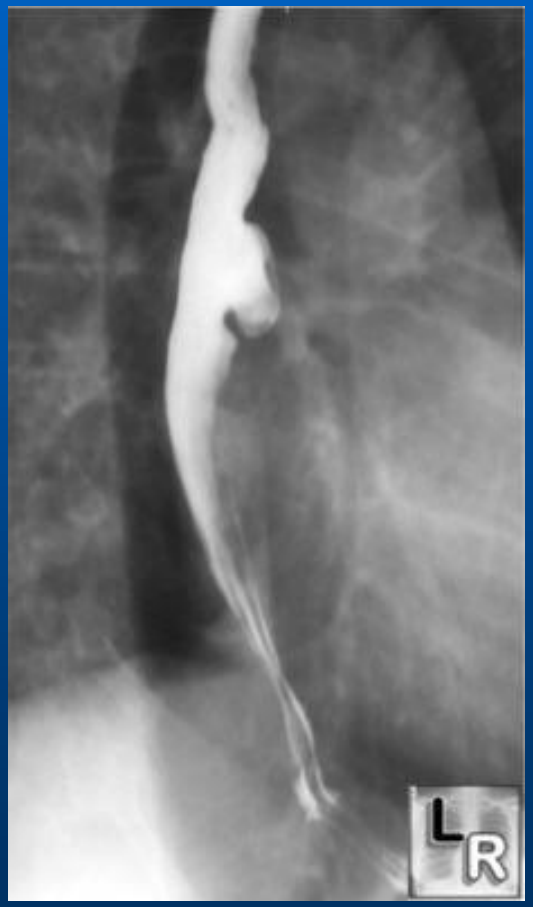
b) types:
    1) Zenker
        - above UES
    2) traction
        - midpoint of esophagus
    3) epiphrenic
        - above LES

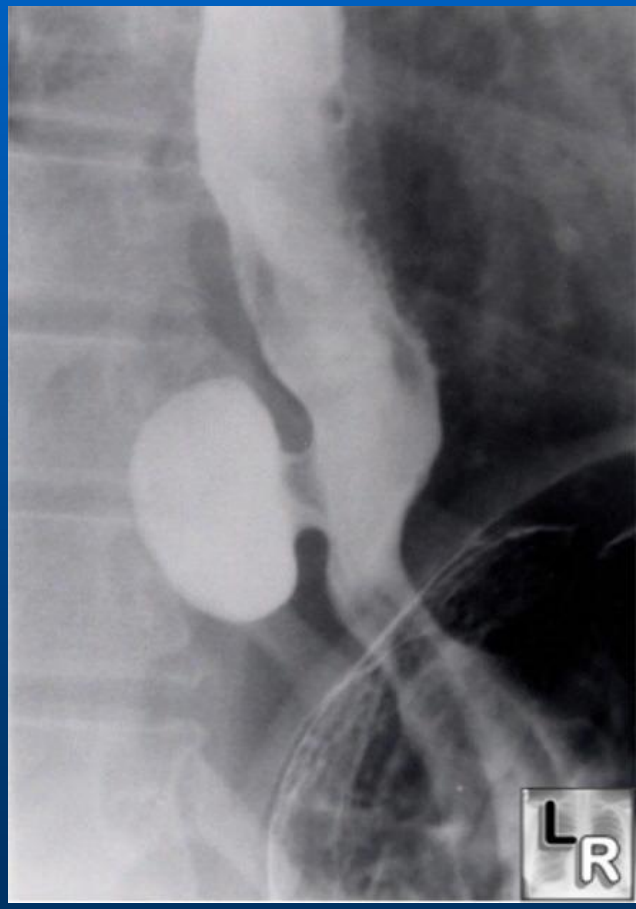
Diverticula



Diverticula



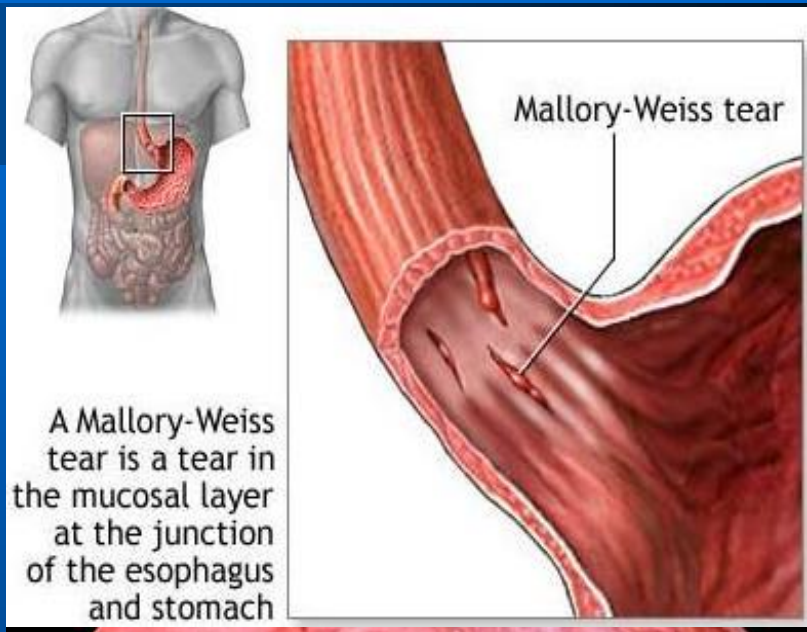


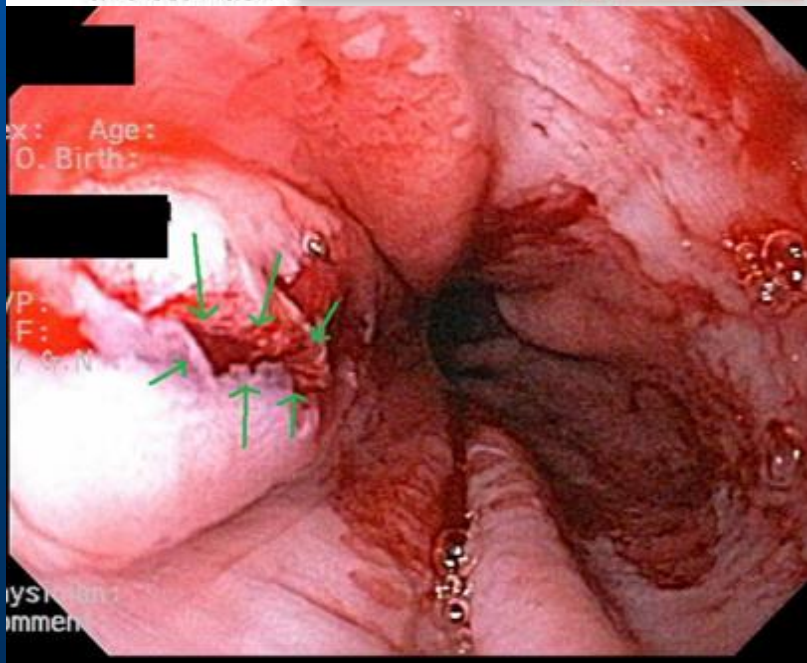


Lacerations
(Mallory-Weiss Syndrome)

- Longitudinal tears in the esophagus at the esophagogastric junction (EGJ).

- The presumed pathogenesis:
  - inadequate relaxation of the musculature of LES during vomiting
  - with stretching and tearing of the EGJ at the moment of propulsive expulsion of gastric contents.
  - supported by the fact that a hiatal hernia is found in more than 75% of patients with Mallory-Weiss tears.



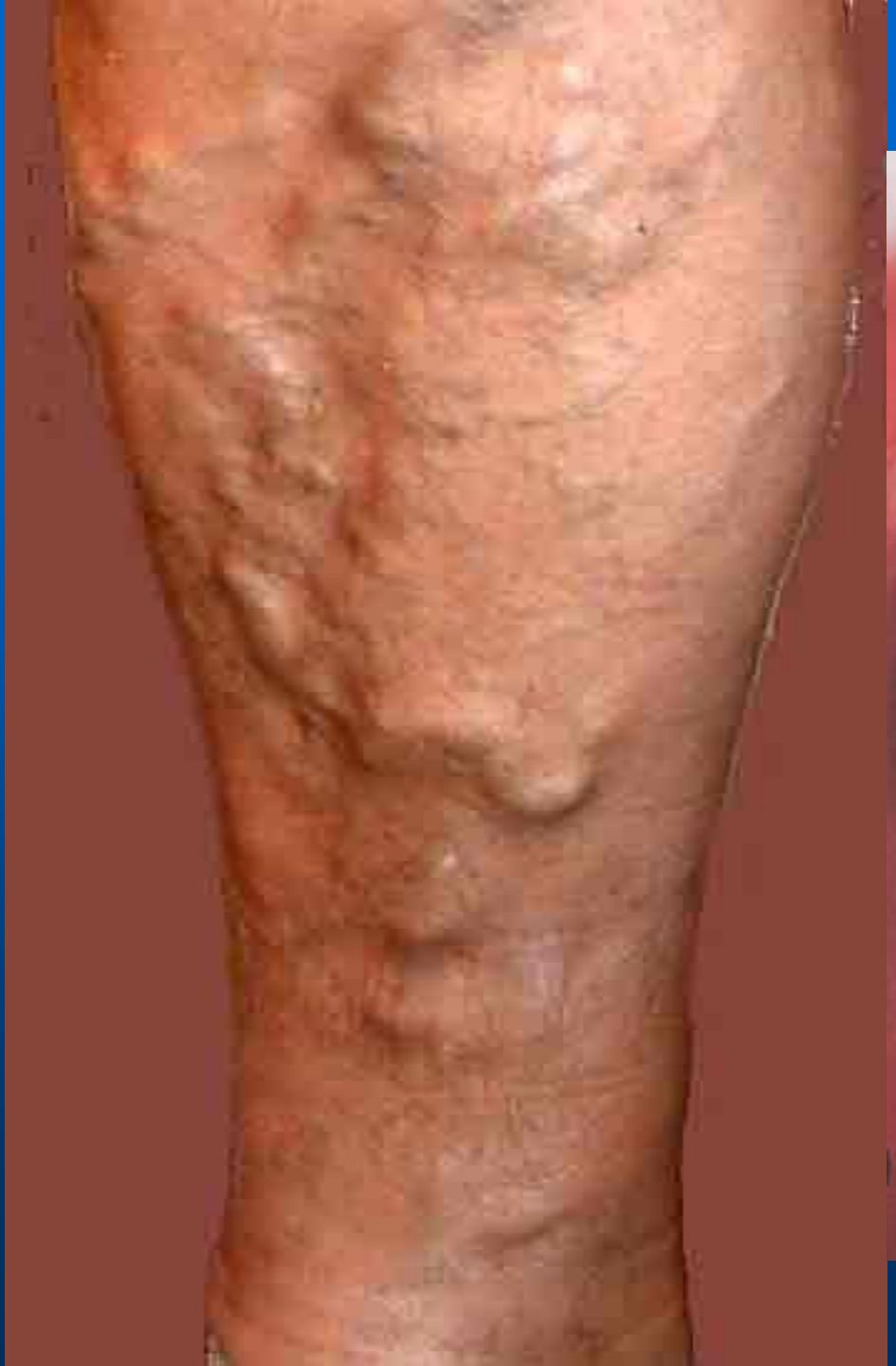


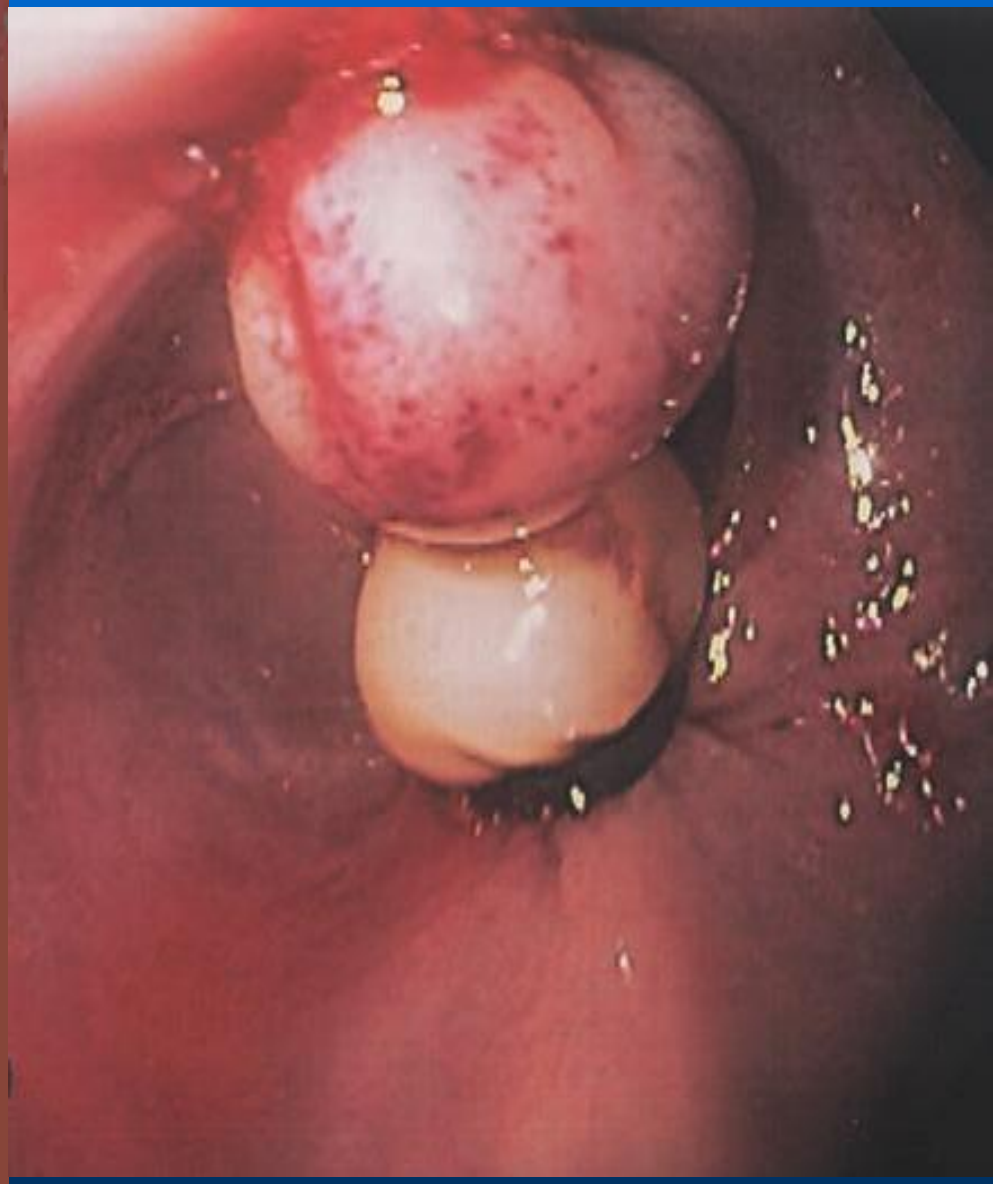
Lacerations (Mallory-Weiss Syndrome)

- Tears usually involve only the mucosa
  - (may penetrate the wall!)
- Infection of the defect may lead to a **mediastinitis**
  - [inflammation of the tissues in the mid-chest].
- Account for 5-10% of upper gastrointestinal bleeding causes.
  - Most often is not profuse and ceases without surgical intervention, but life-threatening hematemesis may occur.
  - If there is a severe blood loss, supportive therapy with vasoconstrictors, transfusions, and sometimes balloon tamponade, is usually required.

Varices

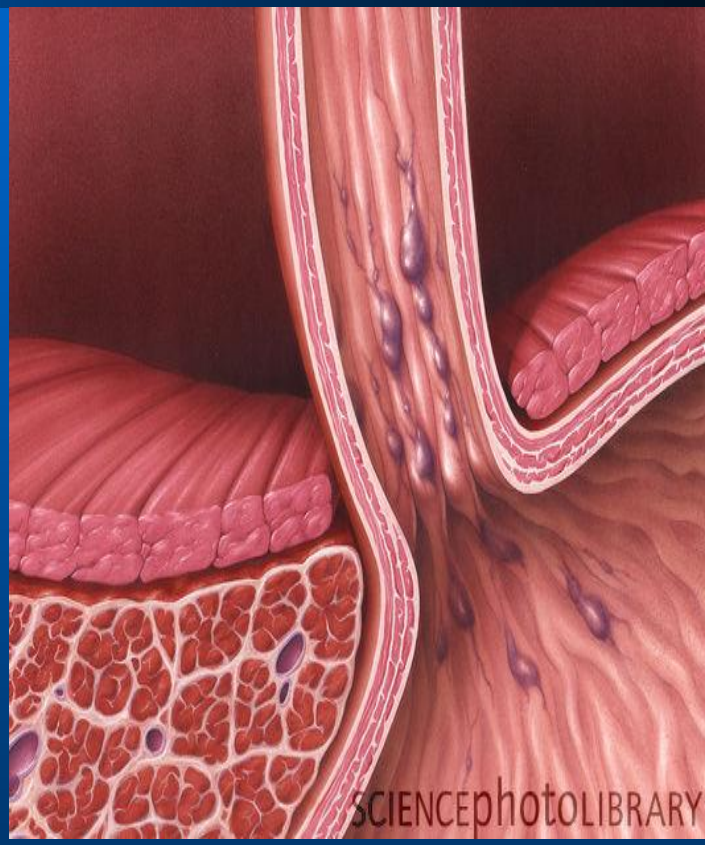
- When portal venous blood flow into the liver is impeded by cirrhosis or other causes, the resultant portal hypertension induces the formation of collateral bypass channels.
- The increased pressure in the esophageal plexus produces dilated tortuous vessels called varices.
- Patients with cirrhosis develop varices at a rate of 5% to 15% per year, so that varices are present in approximately two thirds of all cirrhotic patients. They are most often associated with alcoholic cirrhosis.





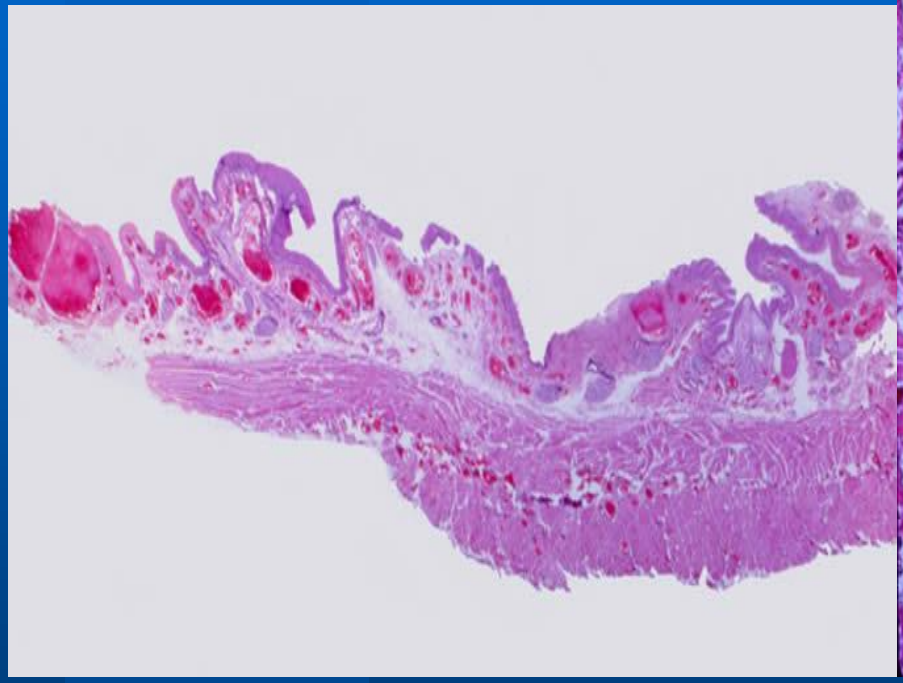
MORPHOLOGY

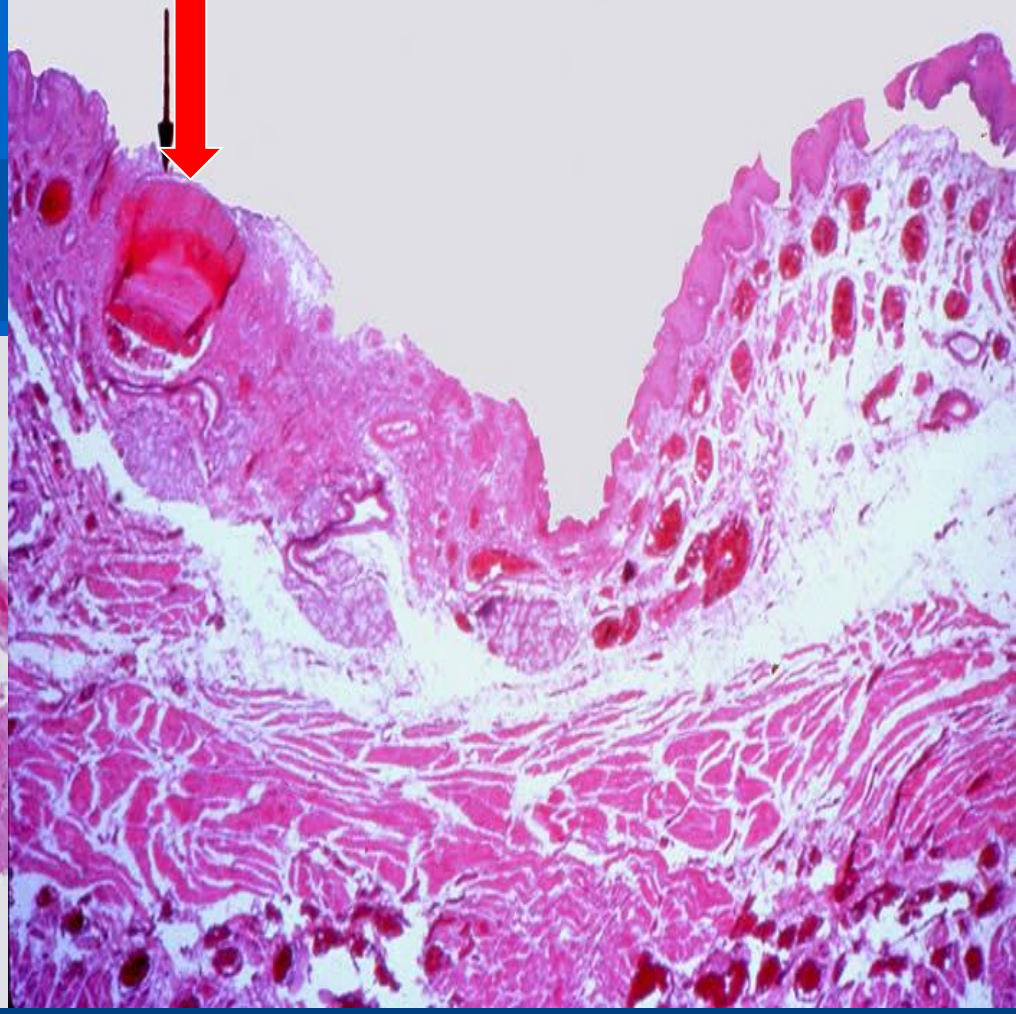
- Varices appear primarily as tortuous dilated veins lying primarily within the submucosa of the distal esophagus and proximal stomach.
- The net effect is irregular protrusion of the overlying mucosa into the lumen
- When the varix is unruptured, the mucosa may be normal, but often it is eroded and inflamed because of its exposed position, further weakening the tissue support of the dilated veins.



a view of the everted esophagus and gastroesophageal junction, showing dilated submucosal veins (varices).

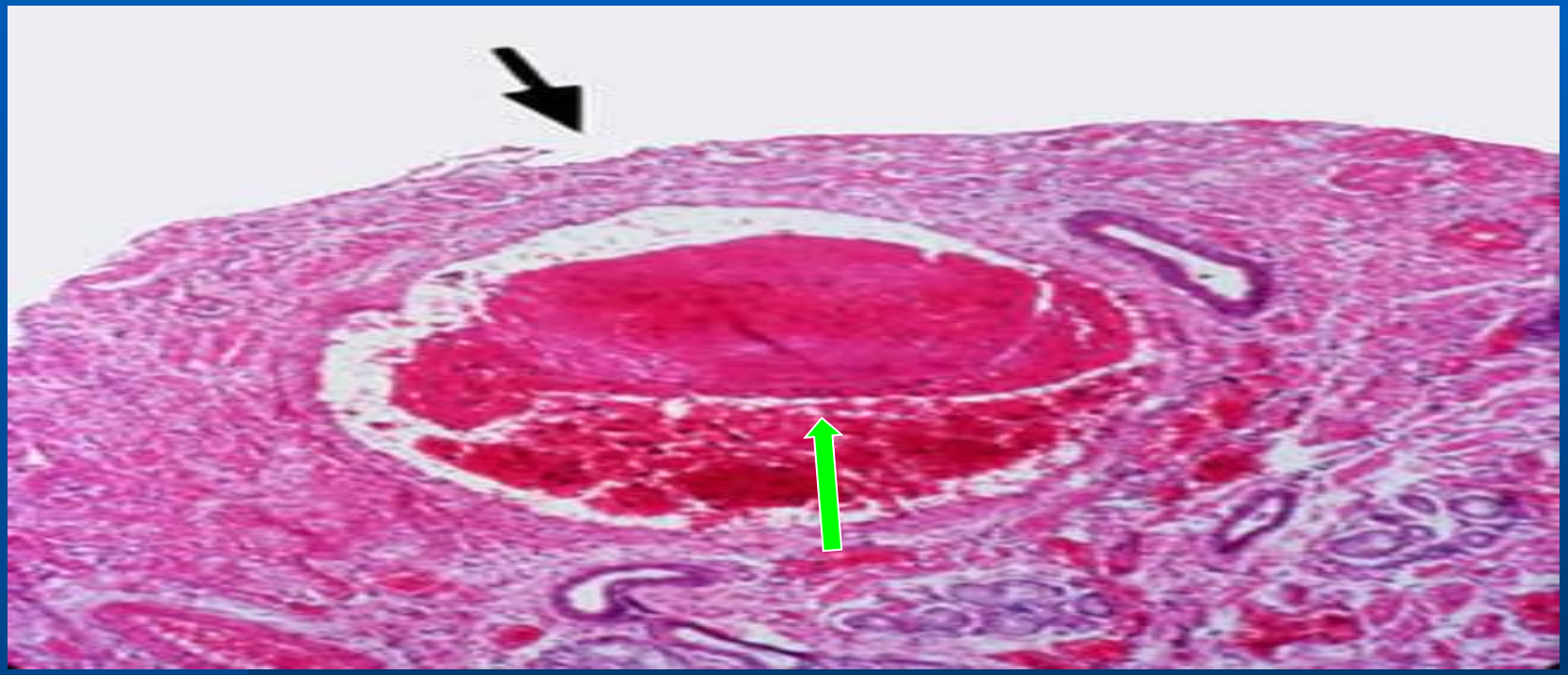
Note the markedly dilated veins in the submucosa and in the muscularis propria of the esophagus.





- Dilated varices often cause pressure atrophy and ulceration of the overlying mucosa, as has happened in this case.
- The subsequent inflammation of the submucosa causes erosion of the thin wall of the varices with subsequent rupture.
- The large varix noted by the arrow communicates directly with the lumen and has probably ruptured in the past.

Thrombosis of a large submucosal varix



Note the ulceration of the overlying mucosa (arrow) and inflammation of the esophagus

Varices

- **The factors leading to initial rupture of a varix are unclear:**
  - increased tension in progressively dilated veins, and vomiting with increased intra-abdominal pressure are likely to be involved.
  - once begun, variceal hemorrhage subsides spontaneously in only 50% of cases
  - endoscopic injection of thrombotic agents (sclerotherapy) or balloon tamponade is often required.
  - rebleeding occurs in approximately 70% within 1 year

ESOPHAGITIS

- Injury to the esophageal mucosa with subsequent inflammation is a common condition

- The inflammation may have many origins
  - prolonged gastric intubation
  - uremia
  - ingestion of corrosive or irritant substances
  - radiation or chemotherapy.

ESOPHAGITIS

- There are many presumed contributory factors:
  - Decreased efficacy of esophageal antireflux mechanisms
  - Inadequate or slowed esophageal clearance of refluxed material
  - The presence of a sliding hiatal hernia
  - Increased gastric volume, contributing to the volume of refluxed material
  - Impaired reparative capacity of the esophageal mucosa by prolonged exposure to gastric juices
- Any one of these influences may assume primacy in an individual case, but more than one is likely to be involved in most instances.

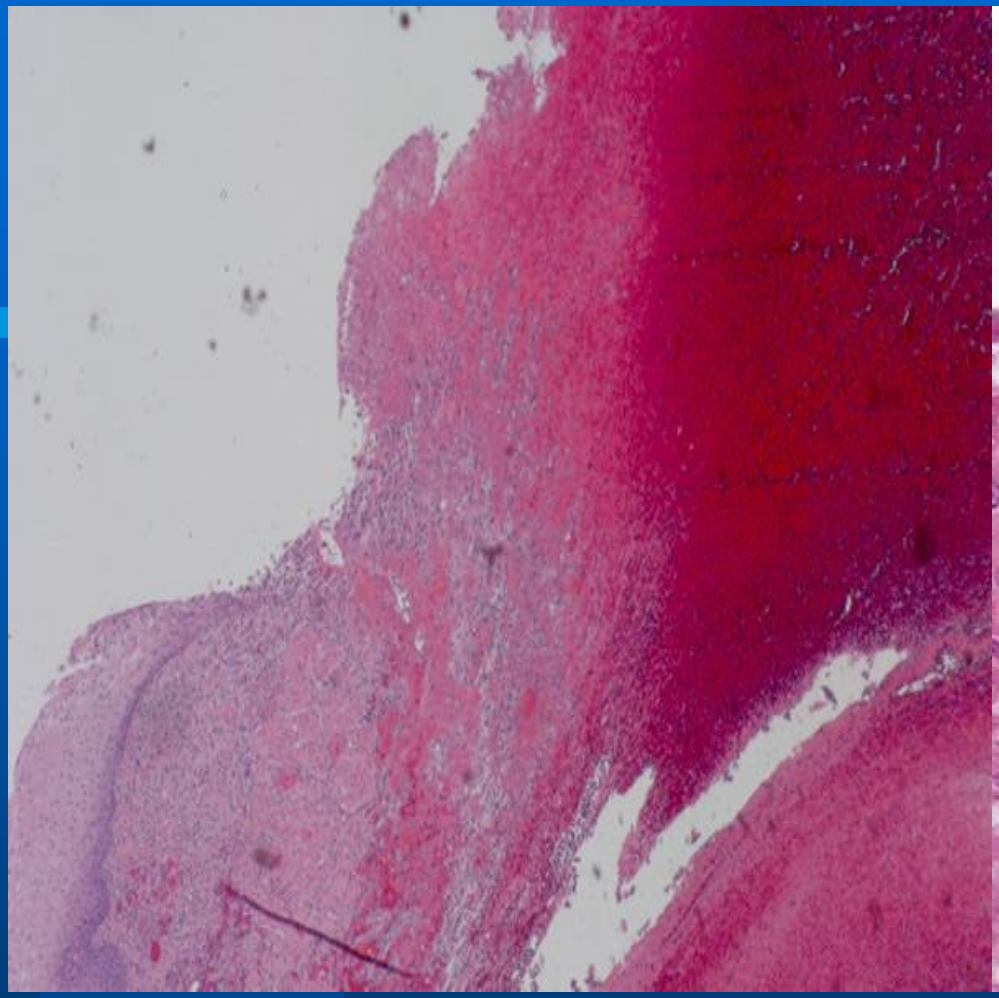
MORPHOLOGY

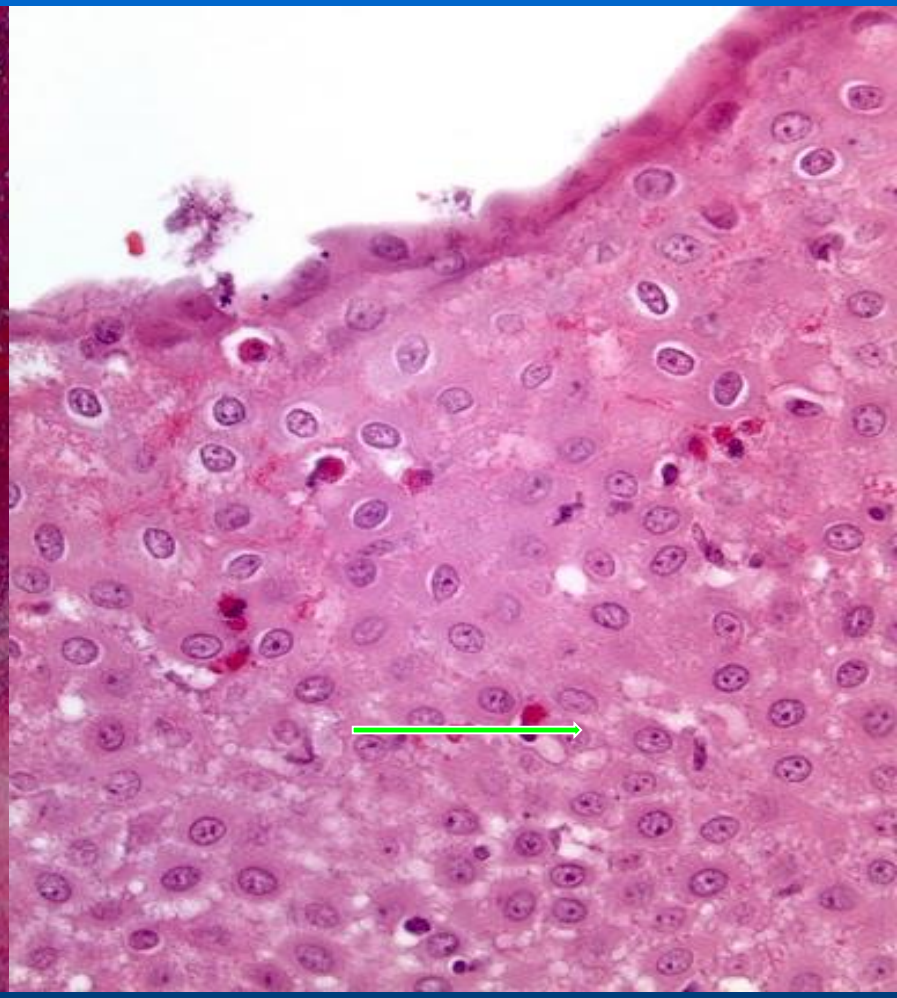
- The anatomic changes depend on the causative agent and on the duration and severity of the exposure.
- Mild esophagitis may appear macroscopically as simple hyperemia, with virtually no histologic abnormality.
- In contrast, the mucosa in severe esophagitis exhibits confluent epithelial erosions or total ulceration into the submucosa.

MORPHOLOGY

- Three histologic features are characteristic of uncomplicated reflux esophagitis:

1. eosinophils, with or without neutrophils, in the epithelial layer;
2. basal zone hyperplasia;
3. elongation of lamina propria papillae. Intraepithelial neutrophils are markers of more severe injury.





Reflux esophagitis showing the superficial portion of the mucosa. Numerous eosinophils (arrows) are present within the mucosa, and the stratified squamous epithelium has not undergone complete maturation owing to ongoing inflammatory damage.

Clinical Features

- The dominant manifestation of GERD is heartburn
- Sometimes accompanied by regurgitation of a sour content.
- Swallowing could be
  - difficult - dysphagia
  - painful - odynophagia
- Chest pain, particularly behind the breastbone
- If occurs with eating swallowed food becoming stuck in the esophagus (food impaction).

Clinical Features

- Rarely, chronic symptoms are punctuated by attacks of severe chest pain mimicking a heart attack.
- Although largely limited to adults older than age 40, GERD is occasionally seen in infants and children.
- The potential consequences of severe reflux esophagitis are bleeding, development of stricture, and Barrett esophagus, with its predisposition to malignancy.

BARRETT ESOPHAGUS

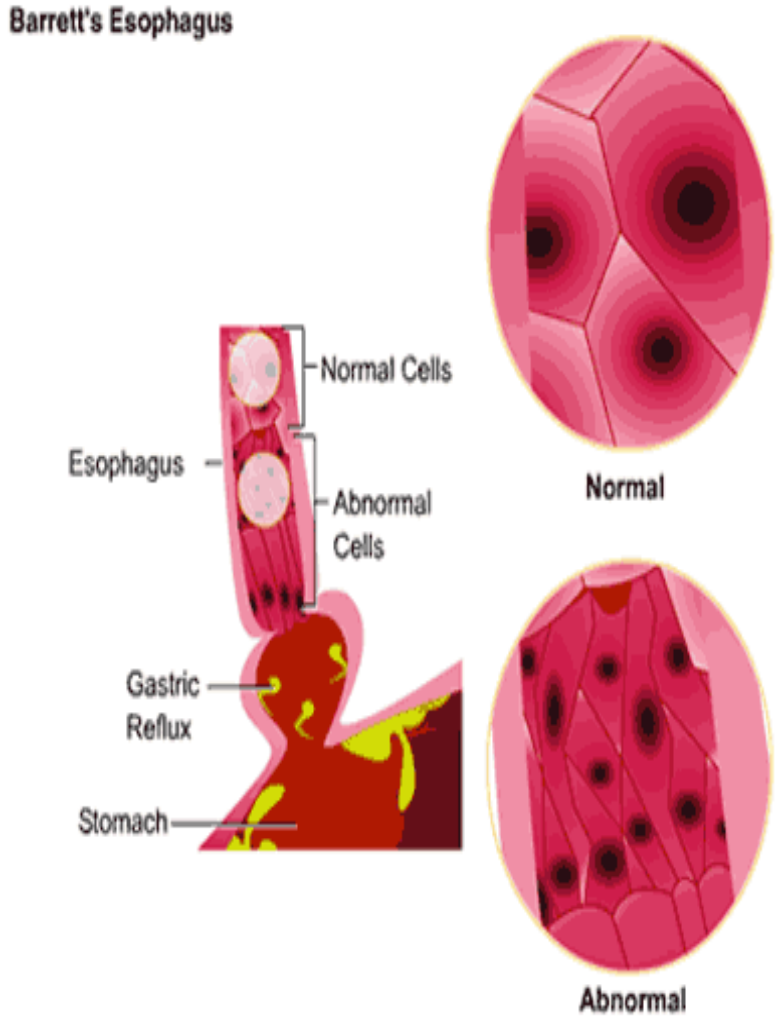
- A complication of long-standing gastroesophageal reflux
- Occurring in up to 10% of patients with persistent symptomatic GERD, as well as in some patients with asymptomatic reflux.
- Defined as the replacement of the normal distal stratified squamous mucosa by metaplastic columnar epithelium containing goblet cells.

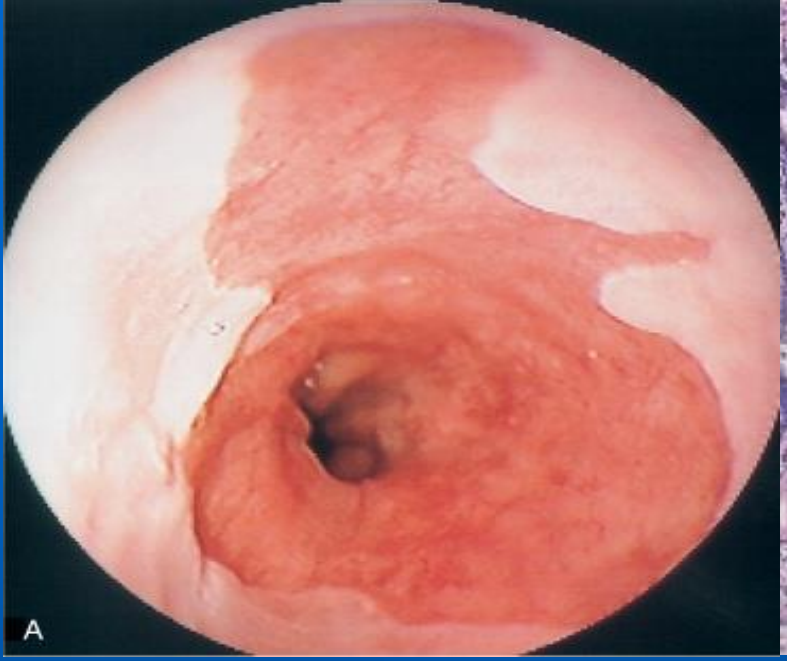
BARRETT ESOPHAGUS

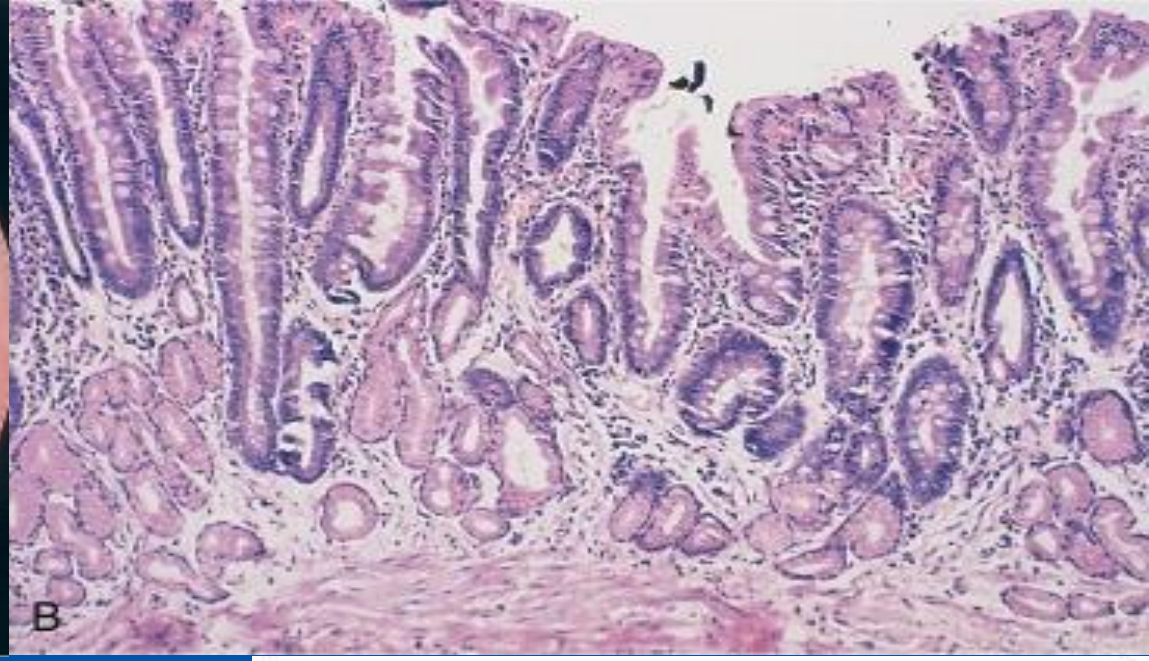
- Prolonged and recurrent gastroesophageal reflux is thought to produce inflammation and eventually ulceration of the squamous epithelial lining.
- Healing occurs by in growth of stem cells and re-epithelialization.
- In the microenvironment of an abnormally low pH in the distal esophagus caused by acid reflux, the cells differentiate into columnar epithelium.

MORPHOLOGY

- Barrett esophagus is apparent as a salmon-pink, velvety mucosa between the smooth, pale pink esophageal squamous mucosa and the more lush light brown gastric mucosa.
- **Microscopically,** the esophageal squamous epithelium is replaced by metaplastic columnar **epithelium (gastric mucosa).**
- Critical pathologic finding is the recognition of **dysplastic** changes in the mucosa that may be precursors of cancer.



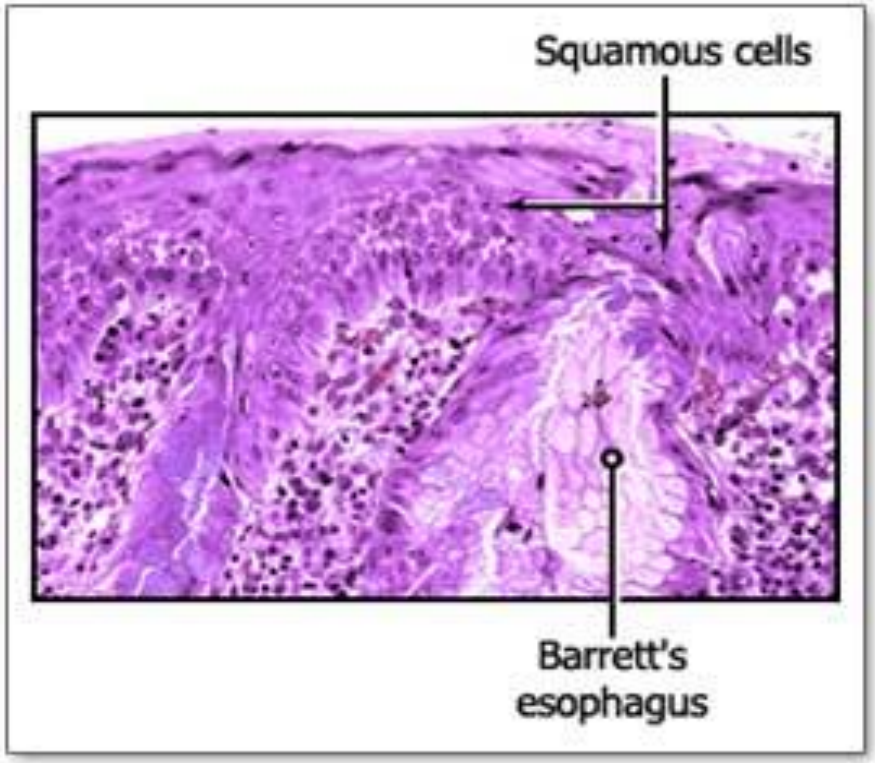




Barrett esophagus.

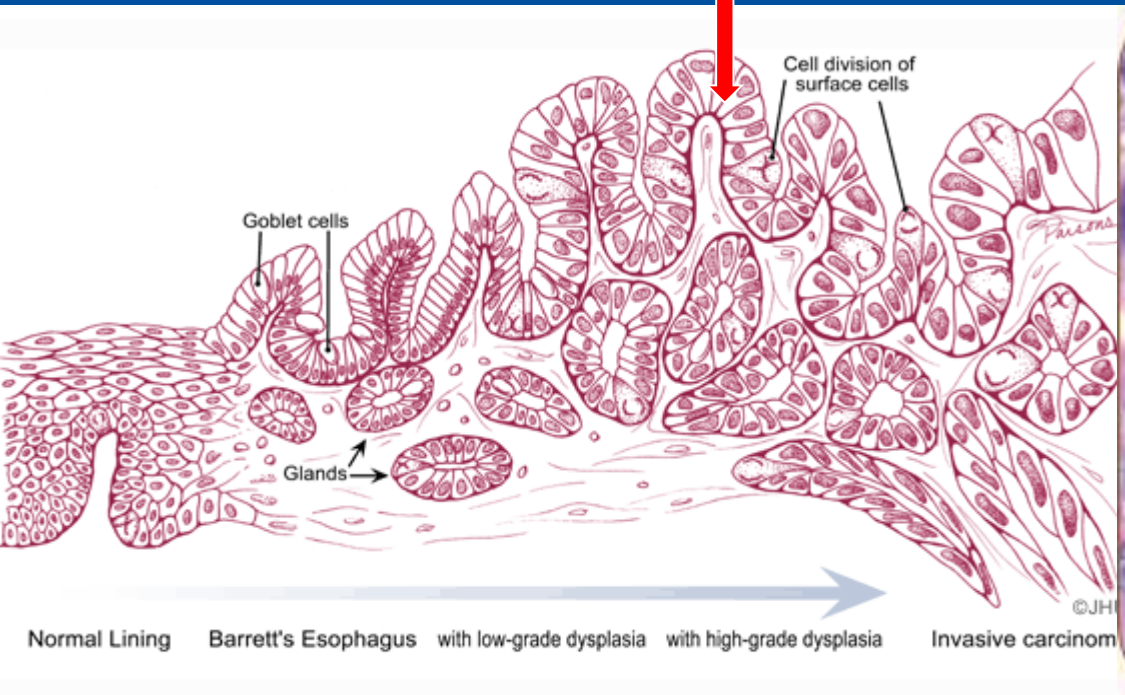
A, Endoscopic view showing red velvety gastrointestinal-type mucosa extending from the gastroesophageal orifice. Note paler squamous esophageal mucosa.

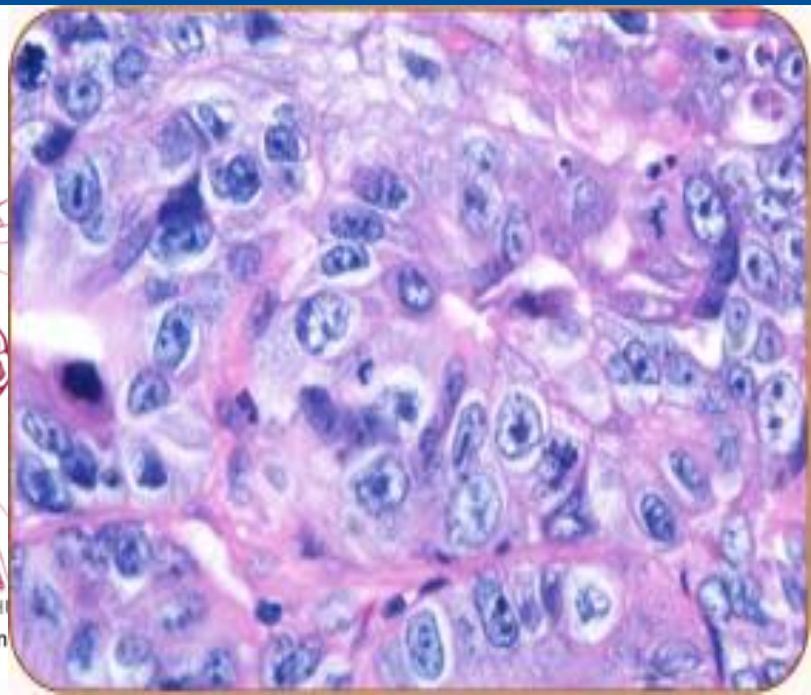
B, Microscopic view showing mixed gastric- and intestine-type columnar epithelial cells in glandular mucosa.



- Barrett esophagus affects males more often than females (ratio of 4:1) and is much more common in whites than in other races. Genetic factors are suggested by clustering in families.

- Ulcer and stricture may develop as a complication of Barrett esophagus. However, the chief clinical significance of Barrett esophagus relates to the development of adenocarcinoma.
- Patients with Barrett esophagus have a 30- to 40-fold greater risk of developing esophageal adenocarcinoma compared with normal populations.





ESOPHAGEAL CARCINOMA

- Benign tumors may arise in the esophagus from both the squamous mucosa and underlying mesenchyme
- Much more important is cancer of the esophagus:
  - squamous cell carcinomas (constitute 90% of all cancers, more common in blacks)
  - adenocarcinomas (arising in Barrett esophagus, more common in whites)

- There are differences in the geographic incidence In US there are about 6 new cases/100,000 population per year.
- In regions of Asia extending from the northern provinces of China to Iran, the prevalence is well over 100 per 100,000.

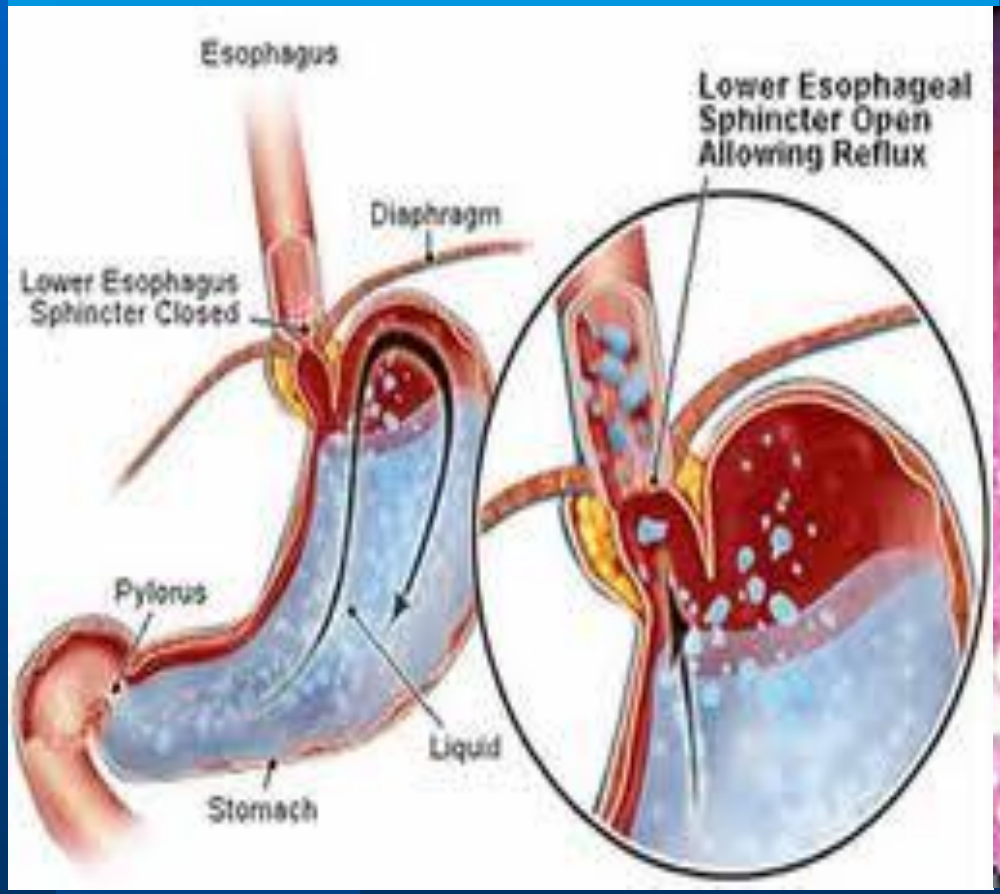
Gastroesophageal reflux disease

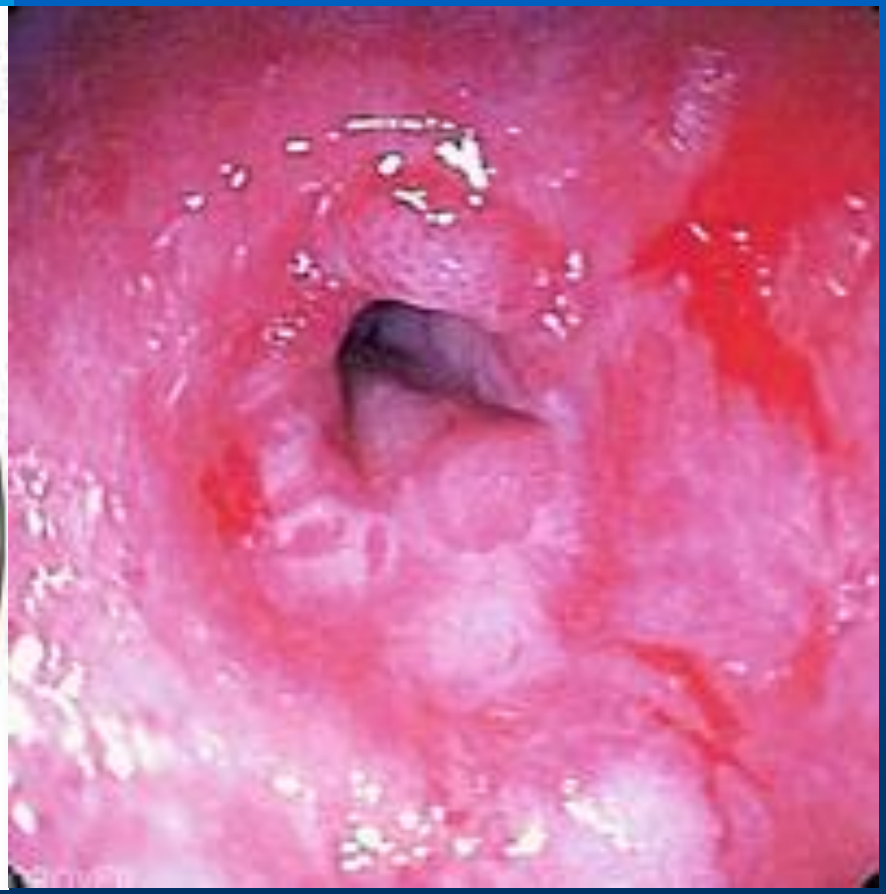
- **Gastroesophageal reflux (GER)** is defined as passage of gastric contents into the esophagus
  - GER is a normal physiologic process that occurs throughout the day in healthy infants, children, and adults.
- **Gastroesophageal reflux disease (GERD)** occurs when gastric contents reflux into the esophagus or oropharynx and produce symptoms.
- **Regurgitation** is defined as passage of refluxed gastric contents into the oral pharynx.
- **Vomiting** is final expulsion of the refluxed contents from the mouth.

Causes

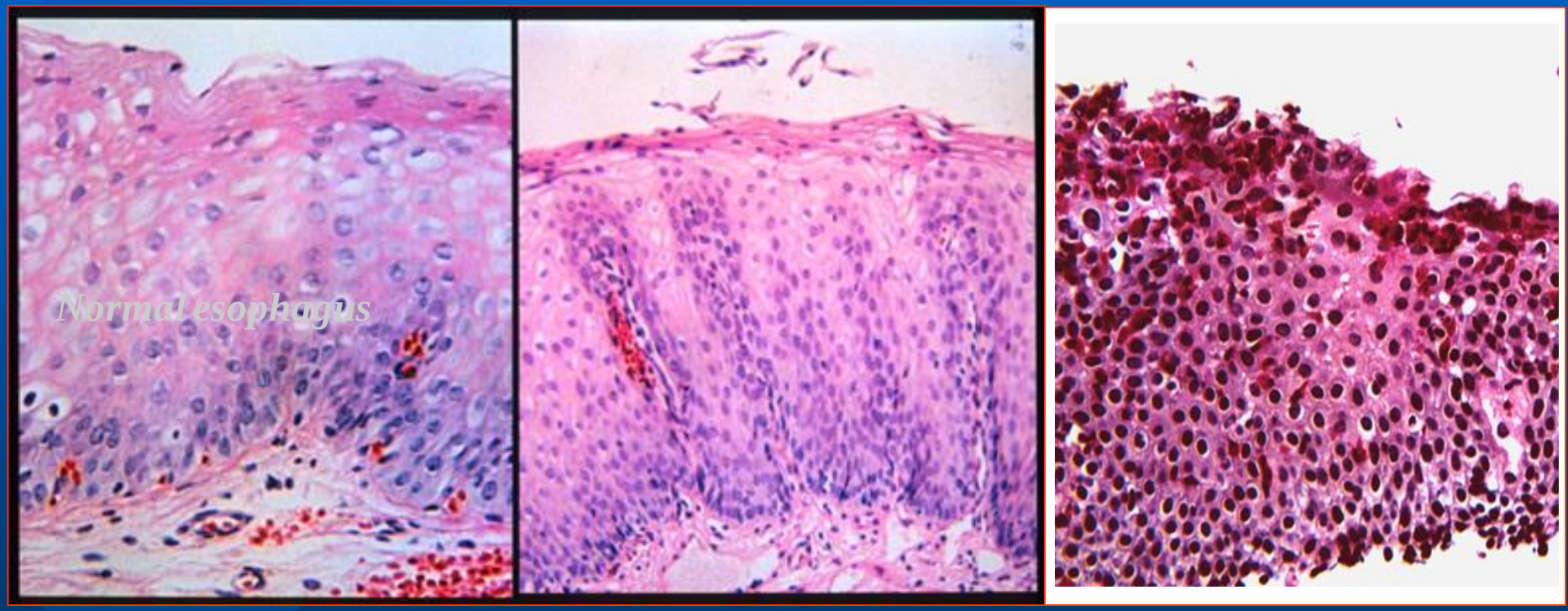
- When you eat, food passes from the throat to the stomach through the esophagus (also called the food pipe or swallowing tube).
- Once food is in the stomach, a ring of muscle fibers prevents food from moving backward into the esophagus.
- These muscle fibers are called the lower esophageal sphincter, or LES

Causes


Esophagus
Lower Esophageal Sphincter Open Allowing Reflux
Diaphragm
Lower Esophagus Sphincter Closed
Pylorus
Liquid
Stomach

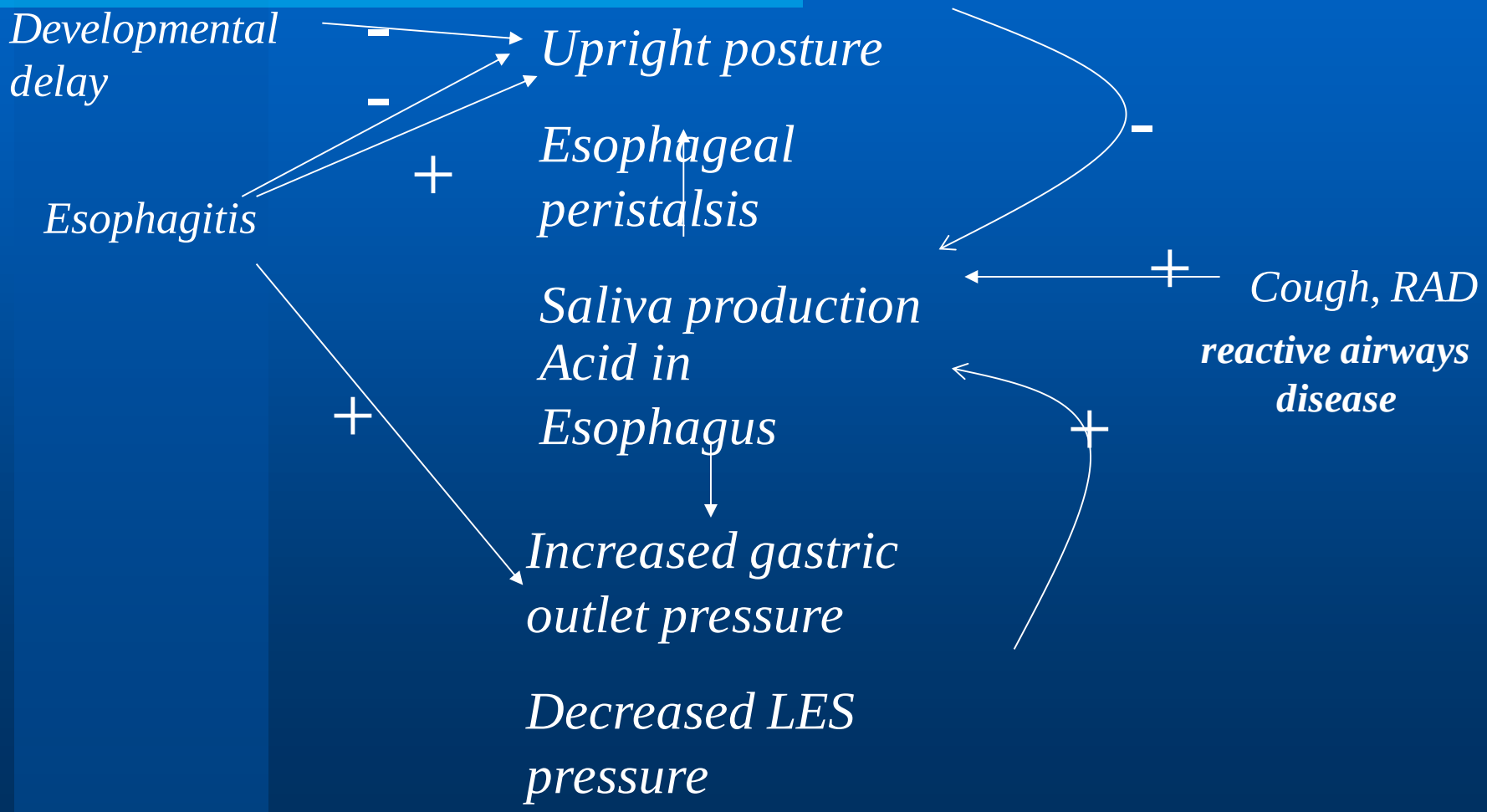


Gastroesophageal reflux disease



1. Normal esophagus (left);
2. GER (center), with approximately 5 eosinophils per HPF;
3. primary eosinophilic esophagitis (right)

Gastroesophageal Reflux



Symptoms

- A burning sensation in your chest (heartburn), sometimes spreading to the throat, along with a sour taste in your mouth
- Chest pain
- Difficulty swallowing (dysphagia)
- Hoarseness or sore throat
- Regurgitation of food or sour liquid (acid reflux)
- Sensation of a lump in the throat

Respiratory Symptoms of GER

- Apnea/ALTE
- Stridor and hoarseness
- Cough
- Wheezing
- Recurrent pneumonia

Diagnosis

- **Esophagoscopy**
  - **To note mucosal changes**
- **Esophageal biopsies**
  - **To note changes at the cellular level**
- **Motilitiy studies**
  - **Low LES pressures are associated with reflux**
- **24 h pH monitoring**
  - **The most precise measure for the presence of acid in the esophageal lumen**

Treatment

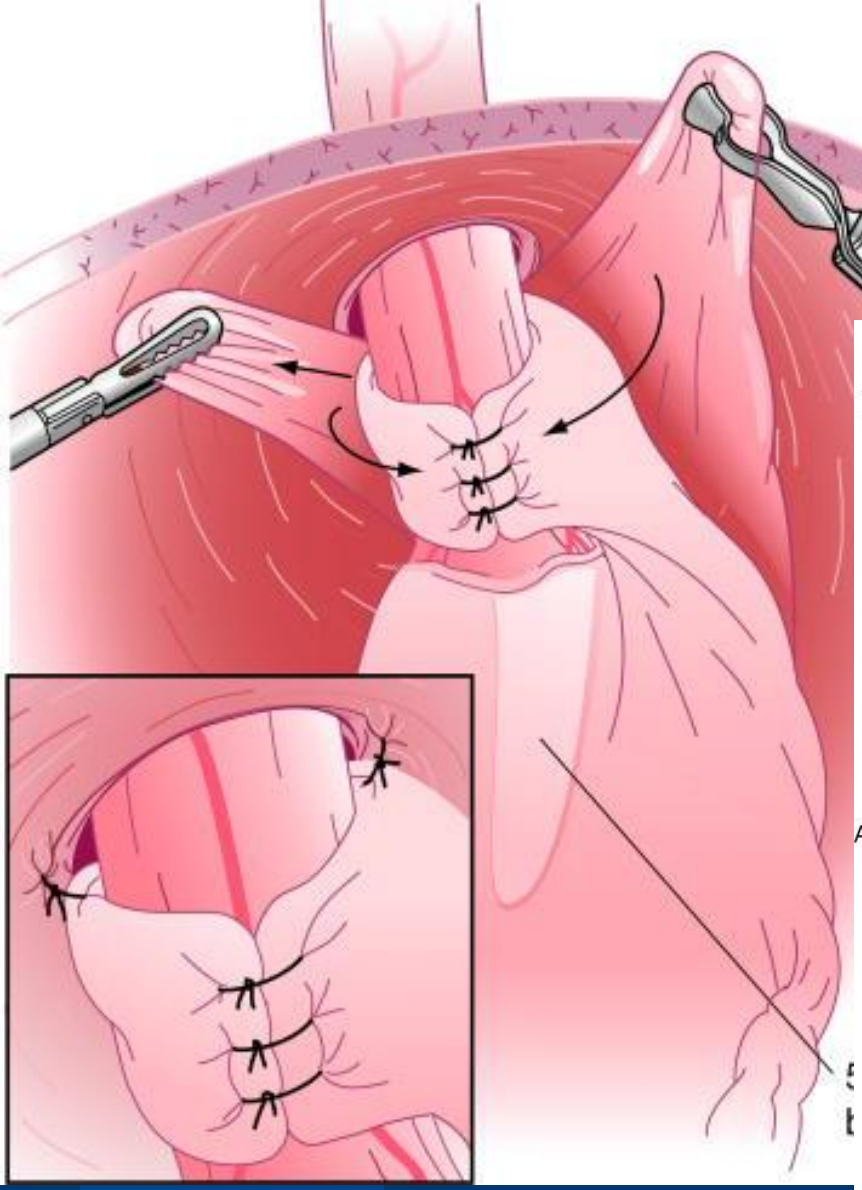
- PPI are standard medical therapy
  - Daily PPI generally has a 80% healing rate for moderate to severe esophagitis and relief of symptoms in up to 90% of patients
- Overall, all PPI are equally effective in treating symptoms. However, there is some variability in response from patient to patient

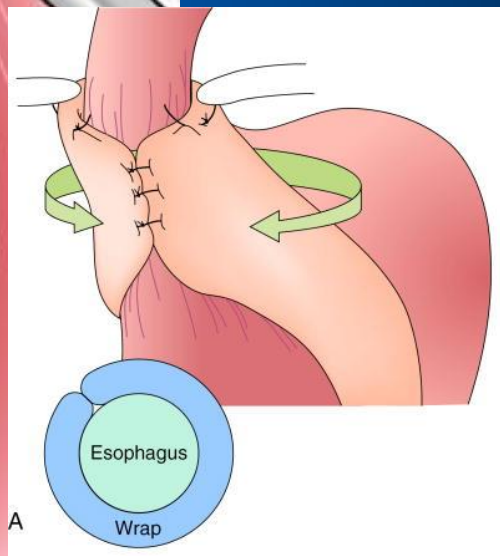
Treatment

- Proper timing of PPI administration is critical for efficacy
- 30 minutes before breakfast or other large meal
- In select patients, a second dose can be added before the evening meal

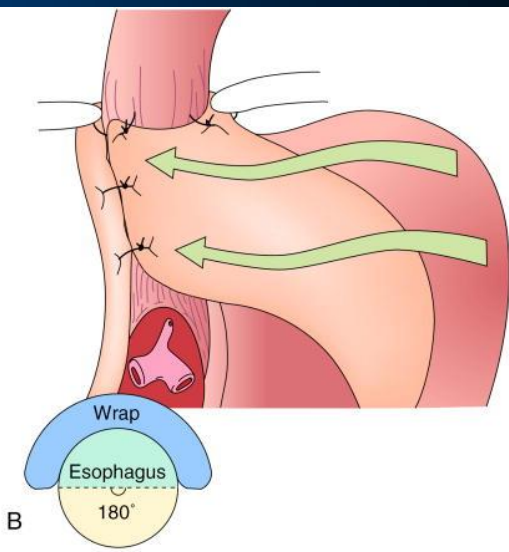
Surgical Treatment

- Indications
  - Esophagitis
  - Stricture
  - Barrett's metaplasia
  - Medication failure
- Purpose of surgery → restoration the LES

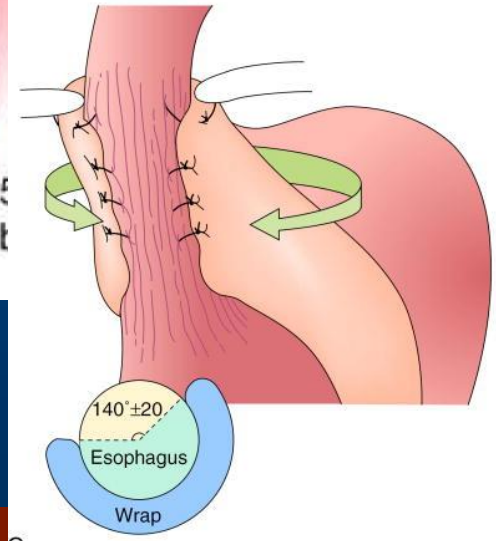




A



B



C

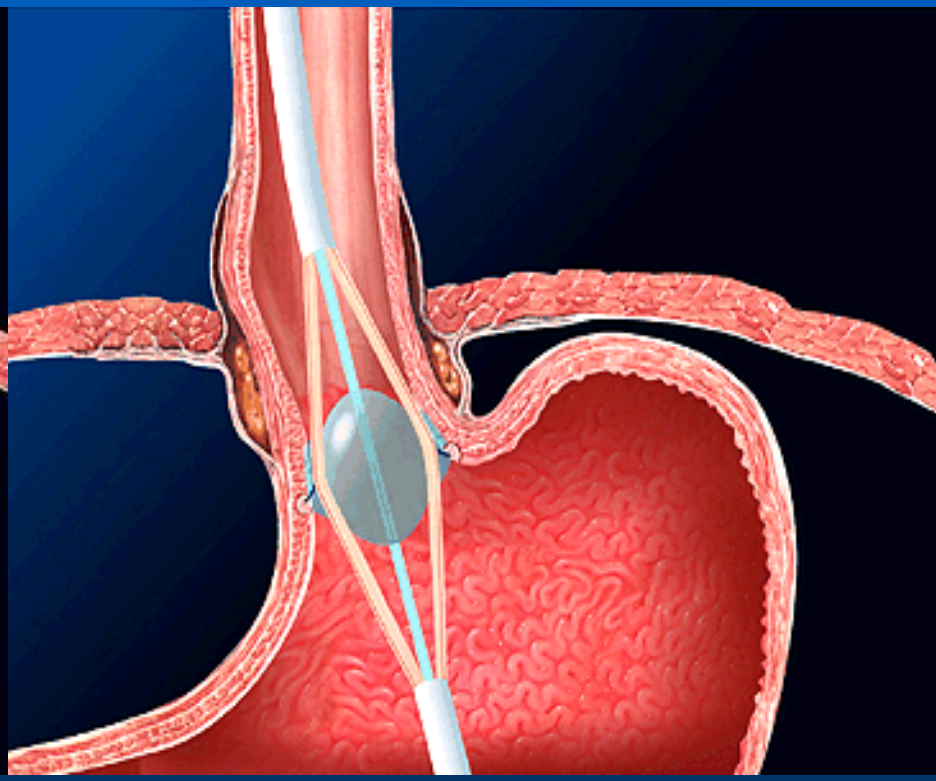
Surgical Treatment

- Most studies indicate that the majority of patients are symptom-free (70-95%)
- Recent studies suggest that after 5 years, up to 1/3 of patients required PPI to control symptoms. At 10 years, up to 50% require PPIs
- Side-effects: gas-bloat symptoms, diarrhea, dysphagia

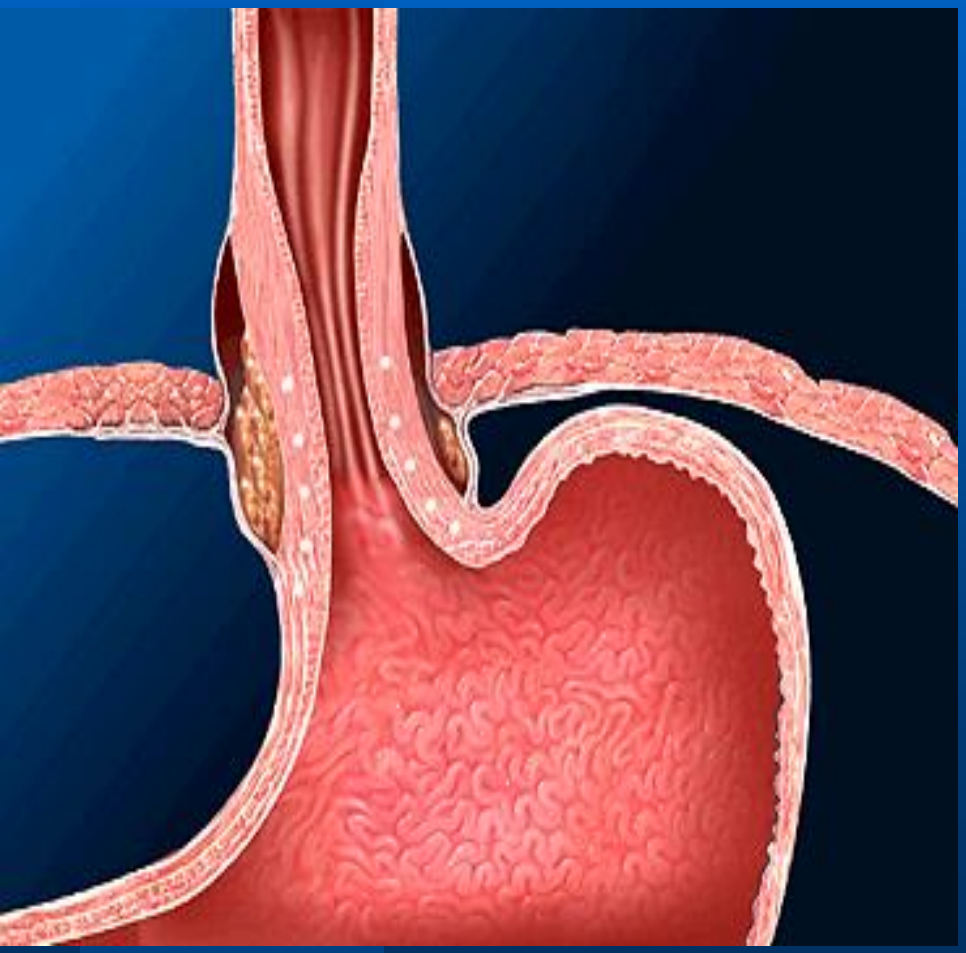
Endoscopic Treatments

- In development with ongoing studies
- Most try to improve LES function in some manner
- Not quite ready for prime time in community practice

Stretta procedure



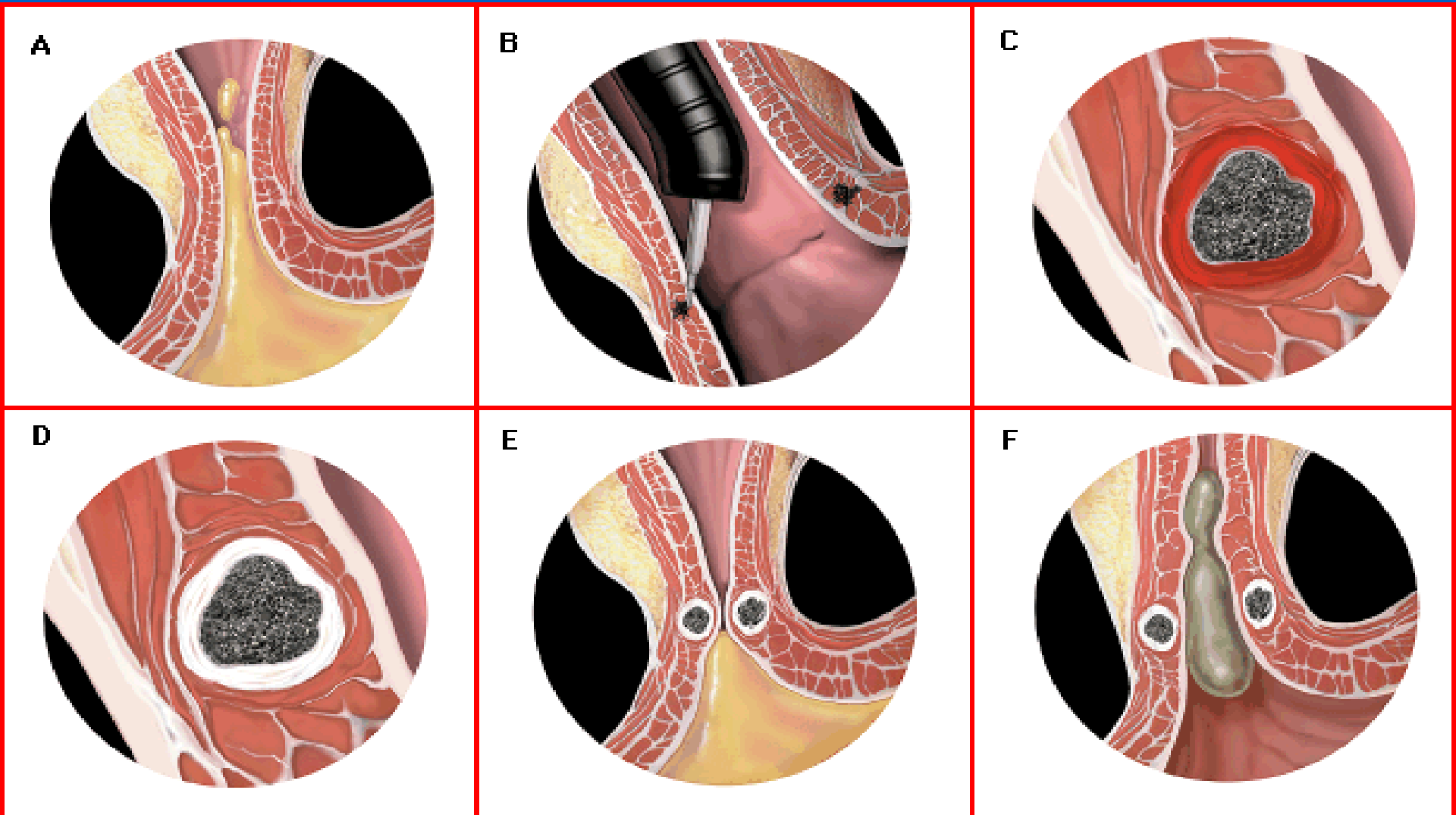
Stretta procedure



- Decrease in symptom score
- Decreased PPI
- No effect on LESP
- No effect on acid exposure

- Some serious thermal injury complications

Enteryx injection

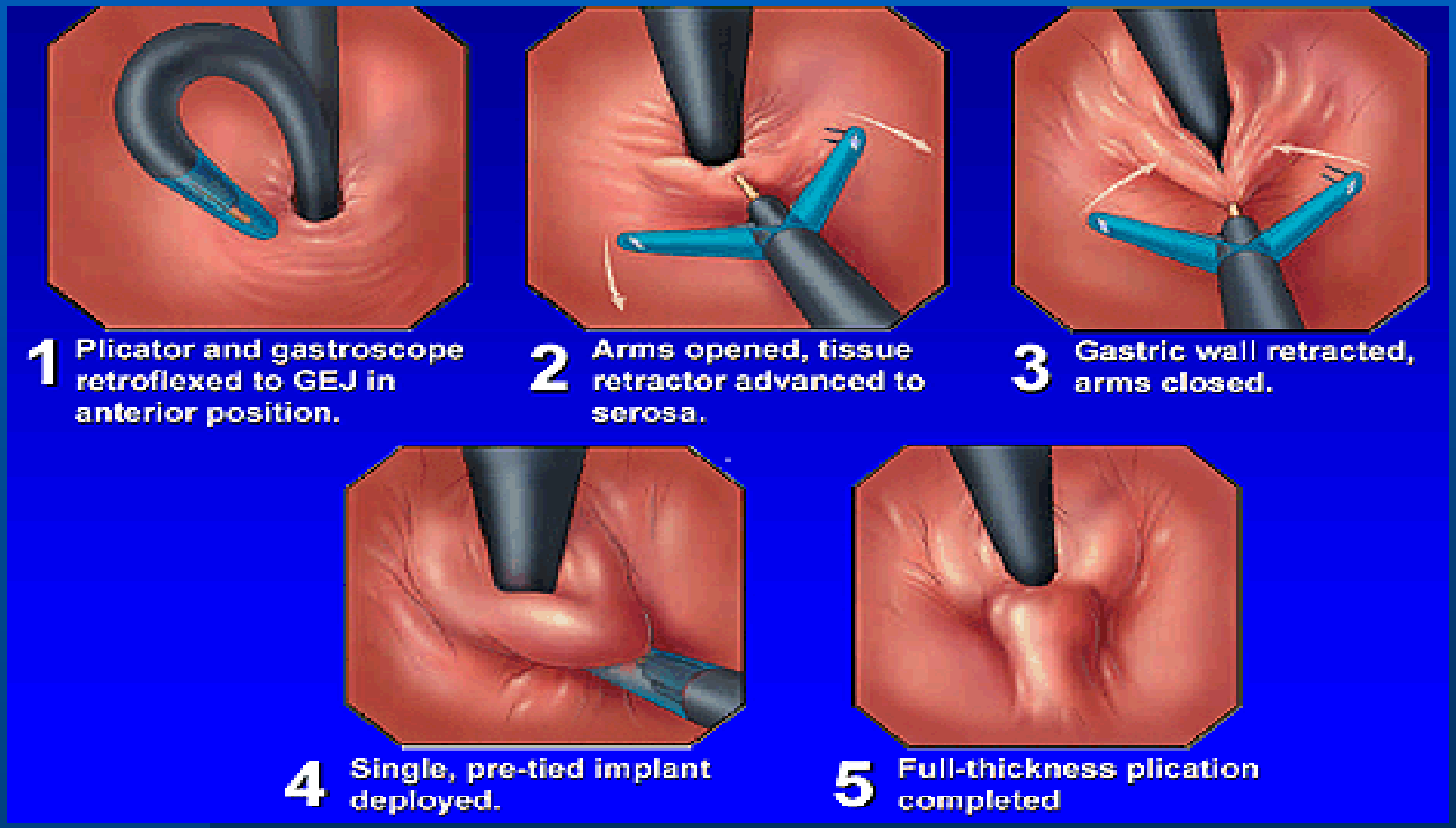


Enteryx injection

- Decreased in heartburn symptoms
- Decreased 24 hour acid exposure
- Decreased need for PPI

- No improvement in severity of esophagitis at EGD
- Long term safety issues not known

Endoscopic suturing



Endoscopic suturing

- Decreased heartburn symptoms
- PPI eliminated in 74% of patients at 6 months
- Decreased esophageal acid exposure; however, only 30% completely normalized

- Long term follow-up needed

Questions?