

Esophagus

Rita Brun, MD

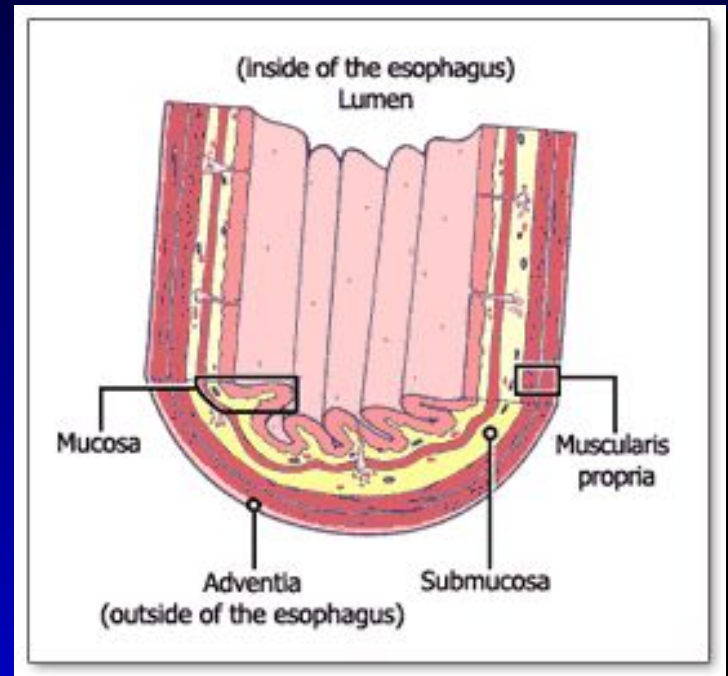
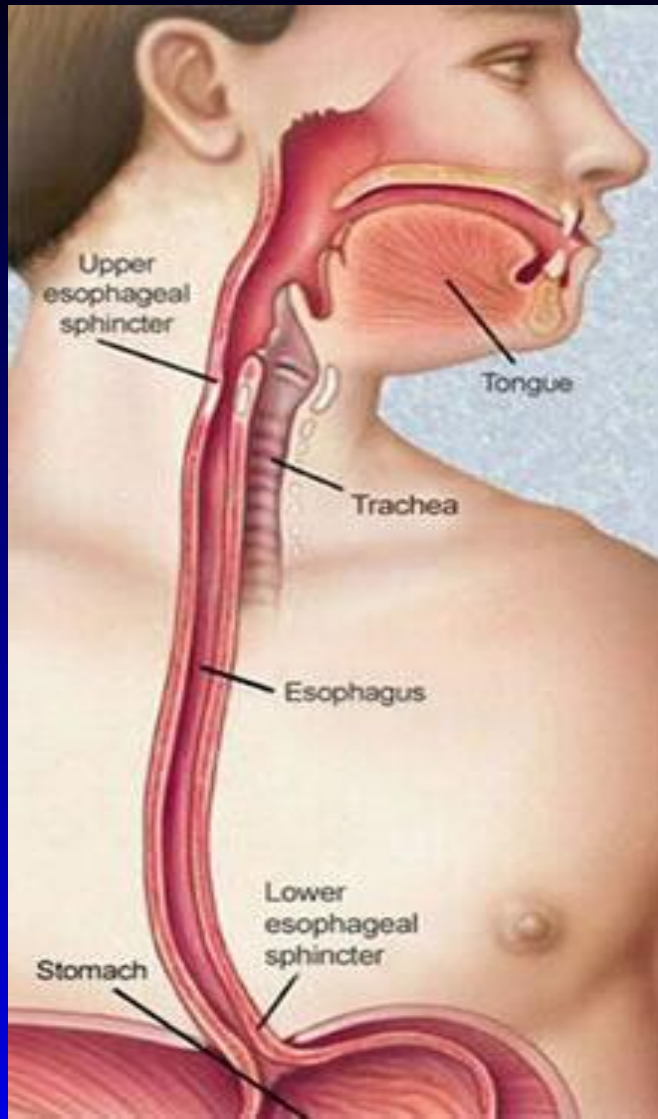
Gastroenterology Department
Rambam Health Care Campus

Esophagus

- **Esophageal anatomy and physiology**
- **Esophageal symptoms**
- **Diagnostic procedures**

- **GERD**
- **Dysphagia**

Esophageal Structure



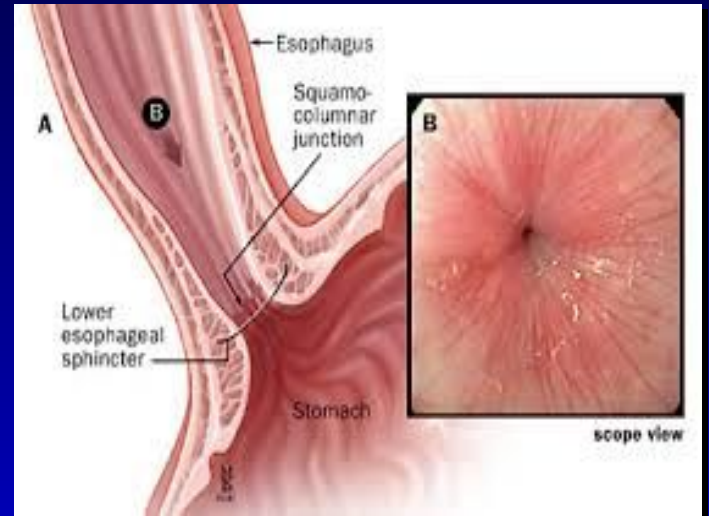
Esophagus Endoscopic View

GEJ



Columnar epithelium

Squamous epithelium



Physiology

- **Upper esophageal sphincter**
- **Lower esophageal sphincter**
- **Diaphragmatic sphincter**
- **Esophageal body**

Function

- **Esophageal bolus transport**

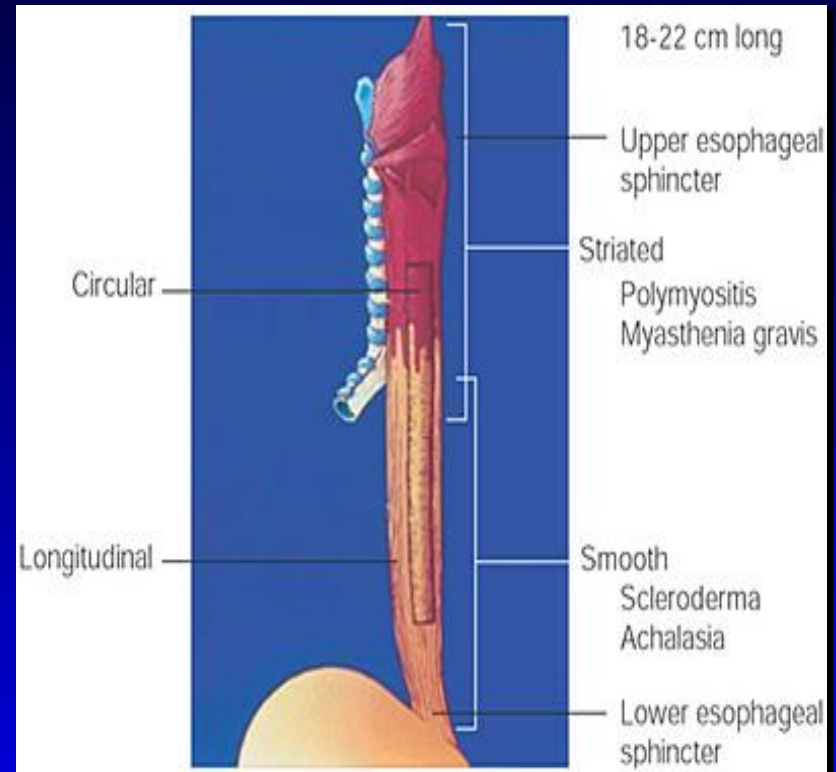
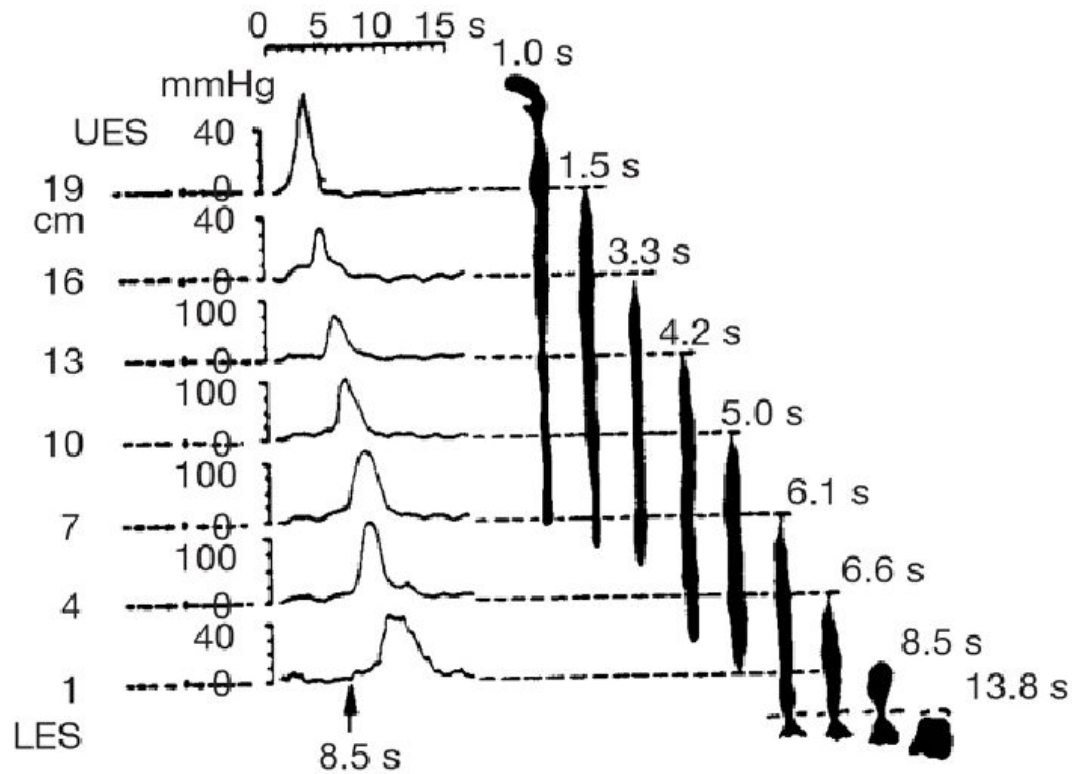


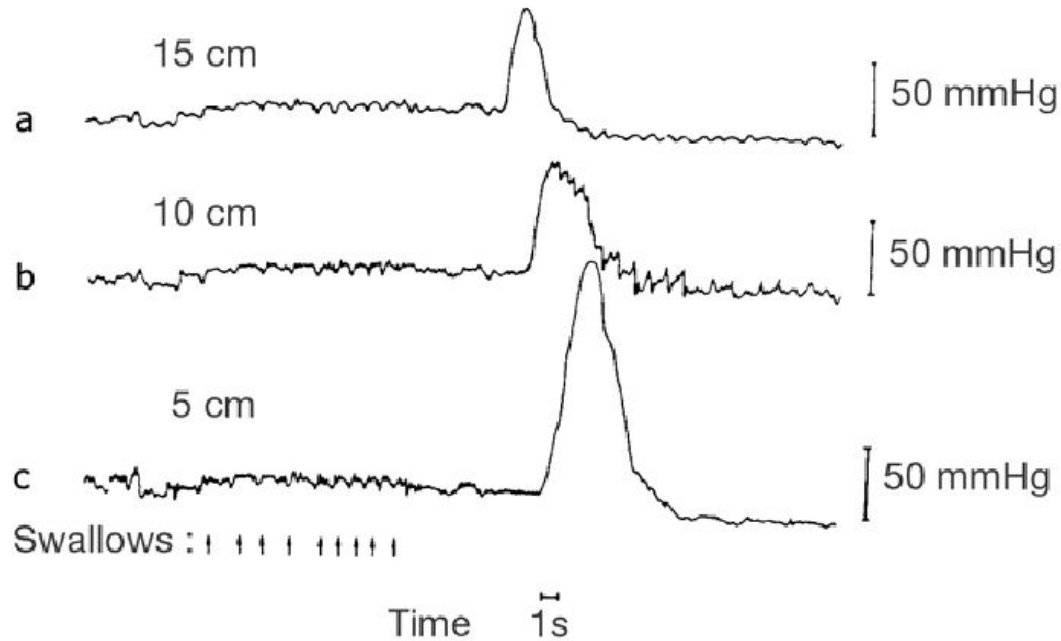
Figure 6 Simultaneous manometry and videofluoroscopy of barium swallow in a



Physiology- Deglutitive Inhibition

- The swallow-evoked peristaltic contraction consist of wave of inhibition followed by that of contraction
- The wave of inhibition that precedes peristaltic contraction is deglutitive inhibition
- Esophageal contraction in response to a single swallow lasts 8 to 10 seconds, and this will obstruct the bolus of a second swallow taken less than 8 second afterward.
- The phenomenon of deglutitive inhibition is essential for drinking of fluids (rate of swallows faster than one swallow every 10 seconds)
- During the usual drinking of water, swallows can be every 1 to 2 seconds, possible by the phenomenon of deglutitive inhibition in which a swallow abruptly inhibits any ongoing contraction in the esophagus.

Figure 8 Diagrammatic representation of manometric tracing demonstrating



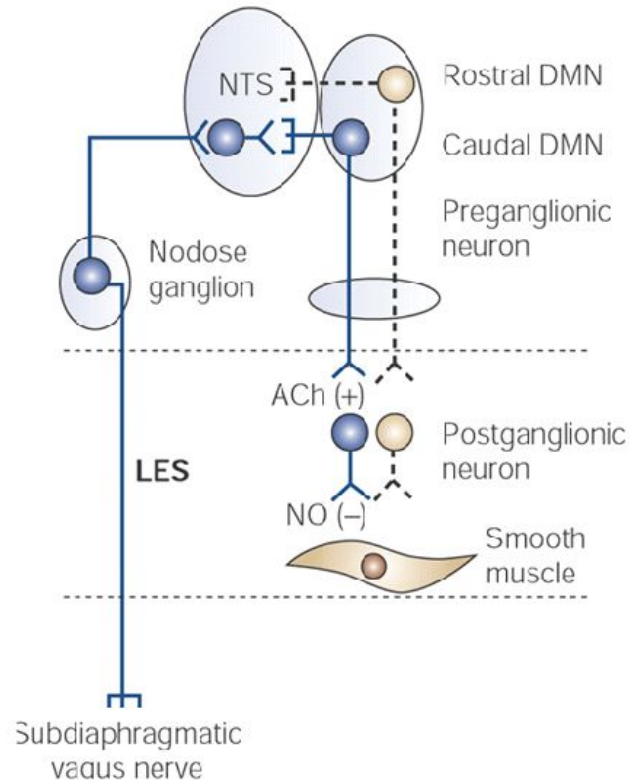
Physiology

- **Primary peristalsis**
 - **esophageal peristaltic contraction wave associated with swallowing**
- **Secondary peristalsis**
 - **It is a reflex that involves esophageal afferents and peristaltic activity restricted to the esophagus**
 - **Not associated with swallowing and does not involve full swallowing reflex**
 - **Residual food in the esophagus can be cleared by what is called secondary peristalsis**

Transient Lower Esophageal Sphincter Relaxations

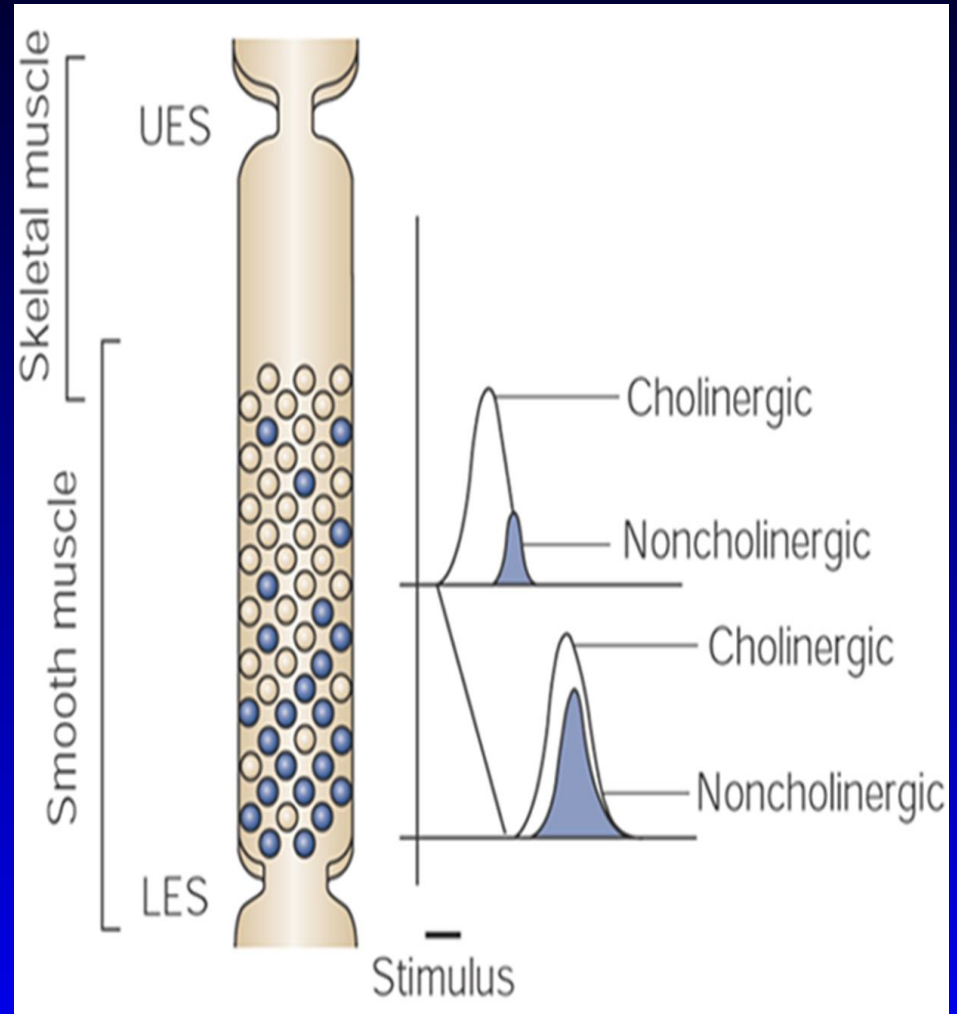
- LES relaxation during belching, retching, vomiting, and rumination
- TLESR are not associated with swallowing
- TLESR are increased after gastric distention or in the presence of a nasogastric tube.
- Vagal afferents in the stomach cause reflex LES relaxation via a vasovagal pathway that involves inhibitory vagal pathway neurons in the caudal part of the DMN and nNOS-containing neurons in the LES
- GERD and TLESR:
 - Most esophageal reflux episodes occurring during TLESR
 - TLESR are increased in patients with reflux esophagitis
 - TLESR associated with reflux of gas, and belch
 - Not all TLESRs were associated with reflux events

Figure 19. Neural circuitry of the enteric nervous system (ENS) and its relationship to the autonomic nervous system (ANS) and the central nervous system (CNS).



Physiology

- The esophagus is innervated by both parasympathetic and sympathetic nerves
- The parasympathetics control peristalsis via vagus nerve



Symptoms

- ***Heartburn* (pyrosis)- the most common esophageal symptom**
 - Discomfort or burning sensation behind the sternum that arises from the epigastrium and may radiate toward the neck
 - Appears after eating, during exercise, and while lying recumbent
 - Relieved with drinking water or antacid

Symptoms

- ***Regurgitation*** - effortless return of food or fluid into the pharynx without nausea or retching
 - Fluid - a sour or burning in the throat or mouth, may also contain undigested food particles
 - Bending, belching, or maneuvers increasing intraabdominal pressure can provoke regurgitation (not *vomiting* or *ruminatio*n)

Symptoms

- ***Chest pain*** - common esophageal symptom with characteristics similar to cardiac pain
 - pressure type sensation in the mid chest, radiating to the mid back, arms, or jaws
 - GE reflux is the most common cause of esophageal chest pain

Symptoms

- ***Dysphagia*** - feeling of food "sticking" or lodging in the chest
 - Solid food dysphagia /liquid and solid
 - Episodic /constant dysphagia
 - Progressive /static dysphagia
 - Oropharyngeal /esophageal
 - ***A patient's localization of food hang-up in the esophagus is very imprecise!***
 - Oropharyngeal dysphagia is often associated with aspiration, nasopharyngeal regurgitation, cough, drooling, or history of CVA

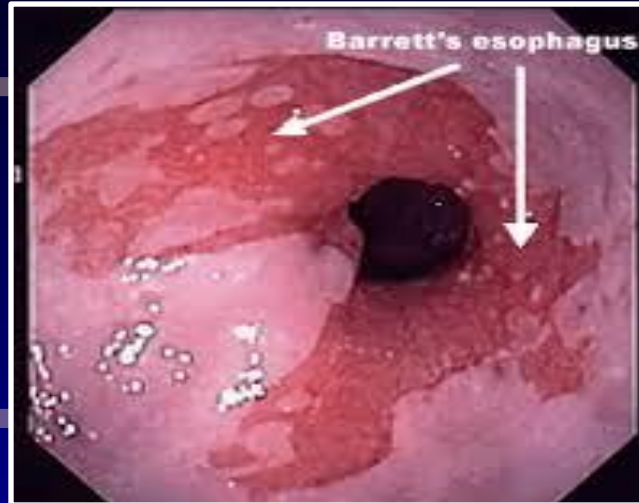
Symptoms

- ***Odynophagia*** - pain caused by swallowing
 - common with pill or infectious esophagitis, esophageal ulcer /erosions
- ***Globus sensation*** - perception of a lump or fullness in the throat that is felt irrespective of swallowing
 - anxiety, GERD
- ***Water brash*** – unpleasant sensation of the mouth rapidly filling with salty thin fluid
 - excessive salivation resulting from a vagal reflex triggered by acidification of the esophageal mucosa

Diagnostic Studies

- *Endoscopy*
- *Radiography*
- *Endoscopic Ultrasound*
- *Esophageal Manometry*
- *Video swallow study*
- *Reflux Testing*

Endoscopy



Radiography- Barium Swallow

Normal barium swallow



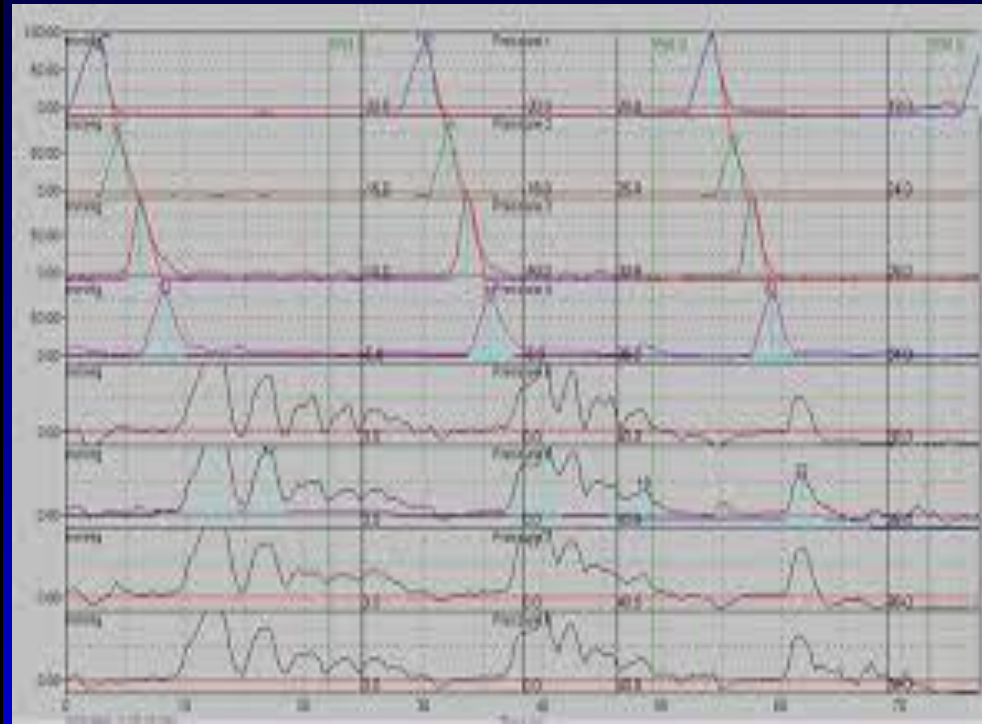
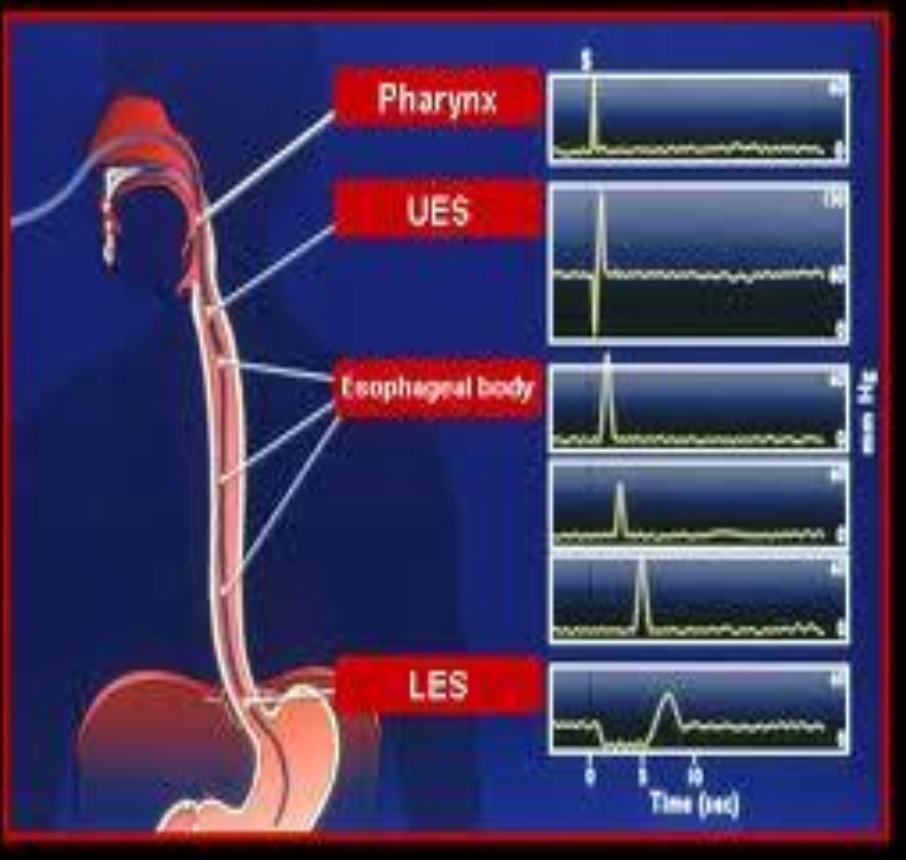
Hiatal hernia



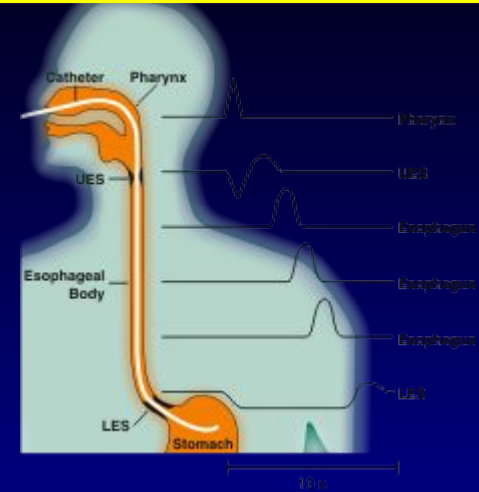
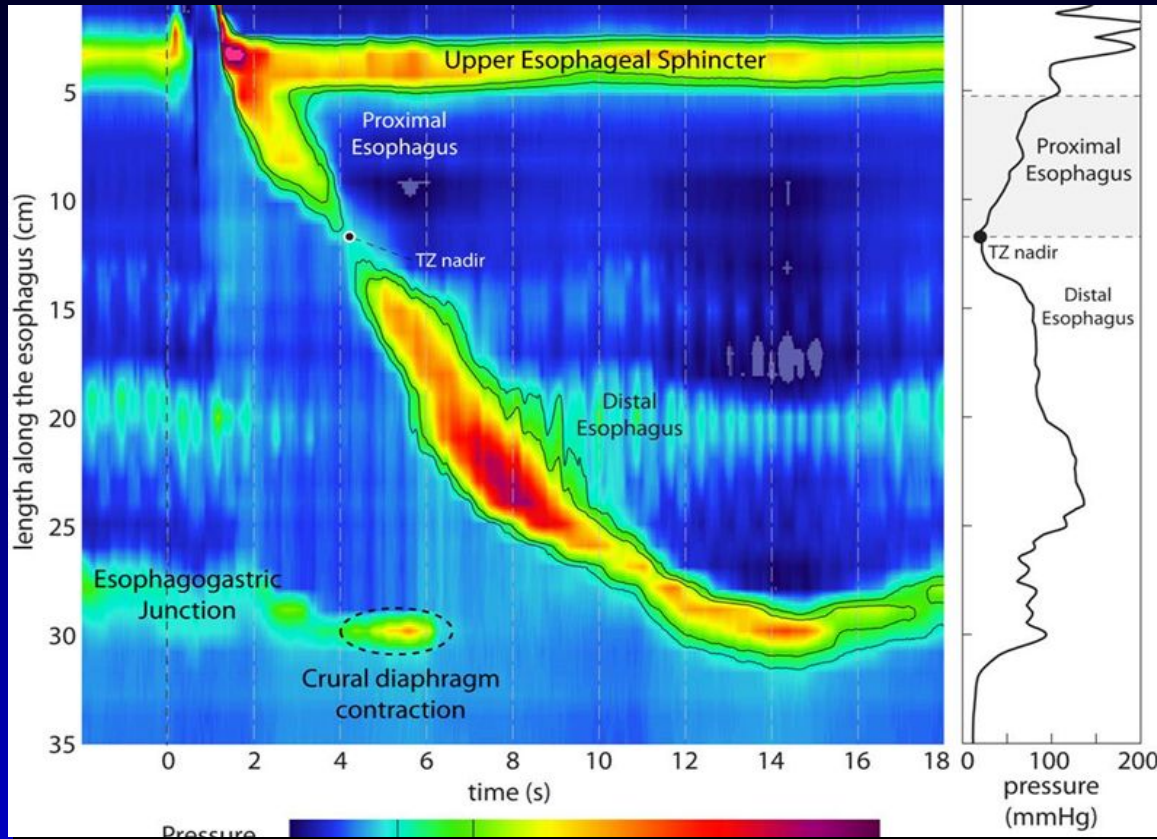
Esophageal spasm
Cork screw esophagus



Esophageal manometry



Motility Testing- Esophageal Manometry

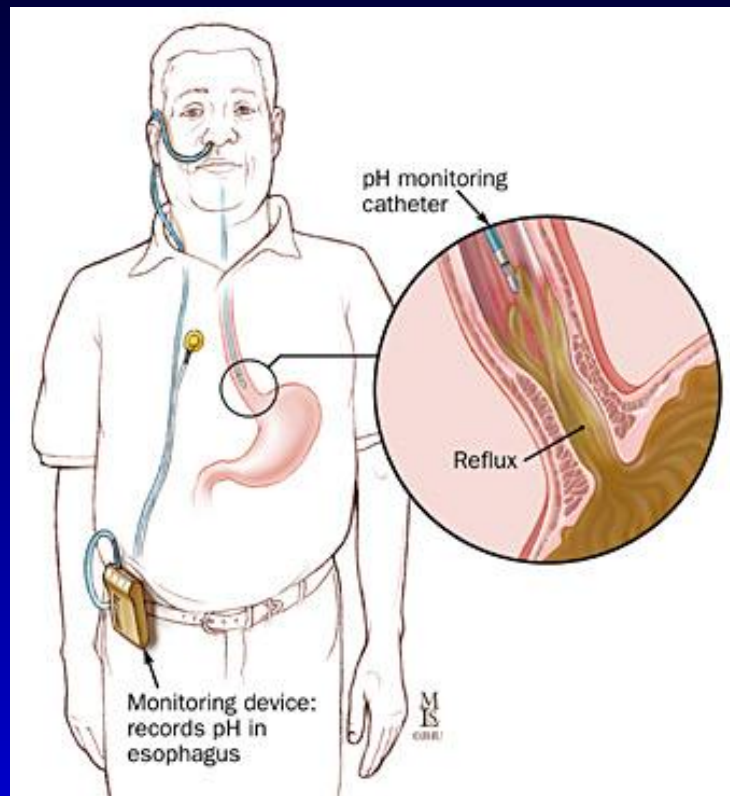


High Resolution Esophageal Manometry

Reflux Monitoring

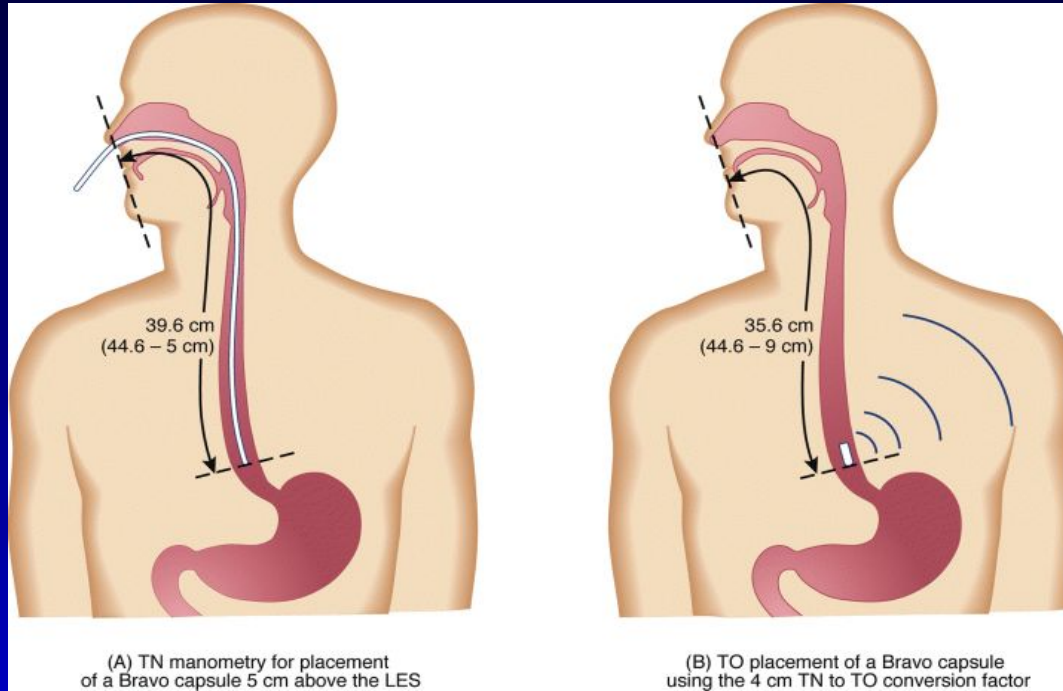
- **24-hour transnasally positioned wire electrode with the tip stationed in the distal esophagus**
- **48-hour esophageal pH recording using a wireless pH-sensitive transmitter (capsule)**
- **Intraluminal impedance monitoring to detect reflux events irrespective of their pH**

Reflux Monitoring



pH study: intranasal wire electrode with the sensor in the distal esophagus.

Reflux Monitoring pH-MII (Impedance)



**Wireless Bravo pH Capsule
for acid reflux detection**

Figure 3 Reflux episode defined by pH monitoring as a rapid drop in pH from

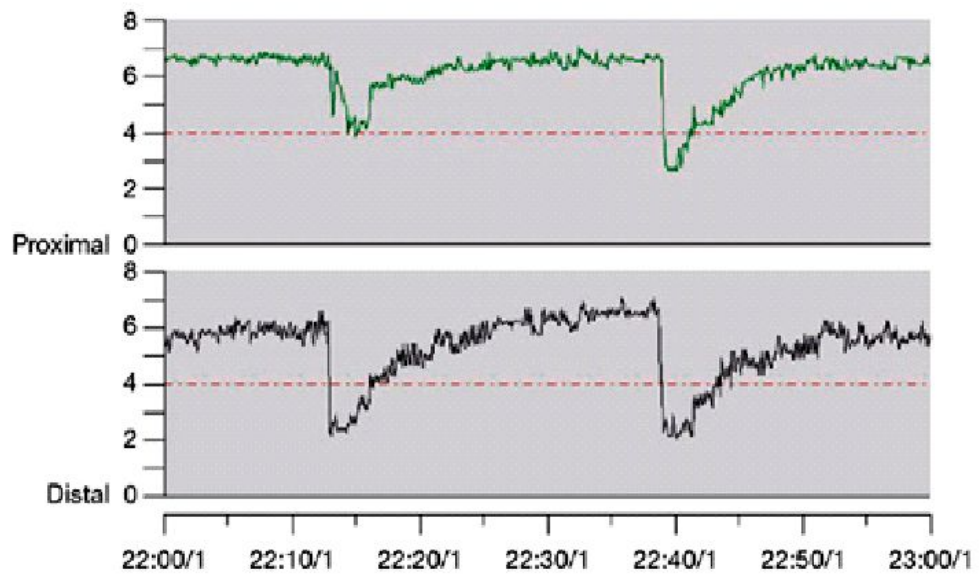
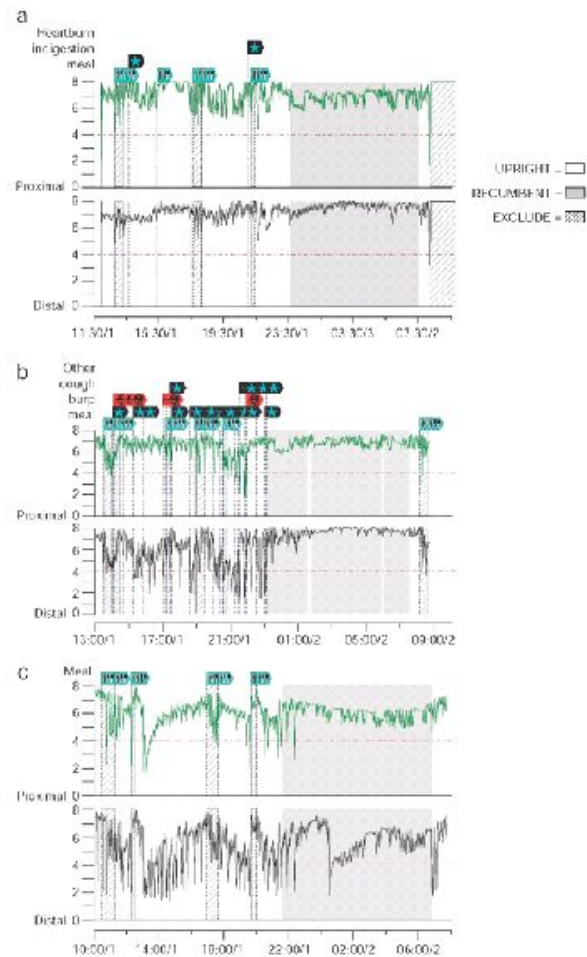
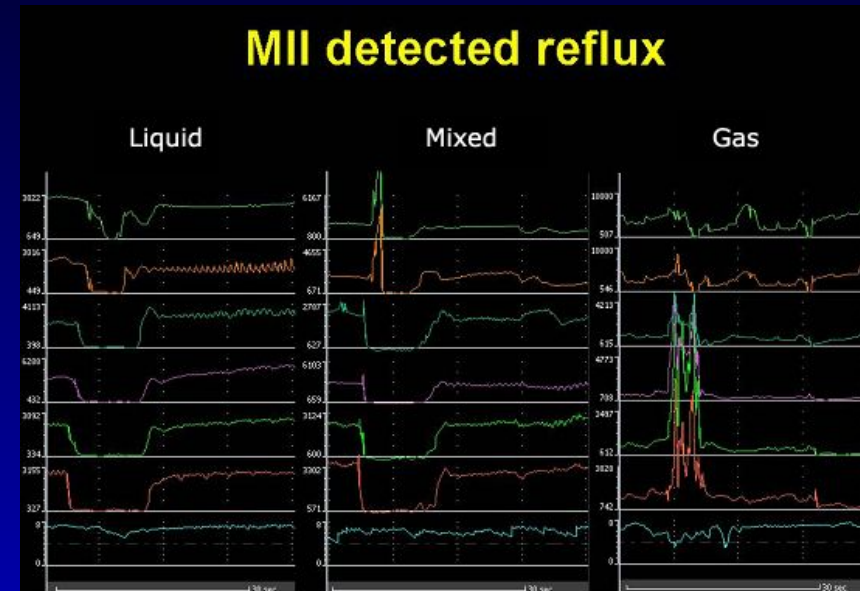
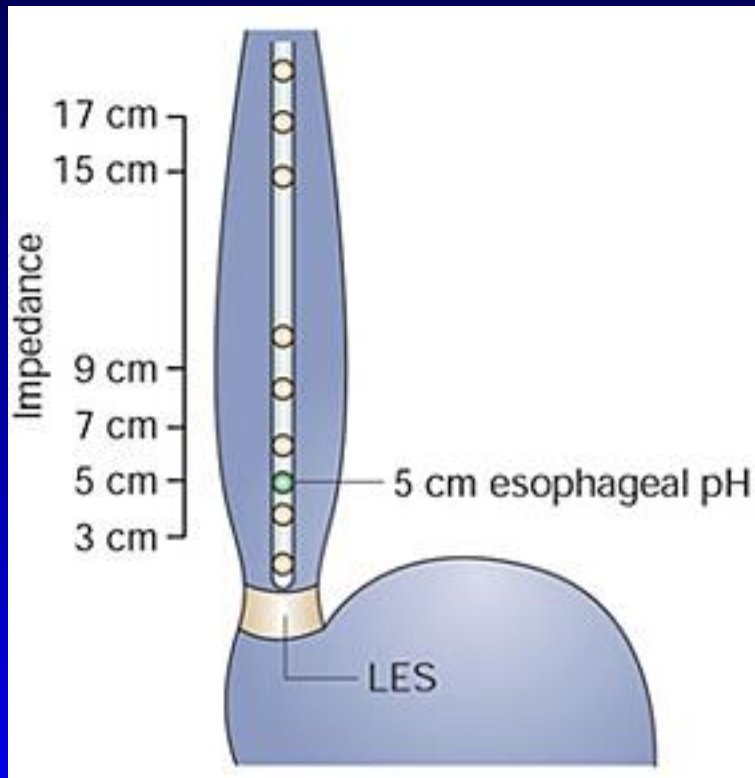


Figure 4 Ambulatory pH monitoring tracings.



Reflux Monitoring: pH- MII Multichannel Intraluminal Impedance Esophageal Reflux Monitoring

Acid and non-acid acid reflux detection
Gold standard of reflux testing



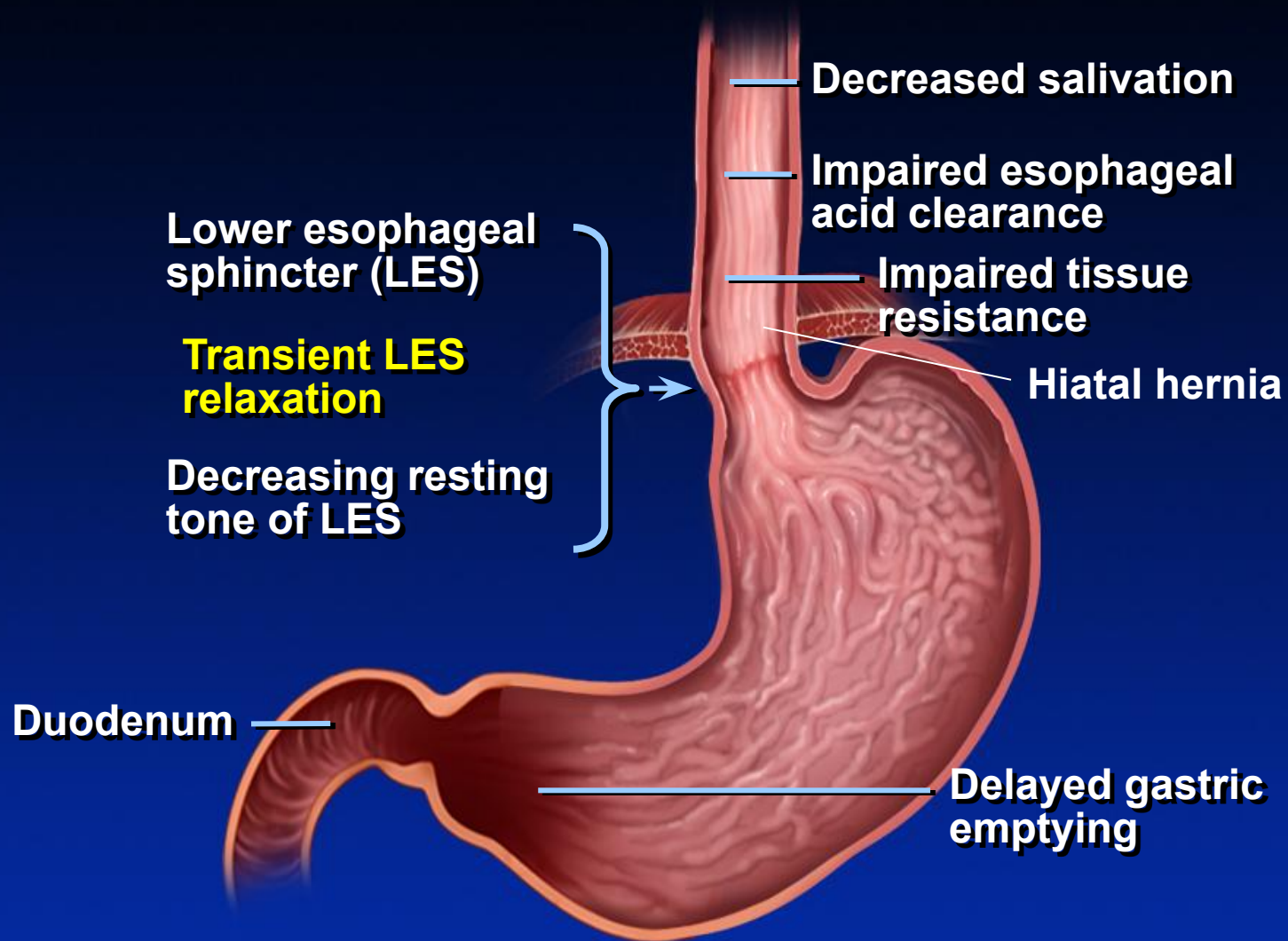
- PH-MII detects intraesophageal bolus movement
- The method is based on measuring the resistance to alternating current (i.e., impedance) of the content of the esophageal lumen
- Pairs of electrodes, separated by an isolator (i.e., catheter), are placed inside the esophagus

Gastroesophageal Reflux Disease (GERD)

GERD- definitions

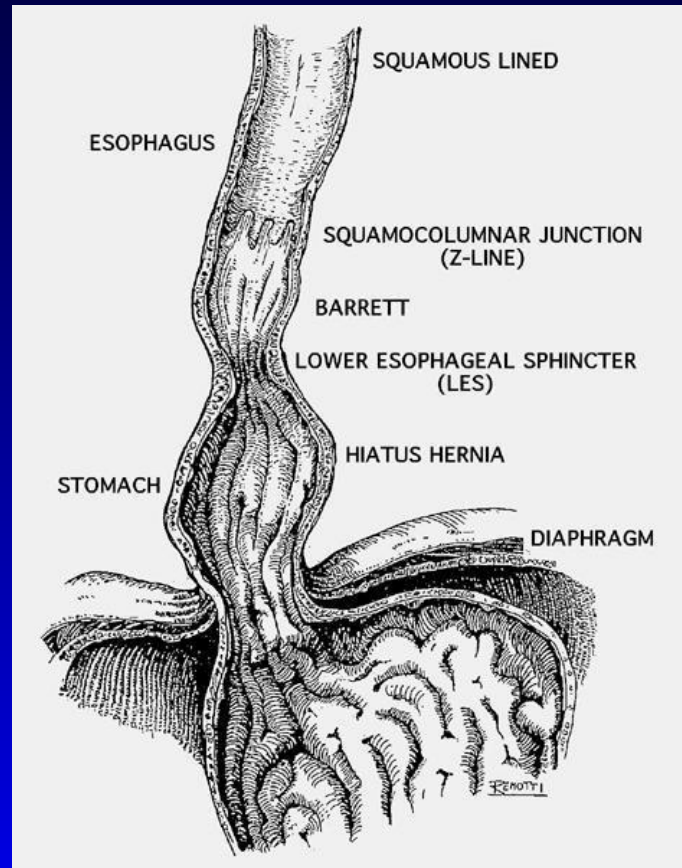
- ***Physiologic reflux*** episodes typically occur postprandially, are short-lived, asymptomatic, and rarely occur during sleep
- ***Pathologic reflux*** is associated with symptoms or mucosal injury, often including nocturnal episodes
- ***Gastroesophageal reflux disease (GERD)*** - a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications
- ***Reflux esophagitis*** - endoscopic or histopathologic evidence of esophageal inflammation in a subset of patients with GERD

Pathophysiology of GERD



Pathophysiology of GERD

Hiatal hernia



GERD

- **Epidemiology**
 - **Prevalence : 10 -20 % in the Western world , < 5 % in Asia**
 - **Incidence : 5 per 1000 person-years**

GERD Symptoms

- **Common: Heartburn and regurgitation**
- **Less common: dysphagia and chest pain**
- **Extraesophageal manifestations of GERD:**
 - **chronic cough**
 - **laryngitis**
 - **hoarsness**
 - **asthma**
 - **dental erosions**

GERD- Ds

- **Ds is usually based on clinical symptoms**
- **Utilization of diagnostic tests: the goal is to confirm the diagnosis of GERD in patients refractory to therapy, assess for complications of GERD, or to establish alternative diagnoses**
- **Upper endoscopy**
 - **Los Angeles classification of esophagitis**
- **pH metry**
- **Manometry**

The Los Angeles Classification System for Esophagitis

Los Angeles Grade A



One or more mucosal breaks no longer than 5 mm, not bridging the tops of mucosal folds

Los Angeles Grade B



One or more mucosal breaks longer than 5 mm, not bridging the tops of mucosal folds

Los Angeles Grade C



One or more mucosal breaks bridging the tops of mucosal folds involving <75% of the circumference

Los Angeles Grade D



One or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference

Lundell LR, et al. *Gut*. 1999;45:172-180.

Armstrong D, et al. *Gastroenterology*. 1996;111:85-92.

GERD Differential Diagnosis

- **Infectious, pill, or eosinophilic esophagitis**
- **Peptic ulcer disease**
- **Dyspepsia**
- **Biliary colic**
- **Coronary artery disease**
- **Esophageal motility disorders**

GERD Treatment

Lifestyle modifications

- **Avoidance of**
 - **Foods that reduce LES pressure -"refluxogenic" (fatty foods, alcohol, spearmint, peppermint, tomato-based foods, coffee and tea)**
 - **Acidic foods**
 - **Smoking**
 - **Carbohydrated beverages**
- **elevated head of the bed**
- **avoidance of eating before lying down**
- **weight reduction**

GERD Treatment

- **Inhibitors of gastric acid secretion**
 - Reducing the acidity of gastric juice does not prevent reflux, but it ameliorates reflux symptoms and allows esophagitis to heal
- **Proton pump inhibitors (PPI) /omeprazole/**
 - PPI is given 20- 30 min before meal for maximal efficacy
- **Histamine₂ receptor antagonists (H₂RAs) /famotidine/**
- PPIs are more efficacious than H₂RAs; and both are superior to placebo
- **Anti- acid /Maalox- aluminium hydroxide and magnesium hydroxide, neutralizes gastric acid/. Symptomatic treatment.**

PPI Mechanisms of Action

- ◆ All PPIs are prodrugs that are converted to active moiety (sulfenamide form) in presence of acid
- ◆ Sulfenamide binds covalently to exposed cysteine residues of H⁺/K⁺-ATPase pump
- ◆ Currently available PPIs have pK_a (pH at which 50% of molecule is protonated) ranging from 3.8 to 5.0
- ◆ Higher pK_a results in more rapid and complete activation, especially at pH above 1-2
- ◆ PPI concentration may be up to 1000-fold higher on luminal side of secretory canaliculus

Besancon M et al. *J Biol Chem.* 1997;272:22438-22446.

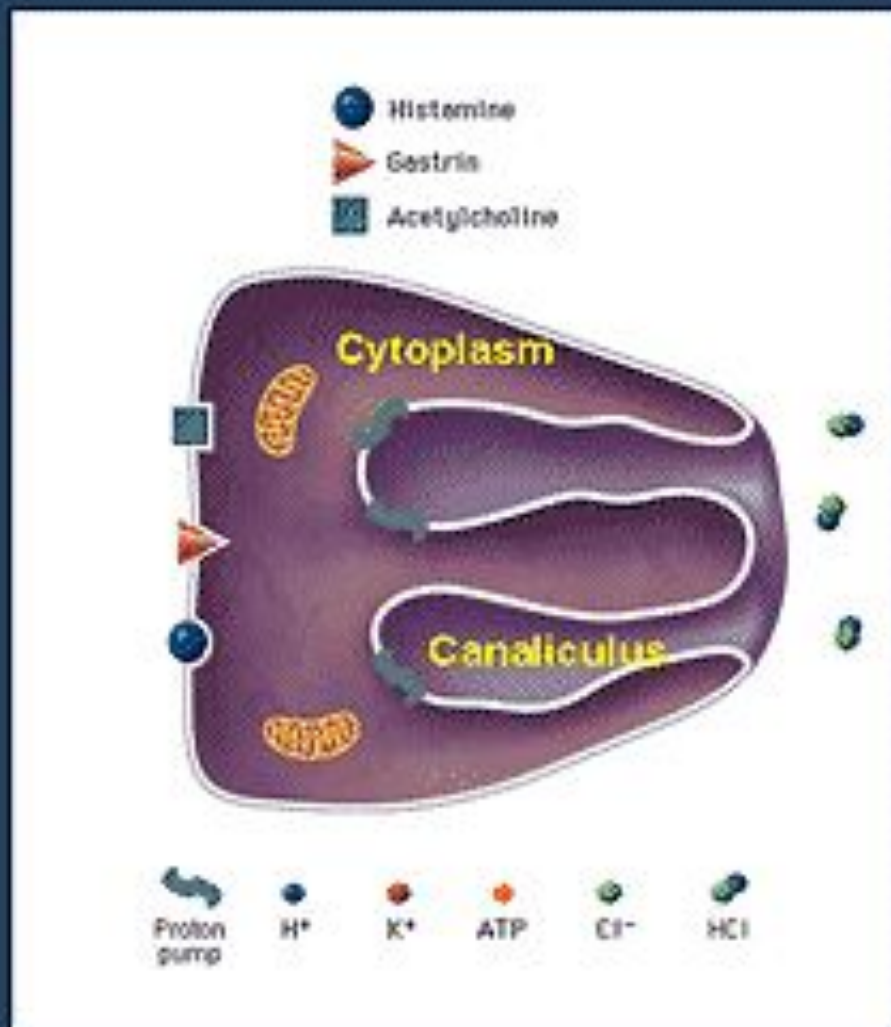
Sachs G et al. *Aliment Pharmacol Ther.* 2000;14:1383-1401.

Horn JR. *Clin Ther.* 2000;22:266-280.

PPI Site of Action: The Parietal Cell

- ◆ Molecules become trapped in canaliculus
 - Suppress gastric acid secretion by inhibiting the final step of acid production at the secretory surface of the gastric parietal cell
 - Inhibit both basal and stimulated acid secretion irrespective of the stimuli

Sachs G et al. *Pharmacotherapy*. 1997;17:22-37.



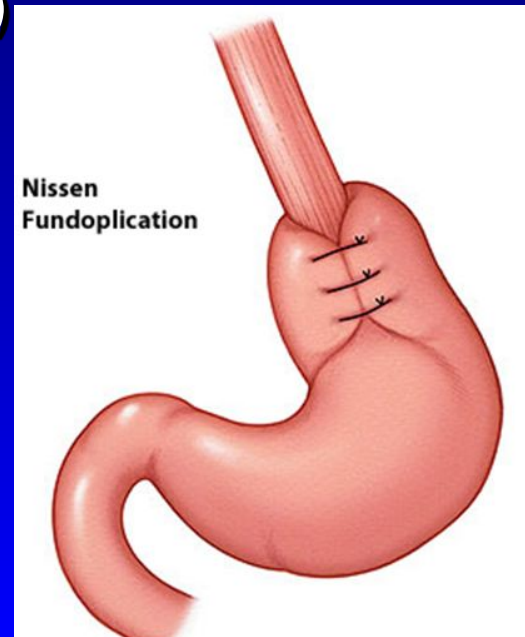
GERD Treatment- surgical

- **Nissen fundoplication**

the proximal stomach is wrapped around the distal esophagus to create an antireflux barrier

- **Potential side effects:**

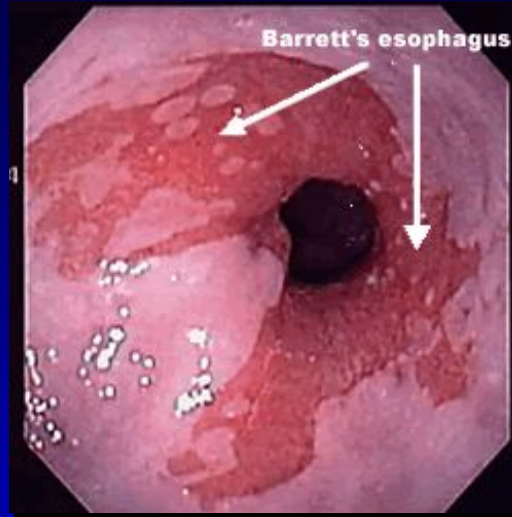
- temporary solution in majority of cases (5-10y)
- surgical morbidity and mortality
- postoperative dysphagia
- failure or breakdown requiring reoperation
- an inability to belch (increased bloating)



GERD Complications

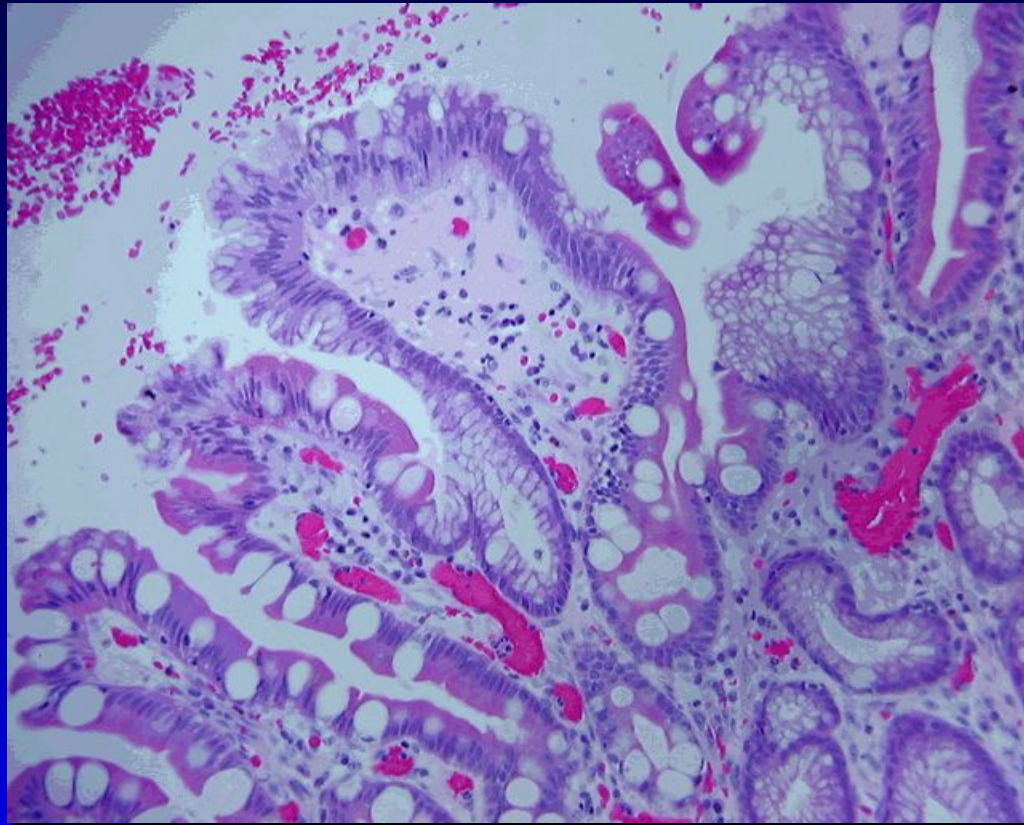
- **Chronic esophagitis (bleeding and stricture)**
 - increasingly rare due to potent antisecretory medications
- **Esophageal adenocarcinoma**
 - Barrett's metaplasia

Barrett's esophagus



Endoscopy: Tongues of reddish mucosa extending proximally from GE junction

Barrett's esophagus



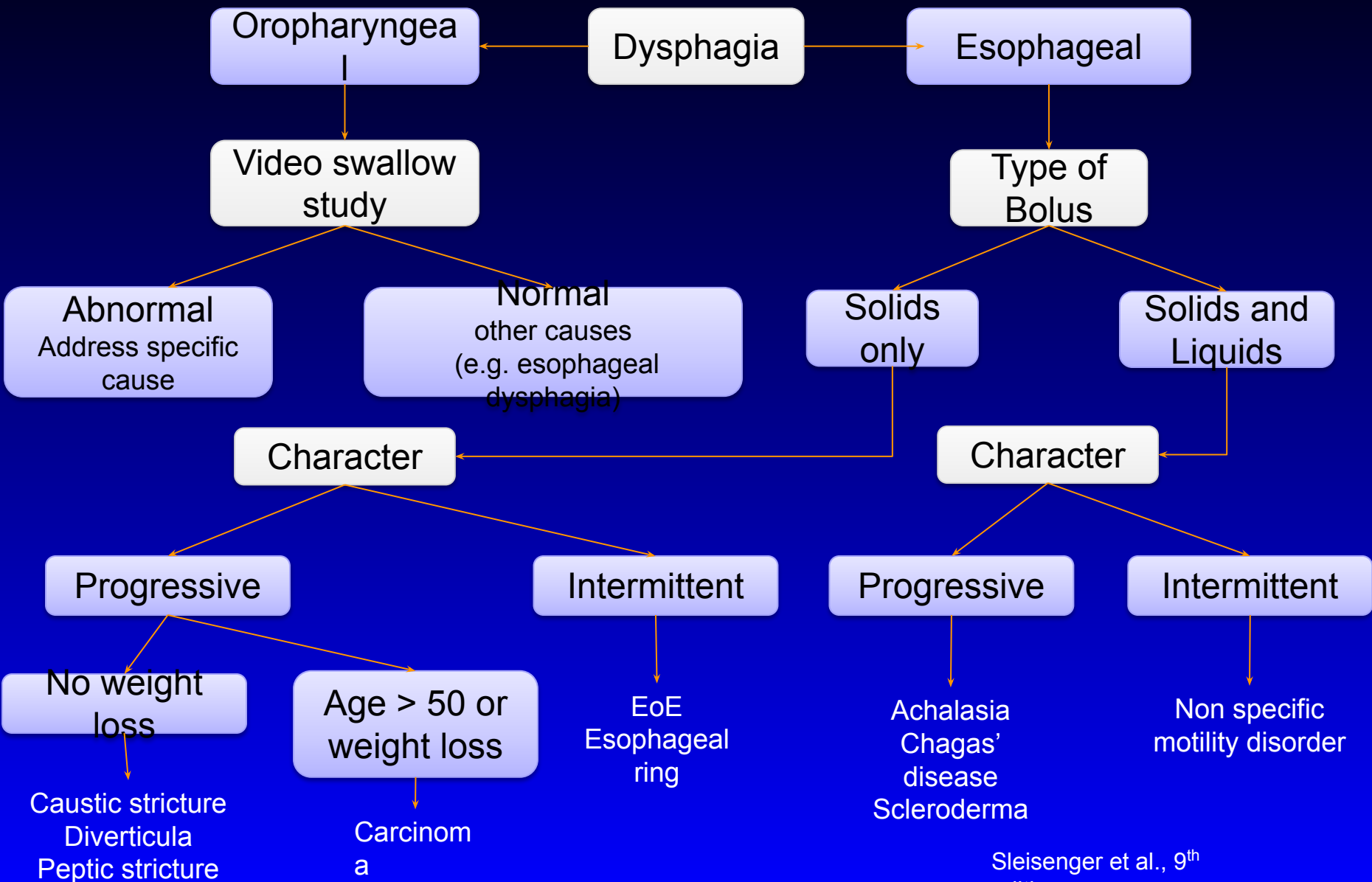
Histology: columnar metaplasia with Goblet cells

GERD Complications- Barrett's

- **Obese white males in 6th decade of life are at greatest risk for Barrett's**
- **Barrett's metaplasia can progress to adenocarcinoma through the intermediate stages of low- and high-grade dysplasia**
- **The rate of cancer development - 0.5% per year**
- **No evidence that aggressive antisecretory therapy or antireflux surgery causes regression of Barrett's esophagus or prevents adenocarcinoma**
- **Management of Barrett's esophagus remains controversial**
- **High-grade dysplasia in Barrett's mandates further intervention**
 - **Esophagectomy**
 - **Mucosal ablation**
 - **Endoscopic Mucosal Resection**

Dysphagia

Approach to Dysphagia



Oropharyngeal Dysphagia

Etiology

- **Neurogenic - major source of morbidity related to aspiration and malnutrition**
 - **CVA**
 - **Parkinson's disease**
 - **ALS**
- **Structural lesions**
 - **Zenker's diverticulum**
 - **cricopharyngeal bar**
 - **neoplasia**
- **Iatrogenic causes**
 - **surgery and radiation (head and neck cancer)**

Zenker's diverticulum

Zenker's
diverticulum

- **Elderly**
- **Prevalence 1:1000 - 1:10,000**
- **Symptoms: dysphagia, regurgitation of particulate food debris, aspiration, halitosis**
- **Pathogenesis: stenosis of the cricopharyngeus, causing diminished UES opening and increased hypopharyngeal pressure during swallowing with development of a pulsion diverticulum immediately above the cricopharyngeus**

Esophageal Dysphagia

- **Solid food dysphagia appears when the lumen is <13 mm**
- **Circumferential lesions are more likely to cause dysphagia**

Esophageal Dysphagia

- **Structural causes**
 - Schatzki's rings
 - Eosinophilic esophagitis
 - Peptic strictures
 - Neoplasia
- **GERD without a stricture, perhaps on the basis of altered function**
- **Propulsive disorders**
 - Abnormalities of peristalsis and/or deglutitive inhibition (achalasia)
- **Diseases affecting smooth muscle**

Esophageal Dysphagia

- **Upper endoscopy**
 - **Dysphagia is an alarm symptom**
- **Esophageal manometry**
- **Barium swallow**

Esophageal Dysphagia- Schatzki's ring



- **Distal esophagus**
- **Mucosal ring**
- **Intermittent dysphagia**
- **Treatment (if symptomatic):
dilatation +/- acid supression**



Achalasia

- Incidence 1-3:100,000
- Age - 25 to 60 yo

Symptoms

- **Dysphagia: solid and liquid food**
- **Regurgitation: food, fluid, and secretions are retained in the dilated esophagus (risk for bronchitis, pneumonia, or lung abscess from chronic regurgitation and aspiration)**
- **Chest pain: a squeezing, pressure-like retrosternal pain, sometimes radiating to the neck, arms, jaw, and back.**
- **Weight loss**

Achalasia

- **Etiology:**
 - **Loss of ganglion cells- inhibitory (nitric oxide) ganglionic neurons within the esophageal myenteric plexus.**
 - **Excitatory (cholinergic) ganglionic neurons are variably affected**
- **Impaired deglutitive LES relaxation and absent peristalsis**
- **Progressive dilatation and sigmoid deformity of the esophagus with hypertrophy of the LES**

Achalasia

Differential diagnosis

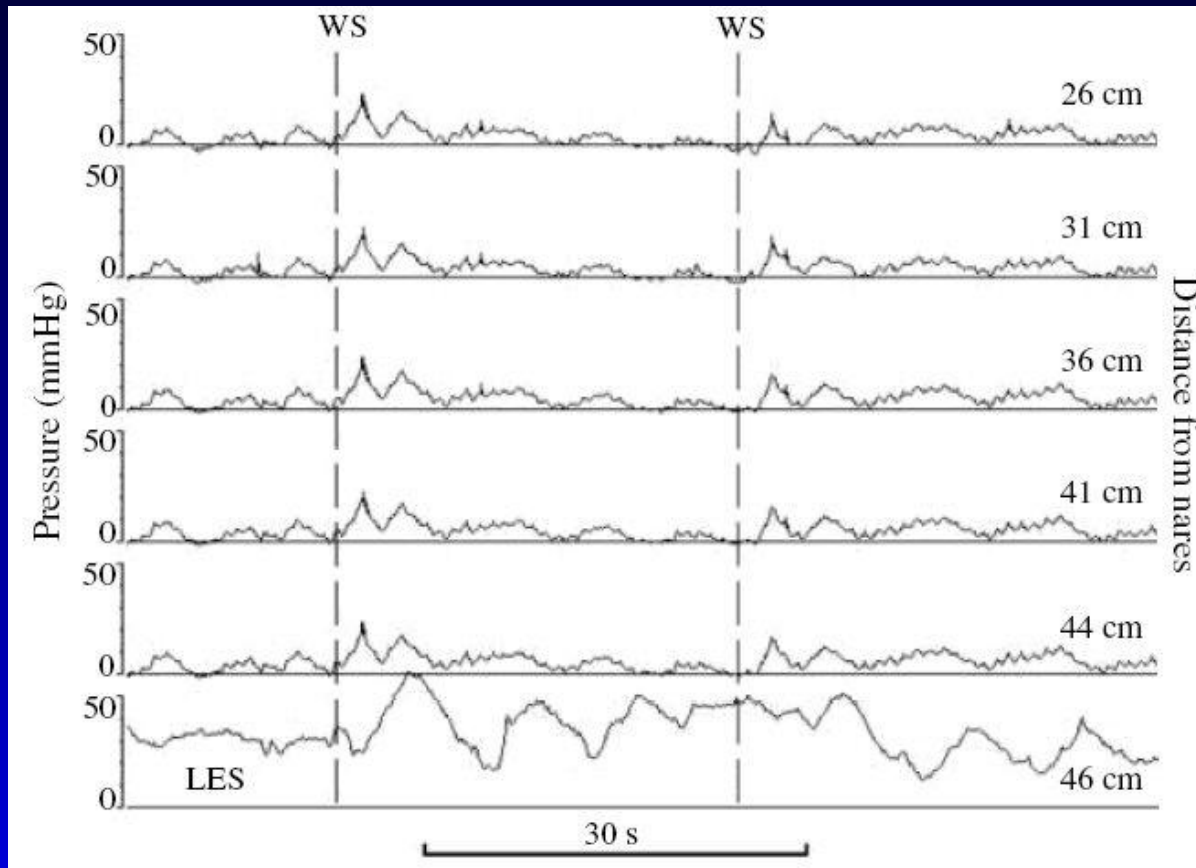
- **Diffuse esophageal spasm (DES)**
- **Chagas' disease (*Trypanosoma cruzi*)**
 - The chronic phase of the disease develops years after infection and results from destruction of autonomic ganglion cells in the heart, gut, urinary tract, and respiratory tract.
- **Pseudoachalasia**
 - Tumor infiltration - up to 5% of suspected achalasia cases (more likely with advanced age, abrupt onset of symptoms, and weight loss).
 - Paraneoplastic syndrome with circulating antineuronal antibodies- rare.

Achalasia Diagnosis

- **Endoscopy**
 - rarely diagnostic, to exclude pseudo-achalasia
- **Manometry**
 - most sensitive diagnostic test
- **Barium swallow x-ray**

Achalasia

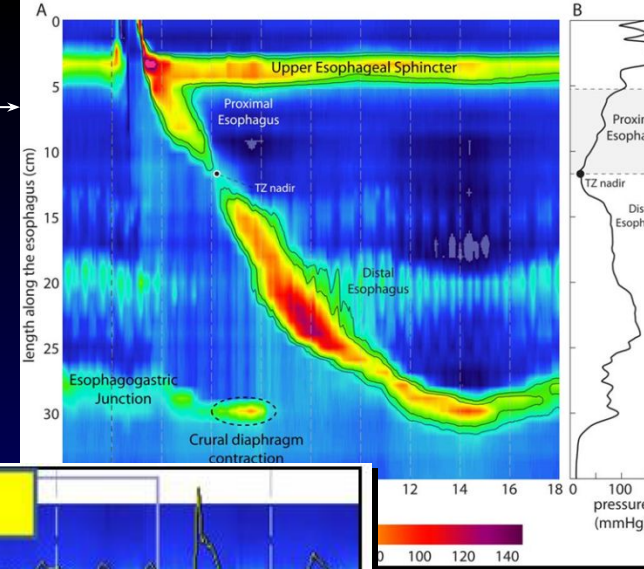
Conventional manometry



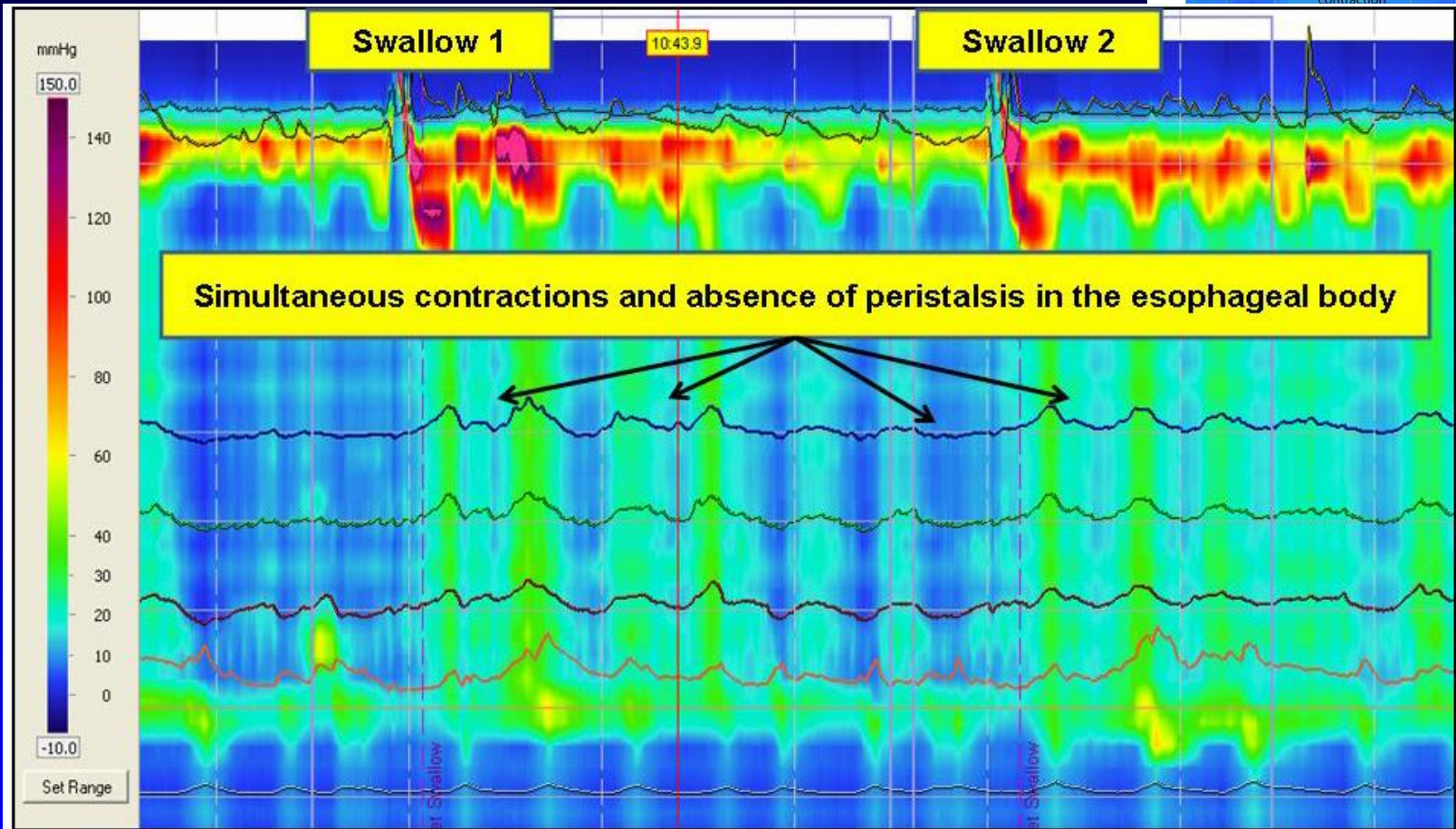
- Impaired LES relaxation
- Absent peristalsis of esophageal body

High Resolution Manometry

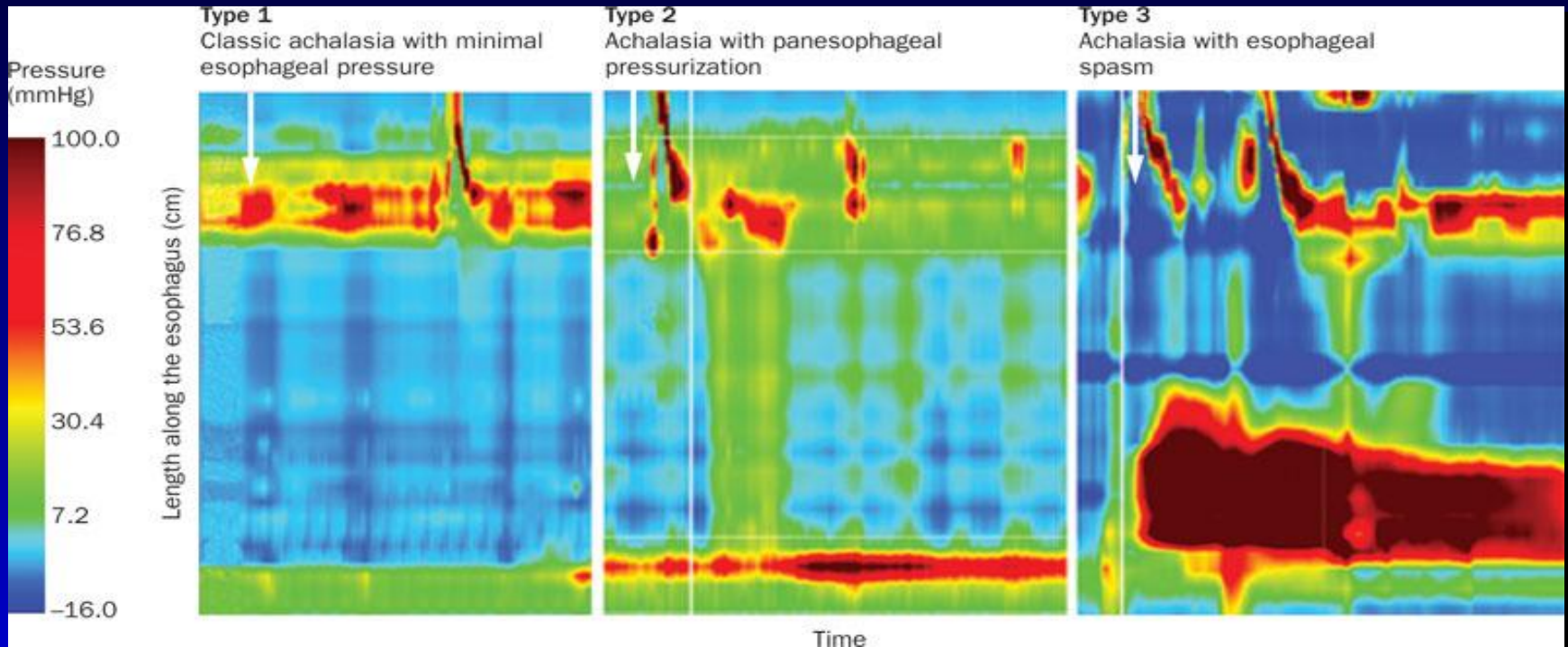
Normal



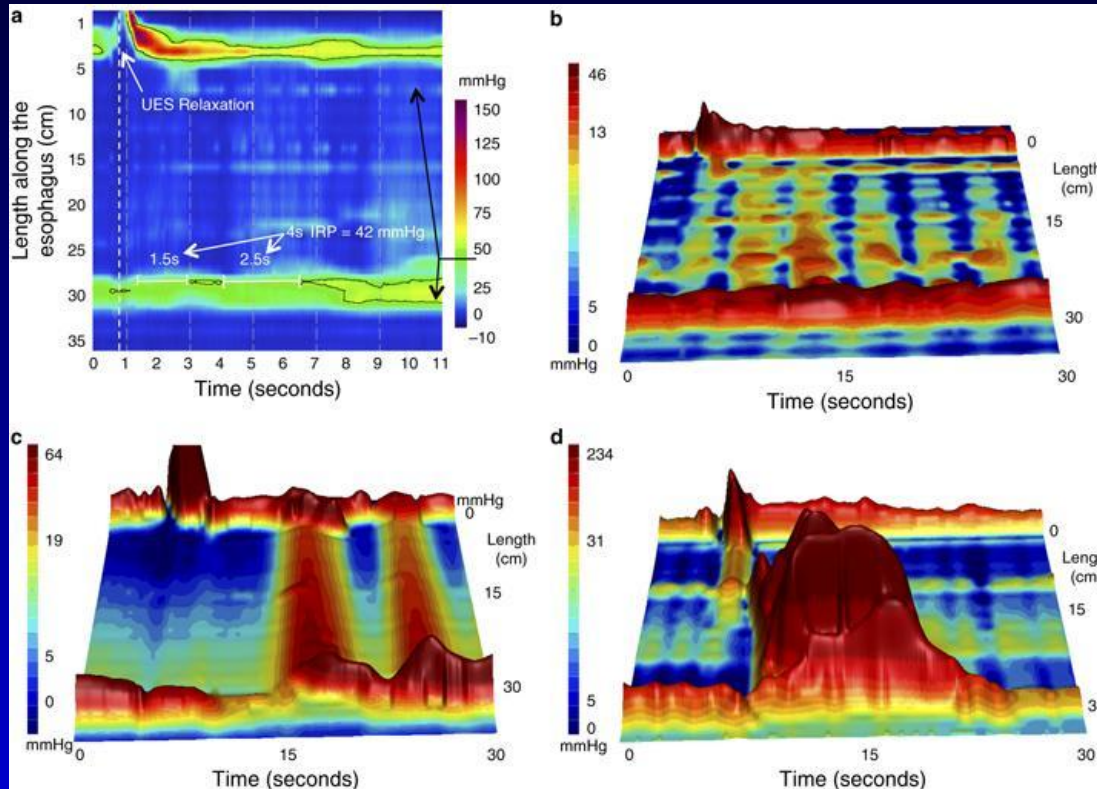
Achalasia



Three Subtypes of Achalasia on High Resolution Manometry



Three Subtypes of Achalasia on High Resolution Manometry



Achalasia

Barium swallow x-ray

- dilated esophagus with poor emptying
- air-fluid level
- tapering at the LES - “bird’s beak”

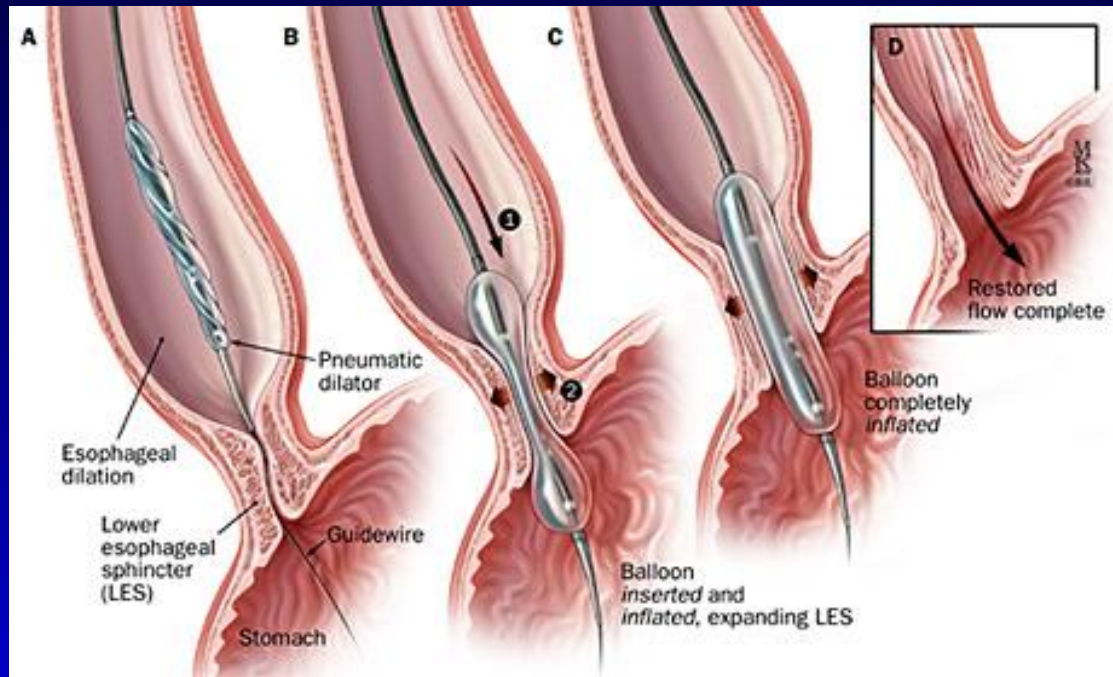


Achalasia Treatment

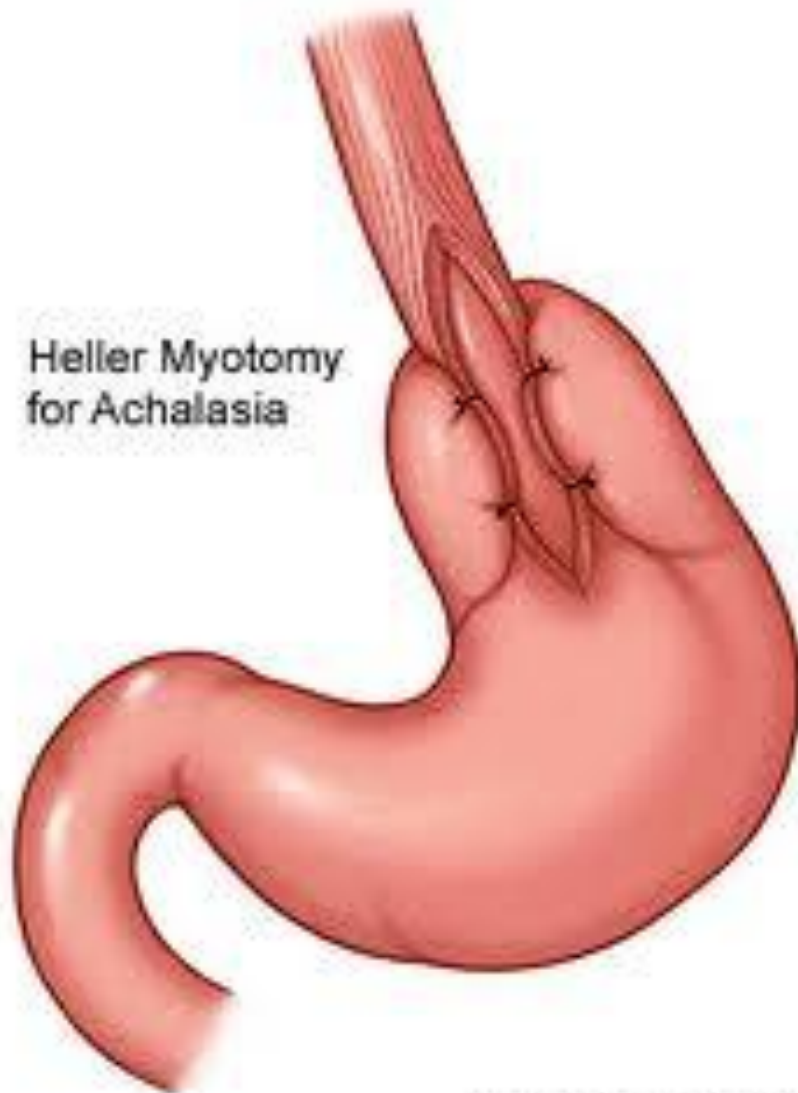
Therapy is directed at reducing LES pressure

- **Pharmacologicals therapies are relatively ineffective**
- **Botulinum toxin, injected into the LES**
- **Pneumatic balloon dilatation**
- **Surgical: Heller myotomy, good to excellent results are reported in 62–100% of cases**

Pneumatic balloon dilation of LES



Heller Myotomy
for Achalasia



Achalasia- Complications

- **Squamous cell carcinoma risk increased 17-fold in inadequately treated achalasia most probably due to stasis esophagitis**
- **Malnutrition**
- **There is no known way of preventing or reversing achalasia**

Diffuse Esophageal Spasm (DES)

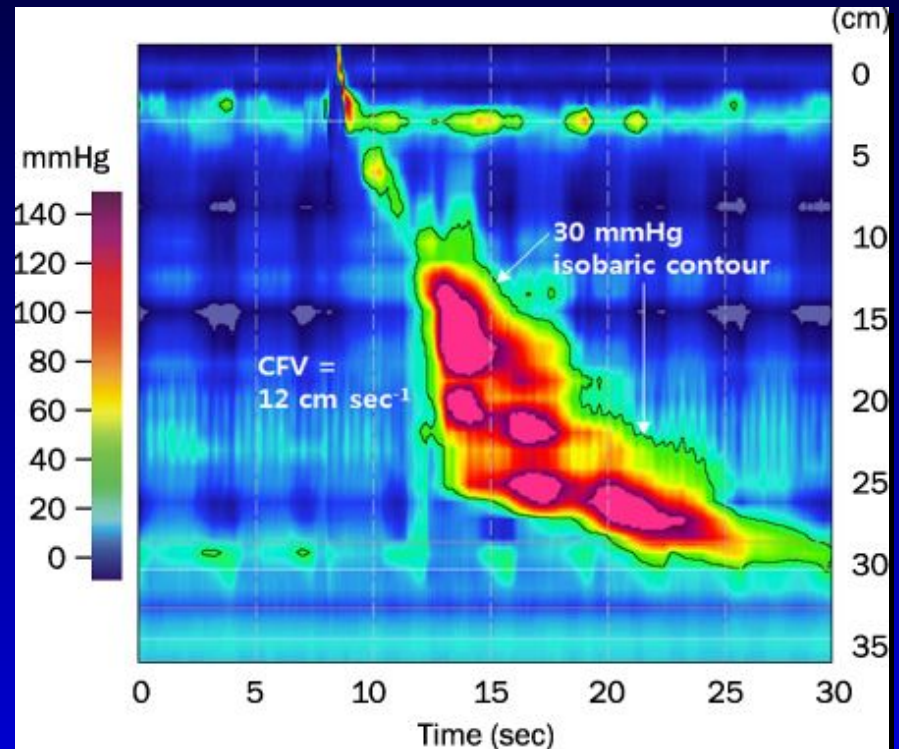
- **Episodes of dysphagia and chest pain attributable to abnormal esophageal contractions.**

Diagnosis

- **Barium swallow: tertiary contractions or a "corkscrew esophagus" , "rosary bead esophagus," pseudodiverticula"**
- **Manometry: simultaneous contractions in the distal esophagus, but normal deglutitive LES relaxation**

Diffuse Esophageal Spasm

Corkscrew esophagus

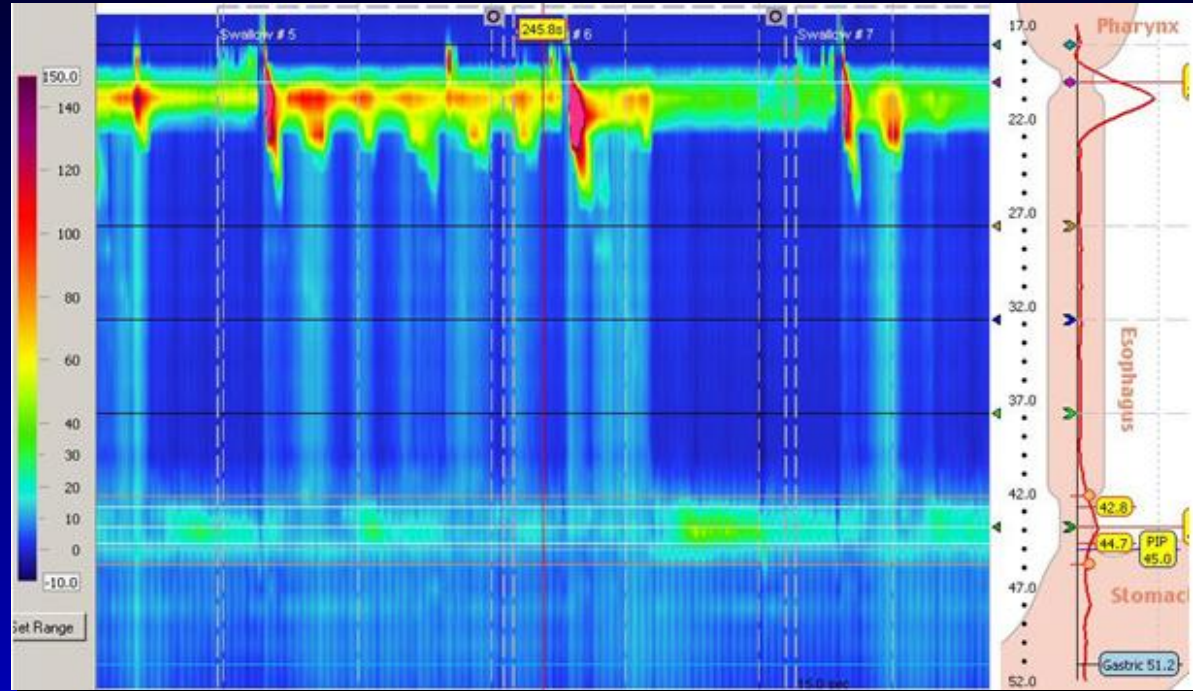
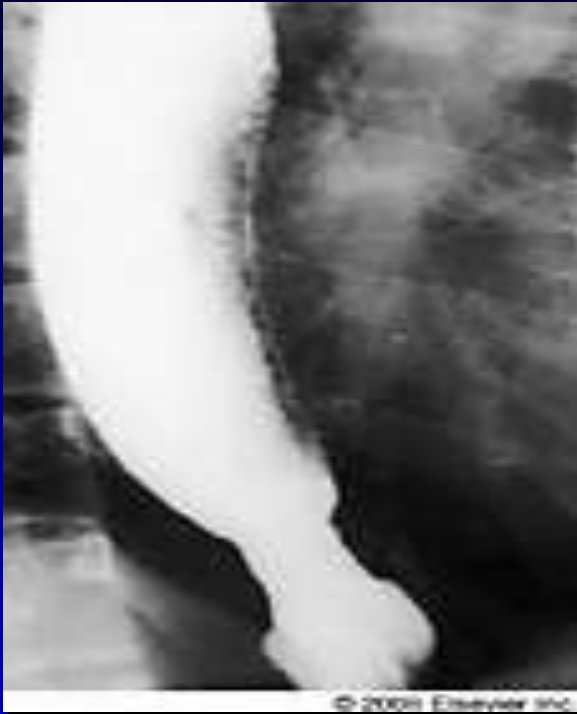


Dysphagia

Diffuse Esophageal Spasm (DES)

- **Differential diagnosis:**
 - **angina pectoris**
 - **peptic or infectious esophagitis**
 - **Achalasia**
- **Treatment**
 - **Partial response to nitrates, calcium channel blockers, hydralazine, botulinum toxin, and anxiolytics**

Scleroderma



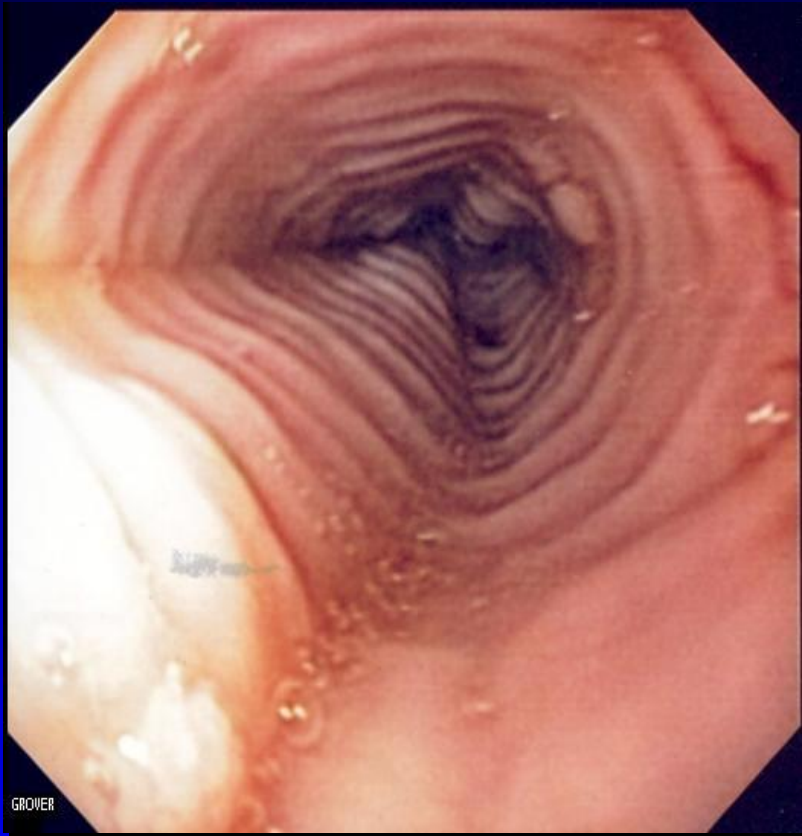
- Dilated esophagus
- Ineffective peristalsis
- Low LES pressure
- Severe GERD

Eosinophilic Esophagitis

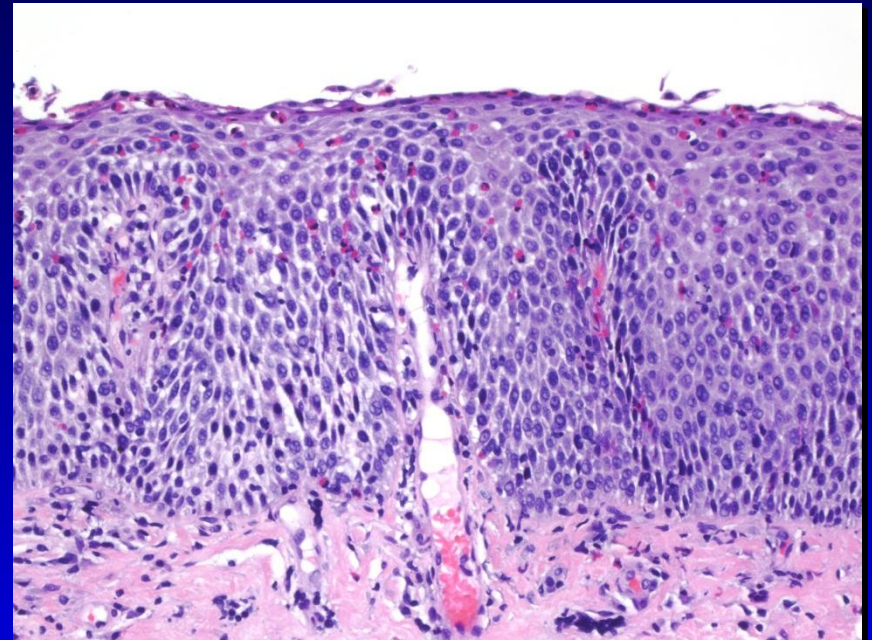
- Prevalence 1:1000 with a predilection for white males, incidence is increasing
- Symptoms: dysphagia, food impaction, atypical chest pain, heartburn, particularly heartburn that is refractory to PPI therapy.
- An atopic history of food allergy, asthma, eczema, or allergic rhinitis is present in the majority of patients
- EoE is an allergic disorder induced by antigen sensitization in susceptible individuals.
 - dietary allergens
 - aeroallergens
- The natural history of the disorder is uncertain

Eosinophilic Esophagitis

Endoscopy: multiple esophageal rings, linear furrows, and punctate exudates



Histology: increased eosinophils in the esophageal mucosa (>15 per high-power field)



Eosinophilic Esophagitis

- **Complications: food impaction and esophageal perforation**
- **Treatment:**
 - **Dietary restrictions**
 - **PPIs**
 - **Systemic or topical (fluticasone) glucocorticoids**
 - **Montelukast**
 - **Immunomodulators**
 - **Endoscopic dilatation of strictures (increased risk of esophageal mural disruption and perforation!)**

Infectious Esophagitis

- **Common infections in Immunocompromized pts (organ transplantation, chronic inflammatory diseases, chemotherapy, AIDS)**
 - **Candida species**
 - **Herpesvirus**
 - **CMV**
- **Nonimmunocompromised pts: herpes simplex and Candida albicans are the most common pathogens**
- ***Odynophagia* is characteristic**
- **Dysphagia, chest pain, and hemorrhage are also common**

Infectious Esophagitis

Candida Esophagitis

- *C. albicans* is the most common.
- Endoscopy with biopsy is diagnostic
- Endoscopic appearance of white plaques with friability
- If oral thrush is present, empirical therapy is appropriate
- Oral fluconazole (200 mg on the first day, followed by 100 mg daily) for 7–14 days is the preferred treatment.
- IV echinocandin or Amphotericin B in severe cases



Infectious Esophagitis

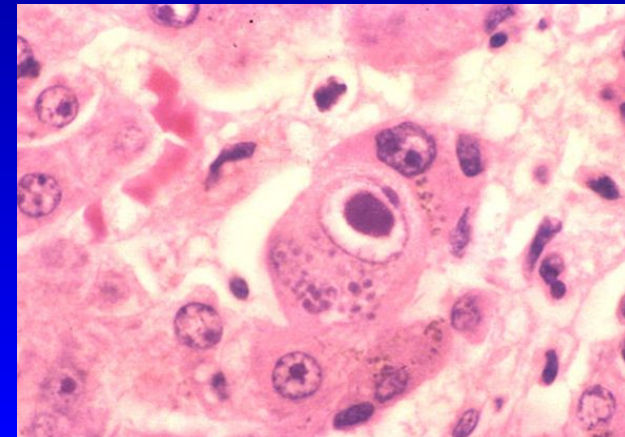
Herpetic Esophagitis

- Herpes simplex virus type 1 or 2 may cause esophagitis
- Endoscopy: vesicles and small, punched-out ulcerations
- Biopsies from the ulcer margins
- Treatment: Acyclovir

CMV esophagitis

- Only in immunocompromised patients, particularly transplant recipients
- Endoscopy: serpiginous ulcers in an otherwise normal mucosa Biopsies of the ulcer bases
- Treatment: Ganciclovir

CMV
esophagitis



Other Types of Esophagitis

- **Radiation esophagitis**
- **Pill-induced esophagitis**
 - doxycycline, tetracycline, minocycline, penicillin, clindamycin, NSAIDs, KCl, Fe, oral bisphosphonates
- **Corrosive esophagitis**

Esophageal Cancer

- Squamous cell carcinoma
- Adenocarcinoma

Esophageal Cancer

- Squamous cell carcinoma risk factors:
 - excess alcohol consumption and/or cigarette smoking
 - ingestion of nitrites
 - smoked opiates
 - fungal toxins in pickled vegetables
 - chronic mucosal injury as extremely hot tea, the ingestion of lye, radiation induced strictures, and chronic achalasia
 - esophageal web in association with glossitis and iron deficiency (Plummer-Vinson syn)

SOME ETIOLOGIC FACTORS BELIEVED TO BE ASSOCIATED WITH ESOPHAGEAL CANCER

Excess alcohol consumption

Cigarette smoking

Other ingested carcinogens

- Nitrates (converted to nitrites)

- Smoked opiates

- Fungal toxins in pickled vegetables

Mucosal damage from physical agents

- Hot tea

- Lye ingestion

- Radiation-induced strictures

- Chronic achalasia

Host susceptibility

- Esophageal web with glossitis and iron deficiency (i.e., Plummer-Vinson or Paterson-Kelly syndrome)

- Congenital hyperkeratosis and pitting of the palms and soles (i.e., tylosis palmaris et plantaris)

? Dietary deficiencies molybdenum, zinc, vitamin A

? Celiac sprue

Chronic gastric reflux (i.e., Barrett's esophagus) for adenocarcinoma

Esophageal Cancer

- incidence of squamous cell cancer decreases over the past 30 years
- incidence of adenocarcinoma has risen dramatically, particularly in white males.
- Adenocarcinomas arise in the distal esophagus in the presence of chronic gastric reflux and gastric metaplasia of the epithelium (Barrett's esophagus)
- Adenocarcinomas arise within dysplastic columnar epithelium in the distal esophagus.
- Adenocarcinomas are >60% of esophageal cancers.

Esophageal Cancer

- Adenocarcinomas arise in the distal esophagus in the presence of chronic gastric reflux and gastric metaplasia of the epithelium (Barrett's esophagus)
- Adenocarcinomas are now >60% of esophageal cancers

Esophageal Cancer

- Location
 - 10% upper third of the esophagus
 - 35% in the middle third
 - 55% in the lower third
- Squamous cell and adenocarcinomas cannot be distinguished radiographically or endoscopically

Clinical features

- Progressive dysphagia (solids)
- Weight loss
- When these symptoms develop, the disease is usually incurable
- The disease most commonly spreads to adjacent and supraclavicular lymph nodes, liver, lungs, pleura, and bone

Esophageal carcinoma

- Endoscopic and cytologic screening for carcinoma in patients with Barrett's esophagus
- Prognosis is poor: < 5% 5 yrs survival
- Treatment: surgery
- radiotherapy
- Chemotherapy
- Palliation with esophageal stents or endoscopic dilatation

Thank you!

תודה רבה!

Спасибо за внимание!