Gastroesophageal Reflux Disease

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GERD: Montreal Definition

"A condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications"

The Montreal definition and classification of GERD 2006

- ≥ 2 heartburn episodes/week
- Adversely affect an individual's well being

From Vakil N et al. Am J Gastroenterol 2006;101(8):1900-20.

Etiology
Factors associated with GERD

More likely to be a cause of GORD ⟷ More likely to be an effect of GORD

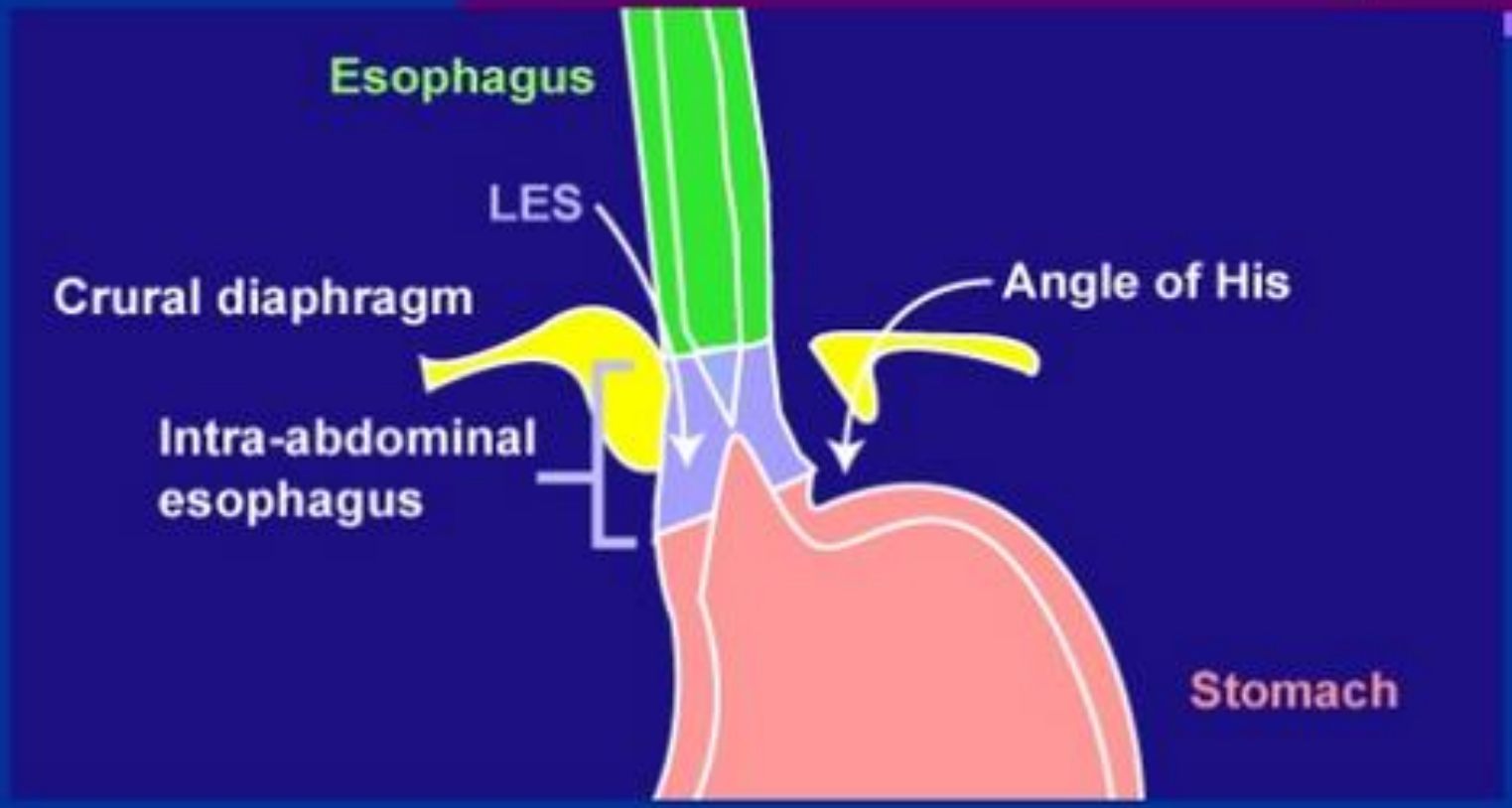
Genetic	Demographic	Behavioural	Comorbid
+ parental family history + GI disease/ symptoms in an immediate relative	+ pregnancy + age + body mass index – educational level	+ smoking + alcohol consumption + drug therapy* – oral contraceptive, – coffee consumption	+ abdominal pain, dysphagia, dyspepsia + asthma + cough + hoarseness + angina + gall bladder disease + laryngitis + otitis + sinusitis + chest pain + anxiety/depression

+ Factor positively associated with GORD in at least one study
– Factor negatively associated with GORD in at least one study
* Drug therapy includes: anticholinergic, NSAID, aspirin, oral steroid nitrate, antirheumatic

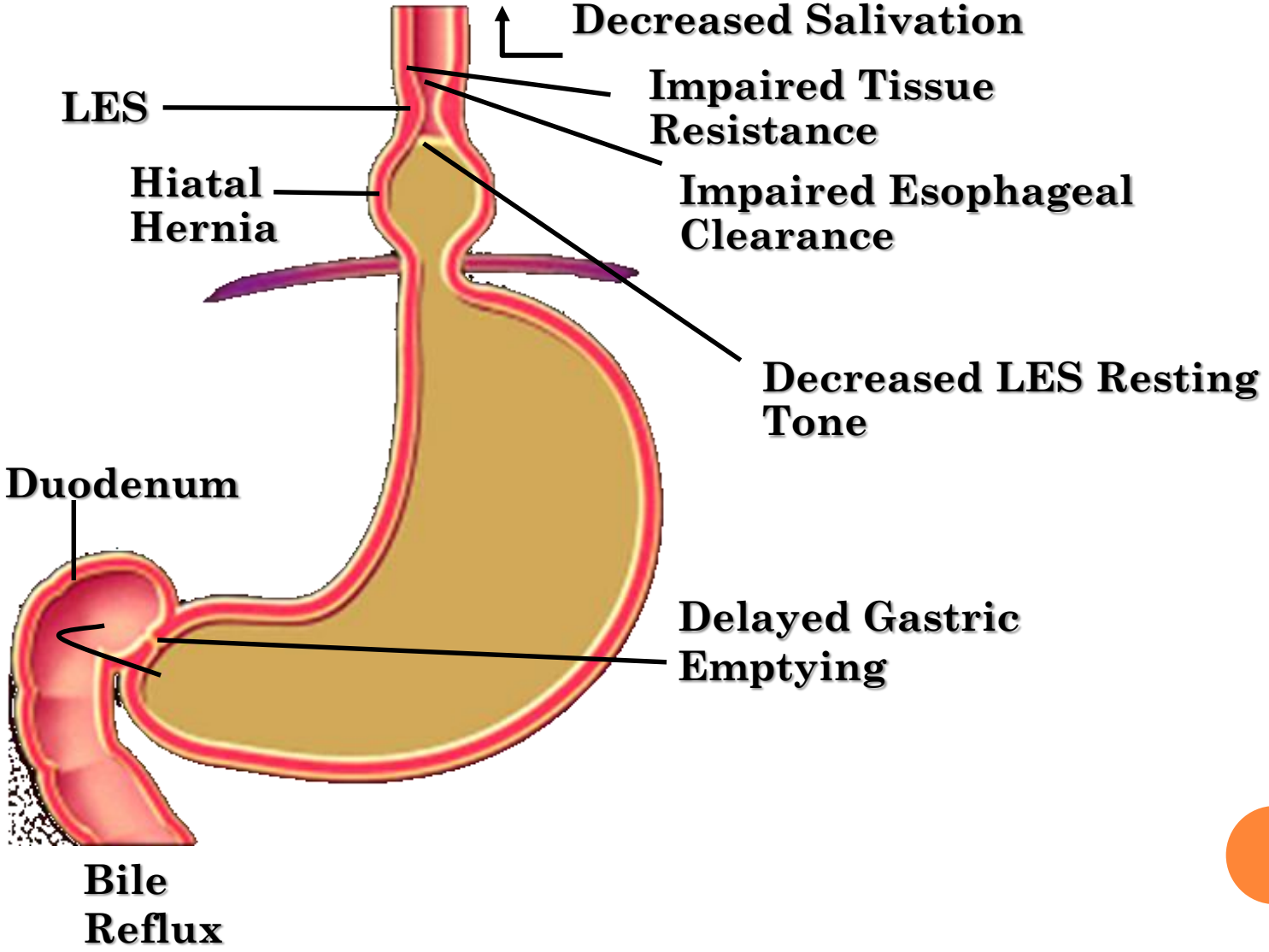
Pathophysiology of GERD

1. Anti-Reflux Barrier
2. Esophageal Contact Time
3. Gastric contents

The Antireflux Barrier



Pathogenesis of GERD



Pathophysiology of GERD
Esophageal Acid Contact

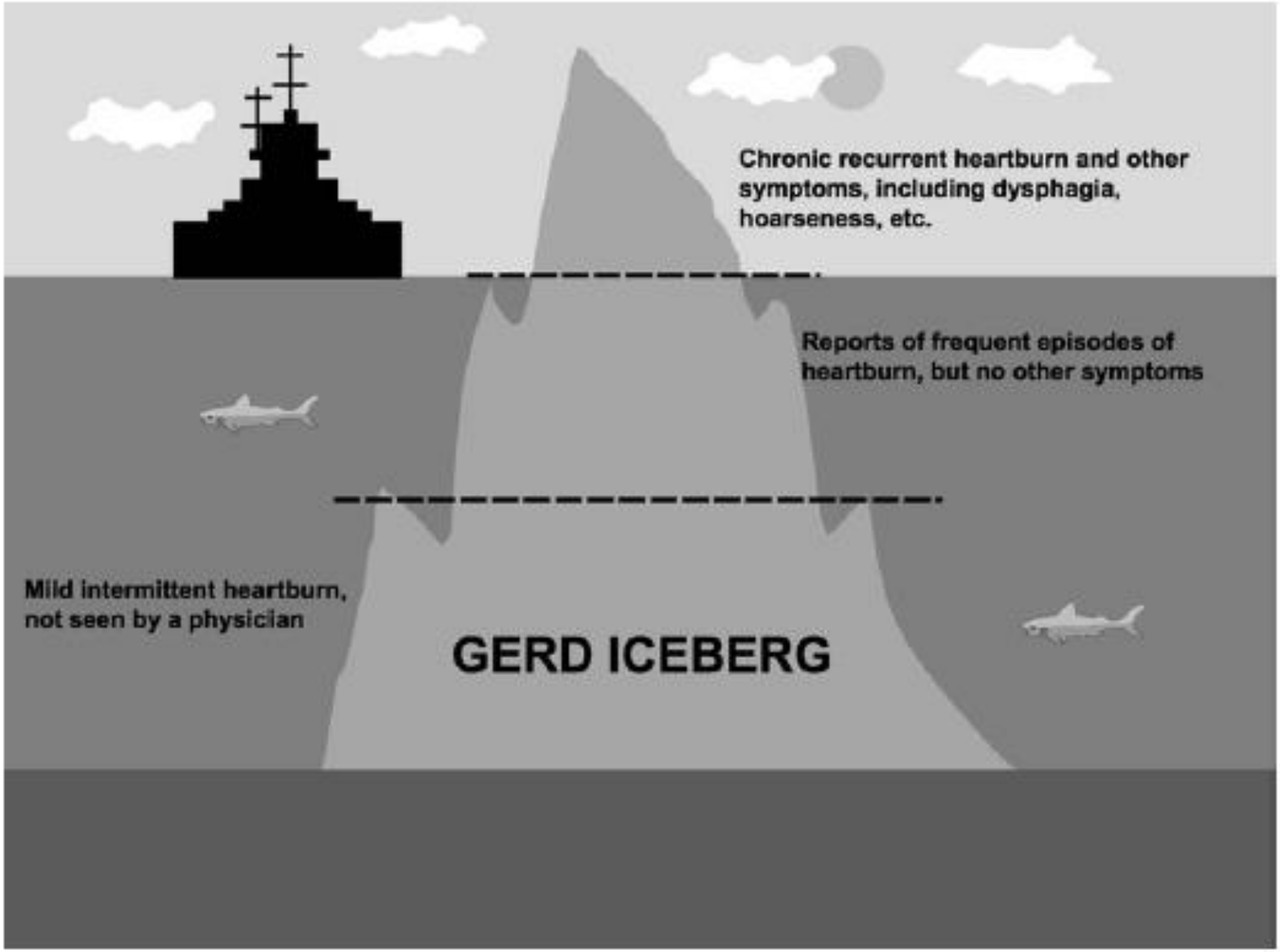
1. Impaired esophageal motility
   - Dysfunctional peristalsis (aging)
   - Poor emptying (hiatal hernia)

2. Salivary function
   - Decreased salivation in sleep
   - Cigarette use <60% saliva HCO_3

Pathophysiology of GERD
Gastric refluxate

- Hydrochloric acid
  - 40-70% Z-E patients have severe esophagitis
  - No difference in basal acid levels in GERD / esophagitis
  - Best treatment results with acid suppression Rx
- Pepsin, bile, pancreatic enzymes
  - Can injure experimental esophagus tissue
  - Effects either limited by acid or too low concentration
  - Role of bile reflux in refractory GERD controversial
- Acid rebound after PPI therapy
- Effect of H. pylori eradication ???

GERD: Clinical features


Chronic recurrent heartburn and other symptoms, including dysphagia, hoarseness, etc.
Reports of frequent episodes of heartburn, but no other symptoms
Mild intermittent heartburn, not seen by a physician
GERD ICEBERG

Typical Symptoms

- Common symptoms most common when pH<4
  - Heartburn
  - Belching and regurgitation
  - Hypersalivation
- May be episodic or nocturnal
- May be aggravated by meals and reclining position

Extraesophageal manifestations of GERD.

Otitis media	Frequent throat clearing
Asthma	Globus
Chronic sinusitis	Tracheobronchitis
Dental erosions	Chronic cough
Aphthous ulcers	Aspiration pneumonia
Halitosis	Pulmonary fibrosis
Pharyngitis	Chronic bronchitis
Laryngitis	Bronchiectasis
Laryngospasm	Noncardiac chest pain
Postnasal drip	Sleep apnea

"Alarm" signs that necessitate further evaluation of GERD.

Dysphagia

Odynophagia

Weight loss

Gastrointestinal (GI) bleeding

Family history of upper GI tract cancer

Anemia

Advanced age

WORKUP

GERD Diagnosis: Menu

- Empiric trial
- Barium esophagram
- Endoscopy
- Manometry
- pH testing
- Impedance

Empiric medical therapy

Guidelines for the Diagnosis and Management of GERD 2013 AGA

- A presumptive diagnosis of GERD can be established in the setting of **typical symptoms of heartburn and regurgitation. Empiric medical therapy** with a proton pump inhibitor (PPI) is recommended in this setting. (Strong recommendation, moderate level of evidence)
- Patients with **non-cardiac chest pain** suspected due to GERD should **have diagnostic evaluation before institution of therapy**. (Conditional recommendation, moderate level of evidence).
- A cardiac cause should be excluded in patients with chest pain before the commencement of a gastrointestinal evaluation (Strong recommendation, low level of evidence)

Barium Esophagram

Guidelines for the Diagnosis and Management of GERD - 2013 AGA

- **Barium radiographs should not be performed to diagnose GERD**

(Strong recommendation, high level of evidence)

Endoscopy Management of GERD: ASGE Guidelines

- GERD despite therapy
- Dysphagia
- Odynophagia
- Unexplained weight loss
- GI bleeding/anemia
- Choking
- Chest pain
- Mass, stricture or ulcer on imaging study
- Recurrent symptoms after antireflux surgery

From Gastrointest Endosc 2007;66:219-24.

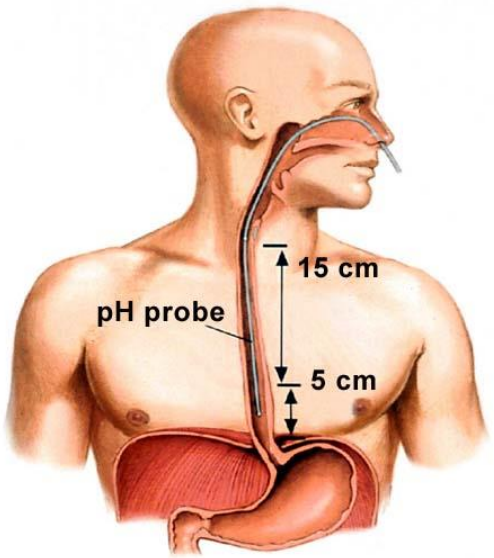
Manometry
AGA Esophageal GERD Practice Guidelines:

- GERD despite therapy
- Negative endoscopy
- Goals:
  - LES location
  - Peristaltic function preoperatively
  - Detection of subtle motility abnormalities
- High resolution manometry superior to conventional manometry for achalasia variants & distal esophageal spasm
- **Esophageal manometry** is recommended for **preoperative evaluation**, but has **no role in the diagnosis of GERD**

From Kahrilas PJ et al. Gastroenterology 2008;135:1383-91.

24-Hour Esophageal pH Monitoring

- Most accurate test for measuring pattern, frequency, and duration of reflux episodes
- Documents correlation between reflux episodes and symptoms
- Sensitivity (77-100%)
  - ***<u>Normal in 25% of esophagitis!</u>***
- Specificity 85-100%
- Most useful when diagnosis still unclear



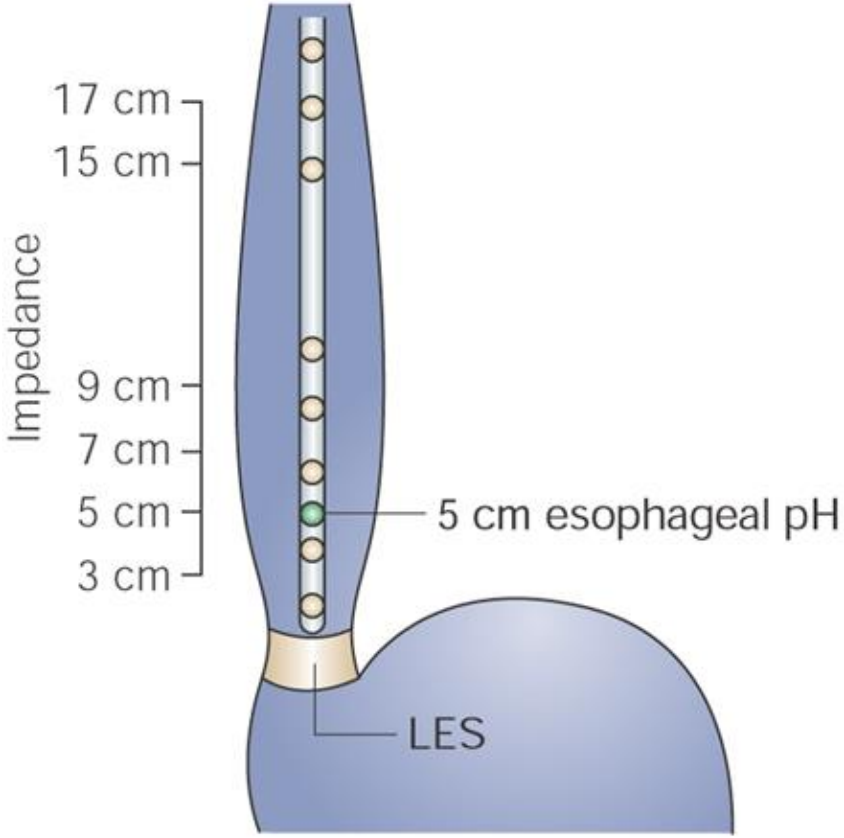
Dent et al. *Gut*. 1999;44(suppl 2):S1-S16.

Impedance

- **In 1991 Silny** was the first to describe multichannel intraluminal impedance (MII), a novel method of detecting intraesophageal bolus movement
- This method is based on measuring the resistance to alternating current (i.e., impedance) of the content of the esophageal lumen
- When a pair of electrodes, separated by an isolator (i.e., catheter), is placed inside the esophagus, the electrical circuit is closed by electrical charges (i.e., ions) present in the esophageal mucosa that surround the catheter
- **The conductivity of the empty esophageal lumen is relatively stable**, with the electrical circuit registering values around 2000 to 4000 ohm

Impedance

Combined multichannel intraluminal impedance and pH catheter.



GI Motility online (May 2006) | doi:10.1038/gimo31

Differential diagnosis

Alternative Diagnosis in GERD

- Coronary artery disease
- Gallstones
- Gastric /esophageal cancer
- Peptic ulcer disease
- Esophageal motility disorders
- Pill induced esophagitis
- Eosinophilic esophagitis

From Kahrilas PJ. N Engl J Med 2008;359:1700-7.

Classification

Montreal Classification of GERD

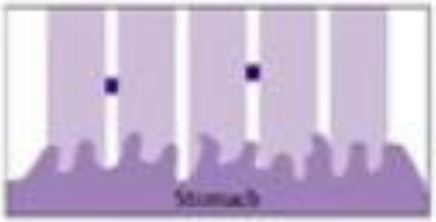
GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications

- Esophageal Syndromes
  - Symptomatic Syndromes
    - 1. Typical Reflux Syndrome
    - 2. Reflux Chest Pain Syndrome
  - Syndromes with Esophageal injury
    - 1. Reflux Esophagitis
    - 2. Reflux Stricture
    - 3. Barrett's Esophagus
    - 4. Esophageal Adenocarcinoma
- Extraesophageal Syndromes
  - Established Associations
    - 1. Reflux Cough Syndrome
    - 2. Reflux Laryngitis Syndrome
    - 3. Reflux Asthma Syndrome
    - 4. Reflux Dental Erosion Syndrome
  - Proposed Associations
    - 1. Pharyngitis
    - 2. Sinusitis
    - 3. Idiopathic Pulmonary Fibrosis
    - 4. Recurrent Otitis Media

From Vakil N et al. Am J Gastroenterol 2006;101:1900-20.

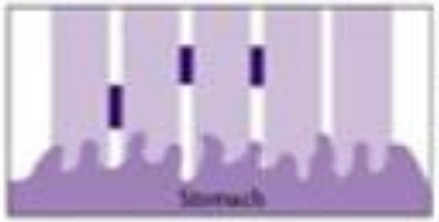
The LA Classification system for the endoscopic assessment of reflux esophagitis

Grade A



One (or more) mucosal break, no longer than 5 mm, that does not extend between the tops of two mucosal folds

Grade B

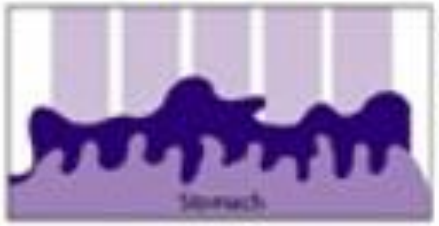


One (or more) mucosal break, more than 5 mm long, that does not extend between the tops of two mucosal folds

Grade C

One (or more) mucosal break that is continuous between the tops of two or more mucosal folds, but which involves less than 75% of the circumference

Grade D



One (or more) mucosal break that involves at least 75% of the esophageal circumference

Treatment

Therapy Goals

- **Alleviate or eliminate symptoms**
- **Diminish the frequency of recurrence and duration of esophageal reflux**
- **Promote healing – if mucosa is injured**
- **Prevent complications**

Guidelines for the Diagnosis and Management of GERD - 2013 AGA

- **Weight loss is recommended for GERD** patients who are **overweight** or have had **recent weight gain**. (Conditional recommendation, moderate level of evidence)

Drug Therapy - Antacids

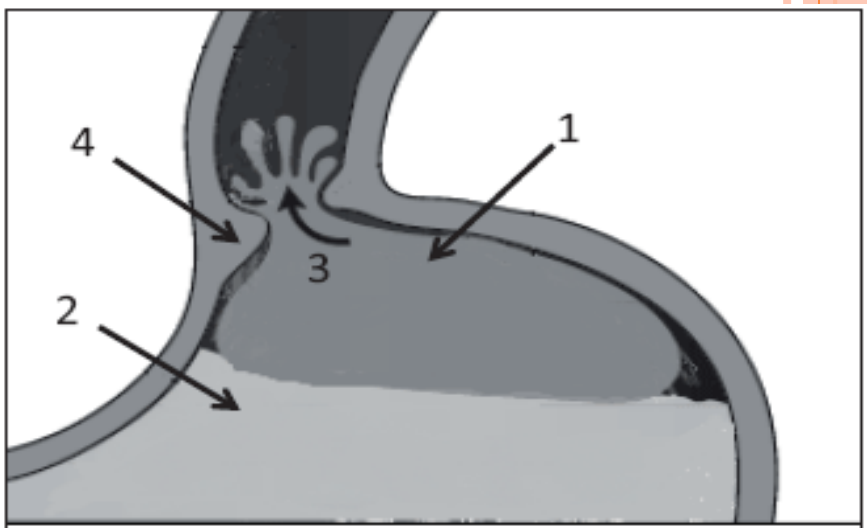
Antacids with or without alginic acid

- Antacids increase LES pressure and do not promote esophageal healing
  - Neutralize gastric acid, causing alkalinization
- Alginic acid (in Gaviscon) forms a highly viscous solution that floats on top of the gastric contents
- Dose as needed – typical action – 1-3 hours
- Not best choice for nocturnal symptoms because pH suppression cannot be maintained

Products: Magnesium salts, aluminum salts, calcium carbonate, and sodium bicarbonate

- Dosing: Initially 40-80 mEq

(no more than 500-600 mEq per 24 hours)



Drug Therapy – H2RA's

	Cimetidine	Famotidine	Nizatidine	Ranitidine
Low dose (qd to bid)	200 mg	10 mg	75 mg	75 mg
Standard dose (bid)	400 mg	20 mg	150 mg	150 mg
High dose	400 mg qid or 800 mg bid	40 mg bid	150 mg qid	150 mg qid

Drug Therapy - PPI's

- Standard dosing
  - Esomeprazole 20 mg qd
  - Rabeprazole 20 mg qd (every day)
  - Pantoprazole 40 mg qd
  - Lansoprazole 15-30 mg qd
  - Omeprazole 20 mg qd
- Timing
  - Best is 30 minutes prior to breakfast

Drug Therapy - Prokinetics

Prokinetic Agents

- Enhances motility of smooth muscle from esophagus through the proximal small bowel
- Accelerates gastric emptying and transit of intestinal contents from duodenum to ileocecal valve
- Results of therapy
  - Improved gastric emptying
  - Enhanced tone of the lower esophageal sphincter
  - Stimulated esophageal peristalsis (cisapride

Drug Therapy – Mucosal Protectants

Sucralfate

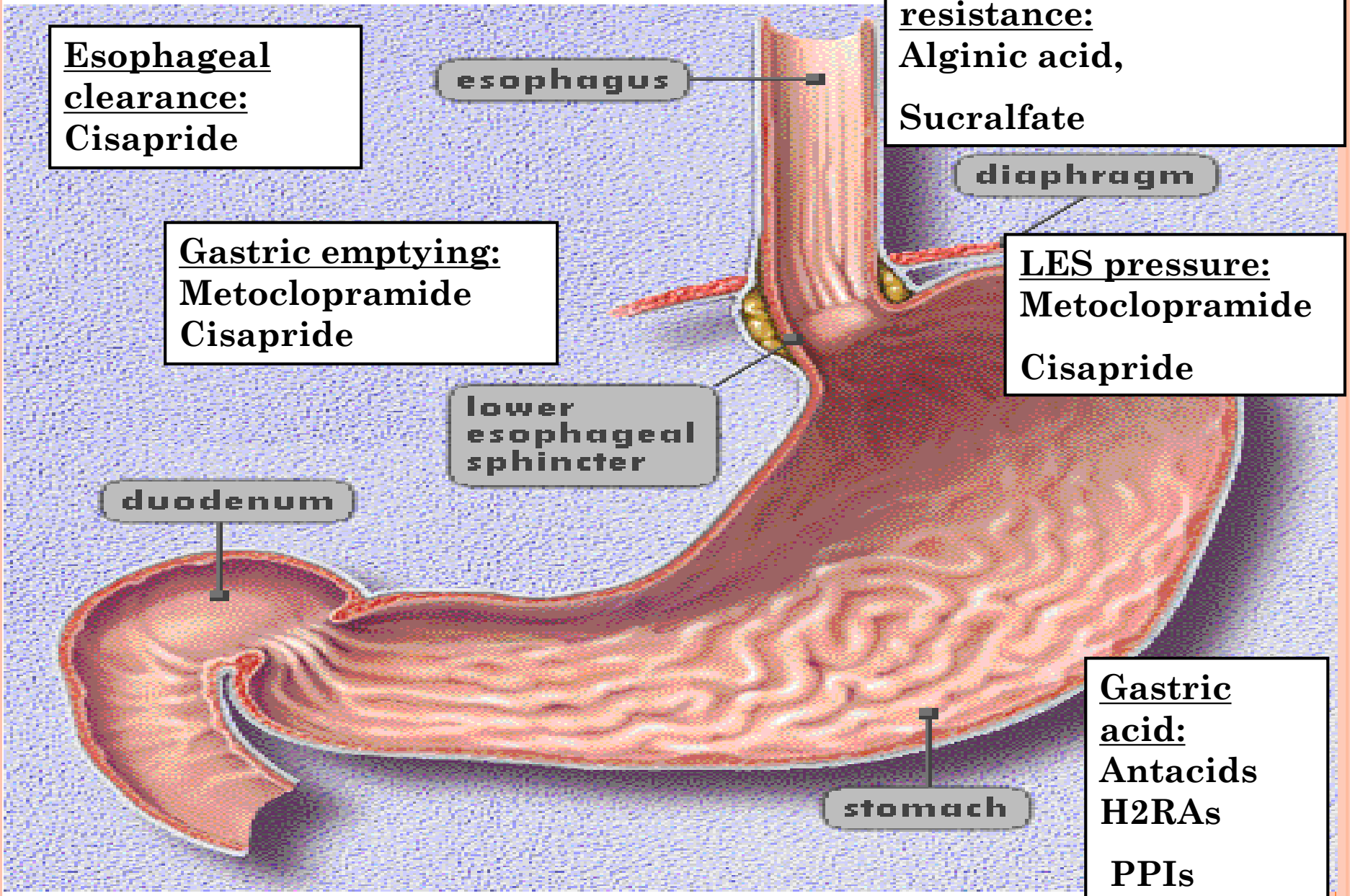
Very limited value in treatment of GERD

Comparisons

Similar healing rate to H2RA in treatment of mild esophagitis

Less effective than H2RAs in refractory esophagitis

Only use in mildest form of GERD



Esophageal clearance:
Cisapride

Esophageal mucosal resistance:
Alginic acid,

Sucralfate

Gastric emptying:
Metoclopramide
Cisapride

LES pressure:
Metoclopramide

Cisapride

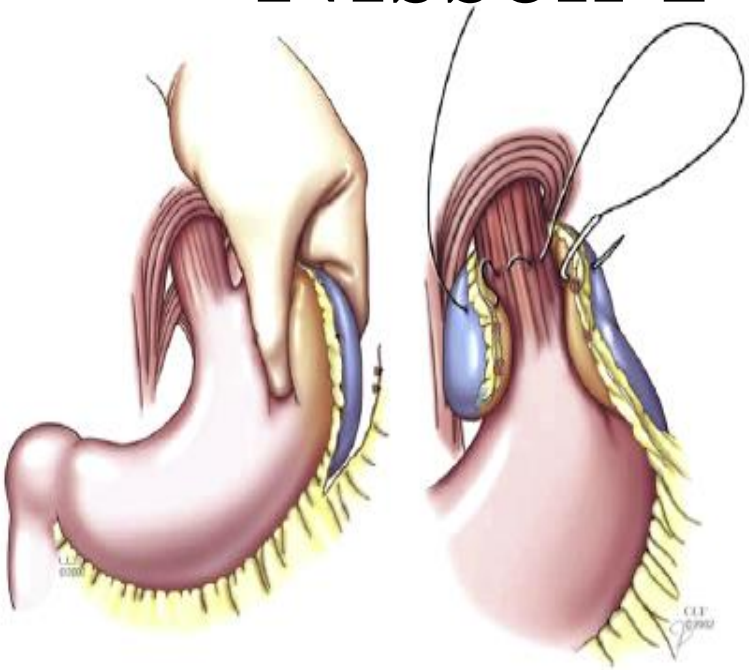
Gastric acid:
Antacids
H2RAs

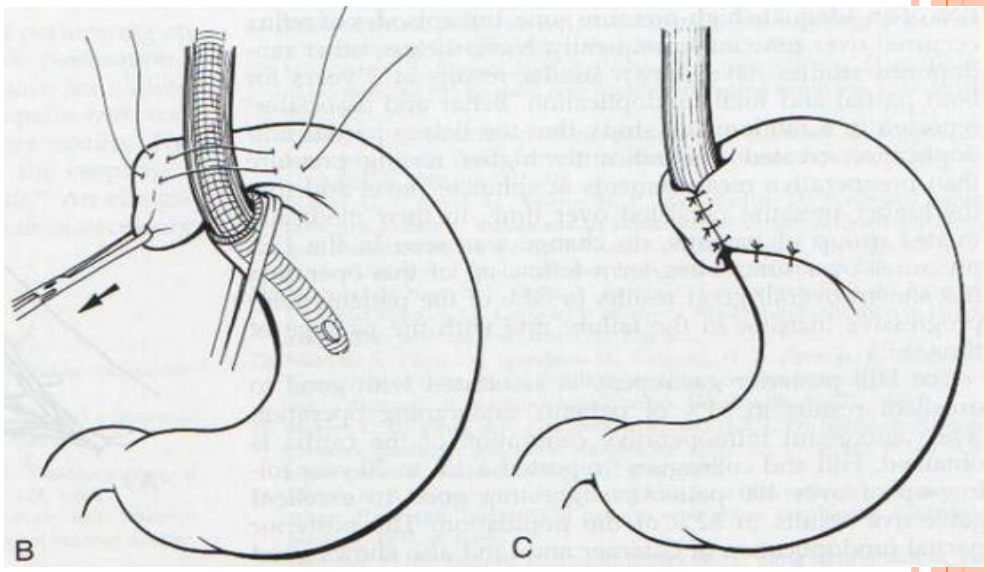
PPIs

http://www.gerd.com/intro/noframe/grossovw.htm

Surgical therapy for GERD

Nissen Fundiplication



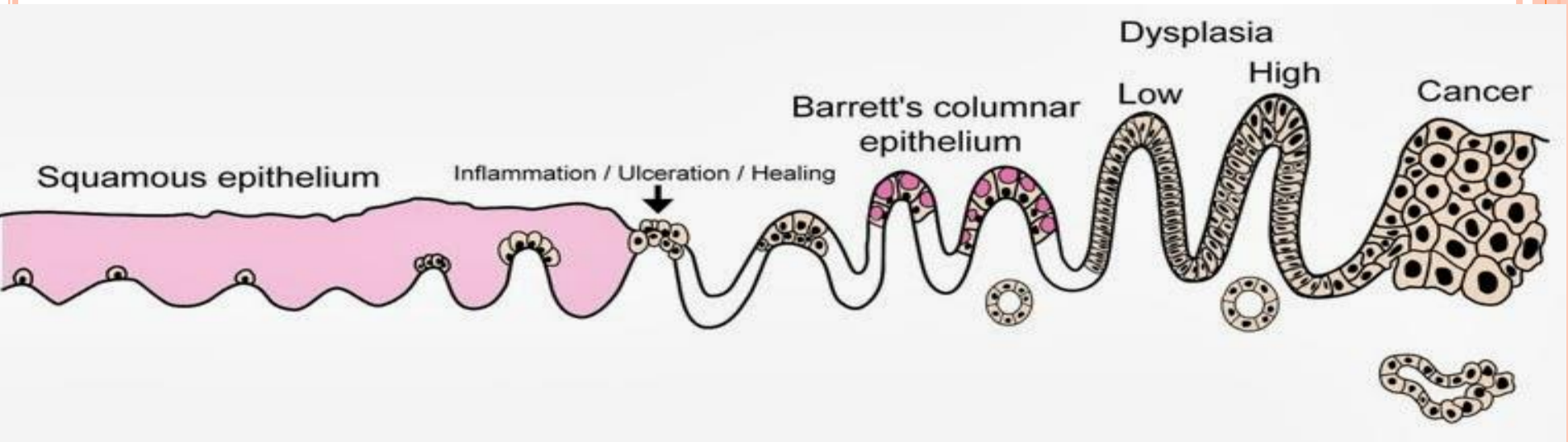


Surgical Reconstruction of Esophageal Hiatus

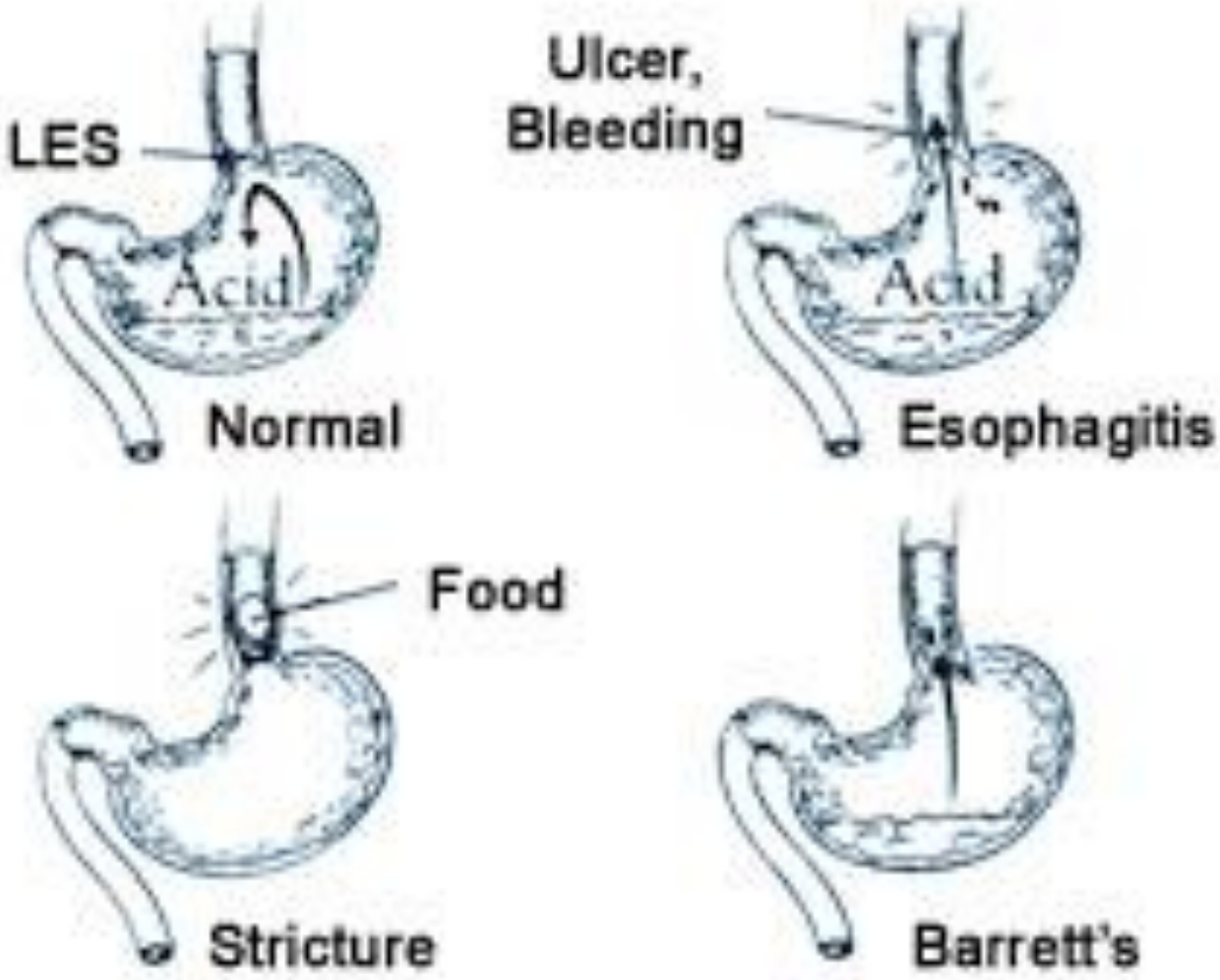
Complications of GERD

Complications

- Esophagitis
- Esophageal strictures and ulcers
- Hemorrhage
- Perforation
- Aspiration
- Development of Barrett's esophagus
- Precipitation of an asthma attack



COMPLICATIONS OF GERD



Barrett's Esophagus

- Barrett's Oesophagus (BO) is a premalignant condition of the oesophagus defined as the presence of metaplastic columnar epithelium,which endoscopically appears as salmon pink mucosa, extending above the gastro-oesophageal junction (GOJ) and into the tubular oesophagus, thereby replacing the stratified squamous epithelium that normally lines the distal oesophagus.

- Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R, Global Consensus Group. *The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus.* Am J Gastroenterol 2006 Aug;101(8):1900-20;
- Shaheen NJ, Richter JE. *Barrett's oesophagus.* Lancet 2009 Mar 7;373(9666):850-61

PRAGUE CRITERIA
For Endoscopically Suspected Esophageal Columnar Metaplasia/Barrett's Esophagus

Developed by the Barrett's Oesophagus Subgroup of the International Working Group for the Classification of Reflux Oesophagitis (IWGCO)

IWGCO — International Working Group for the Classification of Oesophagitis

5 Measure Depth Of Endoscope Insertion* At The **Maximum** Extent Of Suspected Columnar Metaplasia#
= 29 cm

4 Measure Depth Of Endoscope Insertion* At The Most Proximal **Circumferential** Extent Of Suspected Columnar Metaplasia#
= 33 cm

Depth of Endoscope Insertion (cm)

28 30 32 34 36

6 Subtract the Depth of Insertion for **Circumferential** and **Maximum** Extents from the Depth of Endoscope Insertion at the Gastroesophageal Junction†
:36cm - 33cm = **C3**
:36cm - 29cm = **M7**
Prague C3 and M7

3 Look For Displacement Of Squamocolumnar Junction Above Gastroesophageal Junction

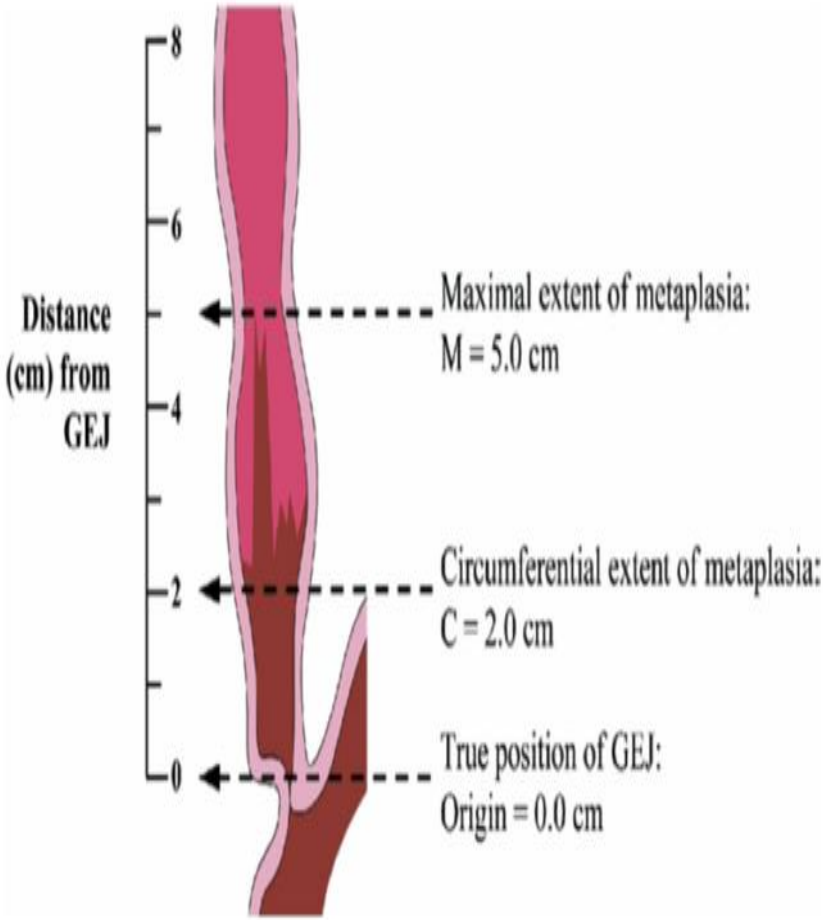
2 Locate Gastroesophageal Junction By Depth Of Endoscope Insertion* At Level Of:
– tops of gastric mucosal folds
– sphincter "pinch"
= 36 cm

1 Ensure Hiatus Hernia Is Recognised By Distinguishing Diaphragmatic Hiatal Impression From Gastroesophageal Junction

Hiatus Hernia

* *To the nearest centimeter*
\# *Squamous and columnar islands do NOT contribute to measures of extent*
† *To the nearest centimeter, except when areas of columnar metaplasia are estimated to be less than 1 cm: report this as <1cm*

Supported by an educational grant from AstraZeneca



Diagrammatic representation of endoscopic Barrett's Oesophagus showing an area classified as C2M5. C: extent of circumferential metaplasia; M: maximal extent of the metaplasia (C plus a distal "tongue" of 3 cm); GEJ: gastroesophageal junction.

Hiatal hernia

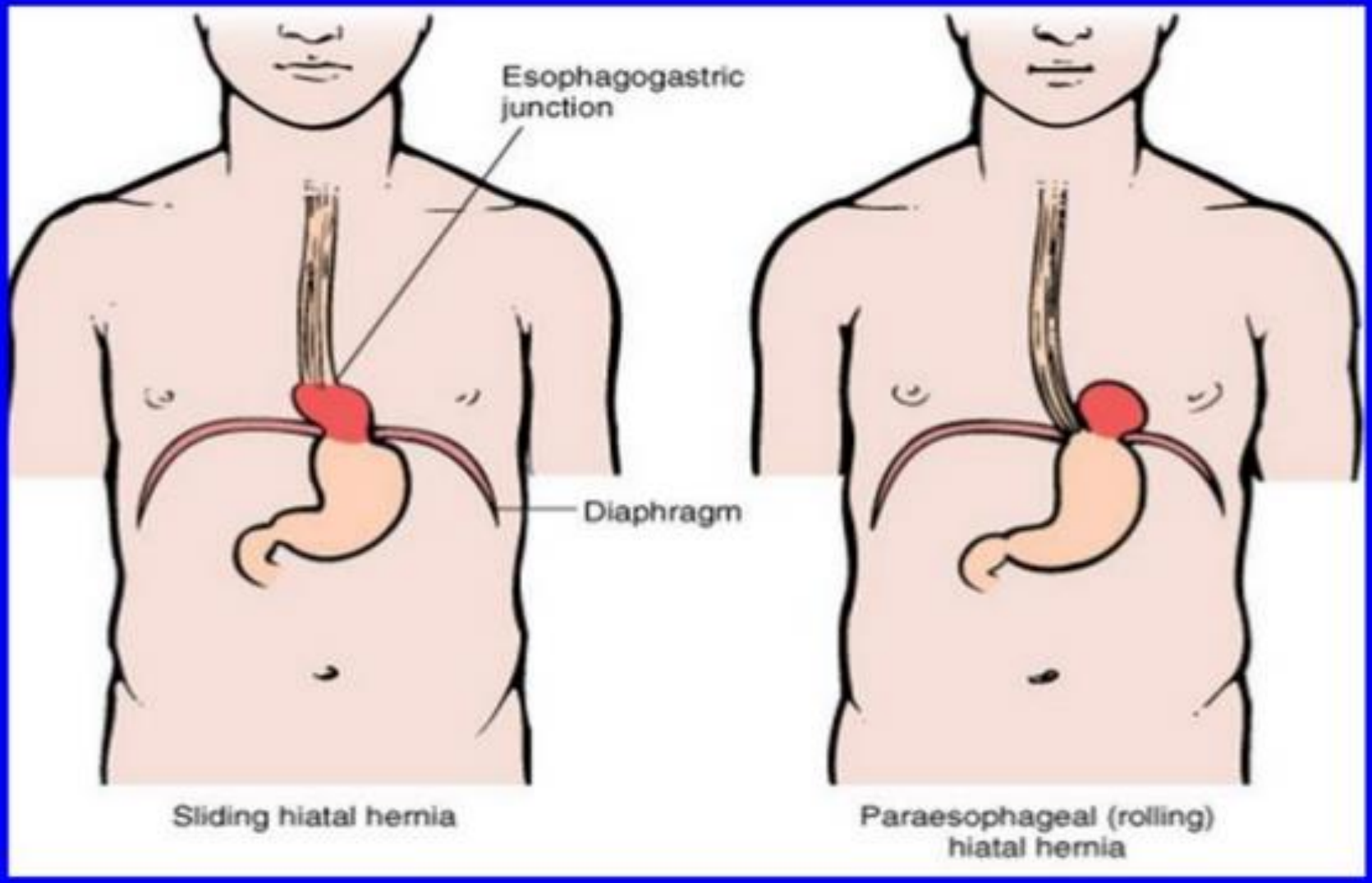
Hiatal Hernia

- Two anatomic patterns are recognized: the **axial, or sliding** hernia and the **nonaxial, or paraesophageal hernia.**

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

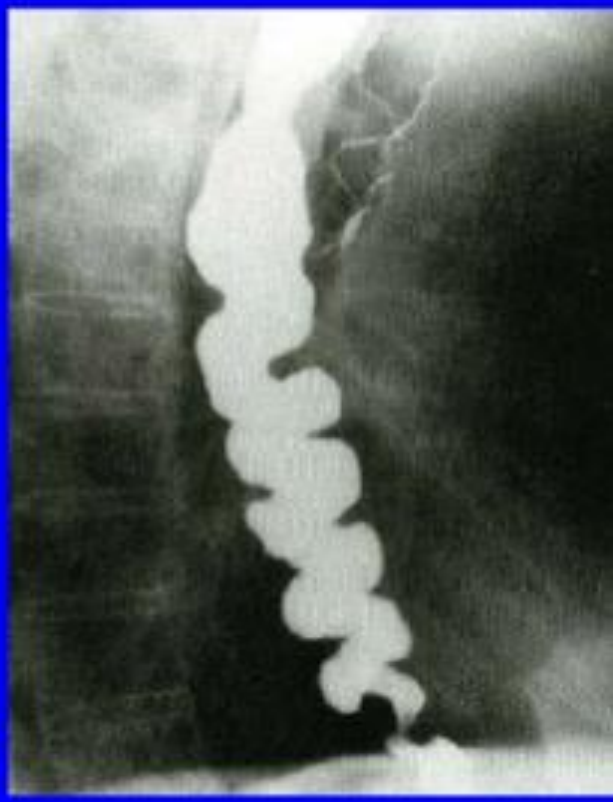
- In **paraesophageal hernias**, a separate portion of the stomach, usually along the greater curvature, enters the thorax through the widened foramen. The cause of this deranged anatomy is obscure.

Comparison of the two forms of esophageal hiatal hernias



Acalasia

Achalasia



- **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.
- **Three major abnormalities in achalasia**:

(1) Aperistalsis (absence of peristalsis)
(2) partial or incomplete relaxation of the lower esophageal sphincter with swallowing
(3) increased resting tone of the lower esophageal sphincter.

ACALASIA

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 sphincte by specific tube through esogh to stomach
- Esophagogastroduodenoscopy
- Upper GI x-ray

Acalasia

Treatment

- The approach to treatment is to reduce the pressure at the lower esophageal sphincter.
- Therapy may involve:
- **Injection with botulinum toxin (Botox).** This may help 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, which can be used to relax the lower esophagus sphincter.
- **Surgery** (called an esophagomyotomy), which may be needed to decrease the pressure in the lower sphincter.
- Wideling (dilation or balloon) of the esophagus at the location of the narrowing (done during esophagogastroduodenoscopy).

Esophagitis

ESOPHAGITIS

- Injury to the esophageal mucosa with subsequent inflammation is a common condition worldwide. The inflammation may have many origins: prolonged gastric intubation, uremia, ingestion of corrosive or irritant substances, and radiation or chemotherapy.

- 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.