UNIVERSITA' DEGLI STUDI DI PERUGIA
DIPARTIMENTO DI MEDICINA E CHIRURGIA

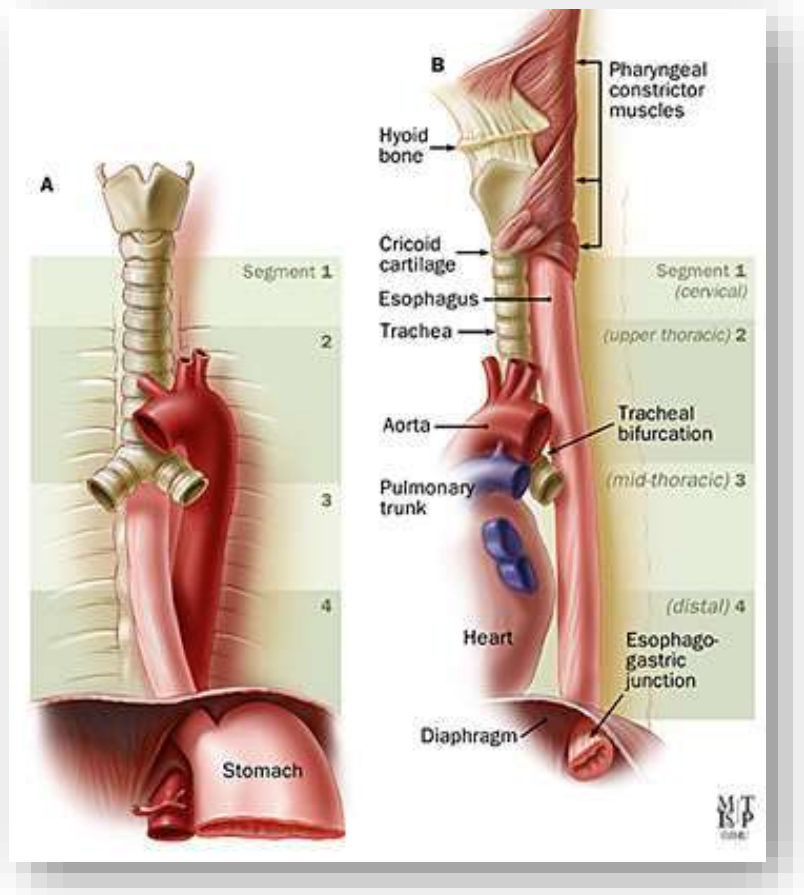
SANU AA 2023/24

Diseases of the esophagus
Anatomy and physiology
Disorders of esophageal motility
Gastroesophageal reflux disease (GERD) and its complications
Esophageal cancer

Prof. Stefano Fiorucci

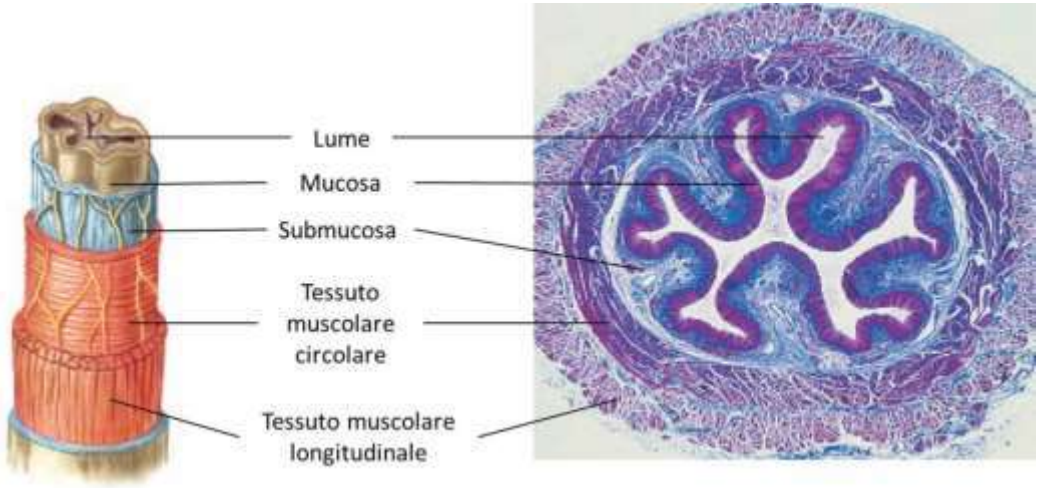
Chair of Gastroenterology - University of Perugia
Director of the Felloship Program in Gastroenterology,
Hepatology and Digestive Endoscopy, University of Perugia

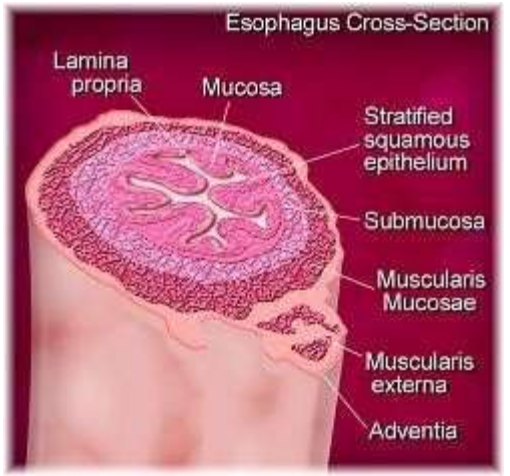
Esophageal anatomy



- The esophagus acts as a conduct for the transport of food from the oral cavity to the stomach.
- The esophagus is a 18- to 26-cm hollow muscular tube with an inner skinlike lining of stratified squamous epithelium.
- Between swallows, the esophagus is collapsed, but the lumen distends up to 2 cm anteroposteriorly and 3 cm laterally to accomodate the swallowed bolus.

Esophageal structure



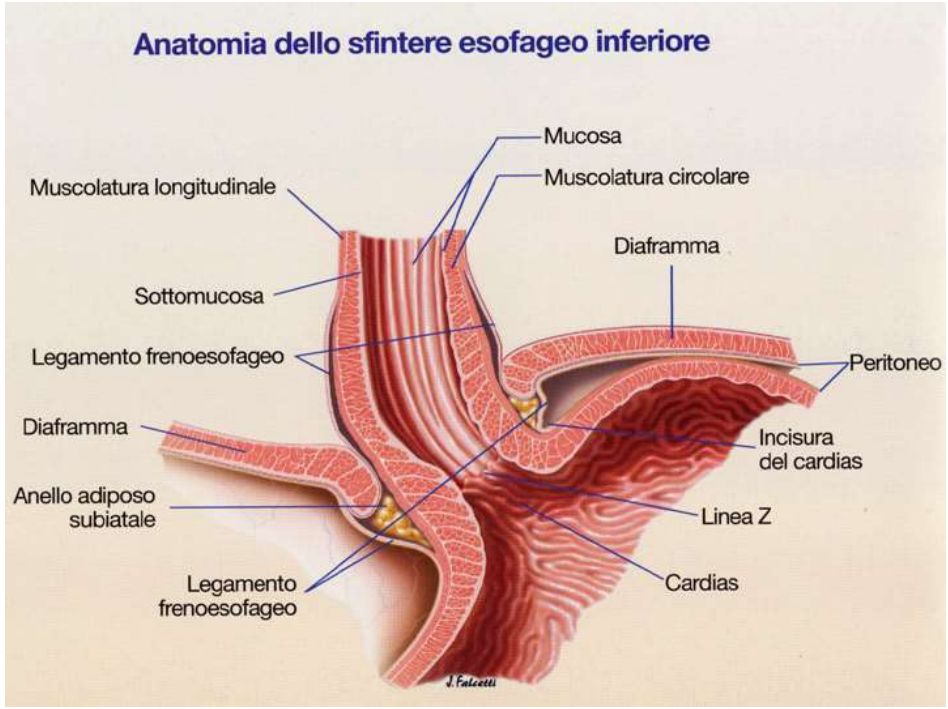


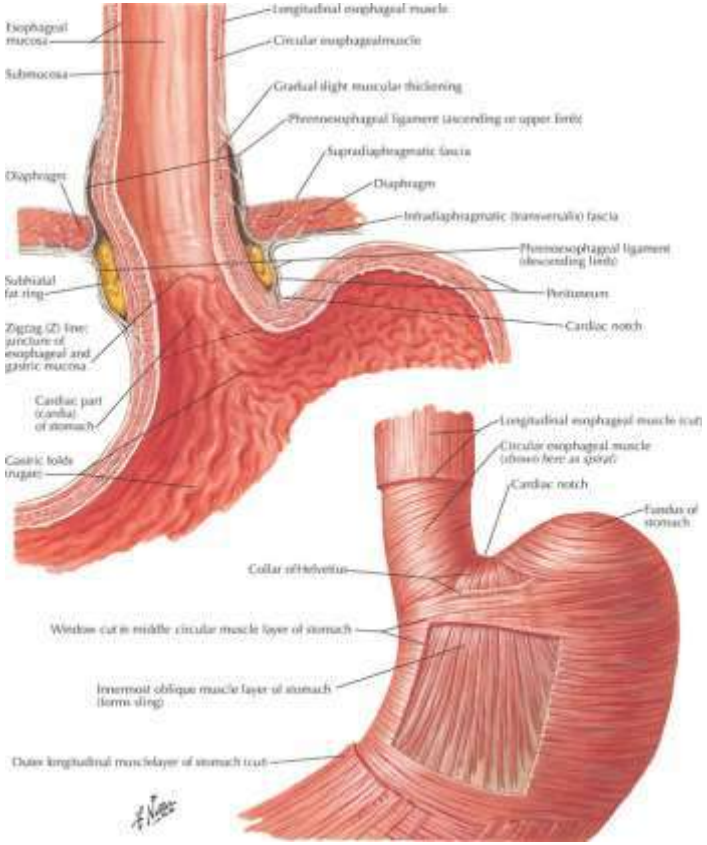
The esophageal wall is composed of four layers:

- innermost mucosa, composed by nonkeratinized stratified squamous epithelium;
- submucosa, that comprises a dense network of connective tissue within which are bood vessels, lymphatic channels, neurons of Meissner plexus and esophageal glands;
- muscularis propria that is responsible for carryng out transport function. The upper 5-33% are composed of skeletal muscle, the distal 33% are composed of smooth muscle and in between is a mixture of both types. The muscular wall separates to inner circular and outer longitudinal layers
- outermost avventitia that is an external fibrous layer that covers the esophagus, connecting it with neighboring structures. It is composed of loose connective tissue and contains small vessels, lymphatic channels, and nerve fibers.

Unlike the remainder of the gastrointestinal tract, esophagus has no serosa.

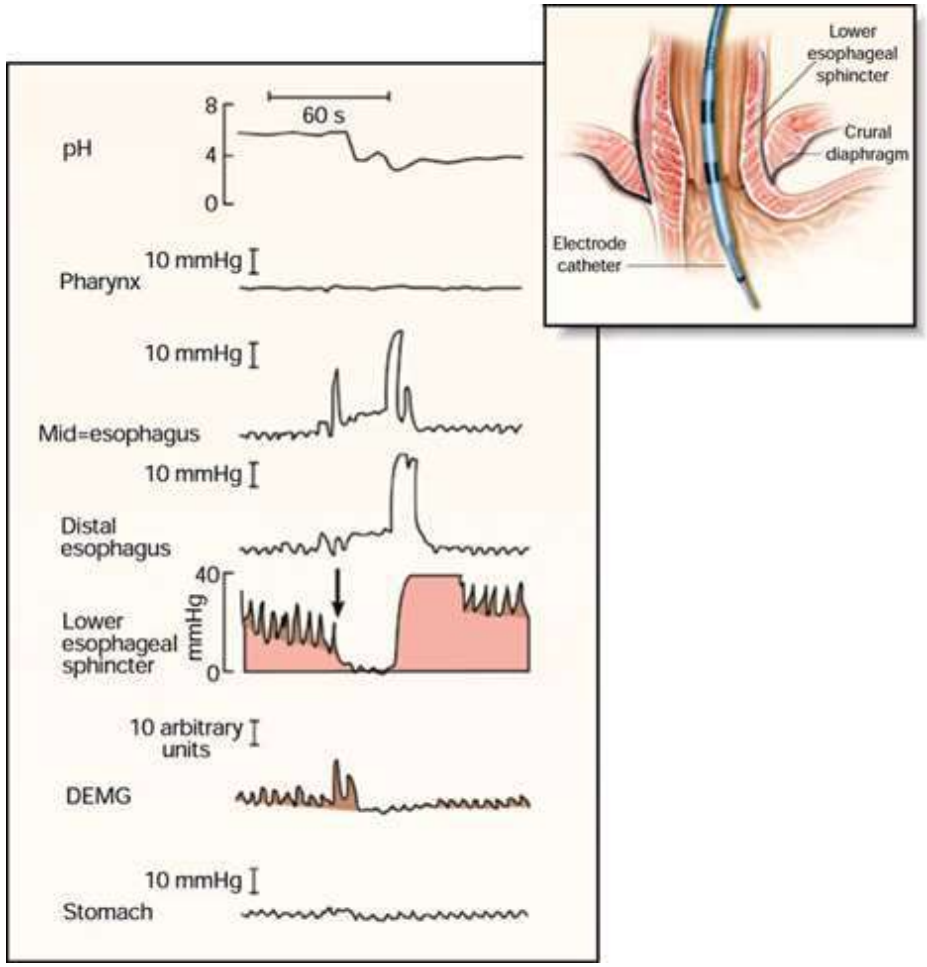
The lower esophageal sphincter (LES)





The esophagogastric junction is the only area of gastrointestinal tract in which contiguous hollows have opposite pressure values: this difference is maintained by a mechanism controlled by LES that permits the presence of a positive intragastric (abdominal) pressure and a negative intraesophageal (thoracic) pressure.

An example of swallow-induced lower esophageal sphincter (LES) relaxation (left) and transient LES relaxation (right)



Esophageal disorders

Symptoms

Pyrosis

Regurgitation

Chest pain

Esophageal dysphagia

Odynophagia

Globus sensation

Water brush

Harrison's Principles of Internal Medicine – 18° Ed. Capter 38-39

Diseases of the esophagus

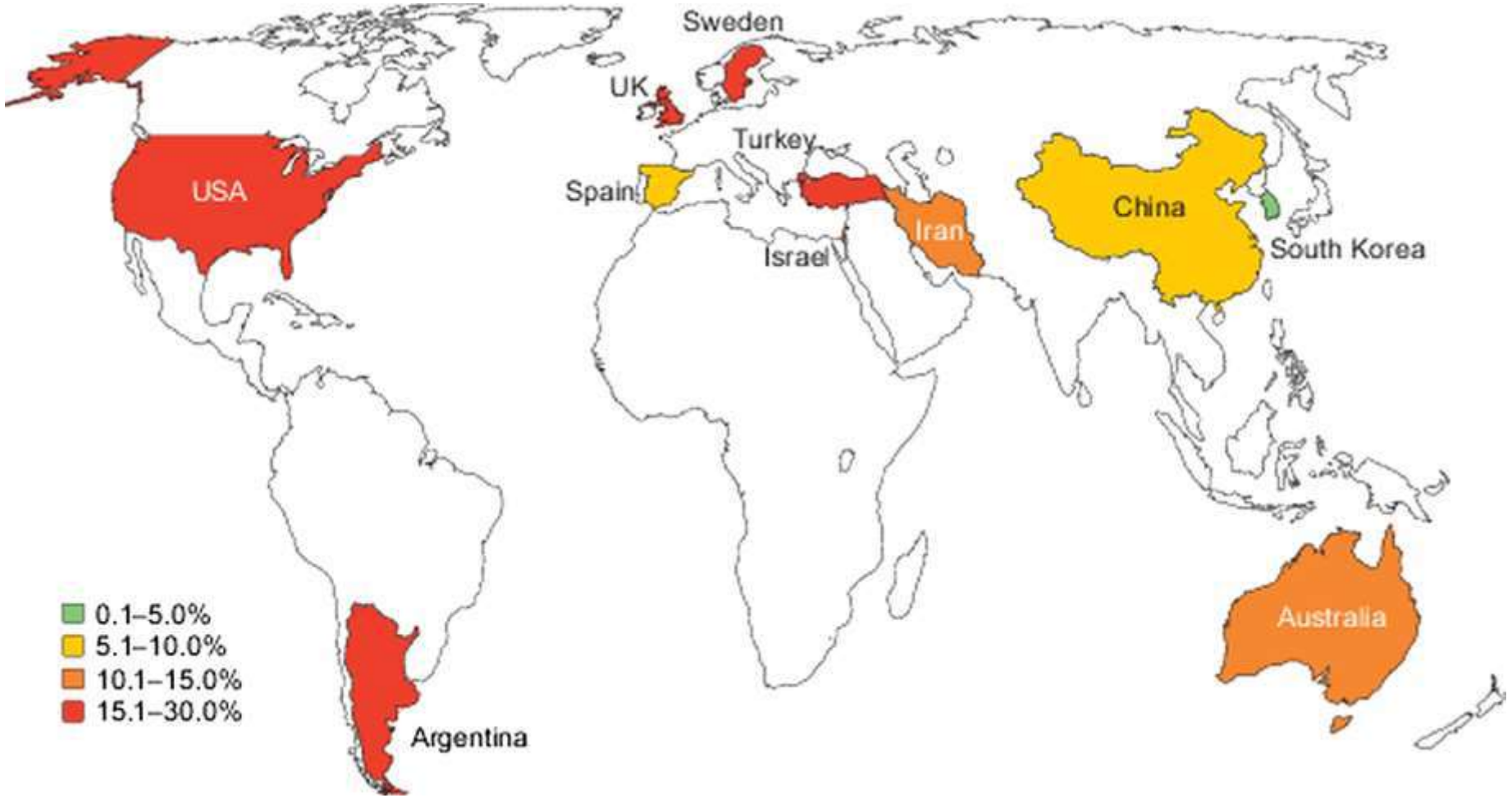
Gastroesophageal reflux disease (GERD)

Prof. Stefano Fiorucci

Gastroesophageal reflux disease (GERD) MRGE

The term Gastro-Esophageal Reflux Disease (GERD) includes any of various conditions resulting from gastroesophageal reflux, ranging in seriousness from mild to life-threatening; principal characteristics are heartburn and regurgitation. When there is damage to the esophageal epithelium, it is known as **reflux esophagitis.**

Gastroesophageal reflux disease (GERD) MRGE



Gastroesophageal reflux disease (GERD) MRGE

Gastroesophageal reflux disease (GERD) is among the most common GI problem seen in primary care settings.

In the United States, 44% of the adult population reported experiencing heartburn at least once a month, 14% weekly, and 7% daily

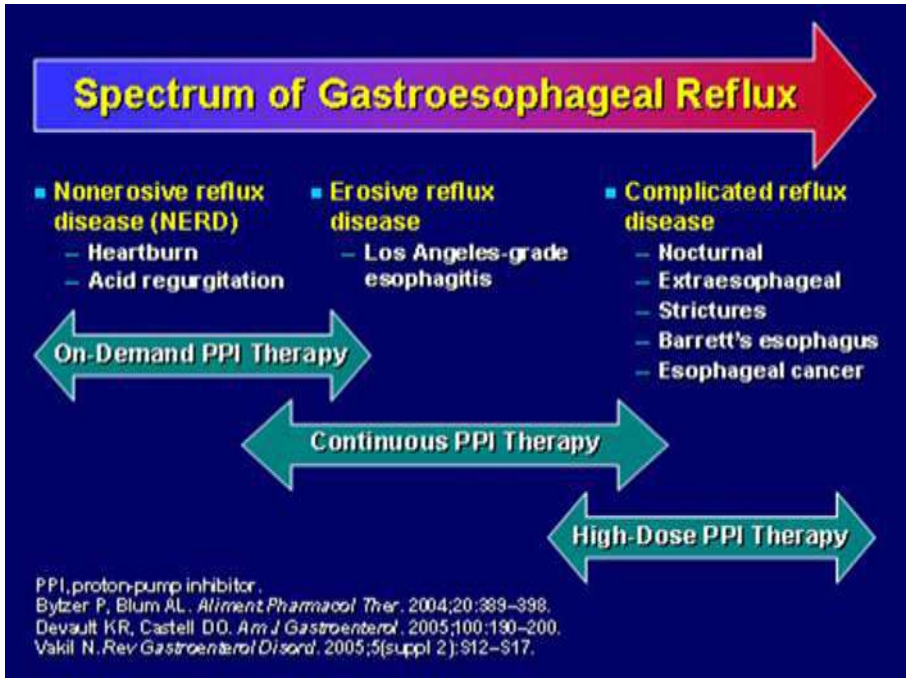
Gastroesophageal reflux disease (GERD) MRGE

GERD has been traditionally approached as a spectrum of disease

On one end of the spectrum, there are those patients with classic symptoms of GERD (heartburn, acid regurgitation) and normal esophageal mucosa (NERD).

As patients progress along the spectrum, patients with GERD symptoms may have advanced grades of erosive esophagitis (again a spectrum of mild to severe).

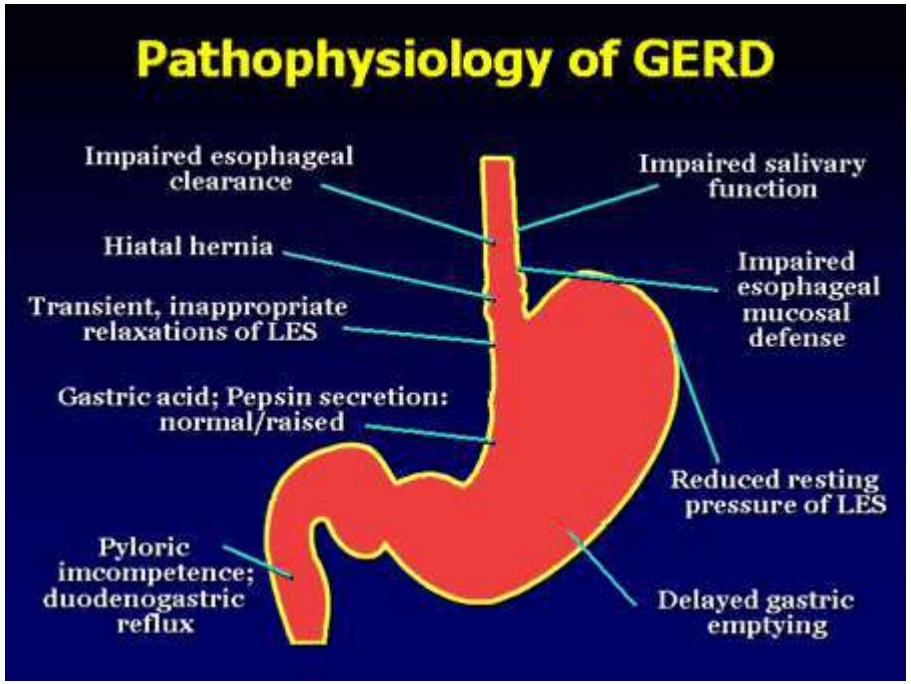
The far end of the spectrum is occupied by patients with GERD complications, such as esophageal ulceration, stricture, Barrett's esophagus, and adenocarcinoma of the esophagus



GERD pathogenesis

The pathophysiology of GERD is multifactorial, including components of the stomach, gastro-oesophageal junction (GEJ), nervous system and the esophagus itself.

There is evidence that LES abnormalities, such as transient LES relaxations (tLESRs) and reduced LES pressure, delayed gastric emptying, suboptimal oesophageal clearance and impaired oesophageal mucosal defence, all contribute.



Gastroesophageal reflux disease (GERD) MRGE

Pathophysiology

GERD is primarily caused by a failure of the lower esophageal sphincter (LES).

Factor that contribute to GERD are

- Hiatal ernia , which increases the likelihood of GERD due to mechanical and motility factors .
- Obesity : increasing body mass index is associated with more severe GERD
- Pregnancy
- Scleroderma and systemic sclerosis , which can feature esophageal dysmotility.
- Drugs, including Ca blockers, Beta agonists, nitrate, steroids, ecc

GERD pathogenesis

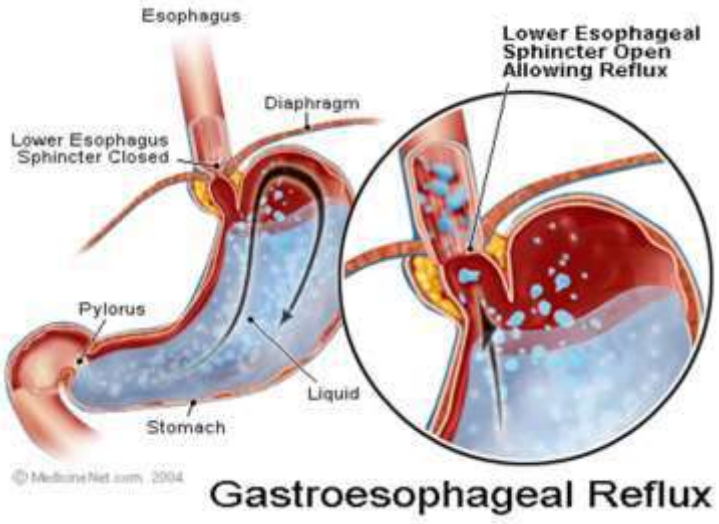
Aggressive factors

Gastro-oesophageal refluxate contains a variety of noxious agents, including acid and pepsin.

Proteolytic enzymes such as pepsin and trypsin have the potential to disrupt epithelial structures by digesting cell surfaces and promoting cell shredding.

In addition, oesophageal refluxate may contain pancreatic secretions and bile as a result of duodeno-gastro-oesophageal reflux (DGER).

Bile acids could disrupt the integrity of the oesophageal mucosa through a detergent effect on cell membranes and cell-to-cell adhesions.



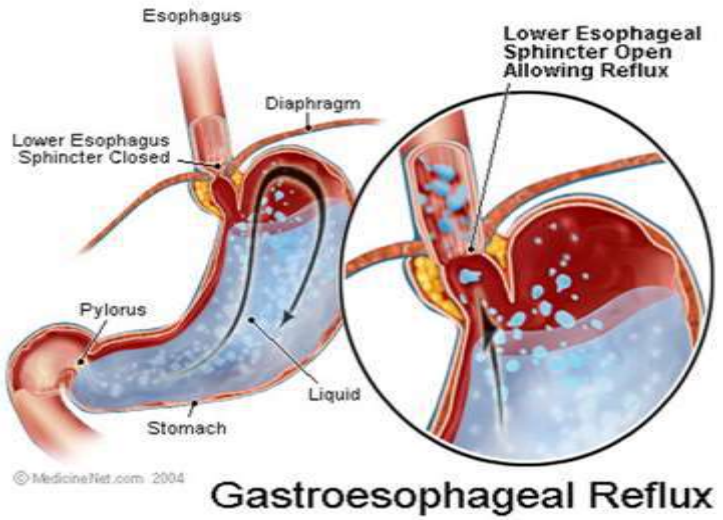
GERD pathogenesis

Aggressive factors

Gastric emptying

In 10–33% of individuals with GERD, gastric emptying is delayed.

A delayed gastric emptying is observed in scleroderma, diabetes, obesity and pregnancy



GERD symptoms

Symptoms of GERD can be divided into two broad categories: typical and atypical symptoms.

Typical symptoms are

heartburn, which is described as a burning sensation in the mid-chest,

regurgitation, which is the sensation of gastric contents coming up into the esophagus/throat.

These symptoms are highly specific

Atypical symptoms are things such as chronic cough, atypical chest pain, which is often confused with chest pain originating from the cardiac region, shortness of breath, asthma, as well as sore throat. These symptoms sometimes are not clearly identified as being due to acid reflux but with the proper testing the final diagnosis can be made.

GERD symptoms

Atypical symptoms

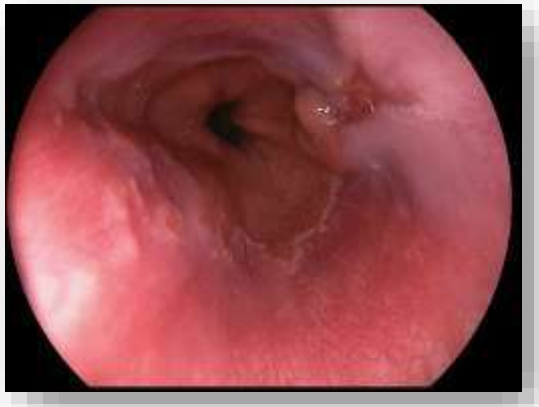
are chronic cough, atypical chest pain, which is often confused with chest pain originating from the cardiac region, asthma, as well as sore throat.

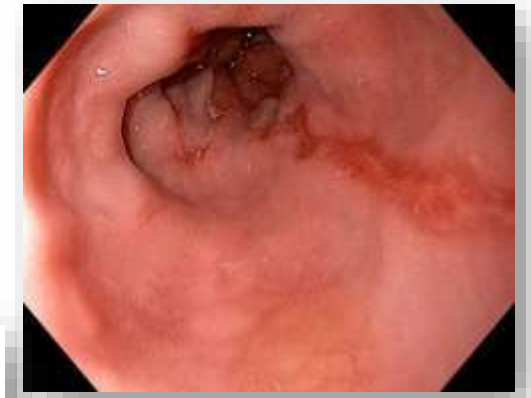
These symptoms sometimes are not clearly identified as being due to acid reflux but with the proper testing the final diagnosis can be made.

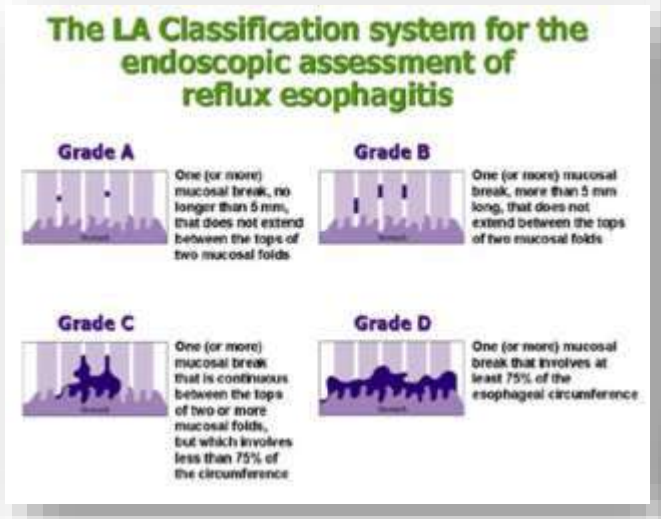
Table 2. Diagnostic testing for GERD and utility of tests

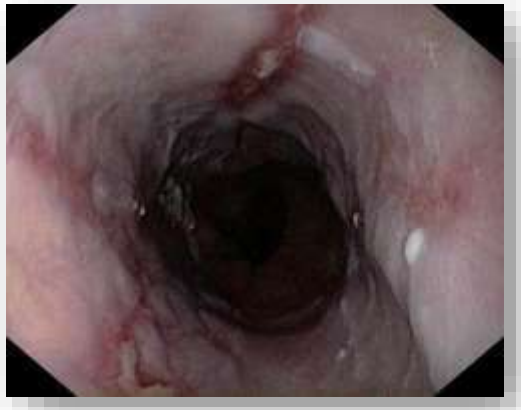
Diagnostic test	Indication	Highest level of evidence	Recommendation
PPI trial	Classic symptoms, no warning signs,	Meta-analysis	Negative trial does not rule out GERD
Barium swallow	Not for GERD diagnosis. Use for evaluation of dysphagia	Case-control	Do not use unless evaluating for complication (stricture, ring)
Endoscopy	Alarm symptoms, screening of high-risk patients, chest pain	Randomized Controlled Trial	Consider early for elderly, those at risk for Barrett's, noncardiac chest pain, patients unresponsive to PPI
Esophageal biopsy	Exclude non-GERD causes for symptoms	Case-Control	Not indicated for diagnosis of GERD
Esophageal manometry	Preoperative evaluation for surgery	Observational	Not recommended for GERD diagnosis. Rule out achalasia/scleroderma-like esophagus preop
Ambulatory reflux monitoring	Preoperatively for non-erosive disease. refractory GERD symptoms, GERD diagnosis in question	Observational	Correlate symptoms with reflux,

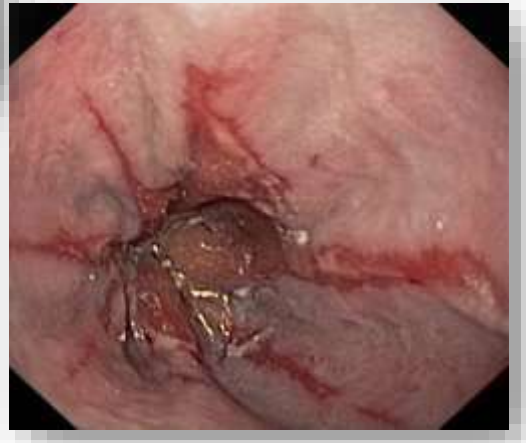
Los Angeles classification of erosive esophagitis











Reflux esophagitis

Therapy

- Lifestyle intervention
- Pharmacological therapy (antisecretive agents)
- Endoscopic and Surgical therapy

Table 3. Efficacy of lifestyle interventions for GERD

Lifestyle intervention	Effect of intervention on GERD parameters	Sources of data	Recommendation
Weight loss	Improvement of GERD symptoms and esophageal pH	Case-Control	Strong recommendation for patients with BMI>25 or patients with recent weight gain
Head of bed elevation	Improved esophageal pH and symptoms	Randomized Controlled Trial	Head of bed elevation with foam wedge or blocks in patients with nocturnal GERD
Avoidance of late evening meals	Improved nocturnal gastric acidity but not symptoms	Case-Control	Avoid eating meals with high fat content within 2–3 h of reclining
Tobacco and alcohol cessation	No change in symptoms or esophageal pH	Case-Control	Not recommended to improve GERD symptoms
Cessation of chocolate, caffeine, spicy foods, citrus, carbonated beverages	No studies performed	No evidence	Not routinely recommended for GERD patients. Selective elimination could be considered if patients note correlation with GERD symptoms and improvement with elimination

BMI, body mass index; GERD, gastroesophageal reflux disease.

The lower esophageal muscle can be weakened by factors other than food. The following recommendations may be helpful in reducing symptoms:

1. Stop using tobacco in all forms. Nicotine weakens the lower esophageal muscle.
2. Avoid chewing gum and hard candy. They increase the amount of swallowed air which, in turn, leads to belching and reflux.
3. Do not lie down immediately after eating. Avoid late evening snacks.
4. Avoid tight clothing and bending over after eating.
5. Eat small, frequent portions of food and snack if needed.
6. Lose weight if overweight. Obesity leads to increased reflux.
7. Elevate the head of the bed six to eight inches to prevent reflux when sleeping. Extra pillows, by themselves, are not very helpful.
8. The following foods aggravate acid reflux, and should be avoided:
    - fatty or fried foods
    - peppermint and spearmint
    - whole milk
    - oils
    - chocolate
    - creamed foods or soups
    - most fast foods
9. The following foods irritate an inflamed lower esophagus and may need to be limited or avoided:
    - citrus fruits and juices (grapefruit, orange, pineapple, tomato)
    - coffee (regular and decaffeinated)
    - caffeinated soft drinks
    - tea
    - other caffeinated beverages
10. Spicy or acidic foods may not be tolerated by some individuals.

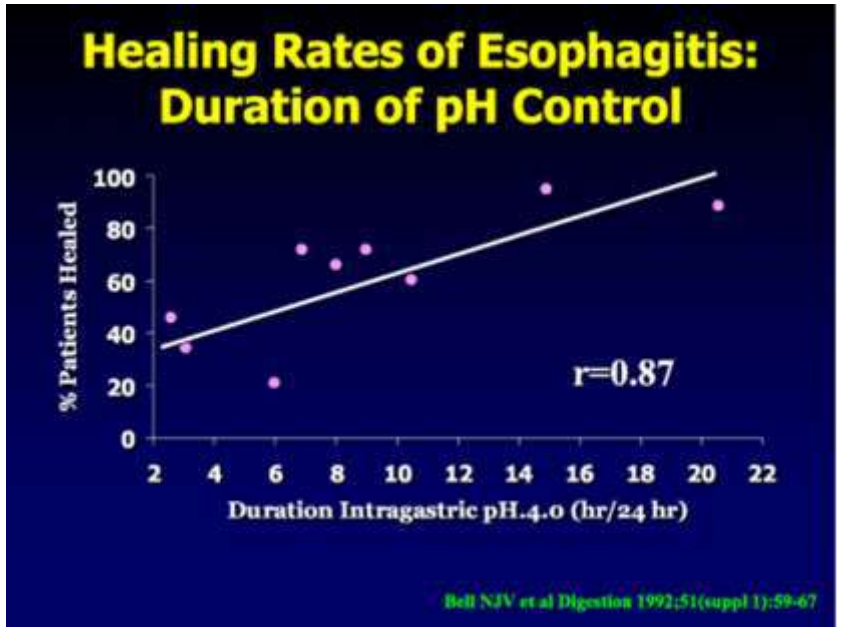
Food Groups		
Group	**Recommend**	**Avoid**
Milk or milk products	skim, 1% or 2% low-fat milk; low-fat or fat-free yogurt	whole milk (4%), chocolate milk
Vegetables	all other vegetables	fried or creamy style vegetables*, tomatoes
Fruits	apples, berries, melons, bananas, peaches, pears	citrus*: such as oranges, grapefruit, pineapple
Breads & grains	all those made with low-fat content	any prepared with whole milk or high-fat I
Meat, meat substitutes	low-fat meat, chicken, fish, turkey	cold cuts, sausage, bacon, fatty meat, chicken fat/skin
Fat, oils	none or small amounts	all animal or vegetable oils
Sweets & desserts	all itmes made with no or low fat (less than or equal to 3 g fat/serving)	chocolate, desserts made with oils and/or fats
Beverages	decaffeinated, non-mint herbal tea; juices (except citrus); water	alcohol, coffee (regular or decaffeinated), carbonated beverages, tea, mint tea
Soups	fat-free or low-fat based	chicken, beef, milk, or cream-based soups
***Individually determined**		

Reflux esophagitis

Therapy

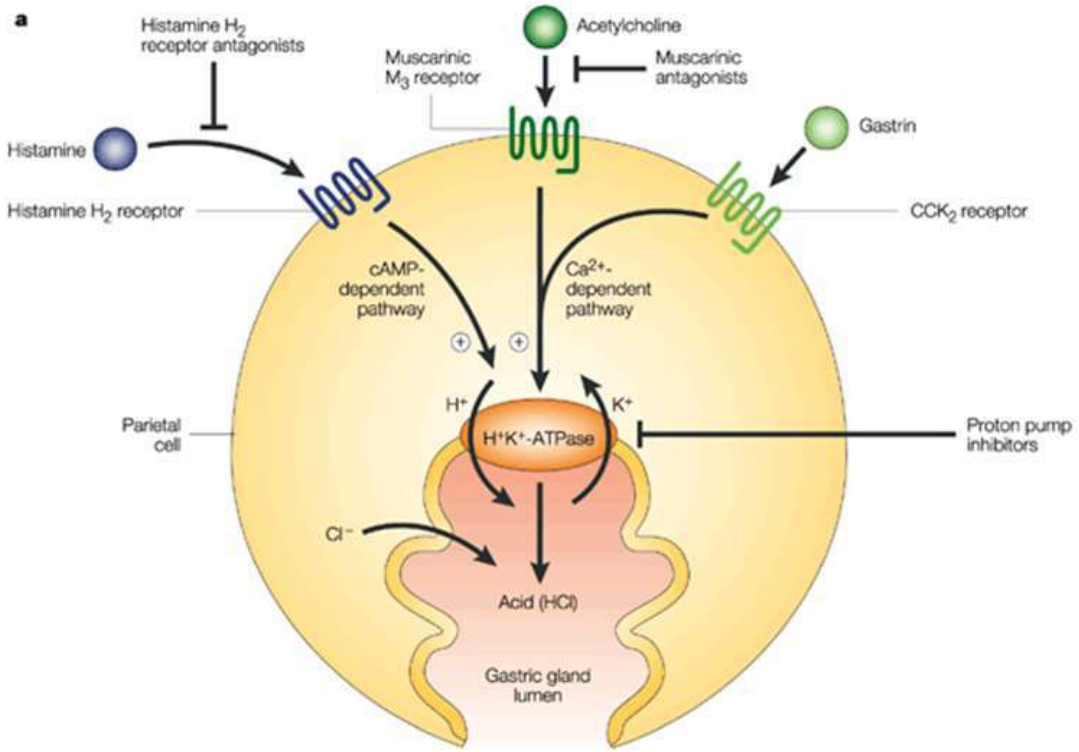
- Lifestyle intervention
- Pharmacological therapy (antisecretive agents)
- Surgical therapy

Reflux esophagitis Antisecretory therapy



$$pH = - \log H^{+}$$

Antisecretory drugs



Pharmacological classes

1. Antimuscarinic agents

2. H_2 Receptors antagonists

3. Proton pump Inhibitors (PPI)

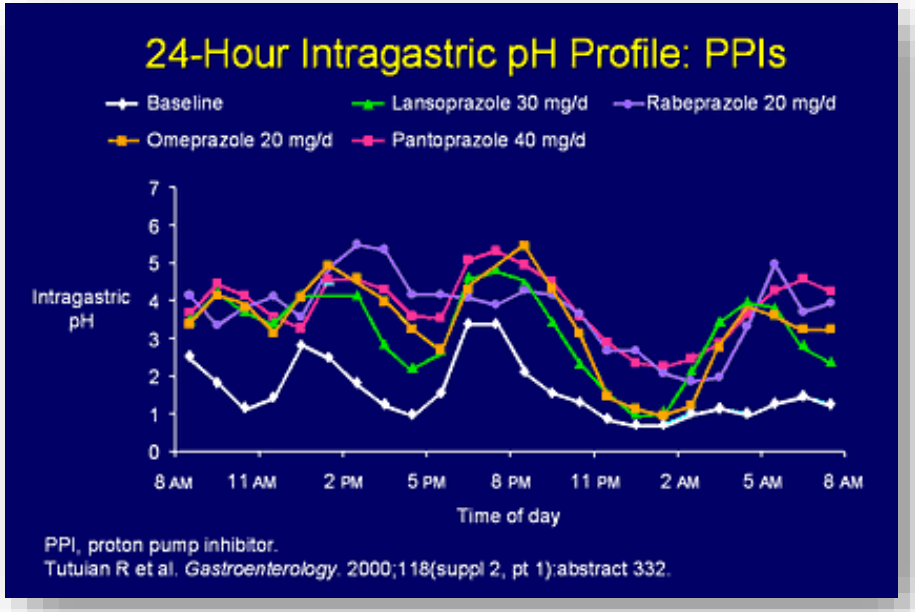
PK of antisecretory agents

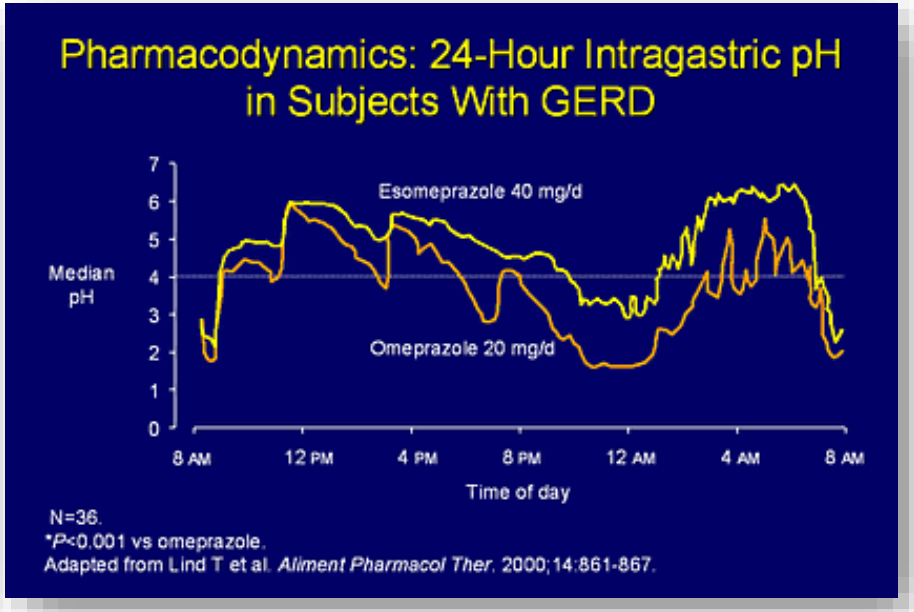
Lenght of action (gastric pH>4)

H_2R antagonists : 8-10 hr
PPI: 12-14 hr

Potency (% acid inhibition /24hr)
H_2R antagonists : 50%
PPI: >80%

Reflux esophagitis: antisecretory therapy



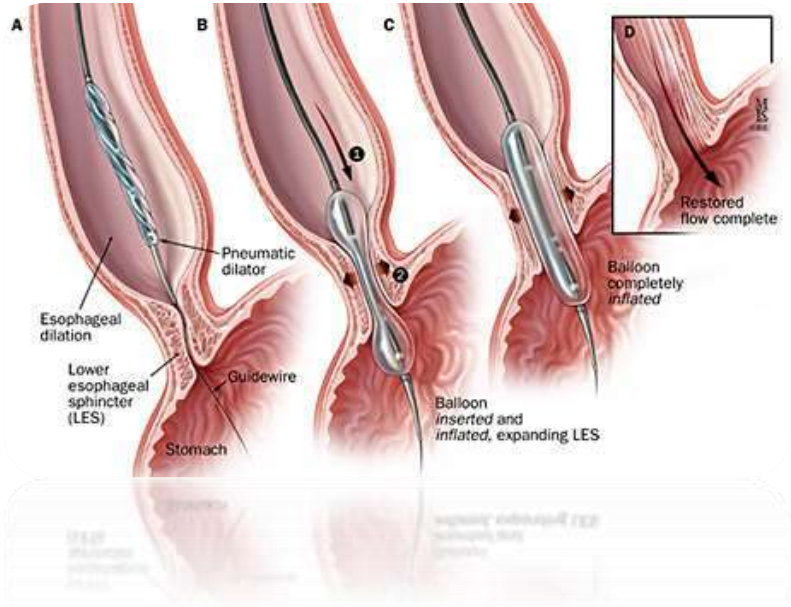


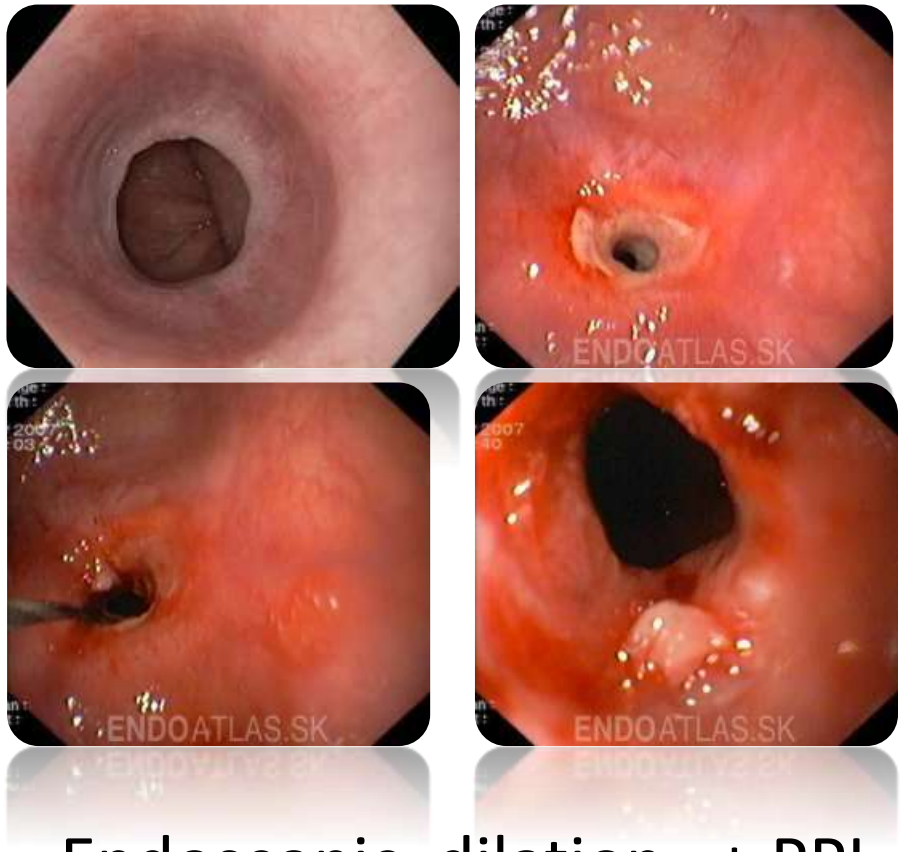
GERD complications

- Stricture
- Hemorrage
- Metaplasia (Barrett’s esophagus)

GERD complications

- **Stricture**



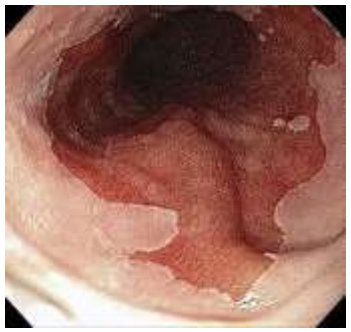


Endoscopic dilation + PPI

GERD complications

It is characterized by the replacement of the normal stratified squamous epithelium_lining of the esophagus by simple columnar epithelium with goblet cells (which are usually found lower in the gastrointestinal tract).

Norman Barrett
(1903-1979)



Barrett’s esophagus

- Barrett's esophagus prevalence was estimated to affect 3.3 million adults over 50 years of age in the United States
- The prevalence of Barrett's esophagus in the adult population is **0.4% to 1.3%,** although recent reports from gastroenterology-selected populations suggest a higher prevalence

Cameron AJ, Zinsmeister AR, Ballard DJ, et al. Prevalence of columnar-lined (Barrett’s) esophagus. Comparison of population-based clinical and autopsy findings. Gastroenterology 1990;

“Study provides first estimate of U.S. population affected by Barrett’s esophagus.” Gastro.org. 2006. American Gastroenterological Association. Accessed August 2007.

Ronkainen J, Aro P, Storskrubb T, et al. Prevalence of Barrett’s esophagus in the general population: an endoscopic study. Gastroenterology 2005; 129:1825-1831.

Barrett’s esophagus

DEMOGRAPHICS OF BARRETT'S ESOPHAGUS

Barrett's esophagus occurs as a result of chronic, pathologic reflux of gastro-duodenal contents into the esophagus.

The diagnosis is made by **endoscopy with biopsy**. **Histologically, Barrett's esophagus is a metaplastic change** in the distal esophageal lining from the normal squamous epithelium to intestinalized columnar epithelium (intestinal metaplasia or IM).

Barrett's esophagus is classified histologically as either non-dysplastic IM , low-grade dysplasia (IM-LGD) or high-grade dysplasia (IM-HGD)

Barrett’s esophagus

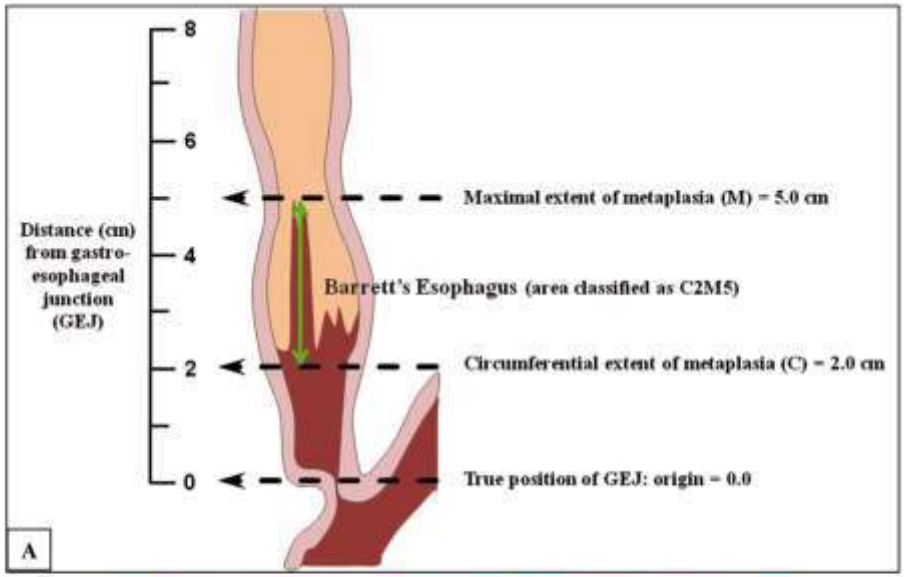
Pathogenesis: GERD

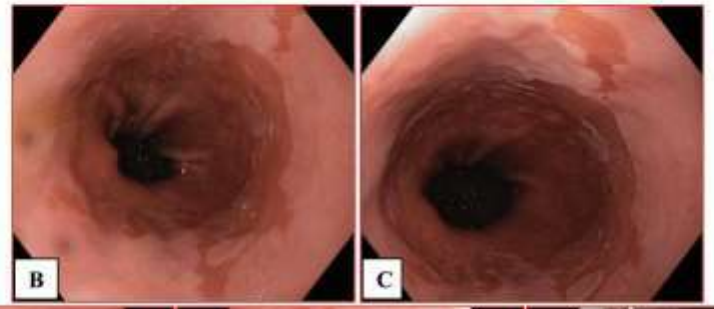
Approximately 13% of Caucasian men over the age of 50, who have chronic reflux, will develop Barrett’s esophagus

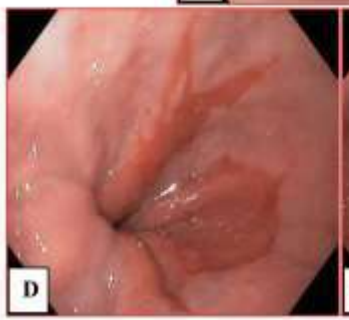
However 25% of patients over 50 years old without GERD symptoms were found to have Barrett's esophagus

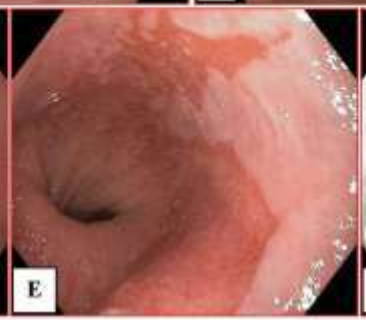
GERD is common in the adult population. Symptoms of GERD, including heartburn, occur monthly in almost 44% of U.S. adults and weekly in 18%

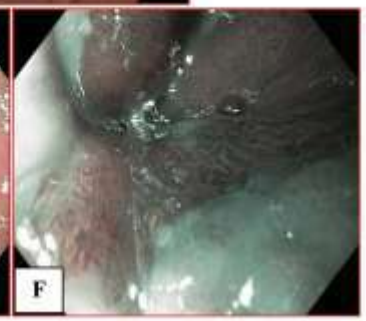
Barrett's esophagus



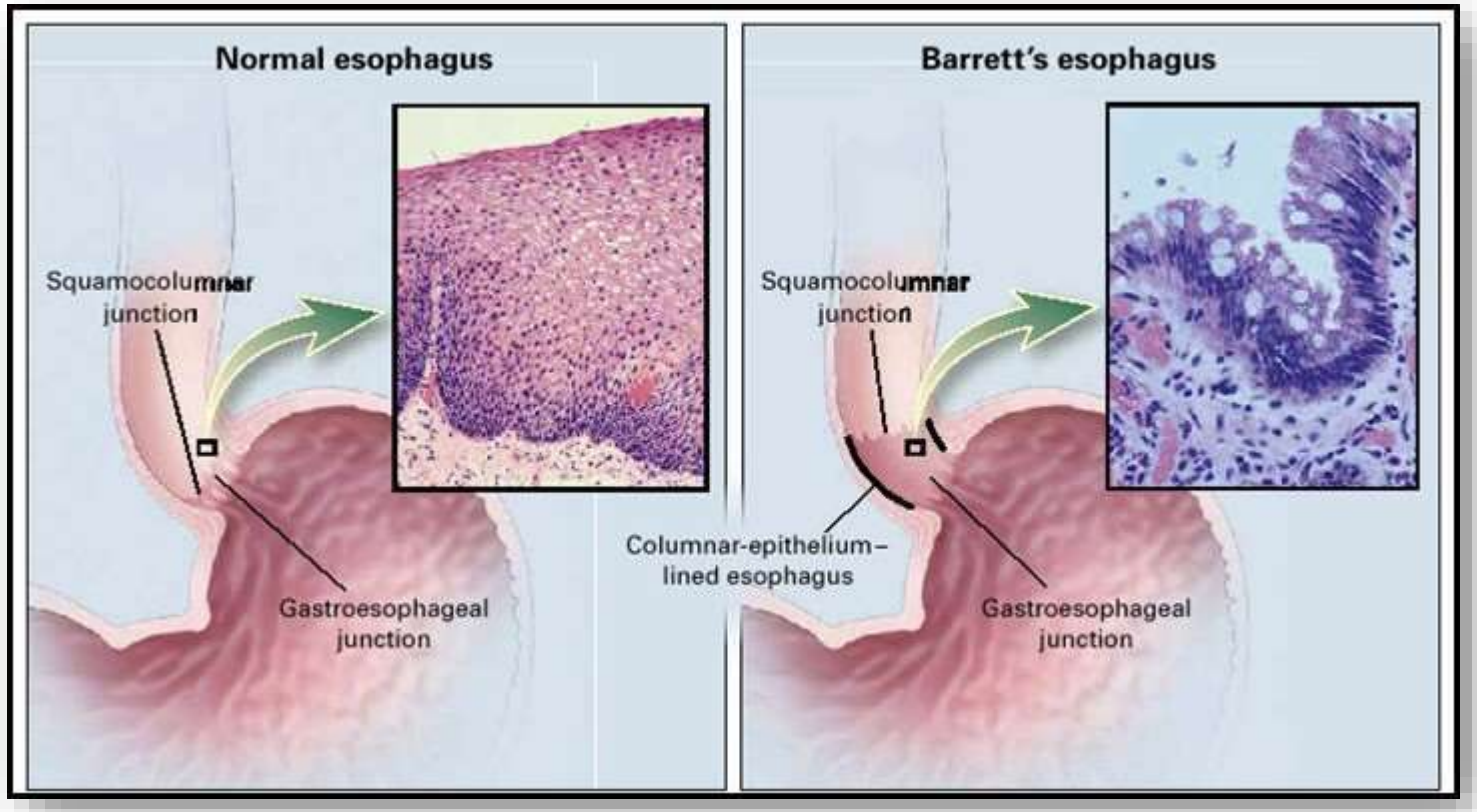




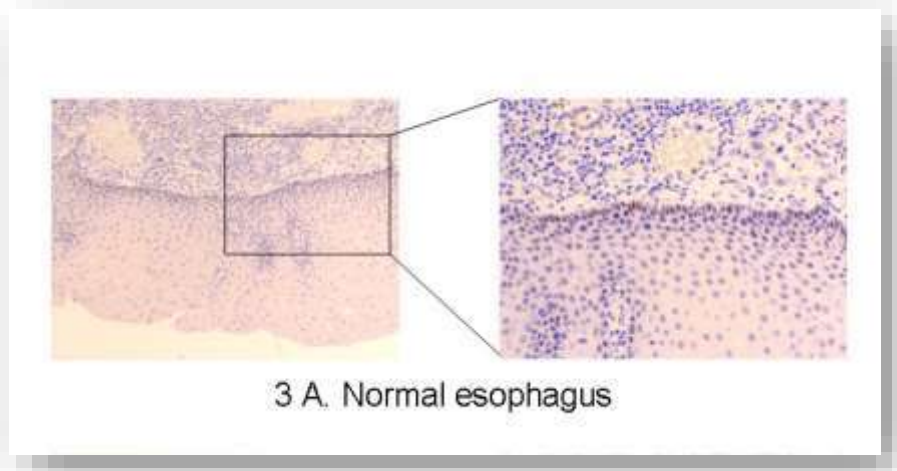


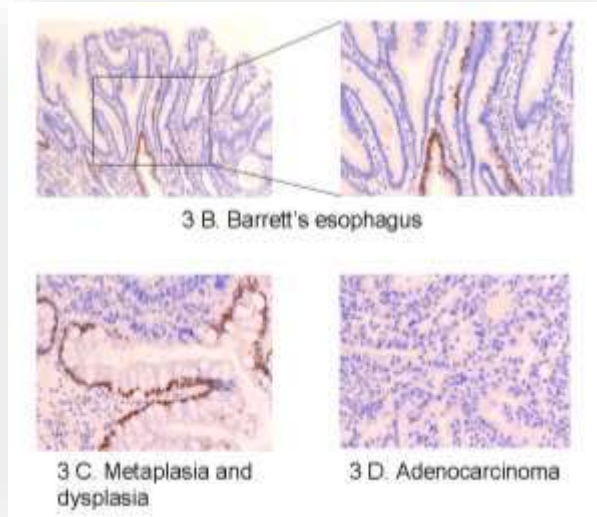


Histology of Barrett's esophagus



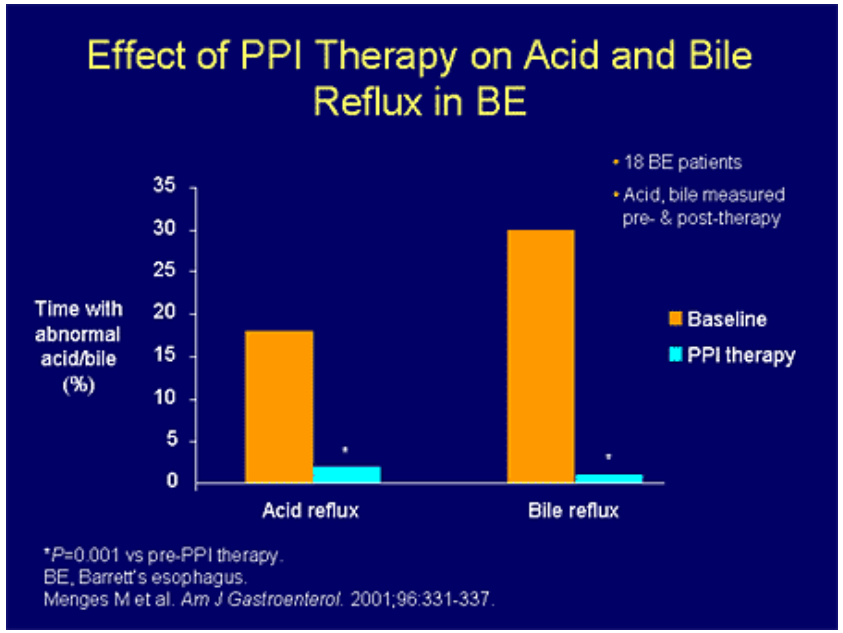
Barrett’s esophagus: histopathology





- Presently, **intestinal metaplasia [with goblet cells] is required for the diagnosis of Barrett's esophagus** because intestinal metaplasia is the only type of esophageal columnar epithelium that clearly predisposes to malignancy.” That statement remains valid to date, and the AGA, the American Society of Gastrointestinal Endoscopy (ASGE), and the American College of Gastroenterology (ACG) all agree that intestinal metaplasia with goblet cells is a requisite diagnostic criterion for Barrett esophagus
- Evans, J.A., Early, D.S., Fukami, N. et al. The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus. Gastrointest Endosc. 2012; 76: 1087–1094

Treatment:
PPIs fail to induce regression

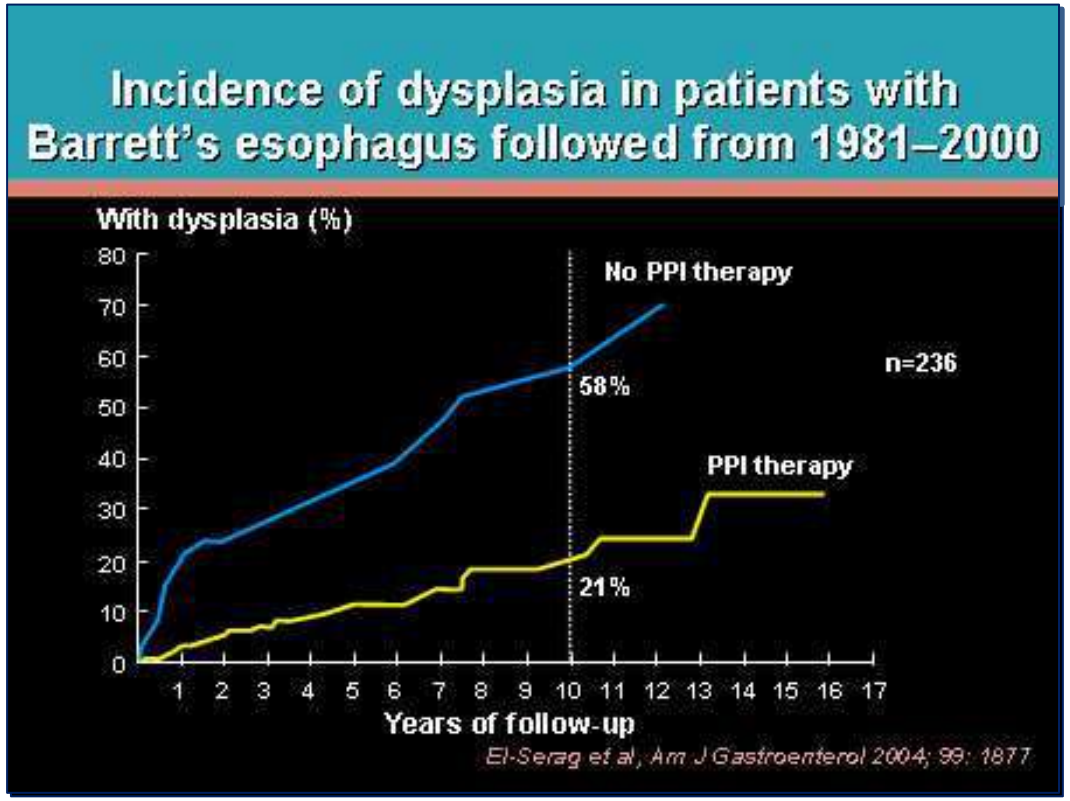


Effect of Long-Term PPI Therapy on Reversal of Barrett's Esophagus

	N	PPI	Duration	Reversal
Gore (1993)	23	Omeprazole 40 mg	24	0
Malesci (1996)	14	Omeprazole 60 mg	12	2
Sharma (1997)	13	Lansoprazole 60 mg	68	0
Cooper (1998)	47	Omeprazole 20 mg	24-72	0
Peters (1999)	31	Omeprazole 80 mg	24	0

Cooper BT et al. *Ailment Pharmacol Ther.* 1998;12:893-897.
Gore S et al. *Ailment Pharmacol Ther.* 1993;7:623-628.
Malesci A et al. *Gastrointest Endosc.* 1996;44:700-705.
Peters FTM et al. *Gut.* 1999;45:489-494.
Sharma P. *Am J Gastroenterol.* 1997;92:582-585.

However: PPIs prevent dysplasia



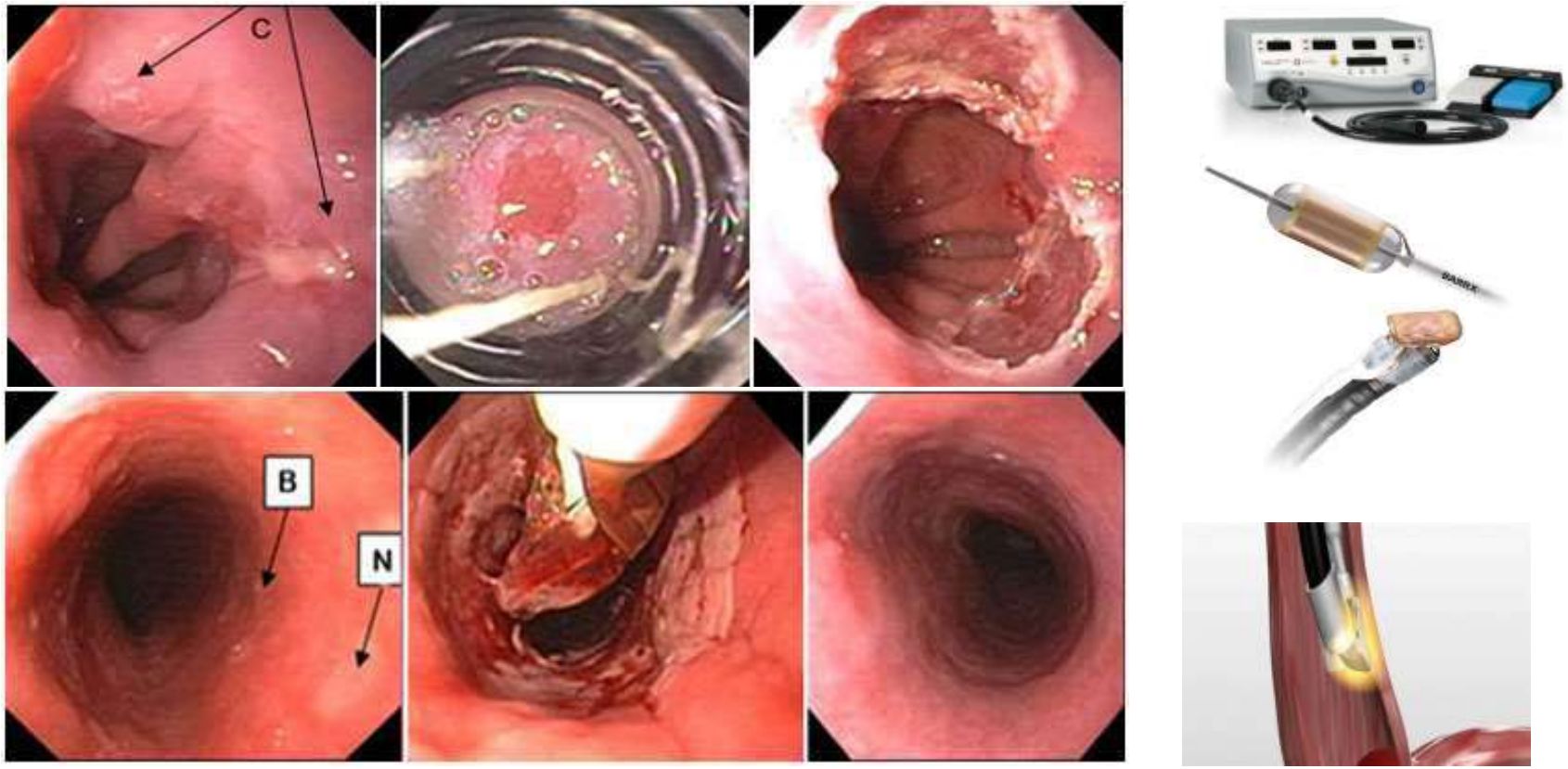
- El-Serag HB, Aguirre TV, Davis S *et al. Proton* pump inhibitors are associated with reduced incidence of dysplasia in Barrett's esophagus. Am J Gastroenterol 2004;99:1877–83.
- Hillman LC, Chiragakis L, Shadbolt B *et al.* Proton-pump inhibitor therapy and the development of dysplasia in patients with Barrett's oesophagus. Med J Aust 2004;180:387–91.

Treatment : endoscopic ablation

Ablation is performed primarily with the goal of decreasing cancer risk.

Given the small risk of cancer development, **in general BE population** however, it will be difficult to demonstrate this benefit in a clinical trial.

Radiofrequency Ablatation



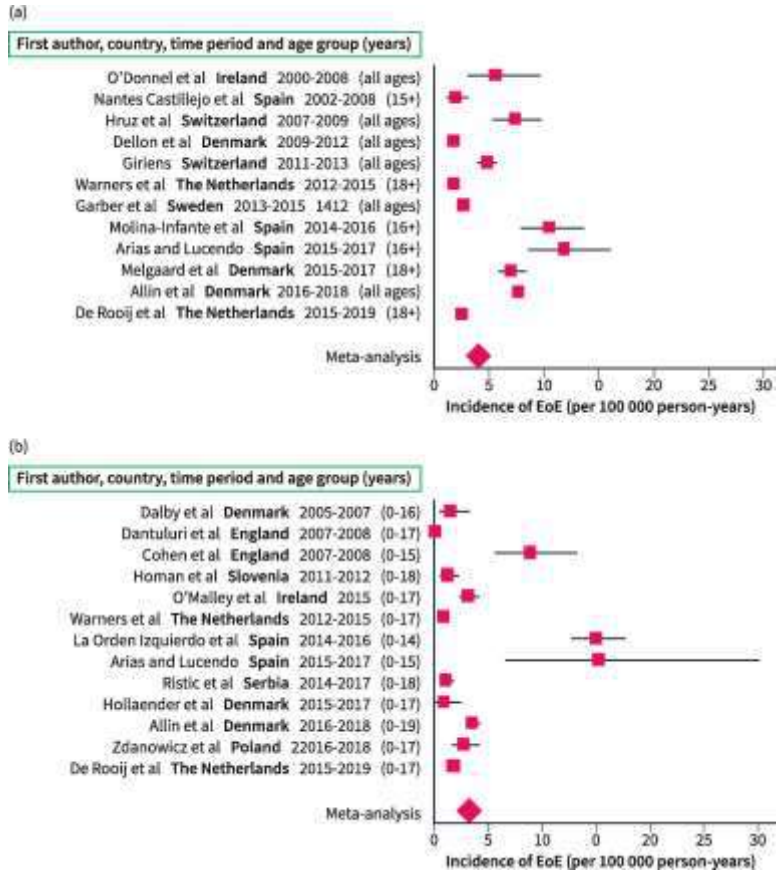
Shaheen, N. J. *et al*. Radiofrequency ablation in Barrett's esophagus with dysplasia. *N. Engl. J. Med.* **360**, 2277–2288 (2009)

Eosinophilic esophagitis

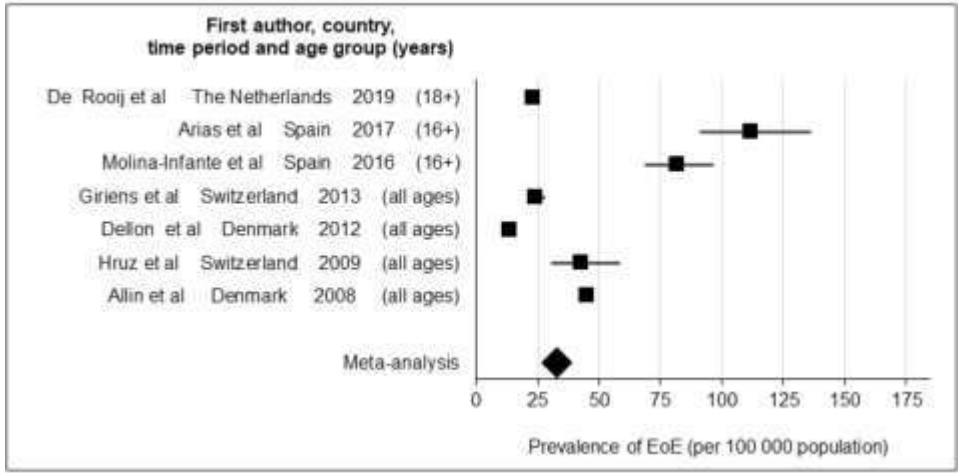
Eosinophilic Esophagitis (EoE) is an allergic, immune-antigen mediated chronic disease of the esophagus.

Histologically characterized by accumulation of eosinophils in the esophageal mucosa.

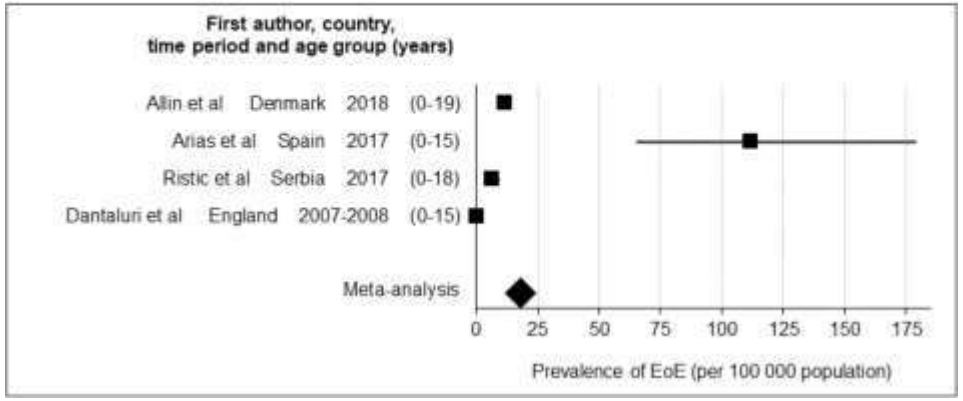
Eosinophilic esophagitis



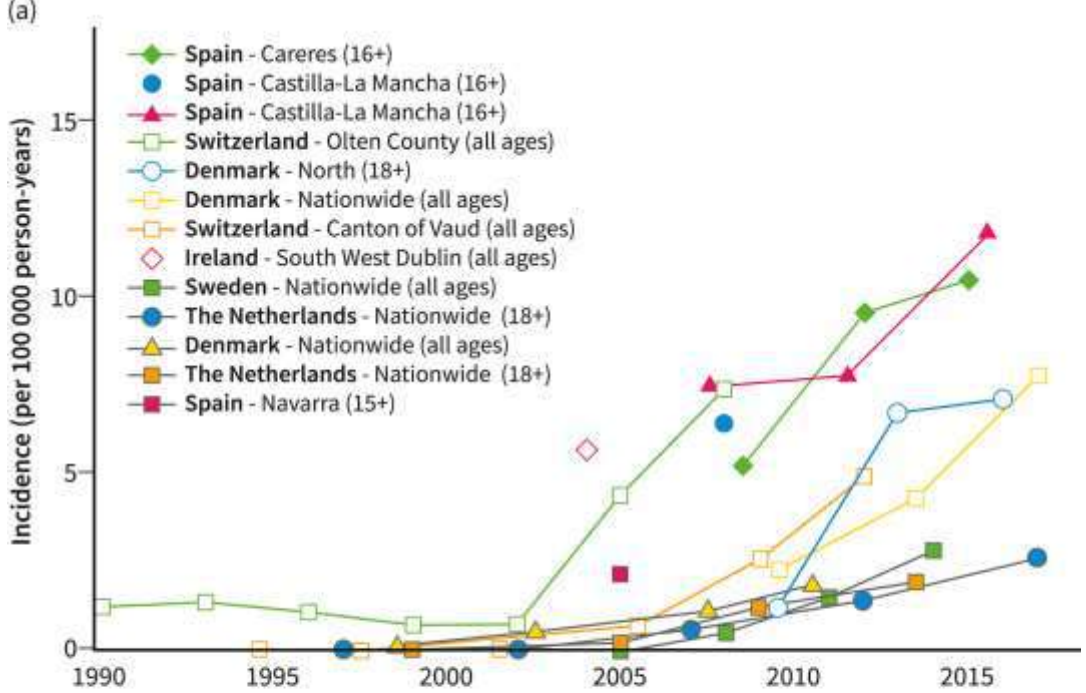
a). **Adults or all age groups:**

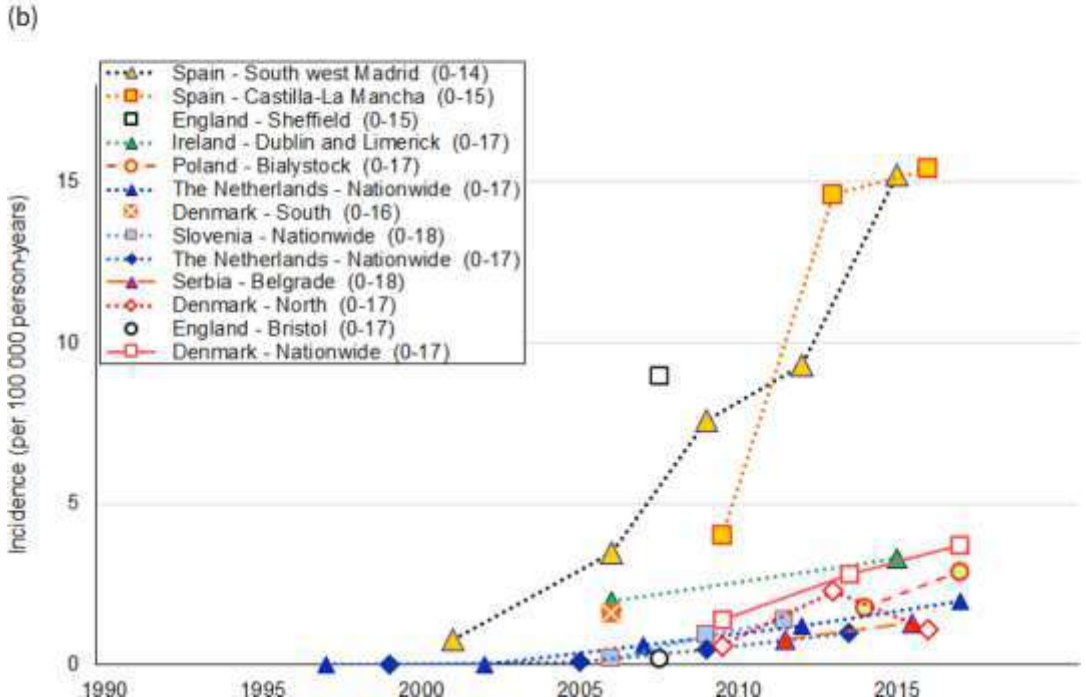


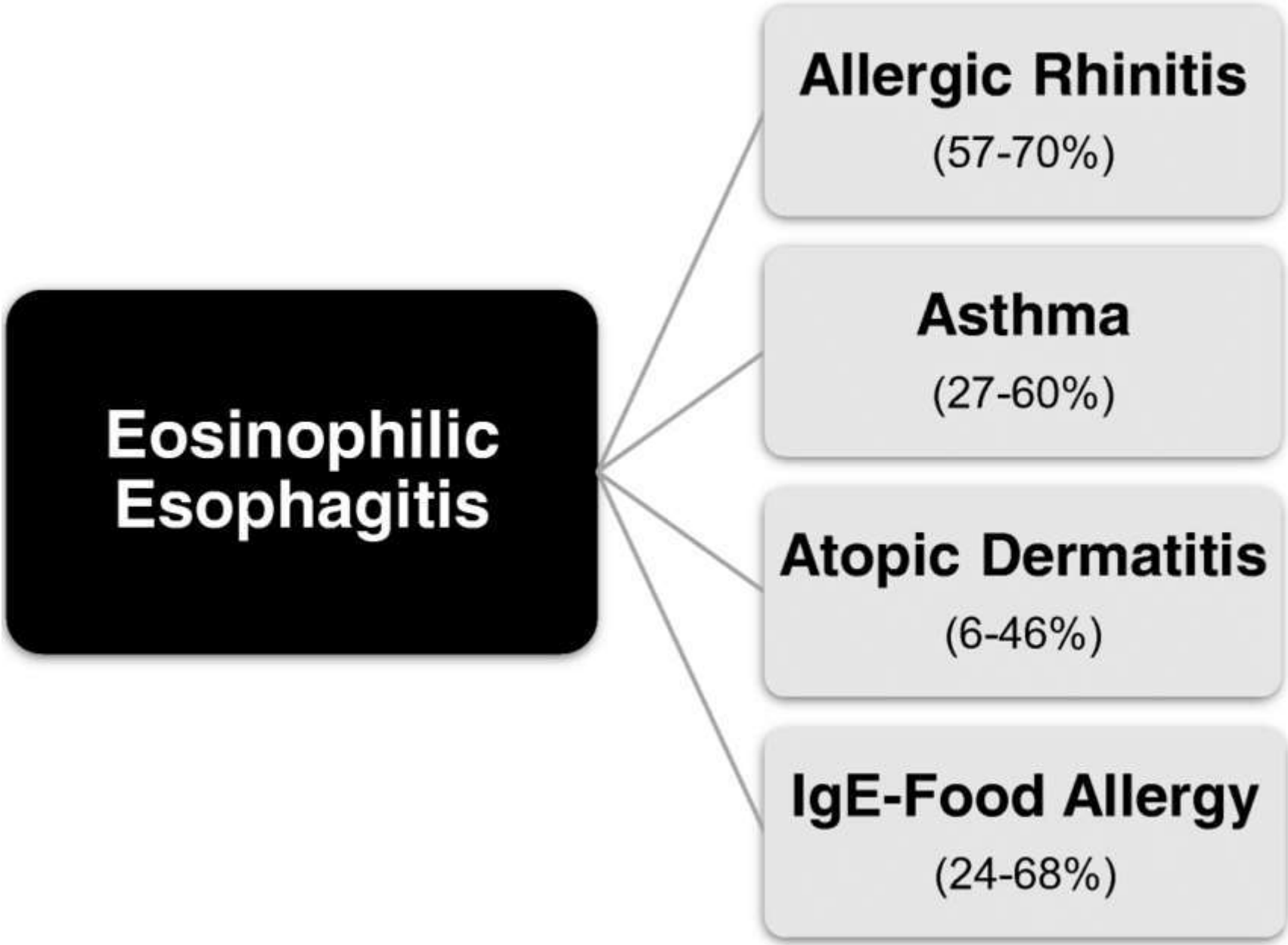
b). **Paediatric age groups**



Eosinophilic esophagitis

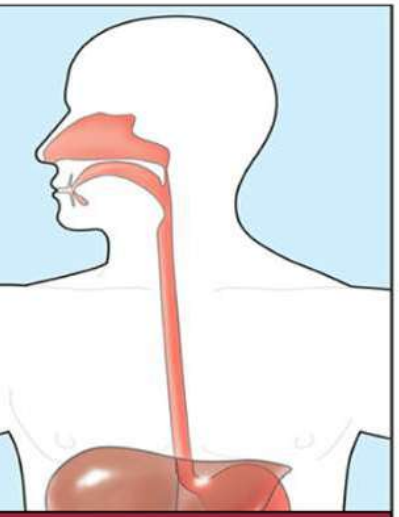




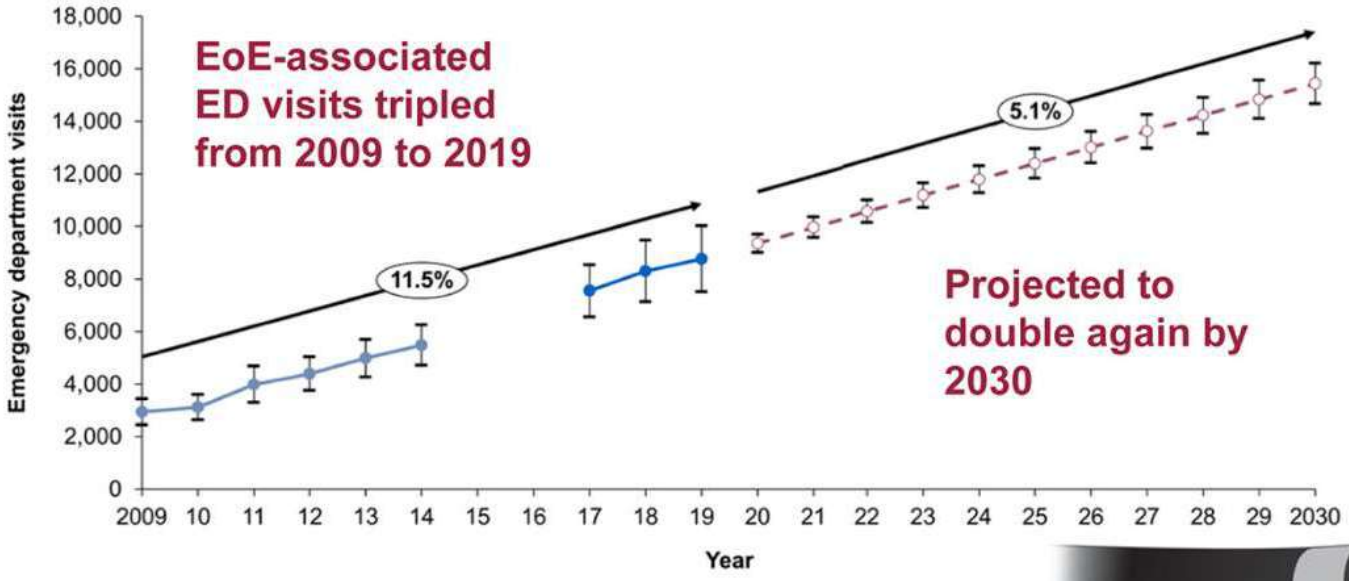

Eosinophilic Esophagitis
Allergic Rhinitis
(57-70%)
Asthma
(27-60%)
Atopic Dermatitis
(6-46%)
IgE-Food Allergy
(24-68%)

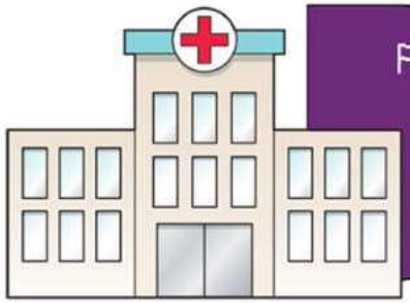
Eosinophilic esophagitis

Burden of Eosinophilic Esophagitis on Emergency Departments in the US



Analysis of ~49,507 EoE-associated ED visits in the US Nationwide Emergency Department Sample (2009-2019)

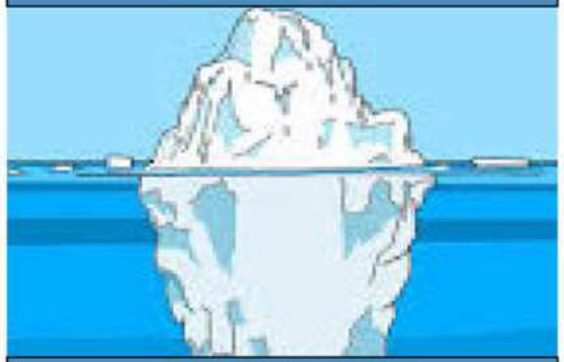




Fewer EoE patients are being admitted to hospital (25% in 2009-2011 to 14% in 2017-2019)

More patients are undergoing upper endoscopy (53% in 2009-2011 to 58% in 2017-2019)

Tip of the iceberg?
~50,000 visits with EoE diagnostic code



>700,000 ED visits for dysphagia, food impaction, or esophageal stricture in men < 40 years old without formal EoE diagnosis

Clinical Gastroenterology and Hepatology

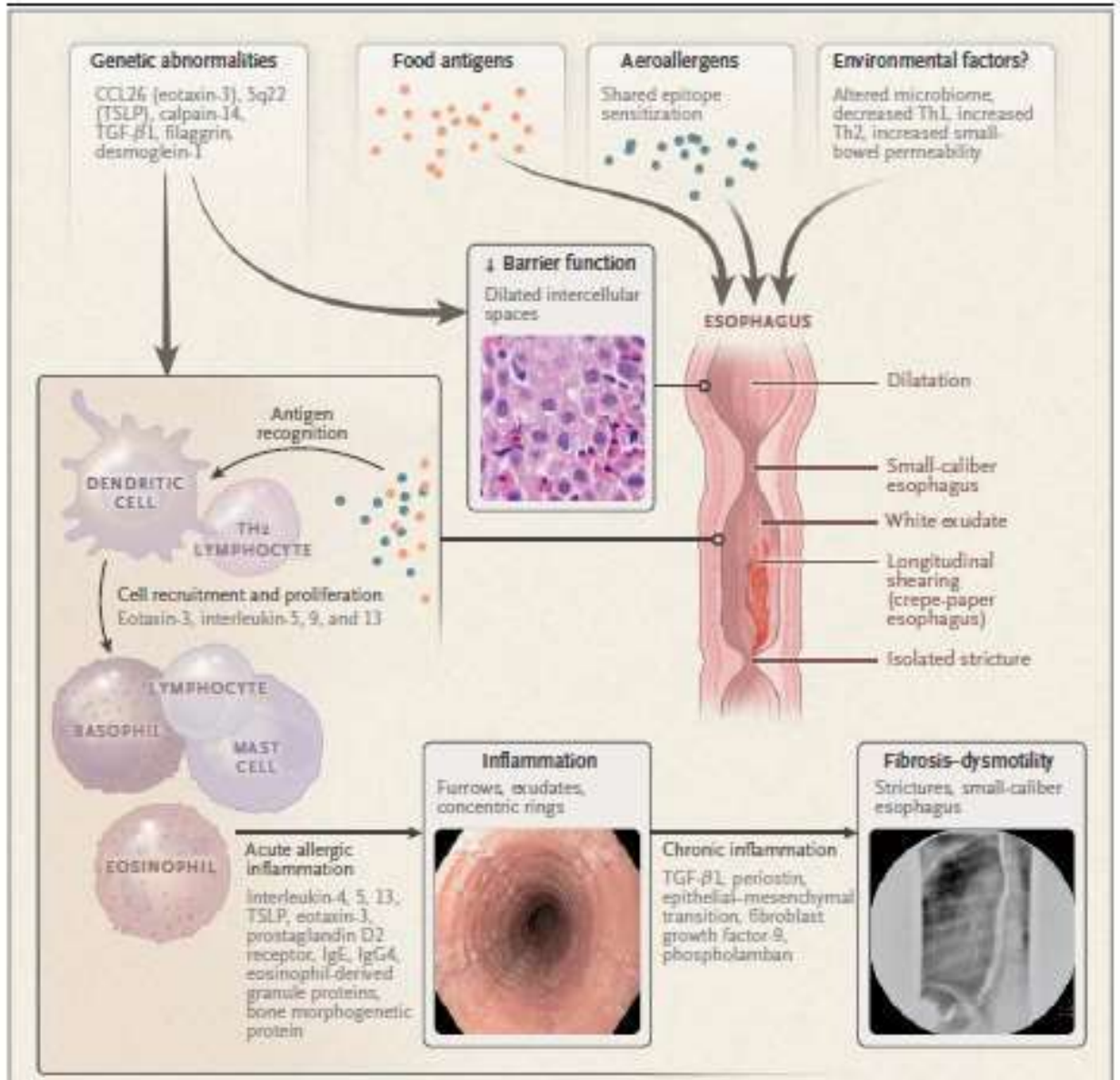
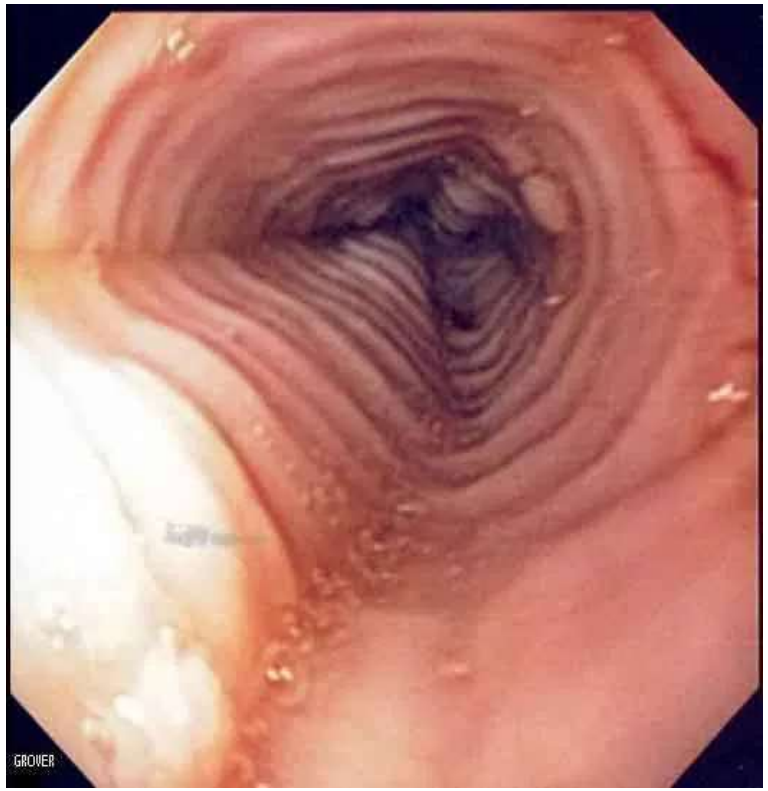


Figure 1. Pathophysiological Mechanisms of Eosinophilic Esophagitis.

Eosinophilic esophagitis is an allergen-mediated disease in which eosinophils are recruited to the esophagus. The functional consequences of this inflammation include stricture formation with proximal dilatation and longitudinal shearing. CCL26 denotes chemokine C–C motif ligand 26, TGF transforming growth factor, Th1 type 1 helper T cell, Th2 type 2 helper T cell, and TSLP thymic stromal lymphopoietin.



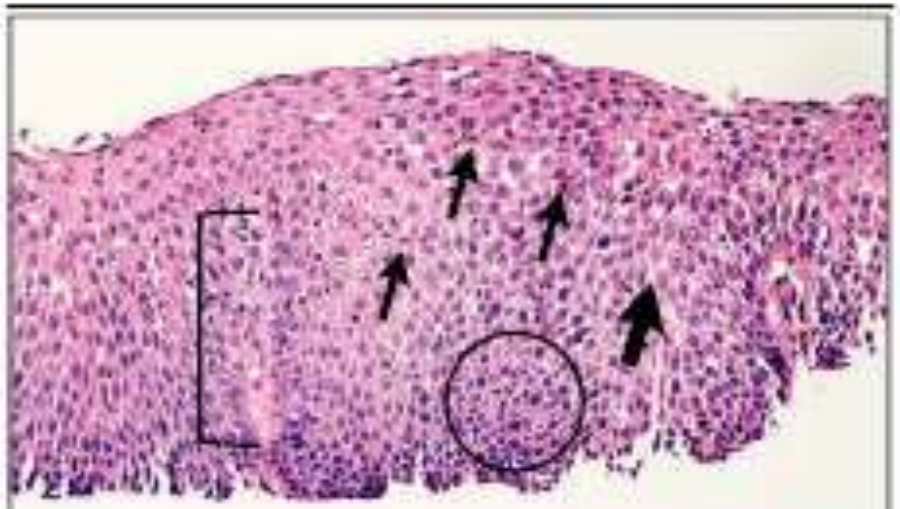


Figure 2. **Histologic Characteristics of Eosinophilic Esophagitis.**

Routine staining with hematoxylin and eosin reveals numerous eosinophils (thin arrows), dilated intercellular spaces (thick arrow), basal zone hyperplasia (circle), and papillary elongation (bracket).

ENDOSCOPIC CLASSIFICATION OF EOSINOPHILIC ESOPHAGITIS

MAJOR ASPECTS

Edema (decreased vascular pattern)
Grade 0: absent
Grade 1: present

Fixed rings (trachealization)
Grade 0: absent
Grade 1: mild (ridges)
Grade 2: moderate (defined)
Grade 3: severe (the endoscope does not pass)

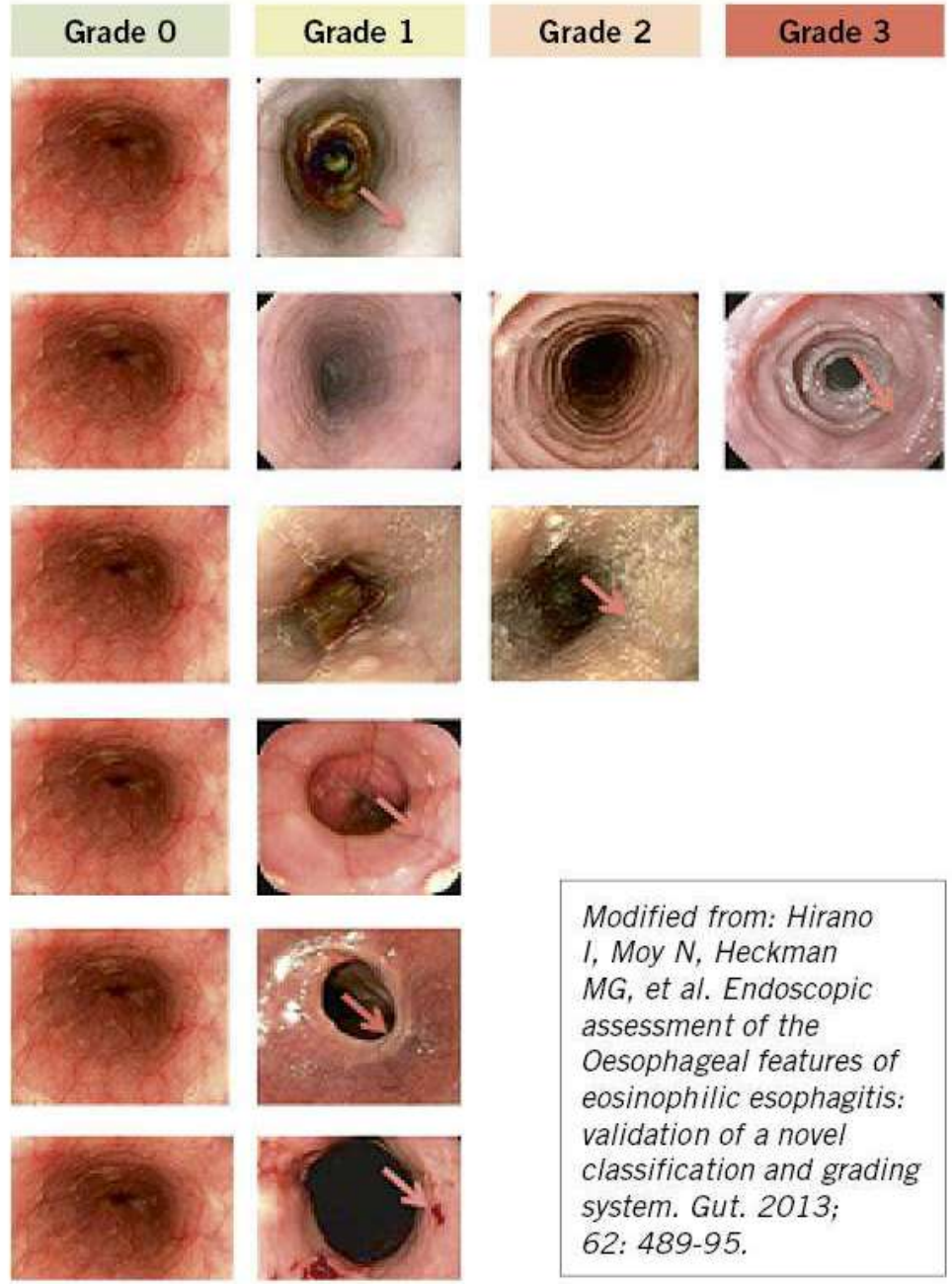
Exudates (whitish plaques or dots)
Grade 0: absent
Grade 1: mild (<10% surface)
Grade 2: severe (>10% surface)

Longitudinal furrows
Grade 0: absent
Grade 1: present

Stenosis
Grade 0: absent
Grade 1: present

MINOR ASPECT

Crepe paper mucosa (fragility/laceration)
Grade 0: absent
Grade 1: present



Modified from: Hirano I, Moy N, Heckman MG, et al. Endoscopic assessment of the Oesophageal features of eosinophilic esophagitis: validation of a novel classification and grading system. Gut. 2013; 62: 489-95.

First line therapy

Proton Pump Inhibitors

Remission:

Acid secretion
STAT6 transcription

Topical steroids

Remission:

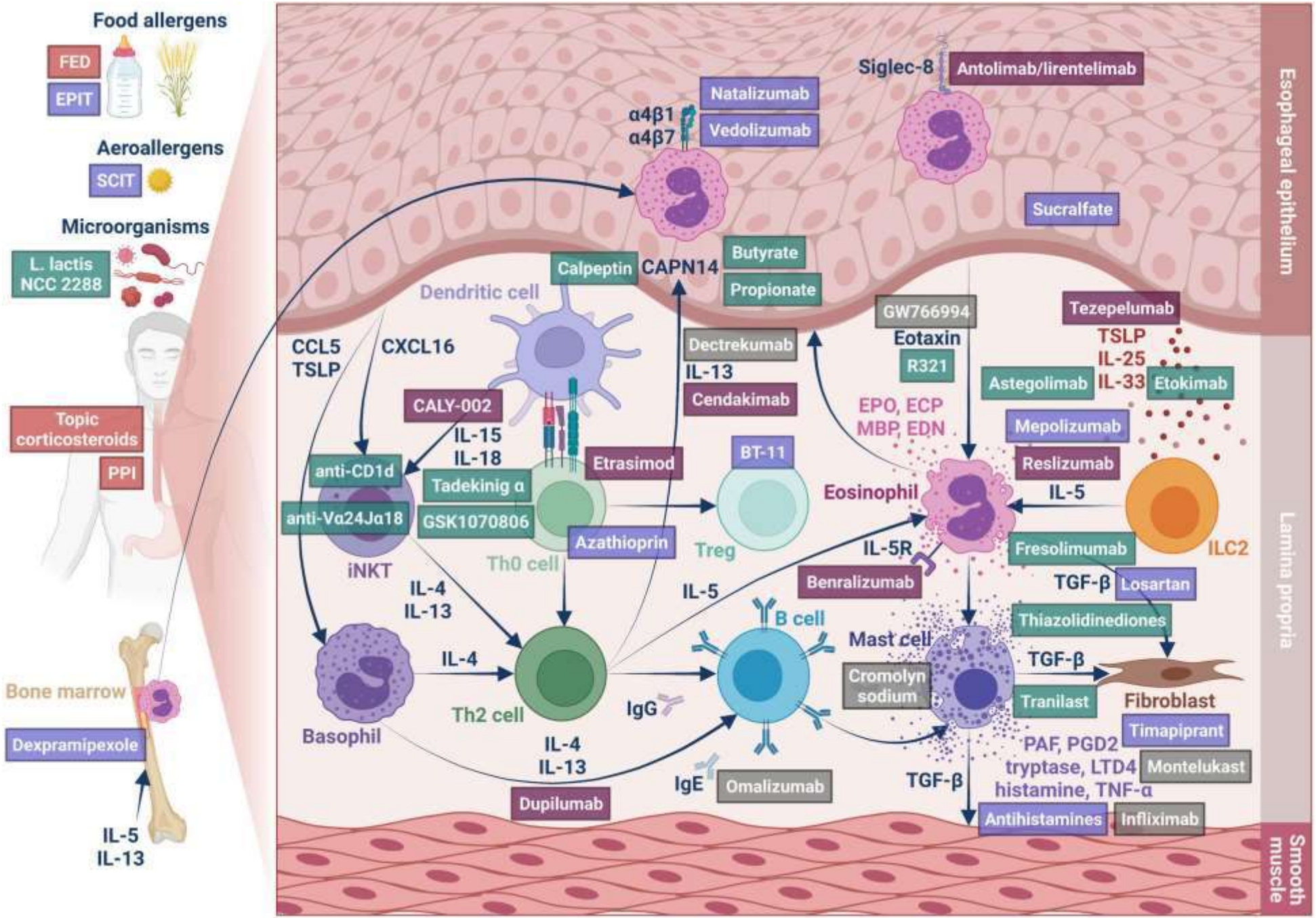
Type 2 inflammation

Elimination diets

Remission:

Food allergy

Endoscopic dilation


Food allergens
FED
EPIT
Aeroallergens
SCIT
Microorganisms
L. lactis NCC 2288
Topic corticosteroids
PPI
Bone marrow
Dexpramipexole
IL-5
IL-13
Esophageal epithelium
Lamina propria
Smooth muscle
Natalizumab
α4β1
α4β7
Vedolizumab
Siglec-8
Antolimab/lirentelimab
Sucralfate
Calpeptin
CAPN14
Butyrate
Propionate
Dendritic cell
CCL5
TSLP
CXCL16
Dectrekumab
IL-13
Cendakimab
GW766994
Eotaxin
R321
Tezepelumab
TSLP
IL-25
IL-33
Astegolimab
Etokimab
CALY-002
IL-15
IL-18
anti-CD1d
anti-Vα24Jα18
iNKT
Tadekinig α
GSK1070806
Etrasimod
BT-11
Treg
Th0 cell
Azathioprin
EPO, ECP
MBP, EDN
Mepolizumab
Reslizumab
IL-5
Eosinophil
ILC2
IL-5R
Benralizumab
Fresolimumab
TGF-β
Losartan
Thiazolidinediones
IL-4
IL-13
IL-5
B cell
Mast cell
Cromolyn sodium
Tranilast
TGF-β
Fibroblast
Basophil
IL-4
Th2 cell
IgG
Timapiprant
PAF, PGD2
tryptase, LTD4
histamine, TNF-α
Montelukast
IL-4
IL-13
IgE
Omalizumab
TGF-β
Dupilumab
Antihistamines
Infliximab

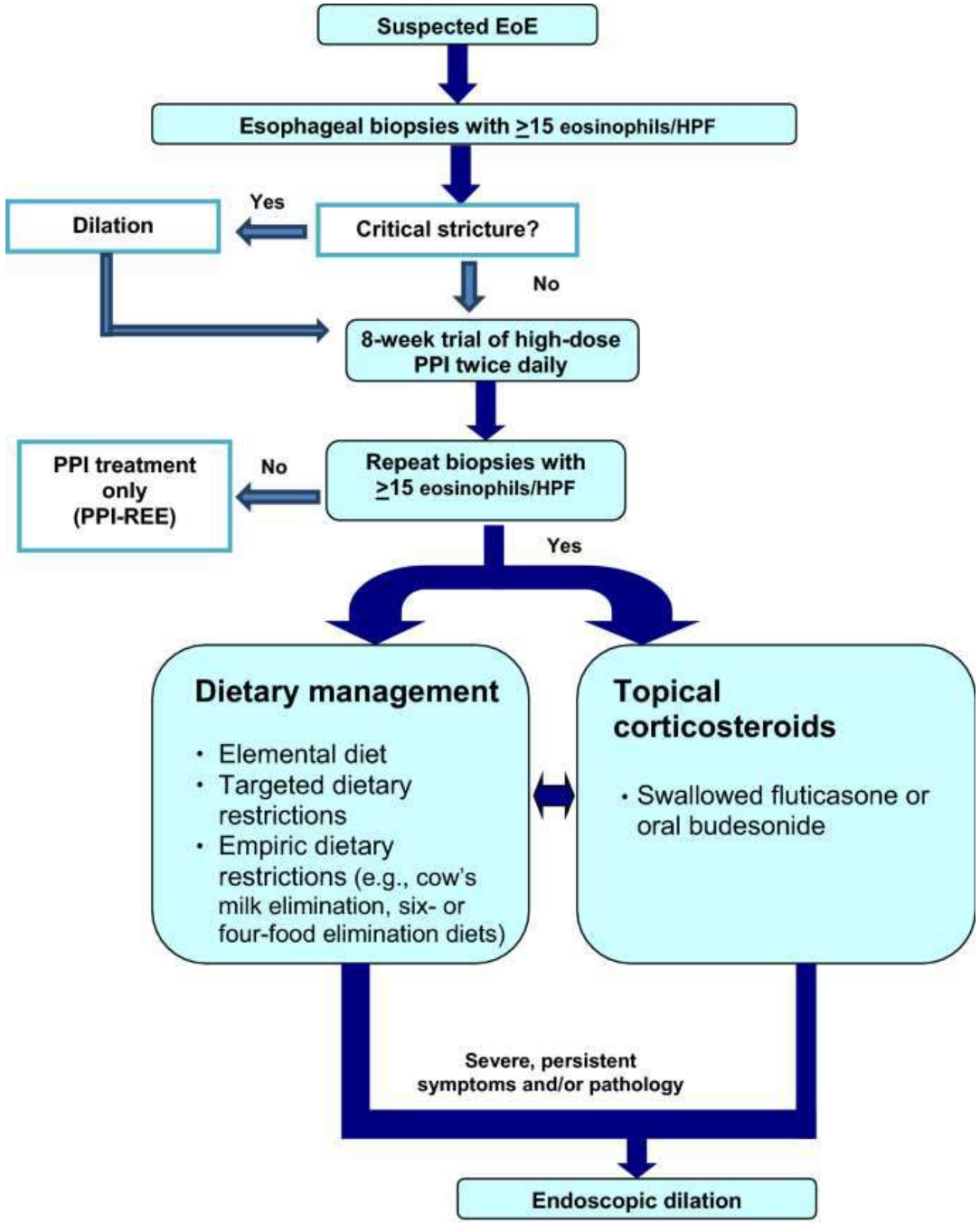


Table 1. Medical Treatment of Active Eosinophilic Esophagitis.

Method	Specific Recommendation or Dosage
Elemental diet therapy	—
Elimination diet therapy	
Six-food elimination	Elimination of milk, wheat, eggs, soy, seafood, and nuts
Four-food elimination	Elimination of milk, wheat, eggs, and soy
Allergy testing–based	Elimination of foods on the basis of results of radioallergosorbent testing, skin-prick testing, or atopy-patch testing*
Omeprazole (proton-pump inhibitor)†	Children with body weight 10 to 20 kg: 10 mg twice a day Children with body weight >20 kg: 20 mg twice a day Adults: 40 mg once or twice a day
Glucocorticoids	
Fluticasone	Children: 220 to 440 μg twice a day Adults: 440 to 880 μg twice a day
Budesonide	Children: 0.25 to 0.5 mg twice a day Adults: 1 to 2 mg twice a day

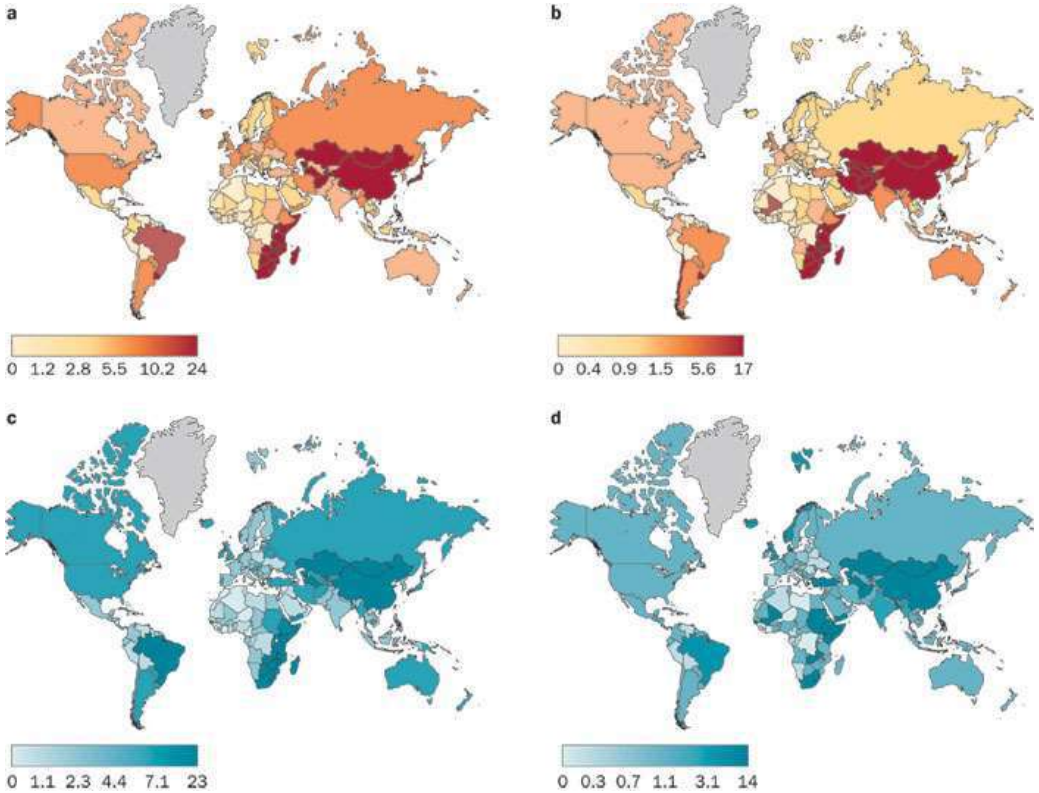
* Approximately 45% of patients have a sustained response to this type of diet therapy.[68]
† An equivalent proton-pump inhibitor can be administered.

Cancer of esophagus

Prof. Stefano Fiorucci

Dipartimento di Scienze chirurgiche e Biomediche
Università degli Studi di Perugia

Esophageal cancer incidence and mortality worldwide—2012 estimates



Lao-Sirieix, P. & Fitzgerald R. C. (2012) Screening for oesophageal cancer
Nat. Rev. Clin. Oncol. doi:10.1038/nrclinonc.2012.35

Cancer of the esophagus

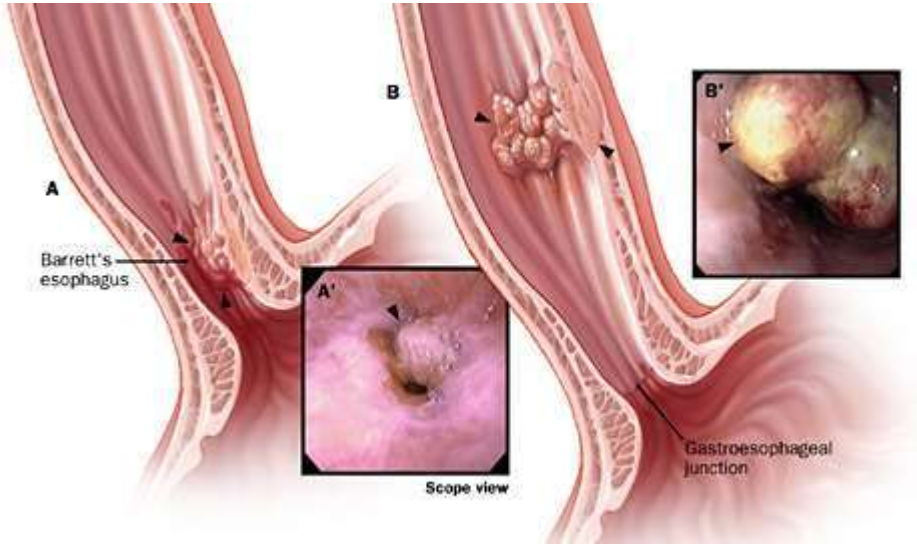
- Cancers arising from the esophagus and gastroesophageal junction account for 14,520 new cases and 13,570 deaths in Europe in 2005.
- Worldwide, esophageal cancer is the eighth most common malignancy and the sixth most common cause of cancer-related death.
- The epidemiology of esophageal cancer changed dramatically during the latter half of the 20th century. Although 40 years ago **squamous cell carcinoma** c accounted for more than 90% of all esophageal tumors in the United States, diagnoses of esophageal **adenocarcinoma** have significantly increased and now represent 80% of cases. However, SCC remains the most common worldwide.
- The mean age at diagnosis is 67 years, and men are affected more frequently than women, particularly among patients with AC.

Cancer of the esophagus

- The most common histologic types are **squamous cell carcinoma (SCC) and adenocarcinoma (AC),** which together constitute more than 90% of esophageal malignancies.
- Rarely, melanoma, sarcoma, small cell carcinoma, or lymphoma may arise in the esophagus.
- Although SCC is more evenly distributed throughout the length of the esophagus, **AC is predominantly a disease of the distal esophagus and gastroesophageal junction**, and is rarely found in the cervical esophagus
- **Squamous cell carcinoma and adenocarcinoma are distinct malignancies of the esophagus, with different risk factors and different natural histories.**

Cancer of the esophagus

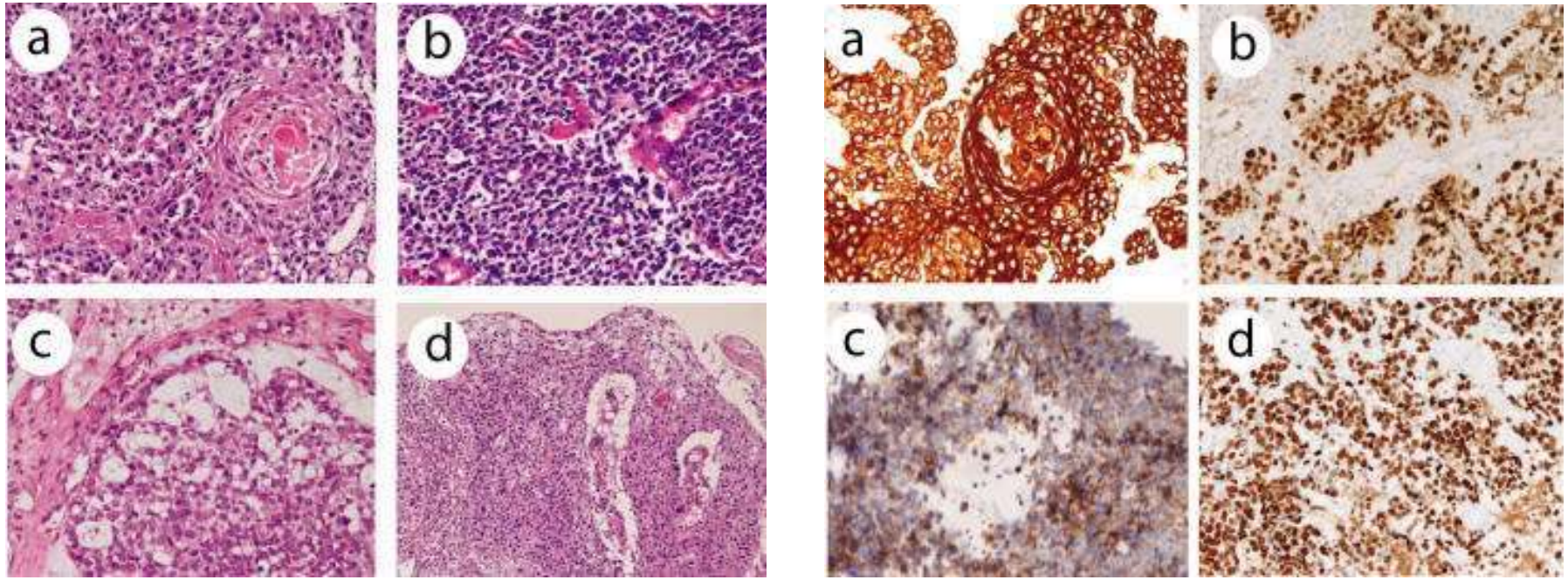
Two histogy types



- **Adenocarcinoma** is the leading histology for esophageal cancer over squamous cell. Adenocarcinoma has increased 350% since 1970 and accounts for 75% of all cases in Caucasian males.
- **Squamous cell** cancer can be estimated based on what level the cancer is in the esophagus. It is seen in 10%-25% of cases involving the upper third, 40%-50% involving the middle third, and 25%-50% involving the lower third

Carcinoma of the esophagus

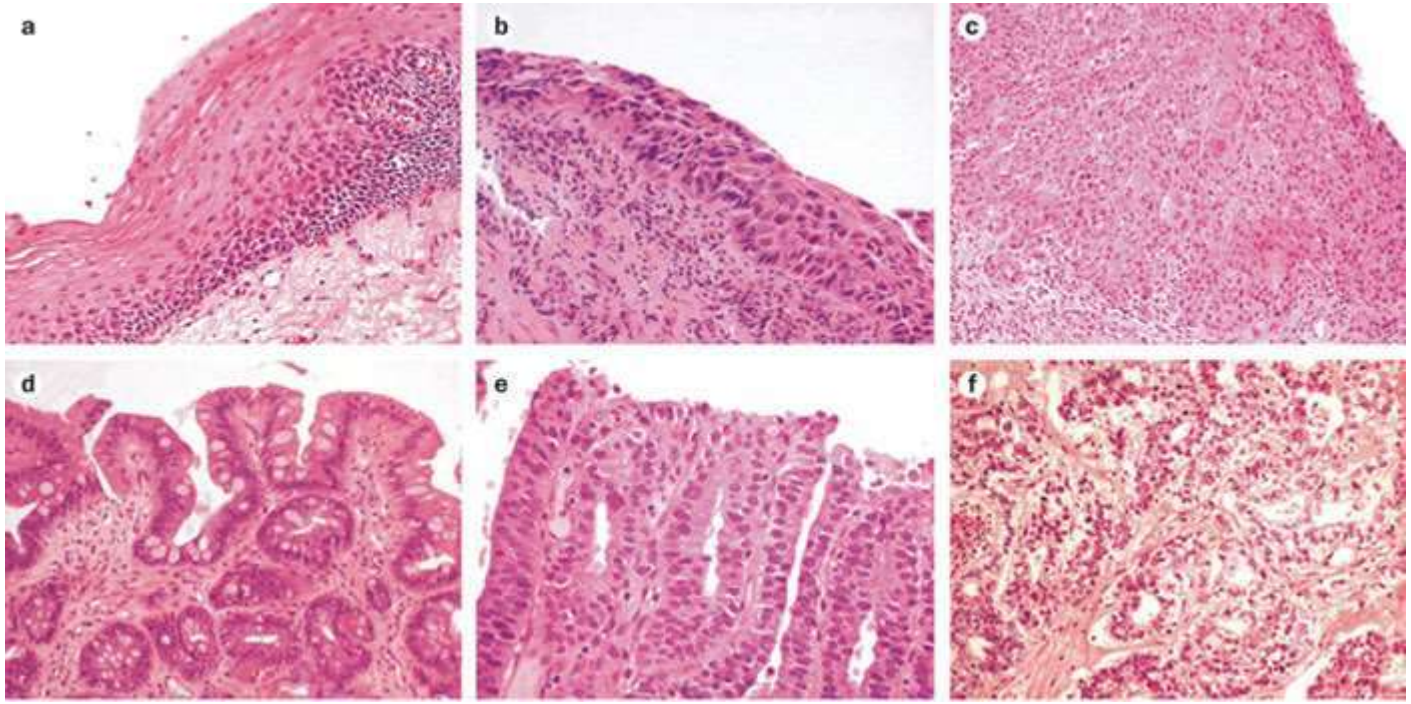
- **SCC**



High molecular weight cytokeratin is positive in the squamous cell carcinoma element.

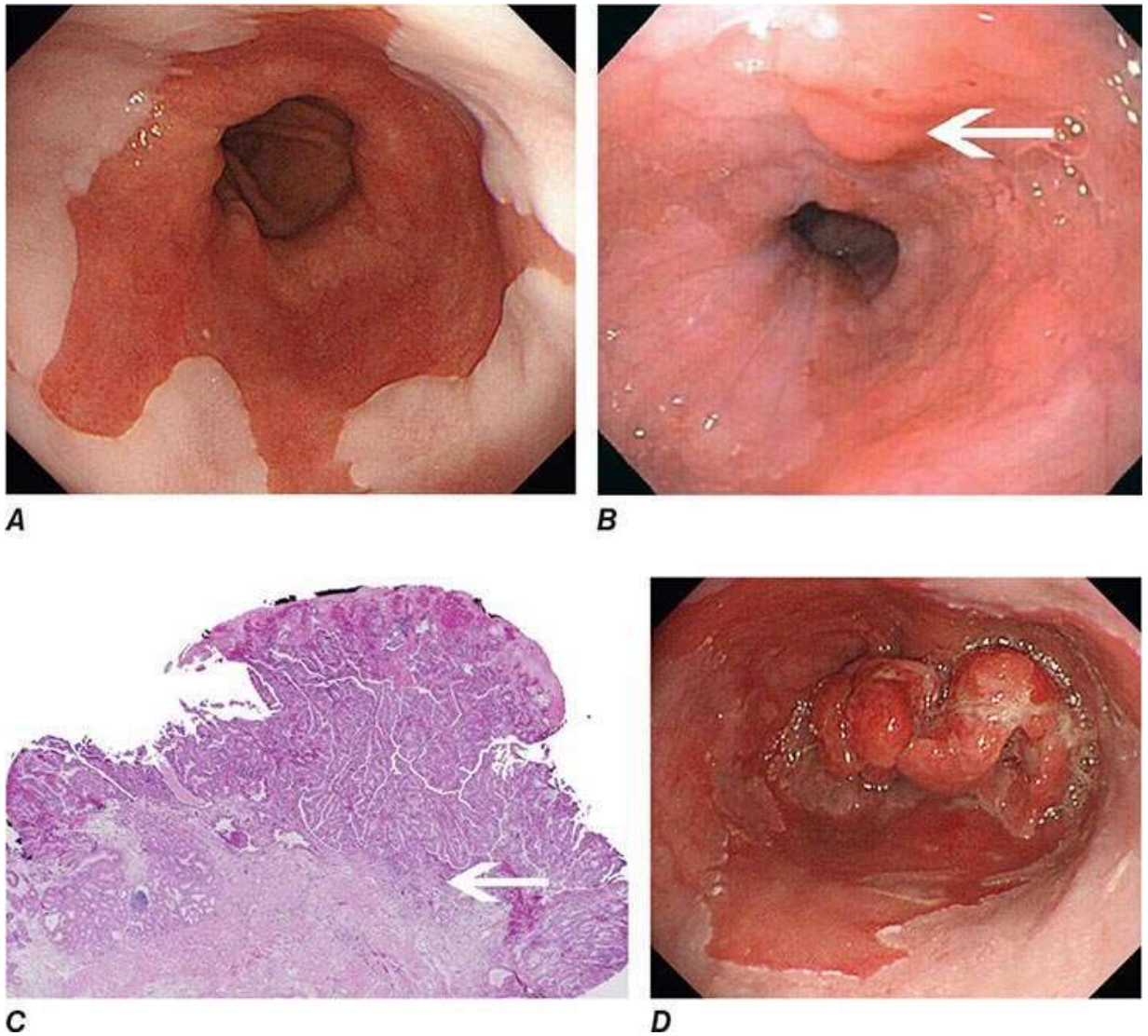
Carcinoma of the esophagus

SCC and AC have different precursors



Progression of a) normal squamous epithelia to b) squamous high-grade dysplasia and c) squamous-cell carcinoma.
Progression of d) Barrett's oesophagus to e) glandular high-grade dysplasia and f) adenocarcinoma.
The sections were stained with haematoxylin and eosin and are displayed at ×100 magnification.

From Barret's esophagus to Adenocarcinoma



Cancer of the esophagus

Risck factors

Causative and Risk Factors for Adenocarcinoma and Squamous Cell Carcinoma

Adenocarcinoma

Barrett's esophagus
Gastroesophageal reflux disease (GERD)
Obesity (by increasing the risk of GERD)

Squamous Cell Carcinoma

Smoking
Alcohol
Dietary and environmental factors that cause chronic irritation and inflammation of the esophageal mucosa
Predisposing underlying conditions, such as tylosis, achalasia, esophageal diverticula and webs, Plummer-Vinson syndrome, and human papillomavirus (HPV) infection

Cancer of the esophagus

Symptoms Caused by Local Tumor Effects

Dysphagia
Cough and regurgitation
Odynophagia
Weight loss
Upper gastrointestinal bleeding

Symptoms Related to Invasion of Surrounding Structures

Respiratory fistula
Hoarseness from recurrent laryngeal nerve invasion
Hiccups from phrenic nerve invasion
Pain caused by local spread

Symptoms Related to Distant Disease

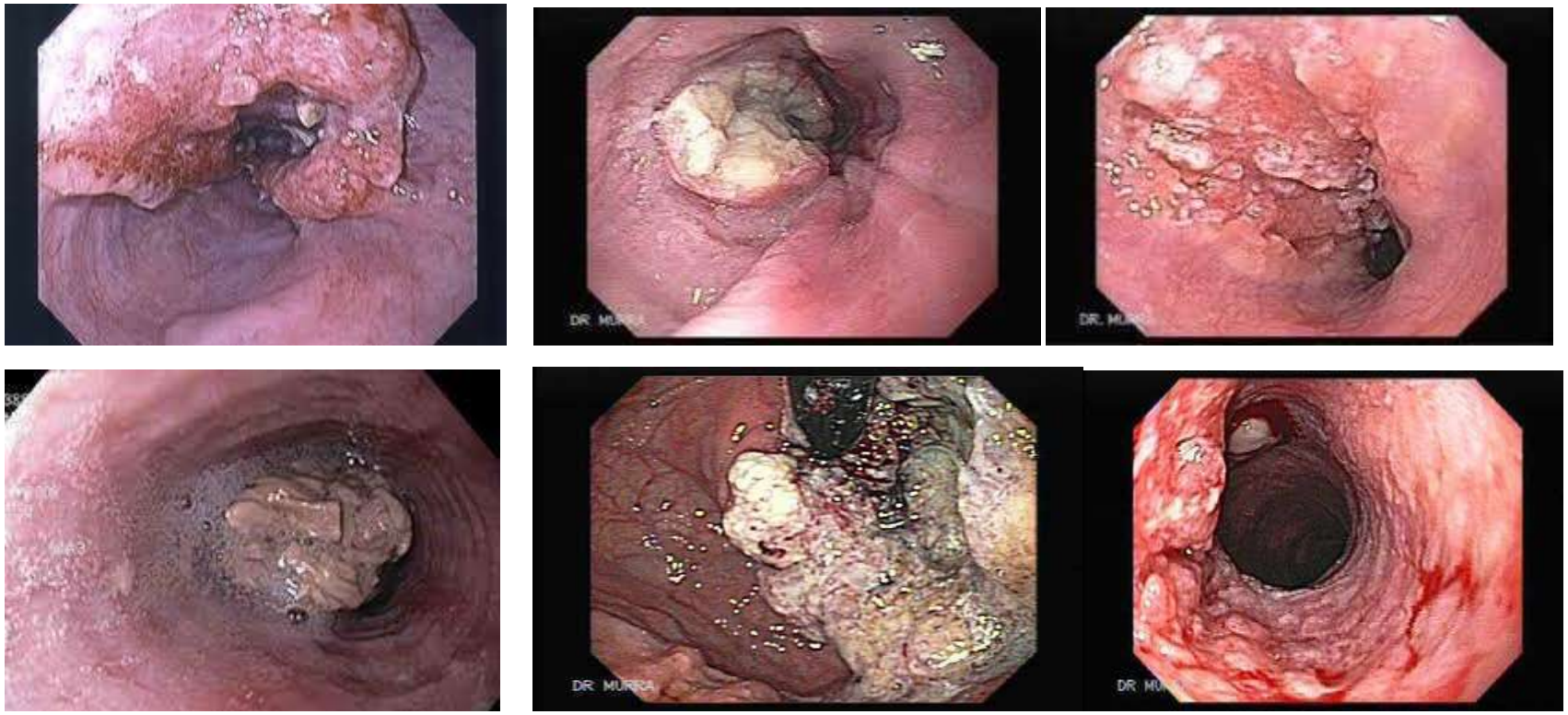
Metastatic disease to the lungs, liver, and central nervous system
Hypercalcemia

Cancer of esophagus

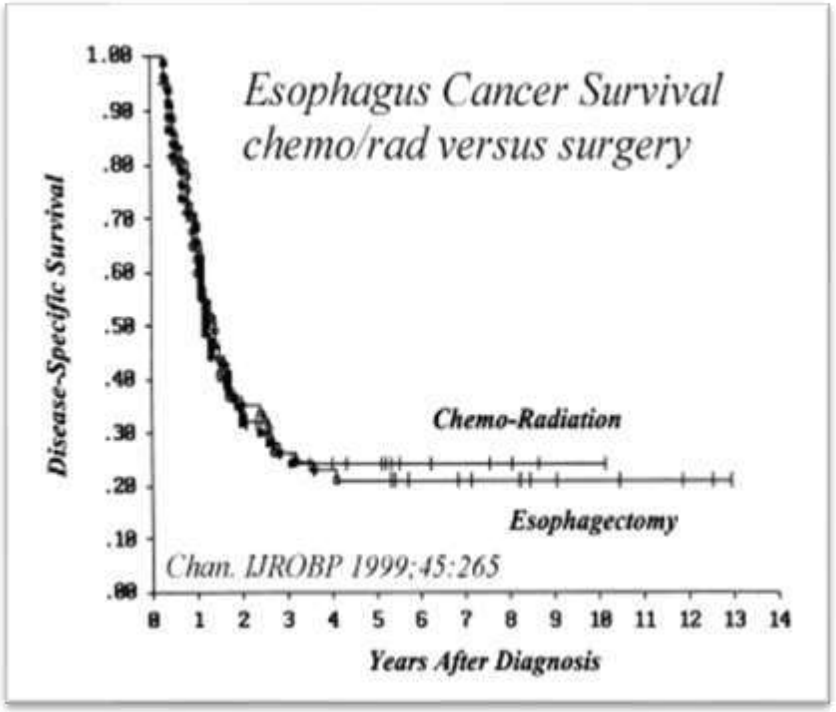
Symptoms

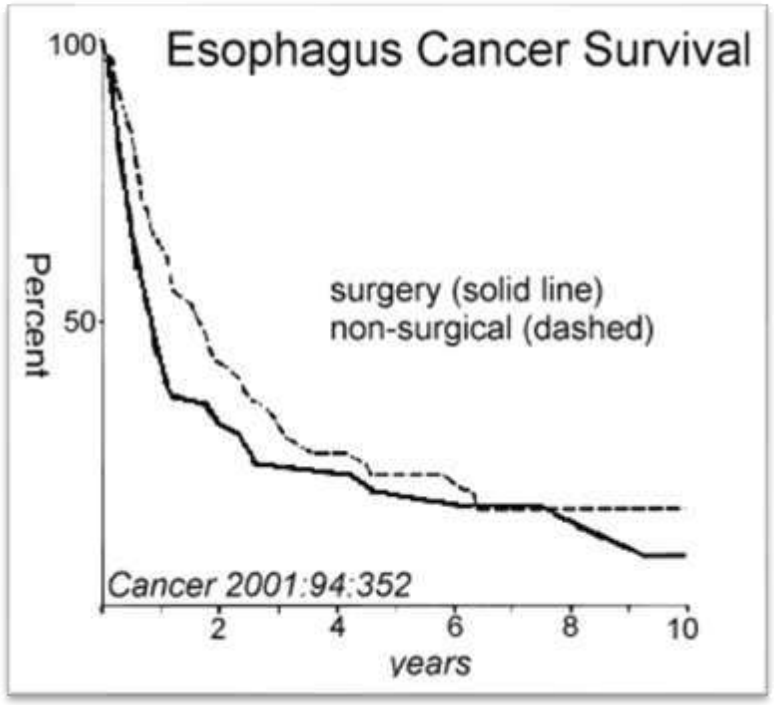
- AC and SCC have similar clinical manifestations, which reflect the extent of local esophageal involvement.
- **Dysphagia**, the most common manifesting symptom, usually develops in response to dense solid food, and progresses gradually to interfere with the intake of softer foods and, finally, liquids.
- This can sometimes be accompanied by **vomiting or regurgitation** of saliva or food.
- **Pain** is frequent and can occur in the absence of dysphagia. It can be related to swallowing itself (**odynophagia**) or to the local extension of the tumor into adjacent structures, such as the pleura, mediastinum, or vertebral bodies.
- **Weight loss** is common and correlates with dysphagia, dietary changes, and tumor-related anorexia. Weight loss is noted in more than 70% of patients and, if present, carries a worse prognosis. Other manifesting signs and symptoms reflect complications from disease spread, such as cough or fever from a respiratory tract fistula, upper or lower gastrointestinal bleeding, hoarseness from recurrent laryngeal nerve involvement, and hiccups from phrenic nerve

Endoscopy



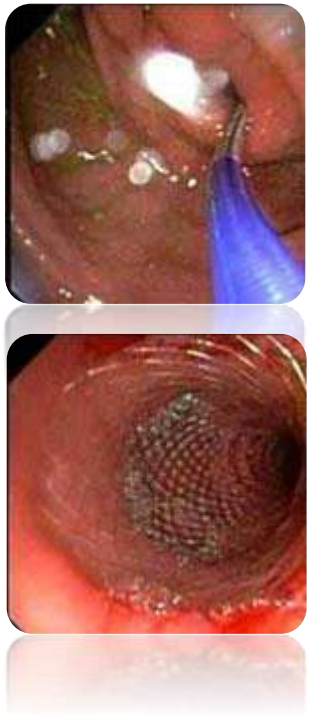
Cancer of esophagus survival

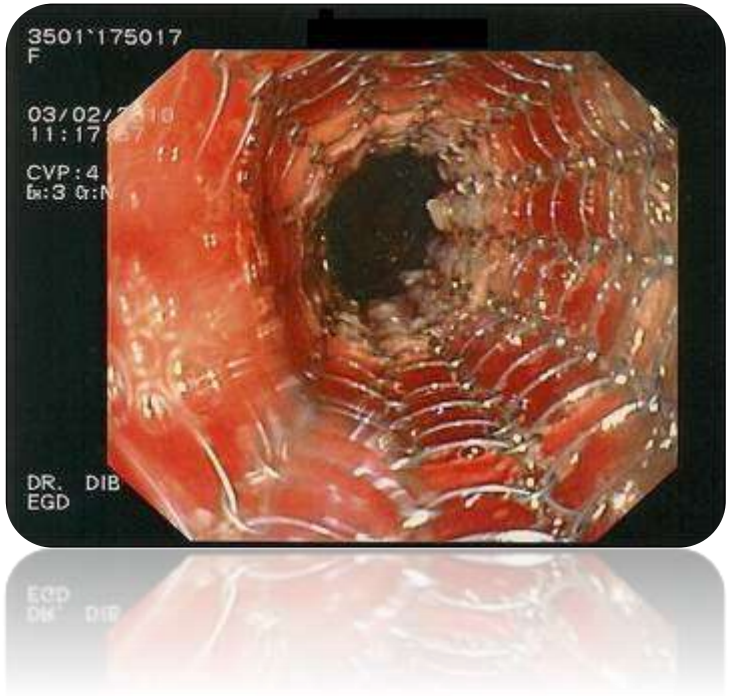




Palliative treatment:

Esophageal stent





Esophageal cancer
Summary

- Squamous cell carcinoma and adenocarcinoma are distinct malignancies of the esophagus, with different risk factors and different natural histories.
- The epidemiology of esophageal cancer in Europe and North America **has changed dramatically** in recent years **with adenocarcinoma now being found in most cases**.
- Dysphagia is an alarming symptom that merits careful evaluation for the possibility of esophageal cancer.
- Patients with locoregionally advanced but non-metastatic disease may be cured with multimodality treatment approaches that often include **chemotherapy**.
- Although patients with metastatic disease cannot be cured, aggressive symptomatic palliation is appropriate.