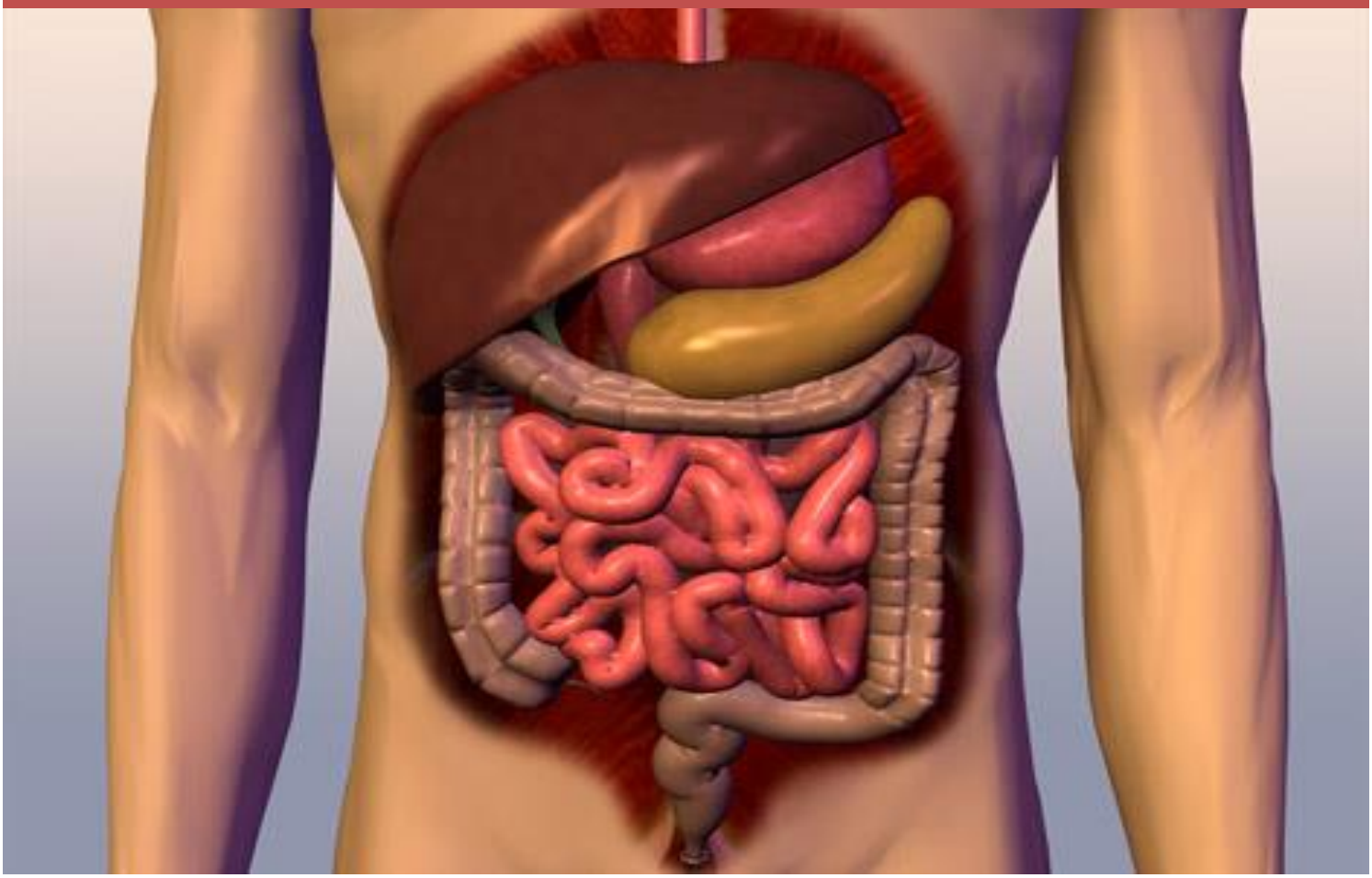

Lecture One

Gastro Esophageal Reflux Disease

432 ***Pathology*** *Team*

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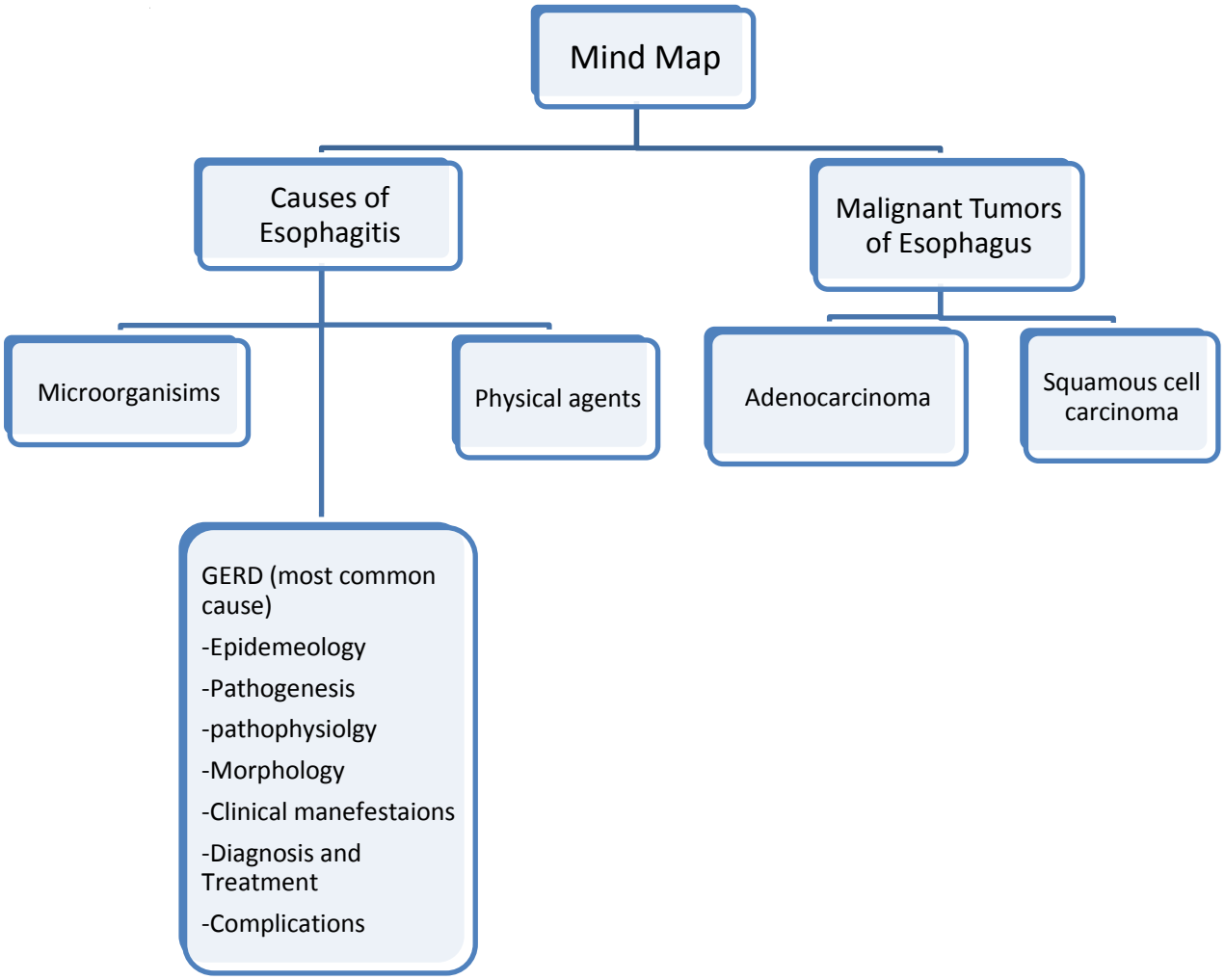
Reviewed By: Ammar *Al-Yamani*

GIT Block

Color Index: female notes are in purple. Male notes are in Blue. Red is important. Orange is explanation.

Gastro-esophageal reflux disease



Gastro Esophageal Reflux Disease

Definition

According to American College of Gastroenterology (ACG)

- Symptoms OR mucosal damage produced by the **abnormal reflux** of gastric contents into the esophagus
- **Often chronic and relapsing**
- May see complications of GERD in patients who lack typical symptoms

Gastroesophageal reflux is a **normal** physiologic phenomenon experienced intermittently by most people, particularly **after a meal**.

Gastroesophageal reflux disease (GERD) occurs when the amount of gastric juice that refluxes into the esophagus **exceeds the normal limit**, **causing symptoms** with or without associated esophageal mucosal injury.

Physiologic GERD

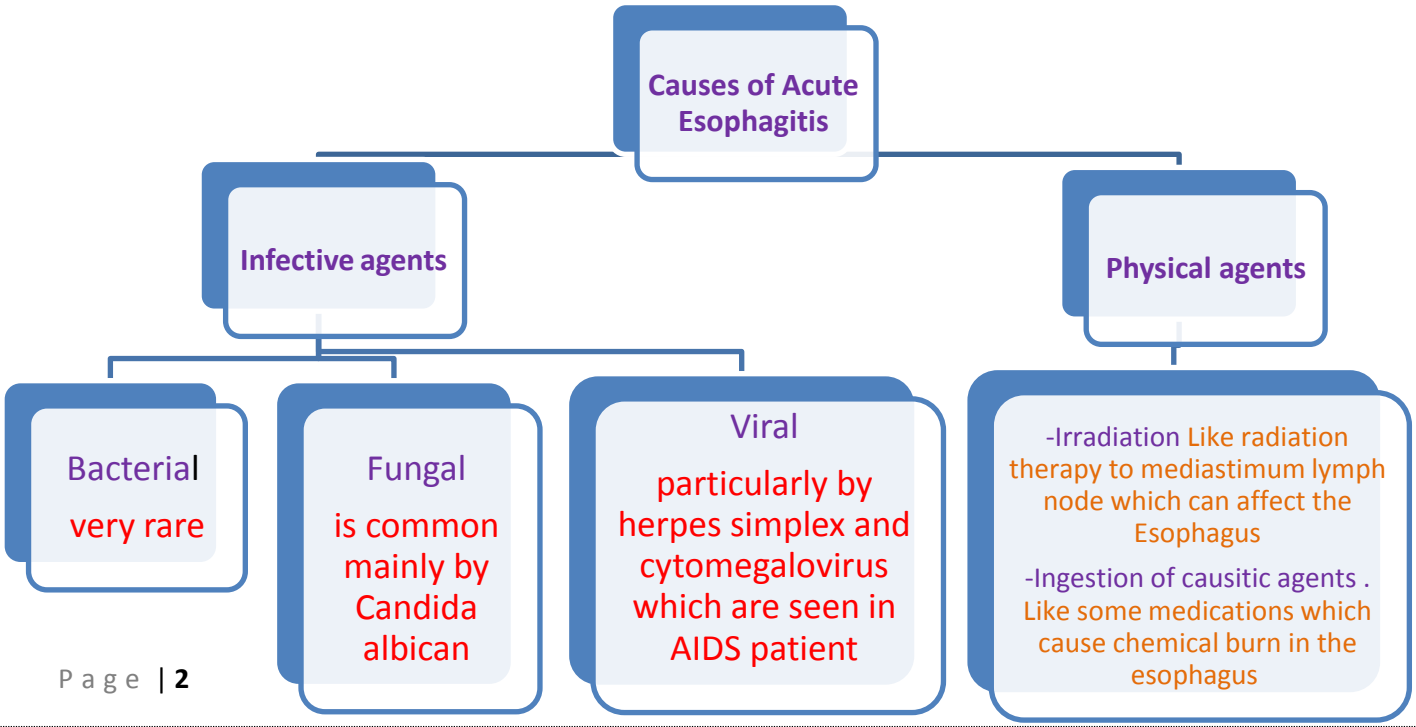
- Post prandial after meal
- Short lived for a period of time
- Asymptomatic
- No nocturnal symptoms while sleeping at night

Pathologic GERD

- Symptoms
- Mucosal injury
- Nocturnal symtopms (problems while sleeping at night)

Esophagitis: is irritation or inflammation of the esophagus.

- Esophagitis is rarely caused by agents than reflux (Most common cause is acid reflux also called Gastroesophageal reflux disease)



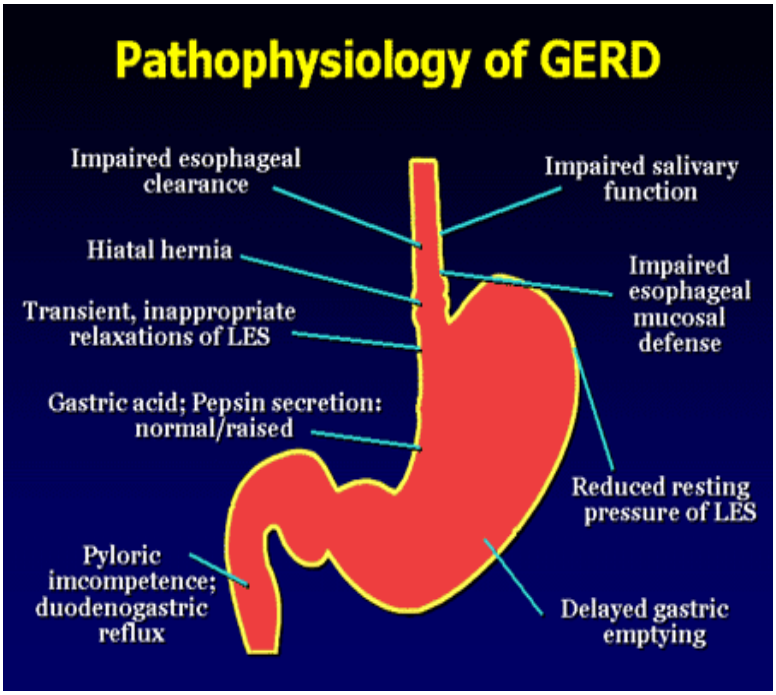
Epidemiology of GERD:

- About 44% of the US adult population have heartburn at least once a month
- 14% of Americans have symptoms weekly
- 7% have symptoms daily

GERD is most common in adults more than 40 years of age but also occurs in infants and children.

Pathophysiology of GERD:

- Primary barrier to gastroesophageal reflux is the lower esophageal sphincter (LES)
- LES normally works in conjunction with the diaphragm
- If barrier disrupted, acid goes from stomach to esophagus



NOTES: (Further information for understanding only)

- The esophagus, lower esophageal sphincter (LES), and stomach all are considered here as one system: the Esophagus act as an antegrade pump (pushes food downward by peristalsis) and LES as a valve and the stomach is the reservoir or the storage.

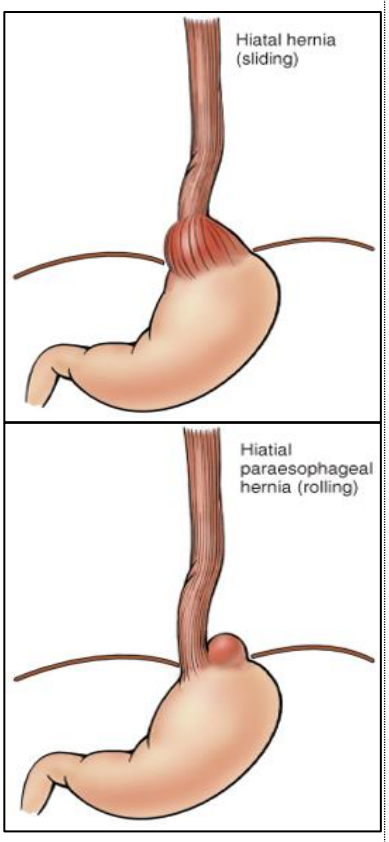
Now any defect in any of the components of this system can contribute to GERD for example:

1) Poor esophageal motility decreases clearance of acids. (Esophageal clearance is an important factor in preventing mucosal injury and there are two types of clearance:
   1- Mechanical by the movement of the esophagus -Peristalsis-.
   2- Chemical by the saliva.
2) A dysfunctional LES allows reflux of large amounts of gastric juice.
3) Delayed gastric emptying can increase volume and pressure in the reservoir (the stomach) until the valve mechanism is defeated (it overcomes the valve pressure and leads to reflux) leading to **GERD**.

A- Abnormal lower esophageal sphincter:

1- **Functional** (frequent transient LES relaxation) (normally the relaxation just after the meals).
2- **Mechanical** (hypotensive LES) (the intra-abdominal pressure will overcome the LES pressure and cause the backflow of the acids –reflux-)
(1 and 2 are the most common cause of GERD)
3- **Foods** (e.g. coffee, alcohol, smoking) (relaxes the LES sphincter)
4- **Medications** (e.g. calcium channel blockers) (decrease the muscle tone).
(3 and 4 both decrease the LES pressure)

5- **Location** … hiatal hernia (check the notes box below)



There are two main types of hiatal hernias:

1) **Hiatal hernia (Sliding):** (More common) the stomach (large portion) and the section of the esophagus that joins the stomach **slide up** into the chest through the hiatus. This is the more common type of hernia.

2) **Paraesophageal hernia (Rolling):** (less common) But it is more dangerous.
The esophagus and stomach stay in their normal locations, but part of the stomach squeezes (small part) through the hiatus next to the esophagus. You can have this type of hernia without any symptoms, but the danger is that the stomach can become "strangled," or and ischemic (no blood supply).

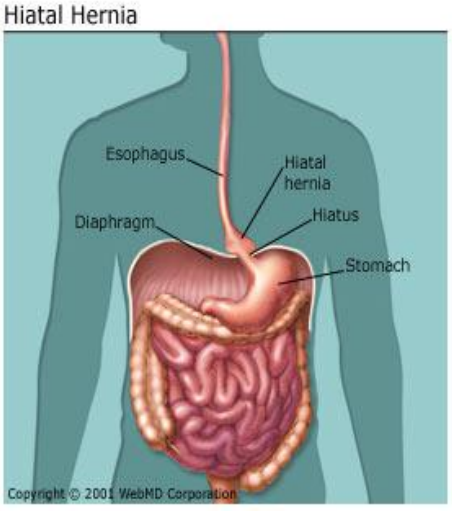
NOTES

- Normally the whole stomach sits below the diaphragm (sheet-like muscle separates the lungs from the abdomen). The esophagus passes through an opening in the diaphragm called **the hiatus** before it enters the stomach. Weakened tissues within and around the hiatus allow **a hiatal hernia** to develop (causes bulging of the stomach through it).

- A **hiatal hernia** occurs when a small portion of the stomach pushes upward through the diaphragm into the thorax through the resulting gap due to separation of the diaphragmatic crura which act as an extrinsic sphincter that **assists the function of LES,** and in order to make this happen the location of **the esophagogastric junction is important to be in the abdomen**, And here in this case it's not.

- Hiatal hernias can be encountered frequently in patients with reflux disease. However, more than 90% of hiatal hernia in adult cases is asymptomatic (no reflux symptoms) and some causes heart-burn sensation.

Hiatal Hernia

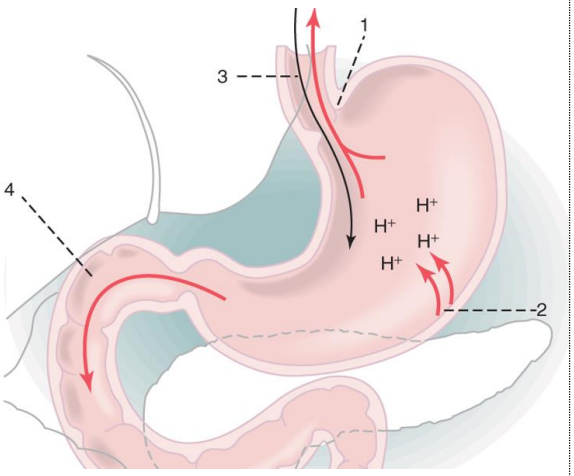


B-Increased abdominal pressure

- Obesity
- Pregnancy
- Increased gastric volume

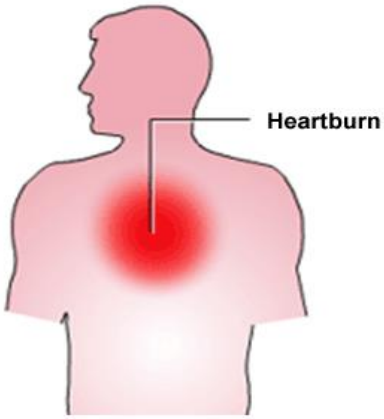
From Robbins: decrease LES tone or increase abdominal pressure all contribute to GERD and include alcohol, tobacco, obesity, central nervous system depressants, pregnancy, hiatal hernia, delayed gastric emptying, increased gastric volume. In many cases no definitive cause is identified.

Pathogenesis of GERD



1. Impaired lower esophageal sphincter.
2. Hypersecretion of acid.
3. Decreased acid clearance resulting from impaired peristalsis or abnormal saliva production.
4. Delayed gastric emptying or duodenogastric reflux of bile salts and pancreatic enzymes.

Clinical Manifestations



- **Typical symptoms (Most common symptoms)**
  -Heartburn—retrosternal burning discomfort
  -Regurgitation—effortless return of gastric contents into the pharynx without nausea, retching, or abdominal contractions.
- Atypical symptoms (alarm symptoms) (extraesophageal) symptoms
  Coughing, chest pain, and wheezing.

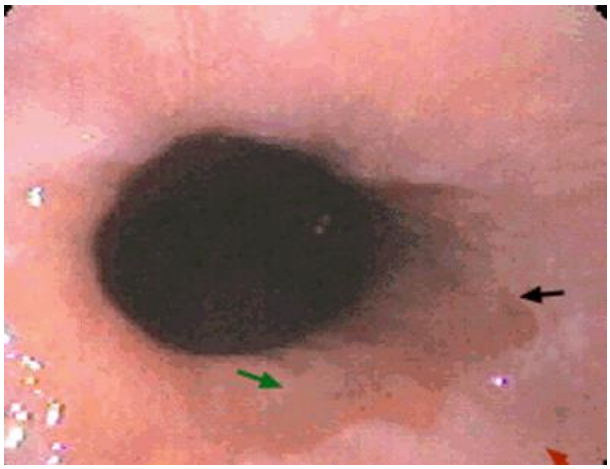
Diagnostic Evaluation

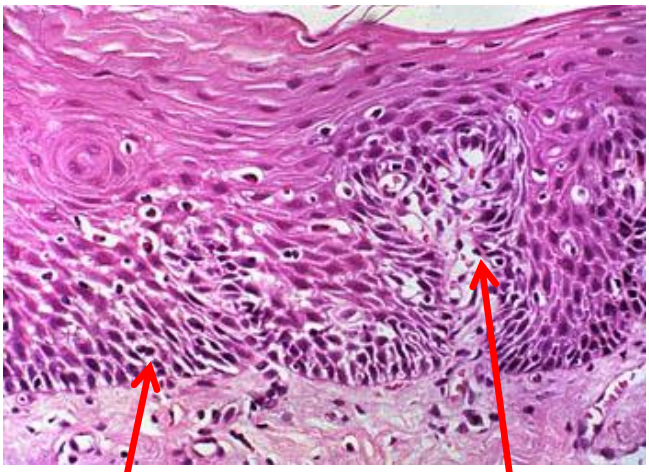
1- **From the signs and symptoms**: If classic symptoms of heartburn and regurgitation exist **with the absence of (alarm symptoms)**, the diagnosis of GERD can be made clinically and treatment can be initiated.

2- **Esophagogastroduodenoscopy:** Endoscopy (with biopsy if needed):
- In patients with alarm signs/ symptoms (atypical symptoms)
- Those who fail a medication trial (because at first we give antacid medications if it failed then we do endoscopy)
- Those who require long-term tx

3- **PH: 24-hour pH monitoring** (the lower end of the Esophagus)
- Accepted standard for establishing or excluding presence of GERD for those patients who do **not have mucosal changes.**
- Trans-nasal catheter or a wireless capsule shaped device.

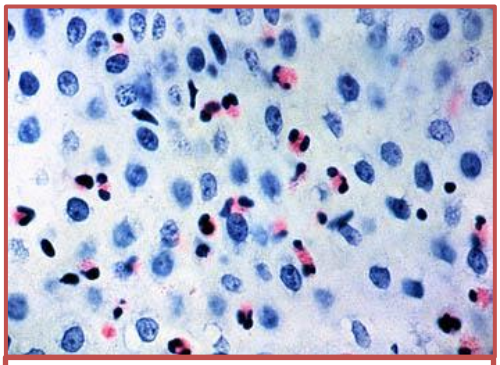
Morphology of GERD





By endoscopy we find **simple hyperemia (redness)** may be the only alteration (1st picture).
In mild GERD mucosal histology is often unremarkable with more significant disease; **eosinophils** are recruited into the squamous mucosa, followed by **neutrophils** in severe injury.

Basal zone hyperplasia exceeding 20% of epithelial thickness and **elongation of lamina propria papillae** and can extend into the upper third of the epithelium.



Eosinophils and neutrophils

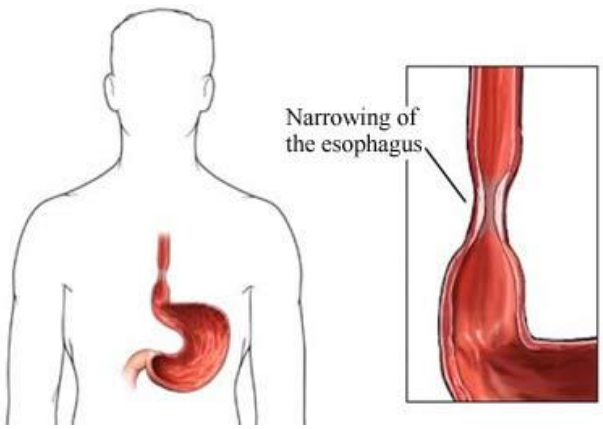
Complications

1- Erosive esophagitis

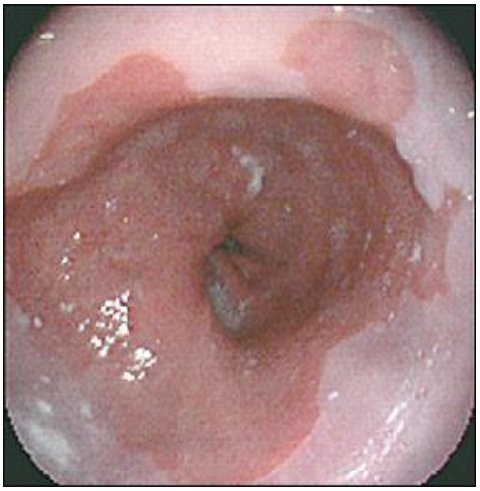
- Responsible for 40-60% of GERD symptoms.
- Severity of symptoms often fail to match severity of erosive esophagitis.
- Red mucosa with erosions.

2- Esophageal stricture

- Result of healing of erosive esophagitis (by fibrosis which cause obstruction)
- May need dilation.

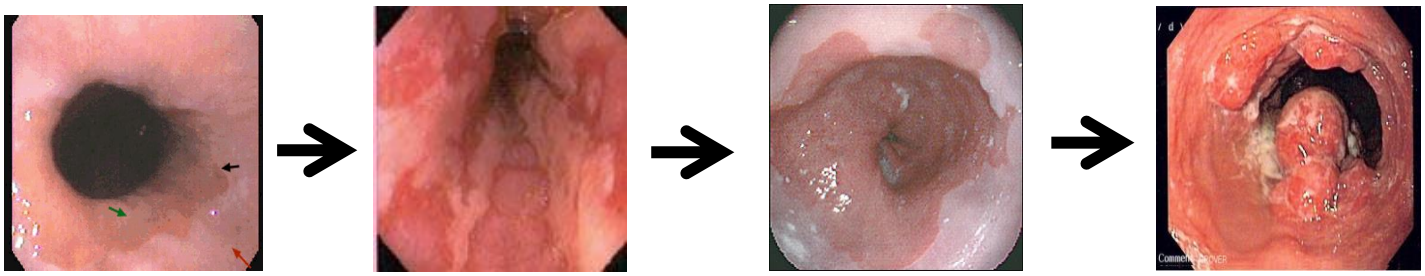


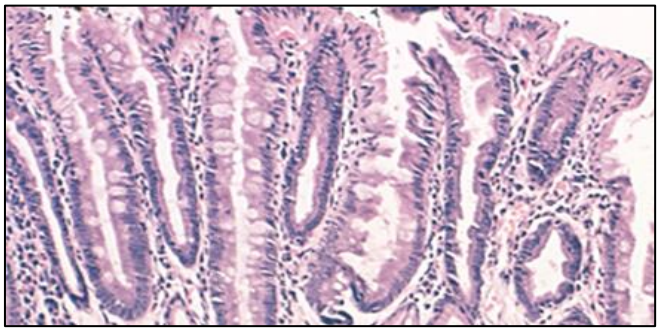
3- Barrett's Esophagus (most sever) 8-15%



- Intestinal metaplasia of the esophagus.
- Associated with the development of adenocarcinoma
- Acid damages lining of esophagus and causes chronic esophagitis.
- Damaged area heals in a metaplastic process (intestinal metaplasia) and abnormal columnar cells replace squamous cells.
- This specialized intestinal metaplasia can progress to dysplasia and adenocarcinoma.

Many patients with Barrett's are asymptomatic and some have symptoms similar to GERD's



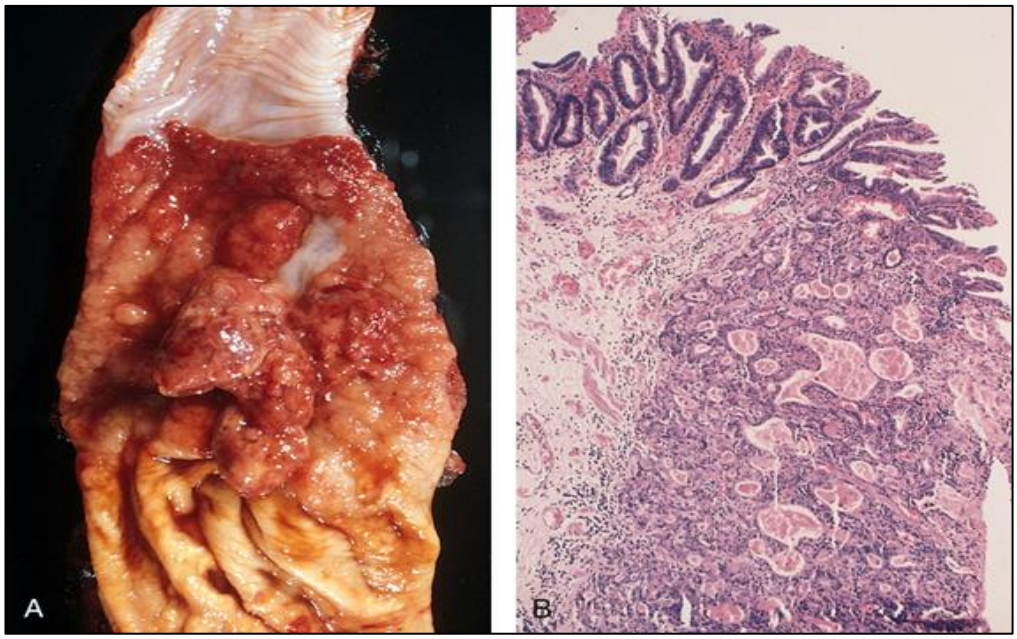


NOTES (from Robbins)

- The strictures in the Esophagus can interfere with eating and drinking by preventing food and liquid from reaching the stomach. They are treated by dilation, in which instrument gently stretches the strictures and expands the narrowing in the esophagus.

- The normal cells that line the esophagus are damaged and replaced by a type of cell not usually found in the esophagus (intestinal epithelium). People with Barrett's esophagus may be at risk of developing adenocarcinoma, but most people with Barrett's esophagus do not develop adenocarcinoma.

- Molecular studies suggest that barrett's esophagus epithelium is more similar to adenocarcinoma than normal esophageal epithelium.



"From Robbins"

Morphology of Barrett:

Patches of red, velvety mucosa extending upward from the gastroesophageal junction. The metaplastic mucosa appear light brown columnar mucosa distally Microscopy: Distal squamous mucosa is replaced by metaplastic specialized (intestinalized columnar) epithelium containing goblet cells.

Treatment:

The goals are to control symptoms and to heal esophagitis, and to prevent recurrent esophagitis or other complications by changing lifestyle and control of gastric acid secretion through medications.

- H2 receptor Blockers
- Proton pump inhibitors

↓

Antireflux surgery (if none of the medications and lifestyle changes worked).

Malignant tumors of the esophagus:

- The most common malignant tumors of the esophagus are squamous carcinomas and adenocarcinomas.

- The prognosis for both types of carcinoma is poor.

Squamous carcinomas: are most common in the middle and lower esophagus. They mostly develop in men who are heavy alcohol drinkers or heavy smokers, and may be preceded by epithelial dysplastic change.

"From Robbins"

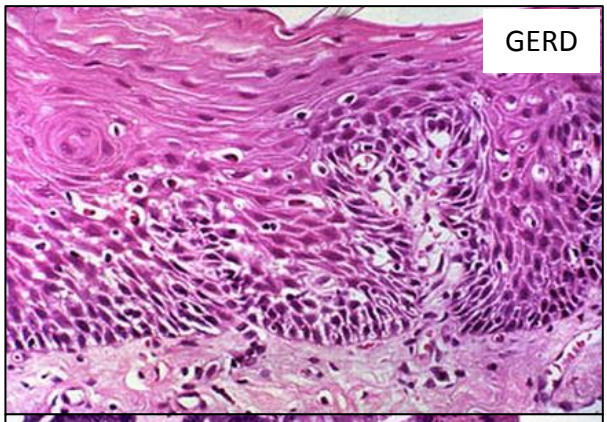
Adenocarcinoma:

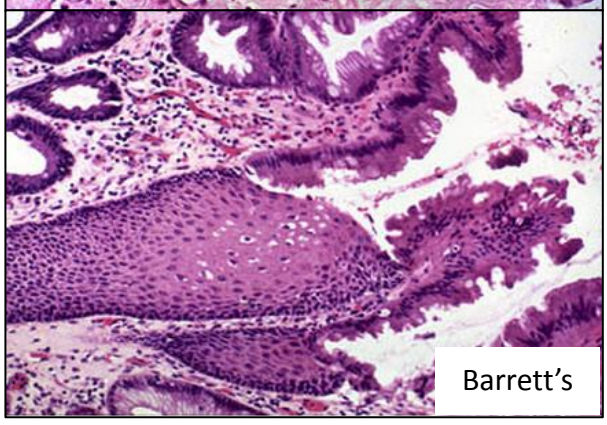
Esophageal adenocarcinoma typically arises in the background of Barrett esophagus and long standing-chronic-GERD.
The risk is greater in patients with documented dysplasia and is further increased by tobacco use, obesity, and previous radiation therapy.

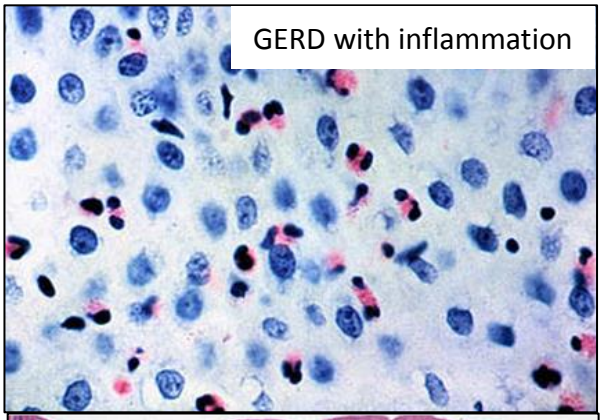
Morphology:

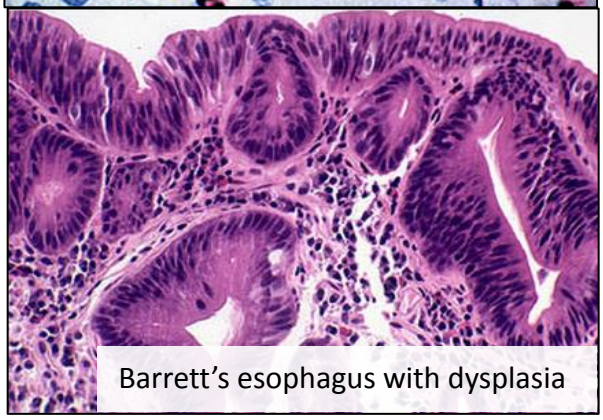
Adenocarcinoma usually occurs in the distal third of the Esophagus and may invade the adjacent gastric cardia.
Early lesion may appear as flat or raised patches in otherwise intact mucosa, tumors may form large exophytic masses, infiltrate diffusely or ulcerate and invade deeply.
Microscopy:Barret esophagus frequently is present adjacent to the tumor. Tumors typically produce mucin and form glands.

Under Microscope









Summary (from Robbins Basic Pathology)

- Esophagitis can result from chemical or infectious mucosal injury. Infections are most frequent in immunocompromised patients.
- The most common cause of esophagitis is gastroesophageal disease (GERD), Which must be differentiated from eosinophilic esophagitis (inflammation of the esophagus at sites far from the gastroesophageal junction with great infiltration of eosinophils superficially).
- Barret esophagus which may develop in patients with chronic GERD is associated with increased risk of esophageal adenocarcinoma
- Esophageal squamous cell carcinoma is associated with alcohol and tobacco use, poverty, caustic esophageal injury, achalasia, tylosis and plummer-vinson syndrome.

Questions from Female doctor's slides

1/ what are the major causes of reflux esophagitis?

Reflux of gastric contents is the major cause of reflux esophagitis. Many factors play a role:

- The presence of a sliding hiatal hernia is the most common.
- Heavy alcohol, tobacco use.
- Increased gastric volume.
- Decreased efficacy of LES.
- Pregnancy.
- CNS depressants.
- Hypothyroidism.

2/ what are other causes of esophagitis?

Ingestion of irritants (e.g. alcohol, corrosive acids); infections in immunosuppressed hosts by fungi (e.g. Candida) or viruses (e.g. CMV, herpes); uremia; radiation therapy; graft-versus-host disease; and cytotoxic anticancer therapy.

3/ what are the major complications of reflux esophagitis?

The potential complications of severe reflux esophagitis are (a) ulcer; (b) bleeding; (c) development of stricture; (d) development of Barrett esophagus.

Case Scenario

- A 57-year-old presents with a history of a retrosternal burning sensation, particularly after large meals, and often on retiring to bed at night. Treatment with antacids has had little effect and he has been referred by his GP for endoscopy.
- Upper gastrointestinal tract endoscopy reveals reddening of the lower esophageal mucosa from the level of the gastroesophageal junction to a point 32 cm from the incisors. There is no evidence of a hiatus hernia. The proximal border of the reddened area is irregular, and this area is biopsied. The biopsy shows gastric and intestinal-type glandular mucosa.

1. What is the likely cause of the symptoms?

- The symptoms of 'heartburn' are suggestive of gastroesophageal reflux disease (GORD), with or without the presence of a hiatus hernia.
- Other important causes of retrosternal pain should not be overlooked, including cardiovascular causes, especially myocardial ischaemia, as well as other rarer causes including pneumothorax and musculoskeletal pain.

2. What is the final diagnosis?

The endoscopic and biopsy appearances confirm a Barrett's oesophagus. This is a metaplastic process which develops as a result of persistent reflux of gastric contents into the esophagus, the normal squamous mucosa being replaced by glandular mucosa of gastric or intestinal type.

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

If there is any mistake or feedback please contact us: 432PathologyTeam@gmail.com