جامعة الملك سعود
King Saud University

MED437
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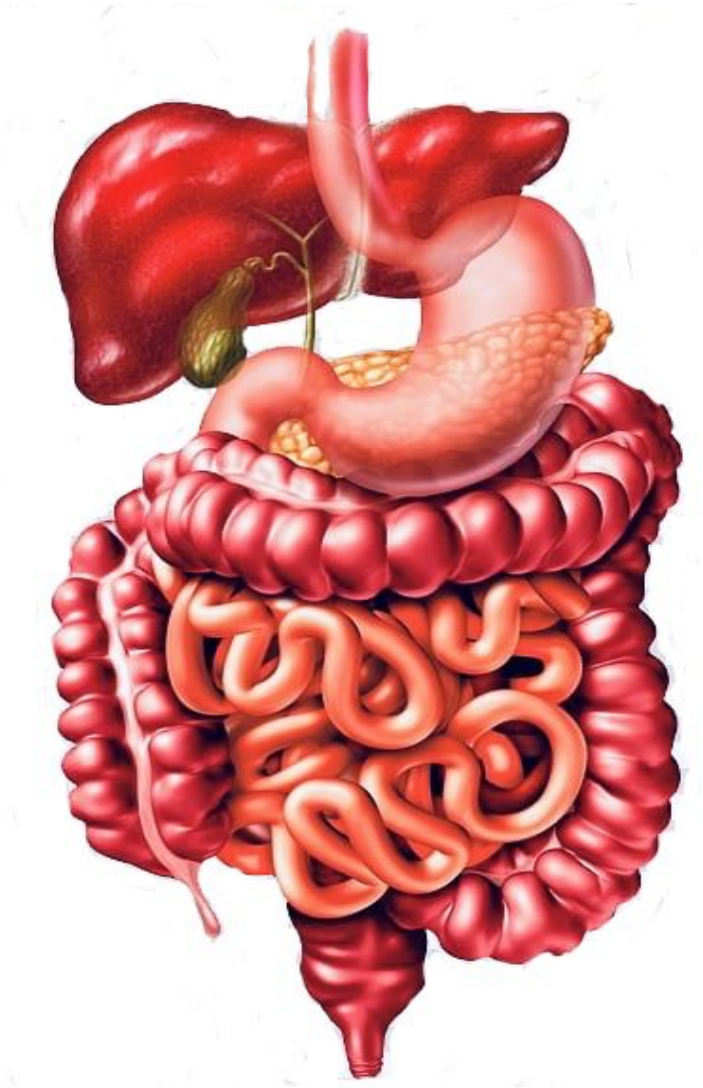
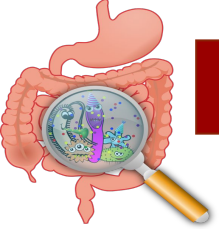
PATHOLOGY
TEAM 437



Gastroesophageal Reflux Disease (GERD) & Peptic Ulcer Disease

Content Explanation Notes Important



Objectives and there answers from Dr slides

Define gastroesophageal reflux disease

- Symptoms OR mucosal damage produced by the abnormal reflux of gastric contents into the esophagus Physiologic vs. pathologic

Understand the Pathophysiology of reflux esophagitis.

- Abnormal lower esophageal sphincter or increased abdominal pressure

Know clinical features of reflux esophagitis

- Heartburn, Regurgitation
- Atypical symptoms….coughing, chest pain, and wheezing

Describe the pathological features of reflux esophagitis

- Eosinophils and neutrophils
- Elongation of lamina propria papillae
- basal zone hyperplasia

Know the complications of reflux esophagitis

- Erosive esophagitis
- Stricture
- Barrett's esophagus ⇨ dysplasia. ⇨ adenocarcinoma

Understand the Pathophysiology and etiology of acute and chronic peptic ulcer:

- Increase Aggressive Factors OR decrease Defensive Factors.
- Acute ulcers: 1-.acute gastritis 2- severe stress response,3-extreme hyperacidity.
- Chronic ulcer:
  A-Gastric: 1-H.Pylori infection 2-NSAIDS 3-Bile Reflux
  B-Duodenal: 1-H.Pylori infection 2-Hyperacidity

Recognize the gross and microscopic features of peptic ulcer:

- The classic peptic ulcer is a round to oval, sharply punched-out defect
- necrotic tissue and polymorph exudate overlying inflamed granulation tissue which merges with mature fibrous (scar) tissue.

Recognize the clinical features and consequences of acute and chronic peptic ulcer:

- **Clinical Features:**Epigastric pain Gnawing or burning sensation
- **Consequences/ Complications:** Some present with
  1-iron deficiency anemia 2- frank hemorrhage 3- perforation

Define gastroesophageal reflux disease.

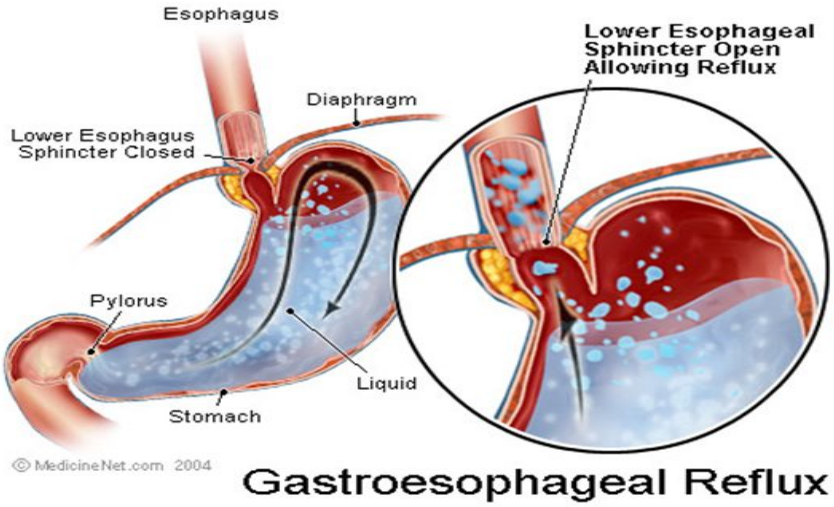


Figure 2 Anatomic radiographic landmarks of the lower esophageal sphincter (LES).

	Gastroesophageal reflux (GER)	Gastroesophageal reflux disease (GERD)
Definitions	is a normal physiologic phenomenon experienced intermittently by most people, particularly after a meal.	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.
Differences	•Physiologic GER –Postprandial (after a meal) –Short lived –Asymptomatic –No nocturnal symptoms (at night)	•Pathologic GERD –Symptoms –Mucosal injury –Nocturnal symptoms

Understand the pathophysiology Of Reflux Esophagitis.

Pathophysiology

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

A. Abnormal lower esophageal sphincter.

-The most common causes:

1. Functional (frequent transient LES relaxation).
"gets loose during swallowing"

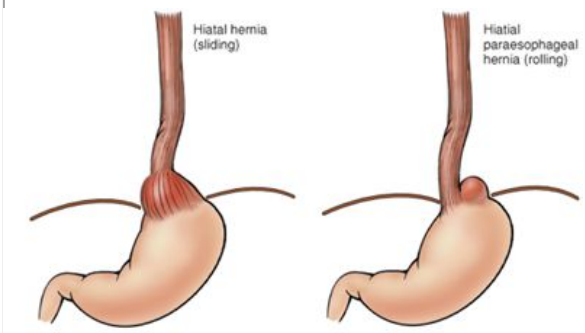
2. Mechanical (hypotensive LES).
"always loose"

-Decrease the pressure of the LES:

3. Foods (eg: coffee, alcohol)

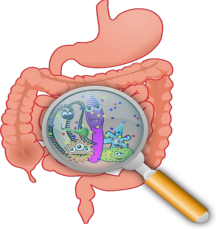
4. Medications (eg: calcium channel blockers)

5. Location: Hiatal hernia (the esophagus is up in the chest so the diaphragm can't aid the sphincter).



B. Increased abdominal pressure.

1.Obesity.
2.Pregnancy.
3.Increased gastric volume.



Know Clinical Features Of Reflux Esophagitis.

Clinical Manifestations:

- **Typical** (most common) symptoms: (When these symptoms occur they are diagnostic, no need for further investigation).

- Heartburn: **retrosternal burning discomfort.**

- Regurgitation: effortless return of gastric contents into the pharynx without nausea.

- **Atypical** symptoms: (These symptoms are not enough for diagnosis, further investigation is needed).

- Coughing.

- Chest pain. (Patients may go to the cardiologist & do ECG due to the mimicry of angina pains)*.

- Wheezing. (Patients may go to the pulmonologist due to mimicry of respiratory symptoms)*.

*Differential diagnosis.

Diagnostic Evaluation:

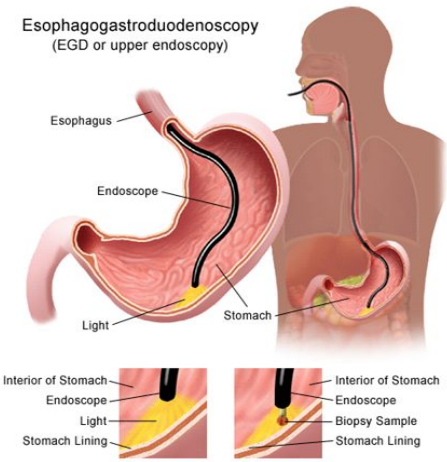
If classic symptoms of heartburn and regurgitation exist in the absence of "alarm symptoms" the diagnosis of GERD can be made clinically and treatment can be initiated.

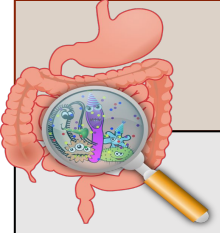
Esophagogastrodudenoscopy:

- Endoscopy (with biopsy if needed)

–In patients with alarm signs/symptoms.(atypical)

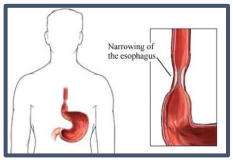
–Those who fail a medication trial.





Know the complications of reflux esophagitis

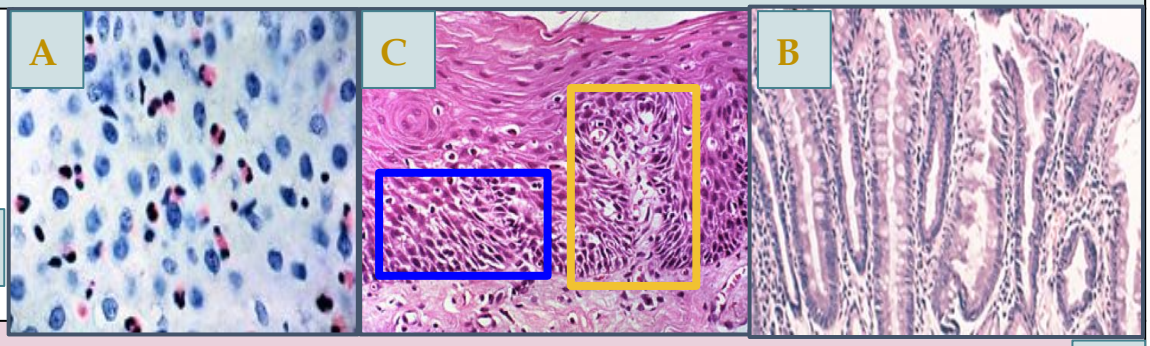
complications

1-Erosive esophagitis.	2-Esophageal stricture.	3-Barrett's Esophagus.		
Responsible for 40-60% of GERD symptoms. Severity of symptoms often fail to match severity of erosive esophagitis	Result of healing of erosive esophagitis. fibrosis May need dilation. 	**8-15% of the cases.**	Associated with the development of adenocarcinoma. B	**Intestinal metaplasia of the esophagus.** it will change from non keratinizing squamous epithelium to columnar with goblet cells.
		Acid damages lining of esophagus and causes esophagitis – Damaged area heals in a metaplastic process and abnormal **columnar cells** replace squamous cells. – This specialized intestinal metaplasia can progress to **dysplasia and adenocarcinoma.**		

Morphology

Eosinophils and neutrophils

A

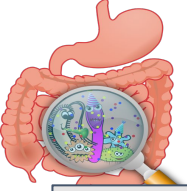


A-basal zone hyperplasia. .B-Elongation of lamina propria papillae.

C

Treatment مو مطلوب عليكم:

1. H 2 receptor Blockers. They both Antacid, reduce gastric acid & relief the symptoms. 2. Proton pump inhibitors. 3. Antireflux surgery. If the meds didn't treat the patient



Peptic Ulcer Disease

Ulcer

It's a breach in the mucosa of the alimentary tract extending through muscularis mucosa into submucosa or deeper.(1)

1-Peptic ulcer A	2-Stress ulcers(acute gastric ulcer)

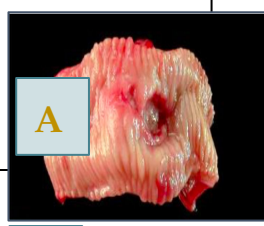
Pathophysiology

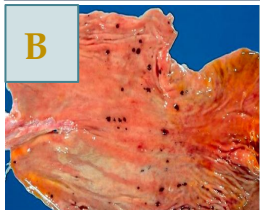
Aggressive factors	Defensive factors
1-H.pylori 2-Drugs (NSAIDs) 3-Acid 4-Pepsin 5-Bile salts	1-Mucus 2-Bicarbonate 3-Blood flow 4- cell renewal 5-Prostaglandins 6-Phospholipid

Any imbalance between these factors will cause a disease, in **peptic ulcer:**
H.pylori causes this imbalance.
(increase in aggressive or decrease in defensive)

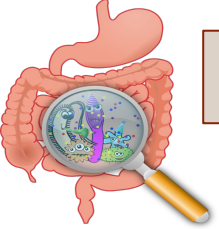
Pathophysiology of Acute Peptic Ulcer B

•As part of an Acute Gastritis:	•As a complication of a severe stress response:(2)	•As a result of extreme hyperacidity:
acute response to an irritant 'chemical' injury by drugs (NSAID) or alcohol.	A-Severe burns (Curling's ulcer), B-Major trauma (cushing ulcer) like car accident C-Cerebrovascular accidents. causes intra cranial hemorrhage	Zollinger- Ellison syndrome.(3)



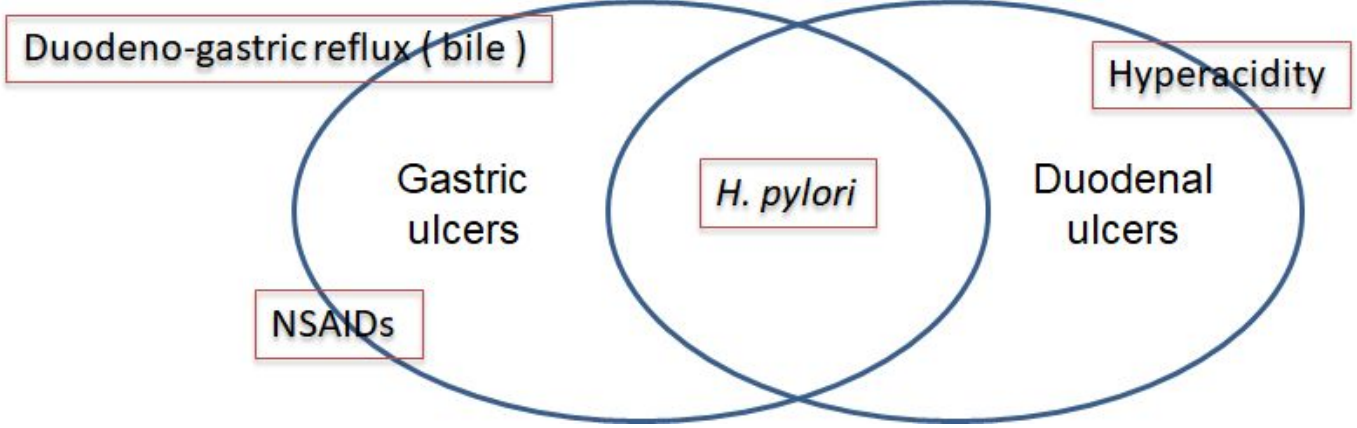


(1) To submucosa : ulcer. / part of mucosa erosion
(2) all of this outside stomach and the result is decrease of blood supply to stomach.
(3) increase stimulation of parietal cells by histamine or gastrien it will lead to acute gastric ulcer or chronic duodenal ulcer.

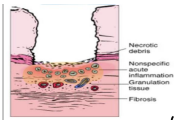


Peptic Ulcer Disease

Chronic Peptic Ulcers		
Locations	May Occur in any portion of the GI tract exposed to gastric Juices 98% are located in the first portion of Duodenum or Stomach Ratio 4:1, Peptic ulcers are four times more common in the proximal duodenum than in the stomach. Can occur in Esophagus due to GERD or ectopic Gastric Mucosa Gastric Mucosa within a Meckel Diverticulum (congenital anomaly) can result in peptic ulceration of adjacent mucosa	
Gastric Ulcers		
Mucosal Defences	Mucus-Bicarbonate barrier Protects Against:Duodenal-gastric reflux (Bile enters the stomach)	Surface Epithelium Protects Against: NSAIDs (Inhibit Prostaglandin synthesis) H Pylori (Produce cytotoxins & Ammonia)
Breakdown of mucosal defence is much more important than excessive acid production in stomach peptic ulcers		
Duodenal Ulcers		
(1)Increased Production of acid assumes more importance in the pathogenesis of duodenal ulceration (2)H Pylori infected individuals secrete 2-6 times as much acid as non-infected controls (3)H pylori does not colonise normal duodenal epithelium (4)Helicobacter is involved in duodenal ulceration because there is gastric metaplasia (metaplasia of duodenal epithelium to gastric epithelium) in response to excess acid (5)Gastric metaplasia paves the way for colonization by Helicobacter		
Increased Acid Production + H Pylori = Duodenal Ulcers		



H pylori infection of the pyloric antrum is present in nearly all patients with chronic duodenal ulcer and approximately 75% of patients with chronic gastric ulcer. Bleeding is a common complication
Although more than 70% of individuals with PUD are infected by *H. pylori*, fewer than 20% of *H. pylori*–infected individuals develop peptic ulcer.

Peptic Ulcers		
Morphology	Gross Important	Usually less than 20 mm in diameter but may exceed 100 mm The classic peptic ulcer is a round to oval, sharply punched-out defect In contrast, heaped-up margins are more characteristic of cancers
	Microscopy Not very import, because any ulcer looks the same under the microscope.	The base consists of necrotic tissue and polymorph exudate overlying inflamed granulation tissue which merges with mature fibrous (scar) tissue. 
Clinical Features	Epigastric pain (the most common symptom) Gnawing or burning sensation Occurs 2-3 hours after meals Relieved by food or antacids Patient awakens with pain at night.	
Complications	Some present with complications such as iron deficiency anemia, frank hemorrhage, or perforation.	
Therapy	Current therapies for PUD are aimed at: 1. H pylori Eradication 2. Acid suppression: 1. Proton Pump Inhibitors 2. H2 Blockers	الثيرابي مو عليكم لكن اذا عرفت 1-etiology 2-pathogenesis بتعرف الثيرابي،الثيرابي انك تقطع واحد منهم

Pathoma

GASTROESOPHAGEAL REFLUX DISEASE (GERD)

A. Reflux of acid from the stomach due to reduced LES tone

B. Risk factors include alcohol, tobacco, obesity, fat-rich diet, caffeine, and hiatal hernia.

C. Clinical features

1. Heartburn (mimics cardiac chest pain)
2. Asthma (adult-onset) and cough
3. Damage to enamel of teeth
4. Ulceration with stricture and Barrett esophagus are late complications.

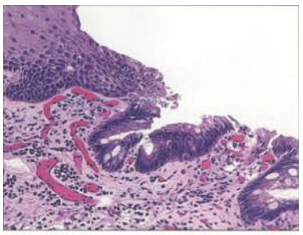


Fig. 10.8 Barrett esophagus.

BARRETT ESOPHAGUS

A. Metaplasia of the lower esophageal mucosa from stratified squamous epithelium to nonciliated columnar epithelium with goblet cells (Fig. 10.8); seen in 10% of patients with GERD

1. Response of lower esophageal stem cells to acidic stress

B. May progress to dysplasia and adenocarcinoma

PEPTIC ULCER DISEASE

A. Solitary mucosal ulcer involving proximal duodenum (90%) or distal stomach (10%)

B. Duodenal ulcer is almost always due to H pylori(> 95%); rarely, may be due to ZE syndrome

1. Presents with epigastric pain that improves with meals
2. Diagnostic endoscopic biopsy shows ulcer with hypertrophy of Brunner glands.
3. May rupture leading to bleeding from the gastroduodenal artery (anterior ulcer) or acute pancreatitis (posterior ulcer)

C. Gastric ulcer is usually due to H pylori (75%); other causes include NSAIDs and bile reflux.

1. Presents with epigastric pain that worsens with meals
2. Ulcer is usually located on the lesser curvature of the antrum.
3. Rupture carries risk of bleeding from left gastric artery.

D. Differential diagnosis of ulcers includes carcinoma.

1. Duodenal ulcers are almost never malignant (duodenal carcinoma is extremely rare).
2. Gastric ulcers can be caused by gastric carcinoma (intestinal subtype).

i. Benign peptic ulcers are usually small(< 3 em), sharply demarcated ("punched-out"), and surrounded by radiating folds of mucosa (Fig. 10 .13A).

ii . Malignant ulcers are large and irregular with heaped up margins (Fig.10.13B)

iii. Biopsy is required for definitive diagnosis.

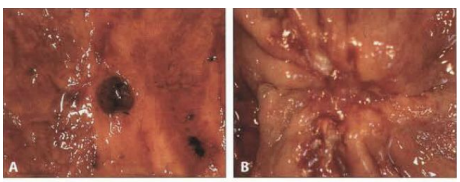


Fig. 10.13 Gastric ulcer. **A**, Peptic ulcer disease. **B**, Carcinoma. (Courtesy of Aliya Husain, MD)

Questions

Q1 : Which one of the following is a defensive factor of peptic ulcer ? .

(A) Bicarbonate
(B) Acid
(C) Pepsin
(D) Bile salts

Q2 : A 40-year-old woman presents with a 2-month history of burning epigastric pain that usually occurs between meals. The pain can be relieved with antacids or food. The patient also reports a recent history of tarry stools. She denies taking aspirin or NSAIDs. Laboratory studies show a microcytic, hypochromic anemia (serum hemoglobin = 8.5 g/dL). Gastroscopy reveals a bleeding mucosal defect in the antrum measuring 1.5 cm in diameter. An endoscopic biopsy shows that the lesion lacks mucosal lining cells and is composed of amorphous, cellular debris and numerous neutrophils. Which of the following is the most important factor in the pathogenesis of this patient's disease?

(A) Achlorhydria
(B) Acute ischemia
(C) Autoimmunity
(D) Gastrinoma
(E) Helicobacter pylori infection

Q3 : Which of the following is NOT a causative agent for a peptic ulcer?

(A) NSAIDS
(B) Helicobacter pylori
(C)Physiological Stress
(D) Augmentin

1-A
2-E
3-D

Q4 : Both gastric ulcers and H.pylori infection are highly associated with ? .

(A) Diff
(B) Gastric malignancy
(C) Uveitis
(D) Esophageal Neoplasms

Q5 : Ulcerations typically occur in regions bathed with acid/pepsin such as the ? .

(A) Jejunum
(B) Cecum
(C) Duodenum
(D) McBurney's point

Q6 : What often describes the pain of PUD?

(A) Sharp, knife-like. Radiates to the right shoulder
(B) Dull, achy. Localized to the stomach.
(C) Diffuse, joint arthralgia.
(D) Burning or gnawing. Radiates to the back.

Q7 : Nsaids induced ulcer differ from h.pylori associated ulcer in that patient with nsaids induced ulcer are more likely to have ?

(A) duodenal ulcer
(B) more severe upper git bleeding
(C) ulcer related epigastric pain
(D) gastric ulcer

4-B

5- D

7- B

Q8 : All of the following are features of gastroesophageal reflux except? .

(A) Postprandial
(B) Physiological
(C) asymptomatic
(D) Nocturnal pain

Q9 :why hiatal hernia may lead to gastroesophageal reflux? .
(A)due to the increase in acidity caused by ach hypersensitivity
(B) due to the decrease in the abdominal pressure
(C) because they are more susceptible to Gastrinoma
(D) because it will decrease the pressure of the lower esophageal sphincter

Q10 : Which one of the following is a typical symptom of GERD?
(A) Coughing
(B).Wheezing
(C) retrosternal burning sensation
(D) Chest pain

Q11:Which of the following is not a histopathologic feature of GERD :
(A) eosinophils recruitment within the mucosa followed by neutrophils
(B) basal zone hyperplasia
(C) elongation of lamina propria
(D) monocytic infiltration with edema and necrosis

Q12 :Which of the following is false regarding GERD clinical presentation ?
(A) the most common symptoms are heartburn and dysphagia
(B) they have noticeable regurgitation of sour-tasting gastric contents
(C) the severity of symptoms is closely related to the degree of histological damage
(D) the degree of histological damage tends to increase with disease duration

Q13: A 50-year-old obese man (BMI = 32 kg/m2) comes to the physician complaining of indigestion after meals, bloating, and heartburn. Vital signs are normal. A CT scan of the abdomen reveals a hiatal hernia of the esophagus. Endoscopic biopsy shows thickening of the basal layer of the squamous epithelium, upward extension of the papillae of the lamina propria, and an increased number of neutrophils and lymphocytes. Which of the following is the most likely diagnosis?
(A) Esophageal varices
(B) Mallory-Weiss syndrome
(C) Reflux esophagitis
(D) peptic ulcer

8-D 9-D 10-C 11-D 12-C 13-C

كل الشكر والتقدير للجهود العظيمة
من قبل أعضاء فريق علم الأمراض الكرام.

قادة فريق علم الأمراض

فايز غياث الدرسوني شيرين العكيلي

اعضاء فريق علم الأمراض

راكان محمد الغنيم
سلطان ناصر الناصر
عادل عبدالعزيز السحيباني
حسن محمد العريني
تركي عيد الشمري
سلطان بن عبيد
عبدالجبار اليماني
عبدالله المعيذر
منصور العبرة
تركي آل ينهار
سعد الفوزان

مها العَمري
مجد البراك
بتول الرحيمي
منيرة المسعد
مشاعل القحطاني
رناد الفرم
غادة الحيدري
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