

Supportive module 2 "Basics of diagnosis, treatment and prevention of major gastroenterological diseases"

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Supportive module 2: Basics of diagnosis, treatment and prevention of major gastroenterological diseases

Gastroesophageal Reflux Disease

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

M. Yabluchansky, L. Bogun, L. Martymianova, O. Bychkova, N. Lysenko, N. Makienko
V.N. Karazin National University Medical School' Internal Medicine Dept.

Plan of the Lecture



- Definition
- Epidemiology
- Mechanisms
- Classification
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic guidelines

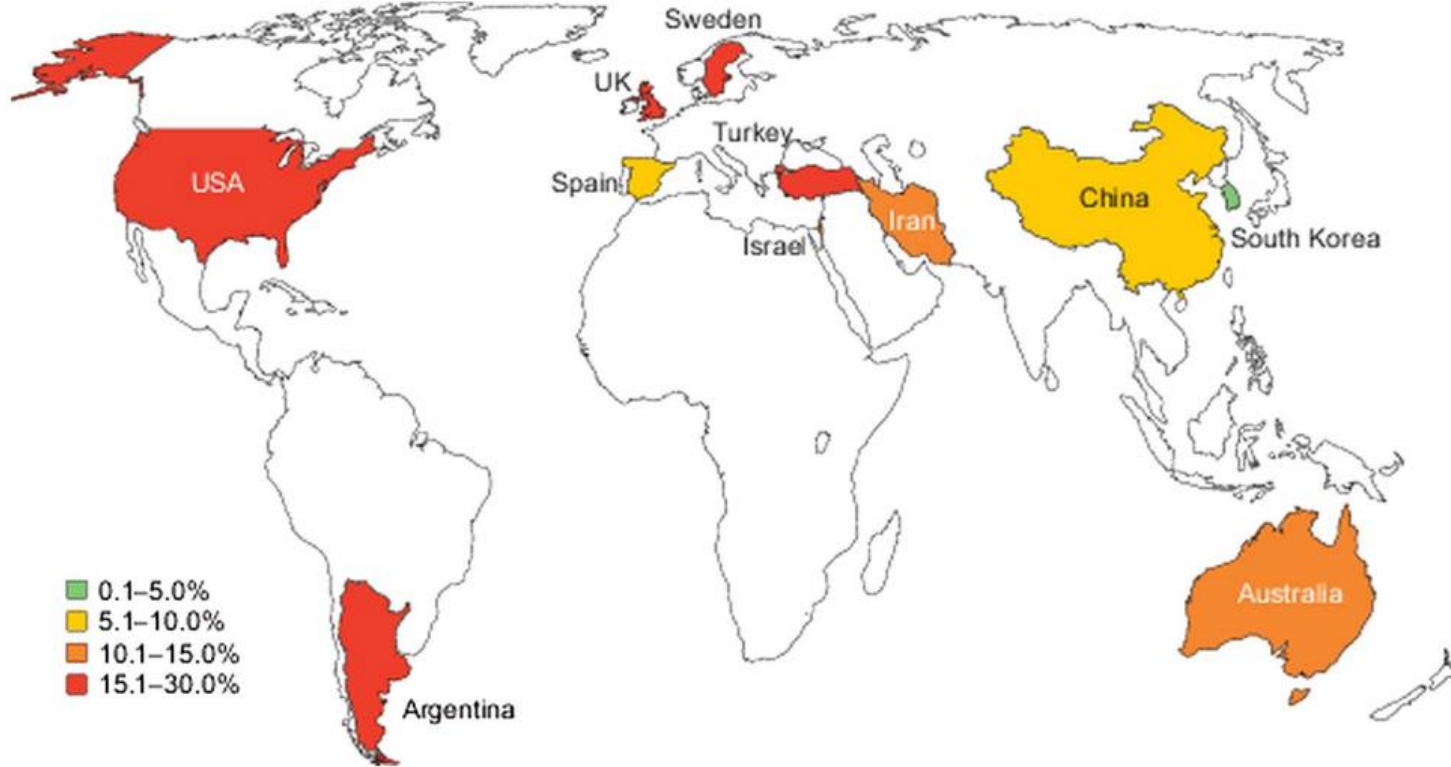
Definition

Gastroesophageal reflux disease (GERD) is a chronic digestive disease that affects the lower esophageal sphincter (LES) with development of its incompetence and reflux of gastric contents into the esophagus, causing symptoms (e.g., the taste of acid in the back of the mouth, heartburn, bad breath, chest pain, vomiting, breathing problems, wearing away of the teeth) with or without associated esophageal mucosal injury (i.e., esophagitis, esophageal strictures, and Barrett's esophagus).

Epidemiology 1

- GERD is prevalent worldwide
- The range of GERD prevalence estimates is (18-28)% in North America, (9-26)% in Europe, (3-8)% in East Asia, (9-33)% in the Middle East, 12% in Australia and 23% in South America
- Incidence per 1000 person-years is approximately 5 in the overall UK and US populations, and 0.84 in pediatric patients aged 1-17 years in the UK
- Evidence suggests an increase in GERD prevalence since 1995 ($p < 0.0001$), particularly in North America and East Asia.

Epidemiology 2



Global distribution of the burden of GERD. Sample-size weighted mean estimates of the prevalence of at least weekly heartburn and/or regurgitation in each country.

Risk Factors

- Weight gain
- Fatty foods
- Caffeinated
- Carbonated beverages
- Alcohol
- Tobacco smoking
- Drugs
- Hiatal hernia
- Increasing body mass index
- Zollinger-Ellison syndrome
- A high blood calcium level (increase gastrin production)
- Scleroderma and systemic sclerosis, which can feature esophageal dysmotility
- Visceroptosis or Glénard syndrome
- A variety of respiratory and laryngeal complaints (laryngitis, chronic cough, pulmonary fibrosis, earache, and asthma)
- Obstructive sleep apnea
- Gallstones
- *H. pylori* infection.

Etiology

- The presence of reflux implies LES incompetence, which may result from a generalized loss of intrinsic sphincter tone or from recurrent inappropriate transient relaxations
- Transient LES relaxations are triggered by gastric distention or subthreshold pharyngeal stimulation
- Factors that contribute to the competence of the gastroesophageal junction include the angle of the cardioesophageal junction, the action of the diaphragm, and gravity (i.e., an upright position)
- Drugs that lower LES pressure include anticholinergics, antihistamines, tricyclic antidepressants, Ca channel blockers, progesterone, and nitrates.

Mechanisms

- A dysfunctional lower esophageal sphincter (LES) allows reflux of large amounts of gastric juice
- Delayed gastric emptying can increase the volume and pressure in the reservoir until the valve mechanism is defeated, leading to GERD
- Esophageal defense mechanisms can be broken down into 2 categories (i.e., esophageal clearance and mucosal resistance)
- Abnormal peristalsis can cause inefficient and delayed acid clearance
- The mucosal resistance factors classified into pre-epithelial, epithelial, and postepithelial defenses, and when the defenses fail, esophagitis and other complications of reflux disease arise.

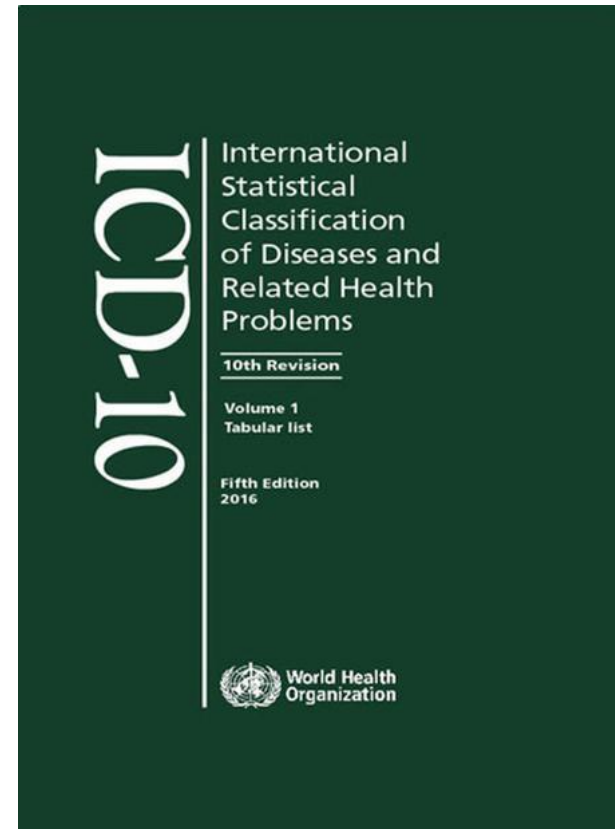
Classification

(International Classification of Diseases (ICD))

XI Diseases of the digestive system

K20-K31 Diseases of oesophagus, stomach and duodenum

K21 Gastro-oesophageal reflux disease



Clinical Investigation

Signs and Symptoms

- Heartburn
- Belching
- Sour taste
- Acid regurgitation
- Nausea and vomiting
- Chronic cough, wheezing
- Difficulty or pain when swallowing
- Sore throat, hoarseness or change in voice
- Chest pain
- Sudden excess of saliva
- Chronic sore throat
- Inflammation of the gums
- Cavities
- Breathlessness
- Esophageal hemorrhage.

Clinical Investigation

Signs and Symptoms: Typical and Atypical

Typical	Heartburn (daytime or night-time) Regurgitation (daytime or nighttime) Water brash (hypersalivation)
Atypical	Nausea, eructation (belching)* Slow digestion, early satiety* Epigastric pain* Bloating* Vomiting Chest pain (precordial) Respiratory symptoms (cough, wheeze, chronic rhinosinusitis) ENT symptoms (hoarseness, pharyngeal pain, globus) Early awakening Nocturnal awakening, nightmares

* Can be considered to be associated with GERD if symptoms improve in response to PPI treatment
ENT, ear, nose and throat.

Clinical Investigation

Signs and Symptoms: Association with Tooth Erosion



Frontal and maxillary occlusal views of severe tooth erosion caused by endogenous acid in a patient with GERD.

Clinical Investigation

Extraesophageal Presentations

- GERD can be considered as a potential co-factor in patients with asthma, chronic cough, or laryngitis
- Careful evaluation for non-GERD causes should be undertaken in all of these patients
- A diagnosis of reflux laryngitis should not be made based solely upon laryngoscopy findings.

Clinical Investigation

Complications

- Esophagitis occur in approximately 50% of patients (see the images below).
- Degrees of esophagitis are described by the Savary-Miller classification as follows:
 - Grade I – Erythema
 - Grade II – Linear nonconfluent erosions
 - Grade III – Circular confluent erosions
 - Grade IV – Stricture or Barrett esophagus (Barrett esophagus with intestinal type metaplasia has malignant potential and is a risk factor for the development of esophageal adenocarcinoma).

Diagnosis

Components

- Clinical diagnosis (a detailed history points to the diagnosis; patients with typical symptoms may be given a trial of therapy; patients who do not improve, or have long-standing symptoms or symptoms of complications, should be studied)
- Endoscopy for patients not responding to empiric treatment, with cytologic washings and biopsy of abnormal areas, is the test of choice
- 24-h pH testing for patients with typical symptoms but normal endoscopy
- Esophageal manometry may be used to guide pH probe placement and to evaluate esophageal peristalsis before surgical treatment.

Diagnosis

Key Points

- A presumptive diagnosis can be established in the setting of typical symptoms of heartburn and regurgitation
- Patients with non-cardiac chest pain suspected due to GERD should have diagnostic evaluation before institution of therapy
- Barium radiographs should not be performed to diagnose GERD
- Upper endoscopy is not required in the presence of typical GERD symptoms
- Endoscopy is recommended in the presence of alarm symptoms and for screening of patients at high risk for complications
- Ambulatory esophageal reflux monitoring is indicated before consideration of endoscopic or surgical therapy.

Diagnosis

Endoscopy and Biopsies

- Endoscopy is not routinely needed if the case is typical and responds to treatment
- Biopsies performed during gastroscopy may show: edema and basal hyperplasia; lymphocytic inflammation; neutrophilic inflammation (usually due to reflux or *Helicobacter* gastritis); eosinophilic inflammation (usually due to reflux); Goblet cell intestinal metaplasia or Barrett's esophagus; elongation of the papillae; thinning of the squamous cell layer; dysplasia, carcinoma.

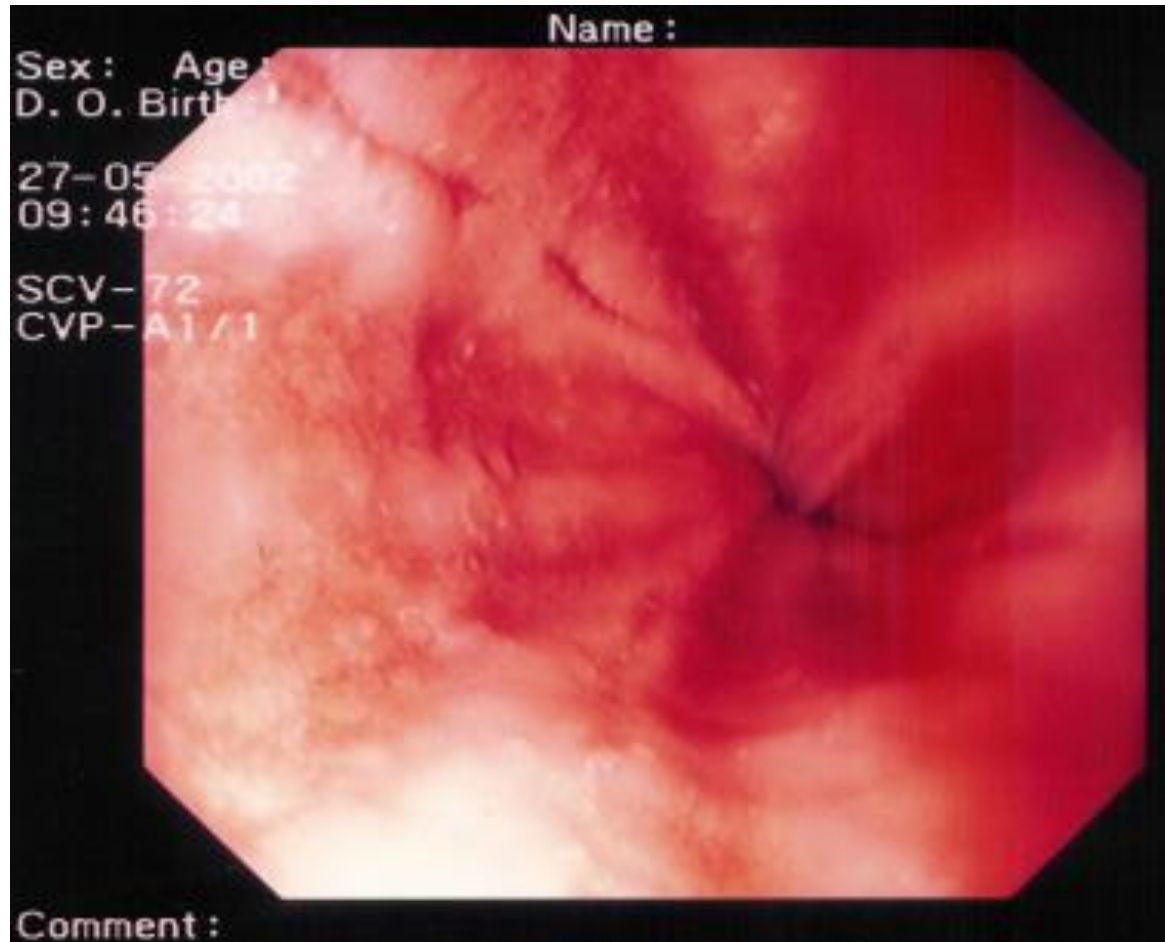
Diagnosis

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Diagnosis

Endoscopy and Biopsies: Peptic Esophagitis



Diagnosis

Endoscopy and Biopsies: Barrett Esophagus



Diagnosis

Esophageal Manometry

- Esophageal manometry defines the function of the LES and the esophageal body (peristalsis) and is essential for correctly positioning the probe for the 24-hour pH monitoring
- Indications for esophageal manometry and prolonged pH monitoring include the following:
 - Persistence of symptoms while taking adequate antisecretory therapy, such as PPI therapy
 - Recurrence of symptoms after discontinuation of acid-reducing medications
 - Investigation of atypical symptoms, such as chest pain or asthma, in patients without esophagitis
 - Confirmation of the diagnosis in preparation for antireflux surgery.

Diagnosis

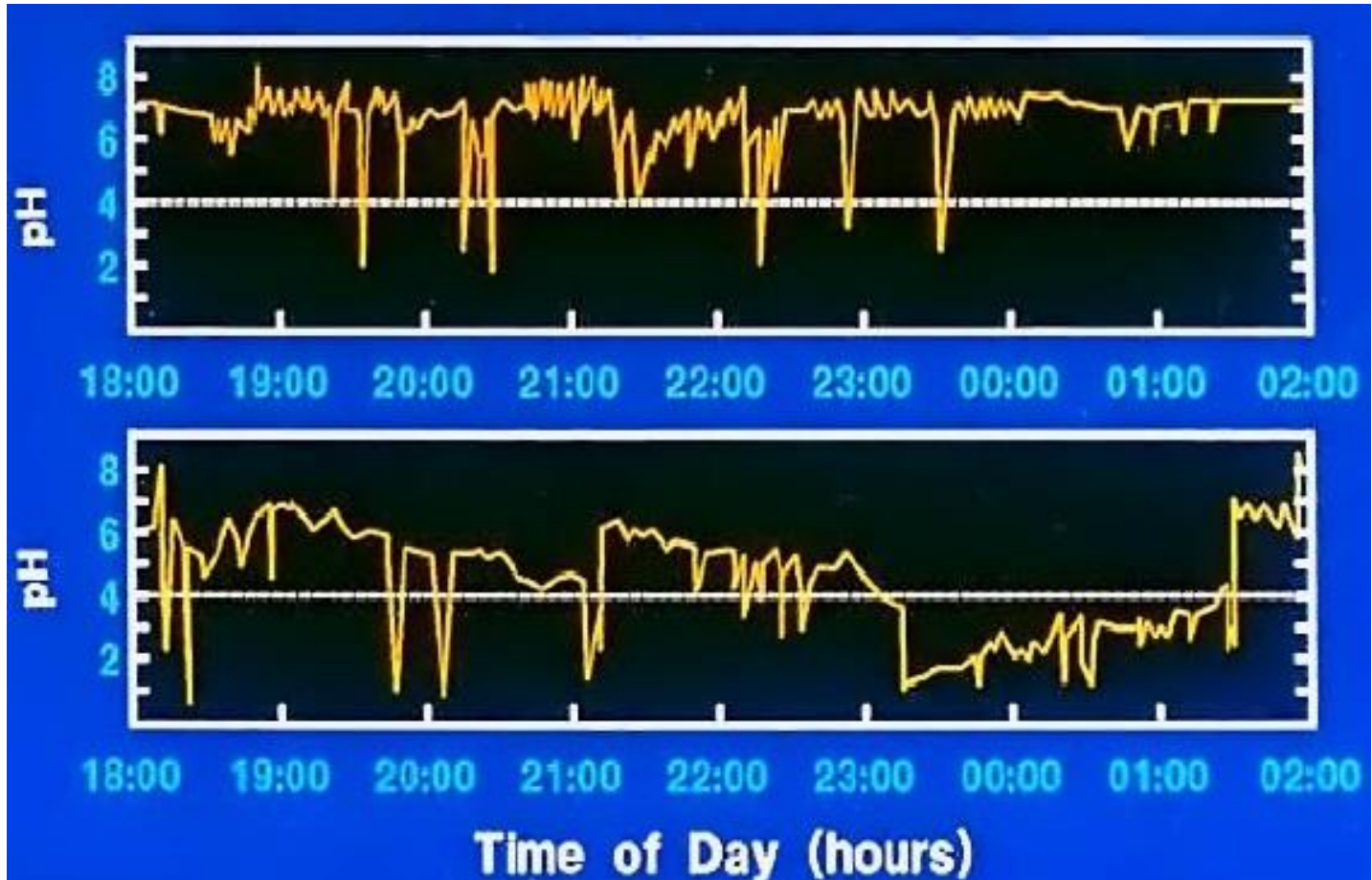
Ambulatory 24-Hour pH Monitoring 1

- Ambulatory 24-hour pH monitoring is the criterion standard in establishing a diagnosis of GERD, with a sensitivity of 96% and a specificity of 95%
- Ambulatory 24-hour pH monitoring quantifies the gastroesophageal reflux and allows a correlation between the symptoms of reflux and the episodes of reflux
- Patients with endoscopically confirmed esophagitis do not need pH monitoring to establish a diagnosis of GERD.

Diagnosis

Ambulatory 24-Hour pH Monitoring 2

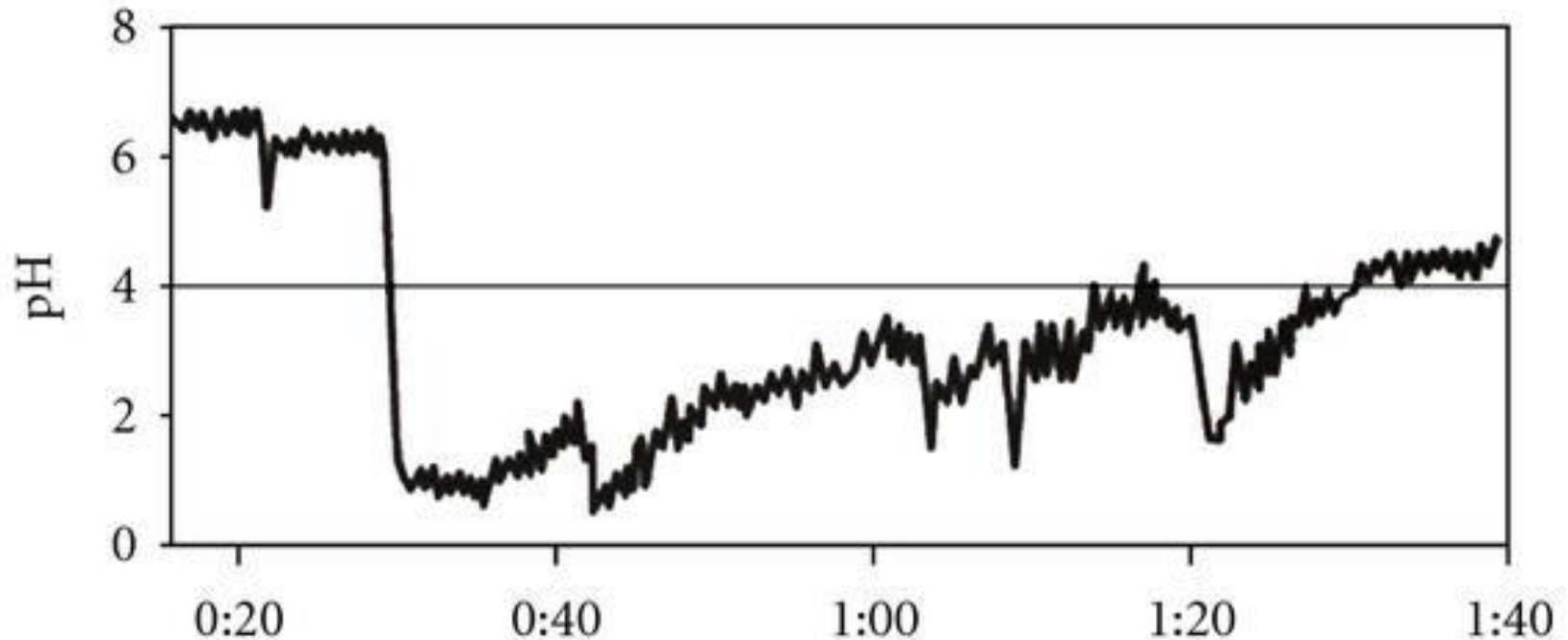
Normal



GERD

Diagnosis

Ambulatory 24-Hour pH Monitoring 3



Pattern of sleep-related esophageal acid exposure in a patient with erosive esophagitis. Night-time acid reflux during supine sleep leads to pH levels <4 that are continuous and sustained.

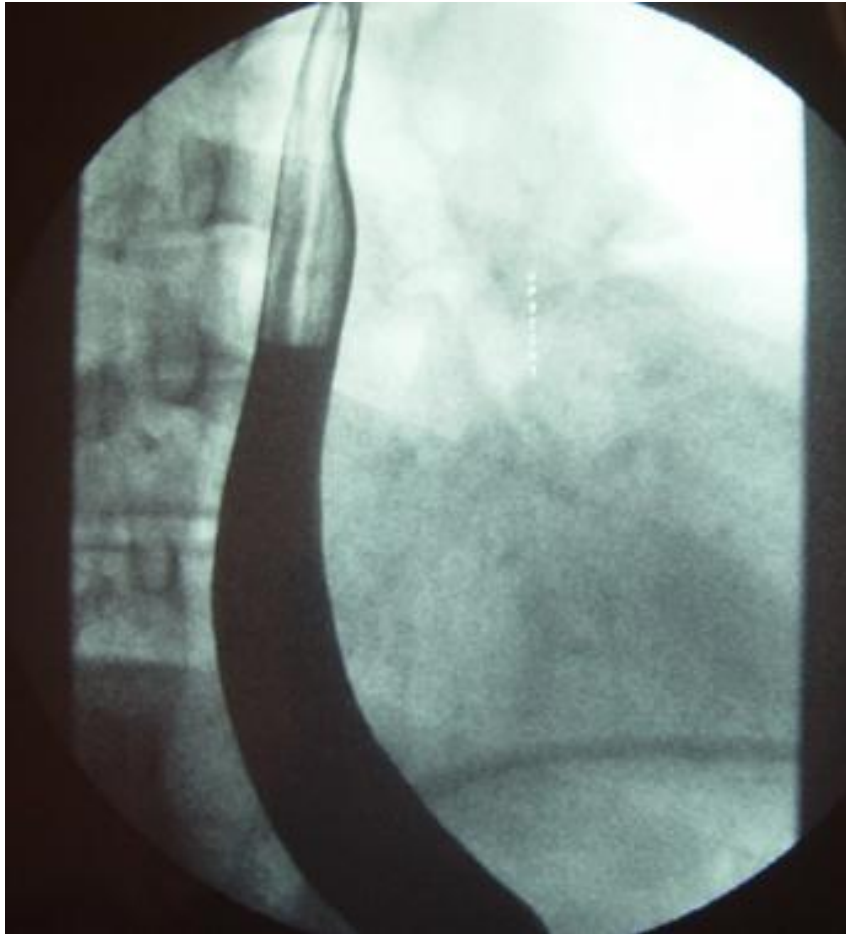
Diagnosis

Imaging

- Plain radiographic findings are not useful in evaluating patients for GERD, but they are helpful in evaluating the pulmonary status
- Chest images may demonstrate a large hiatal hernia, but small hernias can be easily missed
- Upper gastrointestinal (GI) contrast-enhanced studies with double-contrast techniques are the initial radiologic procedure of choice in the workup of the patient in whom GERD is suggested
- Gastric-emptying studies may be worthwhile in the evaluation of patients in whom delayed gastric emptying is believed to contribute to the manifestation of GERD symptoms

Diagnosis

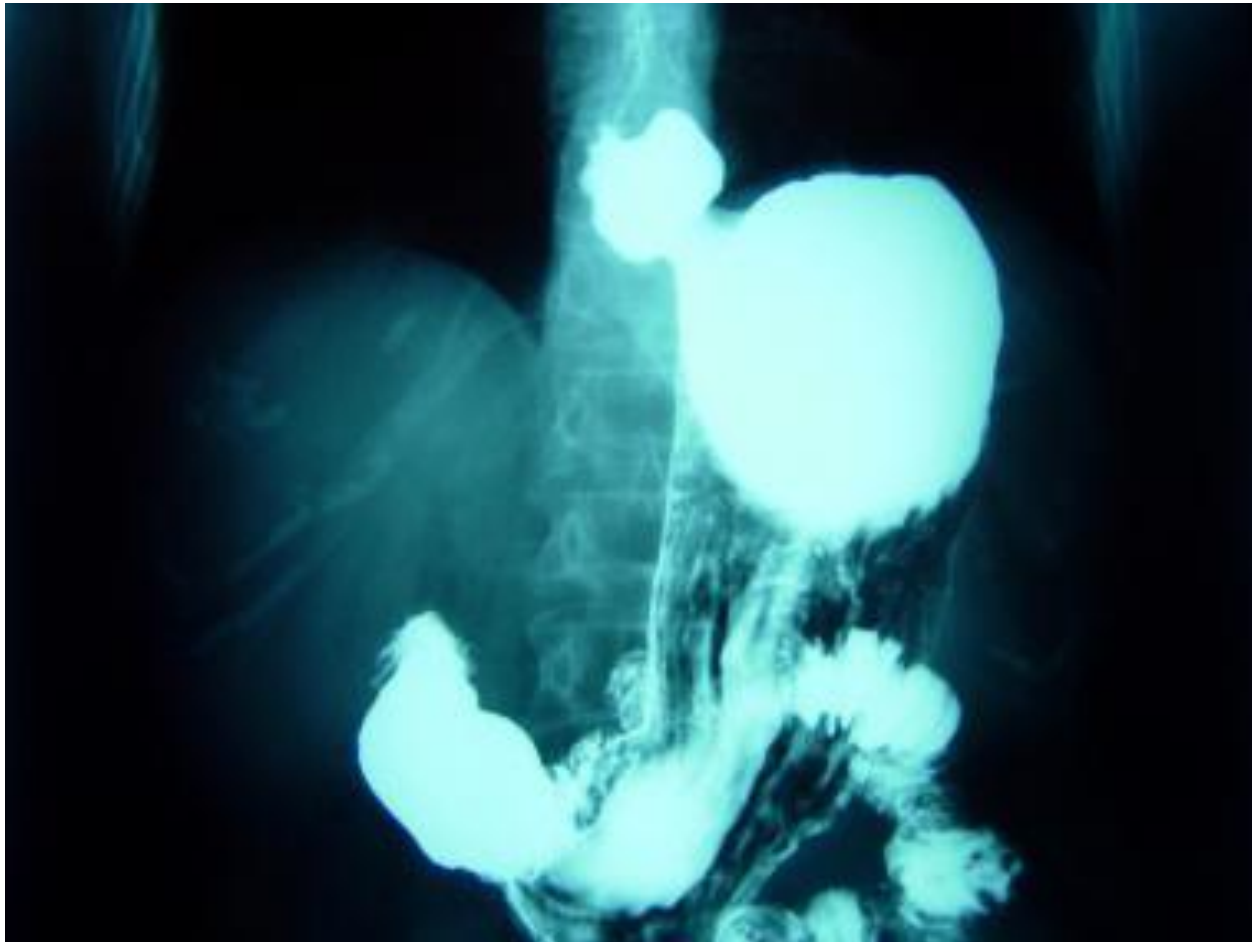
Radiography: Gastroesophageal Reflux



Barium esophagogram demonstrating gastroesophageal reflux with the patient in the upright position.

Diagnosis

Radiography: Hiatal hernia



Diagnosis

Computed tomography: Herniated Stomach



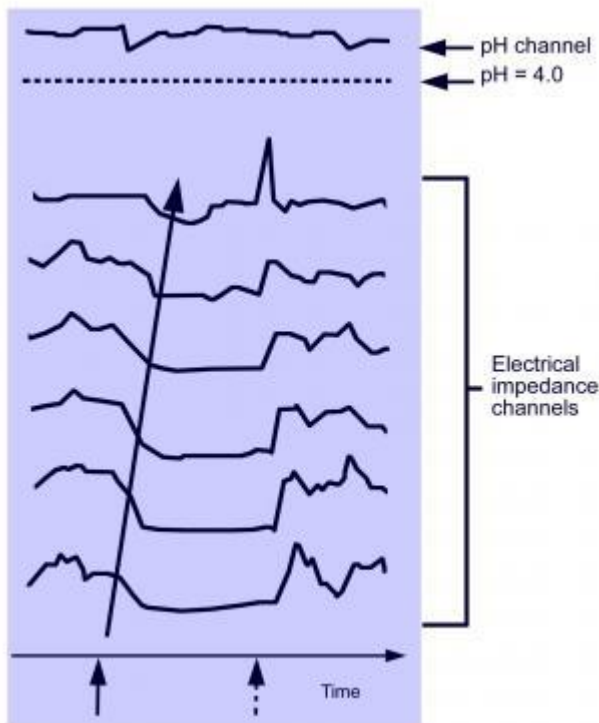
Diagnosis

Intraluminal Esophageal Electrical Impedance 1

- Intraluminal esophageal electrical impedance (EEI), a newer test, is useful for detecting both acid reflux and nonacid reflux by measuring retrograde flow in the esophagus
- Gastroesophageal reflux episodes as brief as 15 seconds may be measured (see the image below)
- In adult studies, impedance measurements have been used in conjunction with 24-hour intraesophageal pH monitoring in order to provide a more complete picture of bolus movement in the esophagus
- EEI has not been thoroughly validated, and normal values have not been determined in the pediatric age group.

Diagnosis

Intraluminal Esophageal Electrical Impedance 2



- The image is a representation of concomitant intraesophageal pH and esophageal electrical impedance measurements
- The vertical solid arrow indicates commencement of a nonacid gastroesophageal reflux (GER) episode (diagonal arrow)
- The vertical dashed arrow indicates the onset of a normal swallow.

Diagnosis

Differential Conditions

- Achalasia
- Acute Gastritis
- Antral Web Cholelithiasis
- Chronic Gastritis
- Coronary Artery Atherosclerosis
- Esophageal Cancer
- Esophageal Motility Disorders
- Esophageal Spasm
- Esophagitis
- Gallstones (Cholelithiasis)
- Helicobacter Pylori Infection
- Hiatal Hernia
- Intestinal Malrotation
- Intestinal Motility Disorders
- Irritable Bowel Syndrome
- Peptic Ulcer Disease

Management

Key Moments

- Treatment involves a stepwise approach
- The goals are to control symptoms, to heal esophagitis, and to prevent recurrent esophagitis or other complications
- The treatment is based on lifestyle modification and control of gastric acid secretion through medical therapy with antacids or PPIs or surgical treatment with corrective antireflux surgery
- Approximately 80% of patients have a recurrent but nonprogressive GERD that is controlled with medications
- Identifying the 20% of patients who have a progressive form of the disease is important, because they may develop severe complications, such as strictures or Barrett esophagus
- . For patients who develop complications, surgical treatment should be considered at an earlier stage.

Management

Lifestyle Modification

- Weight loss is recommended for patients who are overweight or have had recent weight gain
- Head of bed elevation and avoidance of meals 2–3 h before bedtime
- Avoiding large meals
- Routine global elimination of food that can trigger reflux (including chocolate, caffeine, alcohol, acidic and/or spicy foods) is not recommended.

Management

Medications: Proton Pump Inhibitors 1

- An 8-week course of proton pump inhibitors (PPIs) is the therapy of choice for symptom relief and healing of erosive esophagitis
- Traditional delayed release PPIs should be administered 30–60 min before meal for maximal pH control
- PPI therapy should be initiated at once a day dosing, before the first meal of the day
- For patients with partial response to once daily therapy, tailored therapy with adjustment of dose timing and/or twice daily dosing should be considered in patients with night-time symptoms, variable schedules, and/or sleep disturbance.

Management

Medications: Proton Pump Inhibitors 2

- In patients with partial response to PPI therapy, increasing the dose to twice daily therapy or switching to a different PPI may provide additional symptom relief
- Maintenance PPI therapy should be administered for patients who continue to have symptoms after PPI is discontinued, and in patients with complications including erosive esophagitis and Barrett's esophagus
- For patients who require long-term PPI therapy, it should be administered in the lowest effective dose, including on demand or intermittent therapy.

Management

Medications: Proton Pump Inhibitors 3

- Non-responders to PPI should be referred for evaluation
- PPIs are safe in pregnant patients if clinically indicated.
(Conditional recommendation, moderate level of evidence)
- PPIs are safe in pregnant patients if clinically indicated.
(Conditional recommendation, moderate level of evidence)
- Newer PPIs may offer dosing flexibility relative to meal timing
- There are no major differences in efficacy between the different PPIs
- Available PPIs include omeprazole, lansoprazole, rabeprazole, and esomeprazole.

Management

Medications: Proton Pump Inhibitors 4

Potential risks associated with PPIs

- Switching PPIs can be considered in the setting of side-effects
- Patients with known osteoporosis can remain on PPI therapy
- PPI therapy can be a risk factor for *Clostridium difficile* infection, and should be used with care in patients at risk
- Short-term PPI usage may increase the risk of community-acquired pneumonia
- PPI therapy does not need to be altered in concomitant clopidogrel users as there does not appear to be an increased risk for adverse cardiovascular events.

Management

Medications: H2-receptor antagonist

- H2-receptor antagonist (H2RA) therapy can be used as a maintenance option in patients without erosive disease if patients experience heartburn relief
- Bedtime H2RA therapy can be added to daytime PPI therapy in selected patients with objective evidence of night-time reflux if needed, but may be associated with the development of tachyphylaxis after several weeks of use
- Additional H2RA therapy has been reported to be useful in patients with severe disease (particularly those with Barrett esophagus) who have nocturnal acid breakthrough
- Options include ranitidine, cimetidine, famotidine, and nizatidine.

Management

Medications: Prokinetic Medications and Reflux Inhibitors

- Prokinetic agents are somewhat effective but only in patients with mild symptoms; other patients usually require additional acid-suppressing medications, such as PPIs
- The usual regimen in adults is metoclopramide, 10 mg/day orally
- Long-term use of prokinetic agents may have serious, even potentially fatal, complications and should be discouraged
- There is no role for sucralfate in the non-pregnant GERD patient.

Management

Overtreatment

- The use of acid suppression therapy is a common response to GERD symptoms and many patients get more of this kind of treatment than their individual case merits
- The overuse of this treatment is a problem because of the side effects and costs which the patient will have from undergoing unnecessary therapy, and patients should not take more treatment than they need
- In some cases, a person with GERD symptoms can manage them by taking over-the-counter drugs and making lifestyle changes, that is often safer and less expensive than taking prescription drugs
- Some guidelines recommend trying to treat symptoms with an H₂-receptor antagonists before using a proton-pump inhibitor because of cost and safety concerns.

Management

Surgical Options

- Surgical therapy is a treatment option for long-term therapy
- Surgical therapy is generally not recommended in patients who do not respond to PPI therapy
- All patients should undergo preoperative manometry to rule out achalasia or scleroderma-like esophagus
- Surgical therapy is as effective as medical therapy for carefully selected patients when performed by an experienced surgeon
- Obese patients contemplating surgical therapy should be considered for bariatric surgery
- The usage of current endoscopic therapy or transoral incisionless fundoplication cannot be recommended as an alternative to medical or traditional surgical therapy.

Prognosis

- Most patients do well with medications, although a relapse after cessation of medical therapy is common and indicates the need for long-term maintenance therapy
- Identifying the subgroup of patients who may develop the most serious complications and treating them aggressively is important
- Surgery at an early stage is most likely indicated in these patients
- Most cases of gastroesophageal reflux in infants and very young children are benign and respond to conservative nonpharmacologic treatment.

Prophylaxis

- Lifestyle changes that help treat GERD symptoms are effective preventative measures
- These include:
 - Not smoking
 - Avoiding foods and drinks that trigger acid reflux
 - Eating sensible portions
 - Maintaining a healthy weight
 - Wearing loose-fitting clothing
 - Elevating the head during sleep.

Abbreviations

EEl - esophageal electrical impedance

GI - gastrointestinal

H2RA - H2-receptor antagonist

LES - lower esophageal sphincter

PPIs - proton pump inhibitors

GERD - gastroesophageal reflux disease

Diagnostic and treatment guidelines

- [Global Perspective on Gastroesophageal Reflux Disease](#)
- [Updated ACG Guidelines for Diagnosis and Treatment of GERD](#)
- [Gastroesophageal Reflux Disease Treatment & Management](#)
- [Diagnosis and Management of Gastroesophageal Reflux Disease](#)