

Gastroesophageal Reflux Disease (GERD)

Dr. Neda Koulaeinejad

Pharm. D., BCPS.

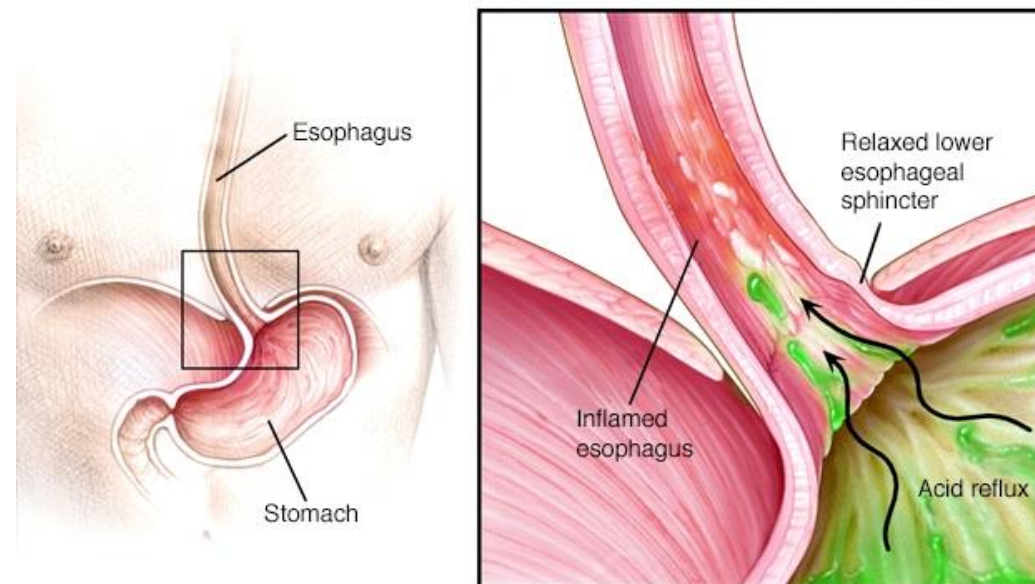
July 2021



➤ Definition

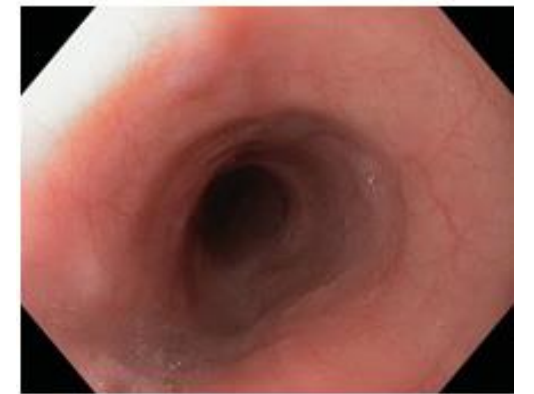
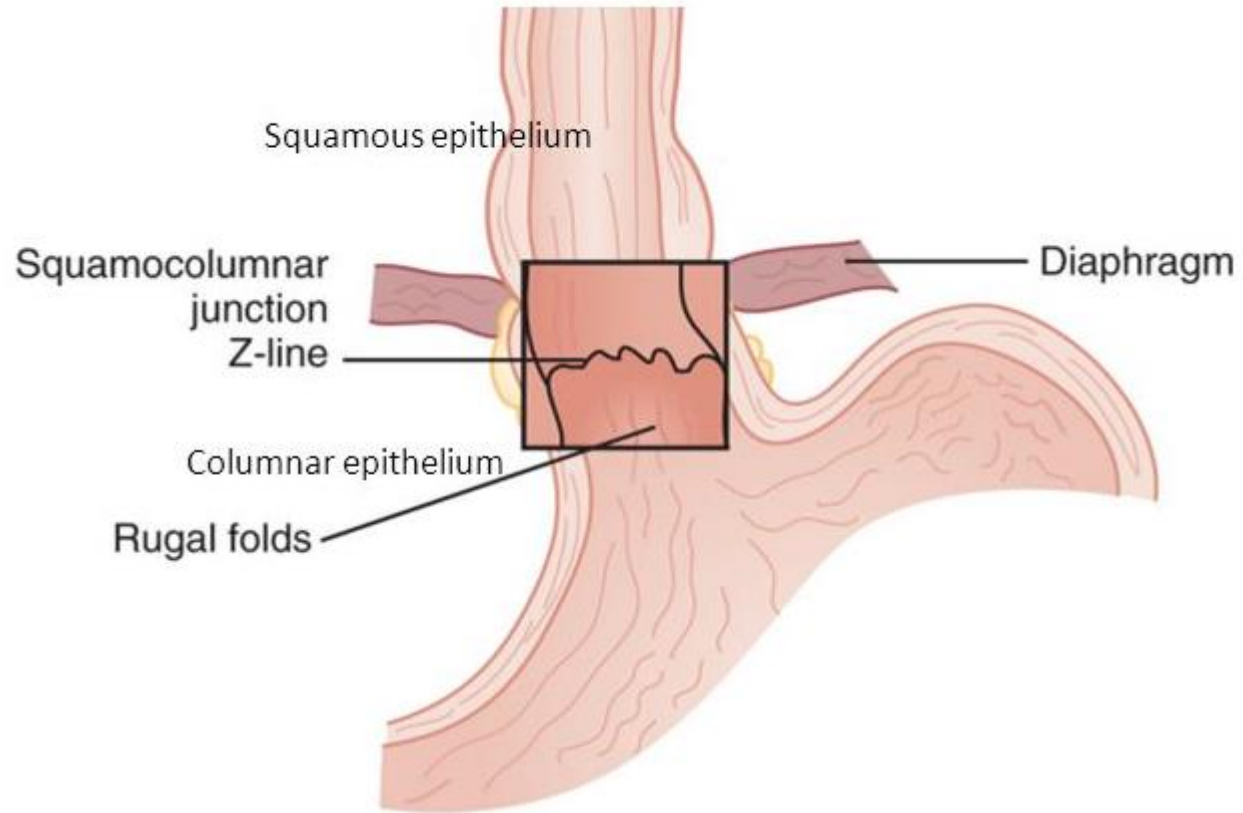
Reflux of the gastric content within the esophagus, causing :

- Troublesome symptoms,
- Impairing quality of life,
- Leading to mucosal damage and complications.





➤ Anatomy



Images: Normal oesophagus



Physiologic reflux

- Typically occur postprandially,
- Short-lived,
- Asymptomatic,
- Rarely occur during sleep.

Pathologic reflux

- Associated with symptoms or mucosal injury
- Often occurs nocturnally.

Based on the appearance of the esophageal mucosa on upper endoscopy :

Erosive esophagitis

Characterized by endoscopically visible breaks in the distal esophageal mucosa with or without troublesome symptoms of GERD.

Nonerosive reflux disease

Characterized by the presence of troublesome symptoms of GERD without visible esophageal mucosal injury.



➤ Epidemiology

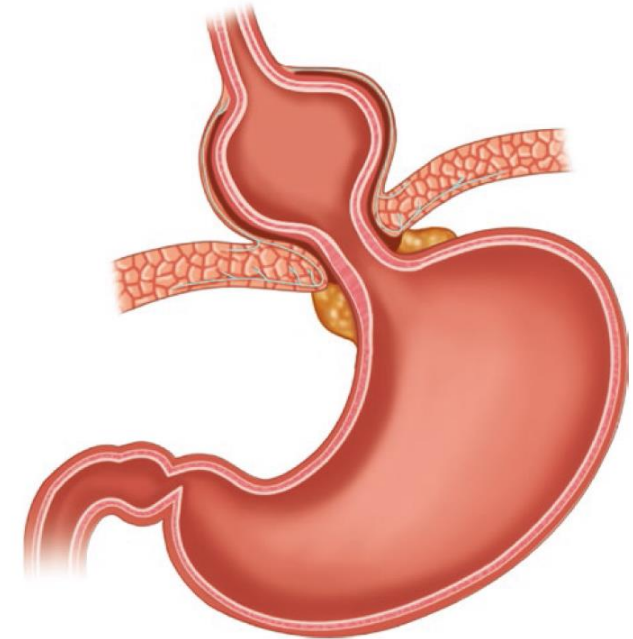
- 10 to 20 percent in the Western world.
 - Less than 5 percent in Asia.
 - Prevalence : Western > Asian countries.
 - Chronic disease.
 - All age groups.
 - Equal distribution between men and women.
 - Symptoms do **not** correlate with the degree of esophageal injury.
- ✓ There are limitations in the epidemiologic estimates of the prevalence of GERD : they are based upon the assumption that heartburn and/or regurgitation are the only indicators of the disease.
(However, patients with objective evidence of GERD (eg, esophagitis or Barrett's esophagus) do not always have heartburn and heartburn is not always sufficiently severe to be indicative of GERD)



➤ Pathophysiology

Gastroesophageal junction incompetence

- (1) Transient LES relaxations :
a vagovagal reflex in which LES relaxation is elicited by gastric distention,
- (2) LES hypotension,
- (3) Anatomic distortion of the esophagogastric junction inclusive of hiatus hernia.





Characteristics of the refluxate

- Increased gastric acid secretion,
- The intragastric pH ($\text{pH} < 2$),
- The amount of time the refluxate is in contact with the mucosa.

Impaired defense against epithelial injury

- Epithelial tight junctions
- Hydrogen ion extrusion

Esophageal hypersensitivity



Impaired esophageal acid clearance

▪ Impaired esophageal emptying

- Ineffective esophageal motility
- Re-reflux

or retrograde flow associated with hiatal hernias also impairs esophageal emptying.

▪ Diminished salivary function

- Oral lozenges or gum chewing will hasten acid clearance.
- Diminished salivation during sleep.





Risk Factors Associated With Gastroesophageal Reflux Disease

Drugs

- α -Adrenergic agonists
- β_2 -Adrenergic agonists
- Dopamine
- Anticholinergics
- CCBs
- Aspirin
- Barbiturates
- Benzodiazepines
- Bisphosphonates
- Estrogen
- Progesterone
- Iron
- Narcotics
- Nitrates
- NSAIDs
- Prostaglandins
- Potassium
- Tetracycline
- Theophylline
- TCAs
- Zidovudine

Medical/Surgical Conditions

- Pregnancy
- Scleroderma
- ZES
- Gastroparesis
- NG tube intubation





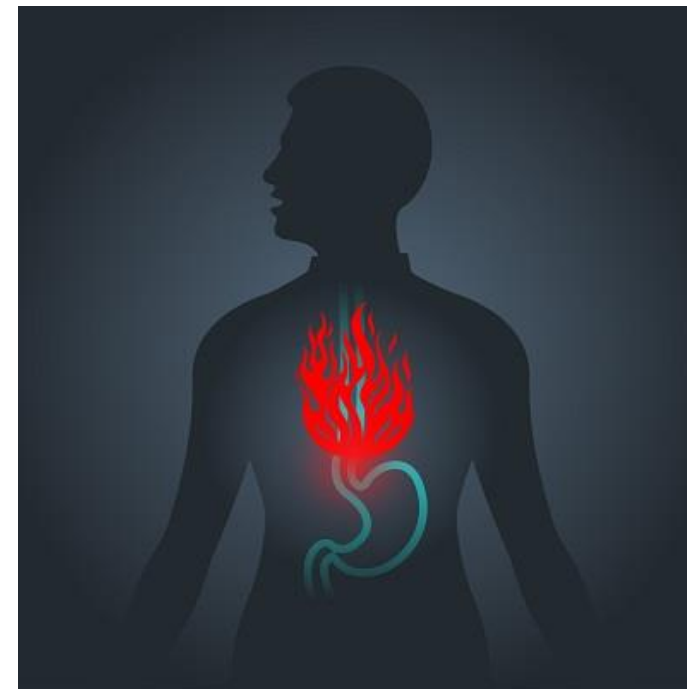
➤ Clinical Presentation

Classic symptoms :

- Heartburn (pyrosis)
- Regurgitation

Other symptoms of GERD include :

- Dysphagia,
- Chest pain,
- Water brash,
- Globus sensation,
- Odynophagia,
- Extraesophageal symptoms (eg, chronic cough, hoarseness, wheezing),
- Nausea : infrequently





Complications from GERD

Esophageal

- Esophageal stricture
- Barrett's esophagus
- Esophageal adenocarcinoma

Extra-esophageal

- Exacerbation of asthma
- Chronic laryngitis
- Laryngeal and tracheal stenosis

Other

- Chronic cough,
- Dental erosions,
- Chronic sinusitis,
- Recurrent pneumonitis.



Examples of Barrett's oesophagus



➤ Diagnosis

Patients with classic symptoms

The diagnosis of GERD can often be based on clinical symptoms **alone** in patients with classic symptoms such as heartburn and/or regurgitation.

Patients without classic symptoms

Other symptoms
(eg, chest pain, globus sensation, chronic cough, hoarseness, wheezing, and nausea)
: Not sufficient to make a clinical diagnosis of GERD.



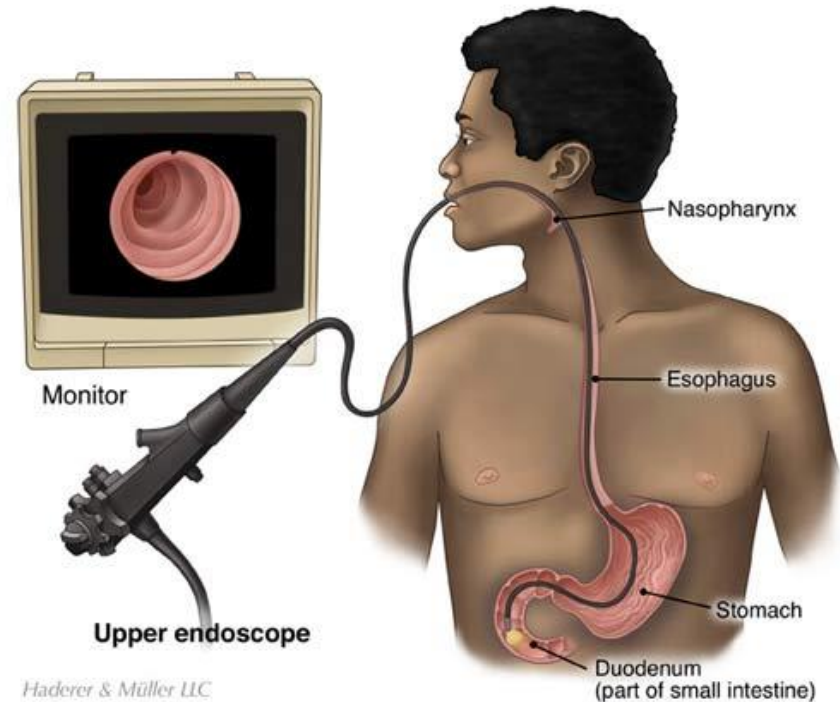
Other disorders need to be excluded before attributing the symptoms to GERD.
(eg, ECG,...



Evaluation in selected patients

Upper gastrointestinal endoscopy

- Patients with suspected GERD to evaluate alarm features.
- Abnormal imaging if not performed within the last 3 months.
- Screen for Barrett's esophagus in patients with risk factors.
- Can also rule out other etiologies in patients with GERD symptoms that are refractory to a trial of PPI therapy.





(((**Alarm features**)))

- New onset of dyspepsia in patient ≥ 60 years
- Evidence of gastrointestinal bleeding
(hematemesis, melena, hematochezia, occult blood in stool)
- Iron deficiency anemia
- Anorexia
- Unexplained weight loss
- Dysphagia
- Odynophagia
- Persistent vomiting
- Gastrointestinal cancer in a first-degree relative



(((Risk factors for Barrett's esophagus)))

- Duration of GERD of at **least 5 to 10 years**
- Age **50 years** or older
- **Male** sex
- White race
- Hiatal hernia
- Obesity
- Nocturnal reflux
- Tobacco use (past or current)
- First-degree relative with Barrett's esophagus and/or adenocarcinoma



Ambulatory esophageal pH monitoring

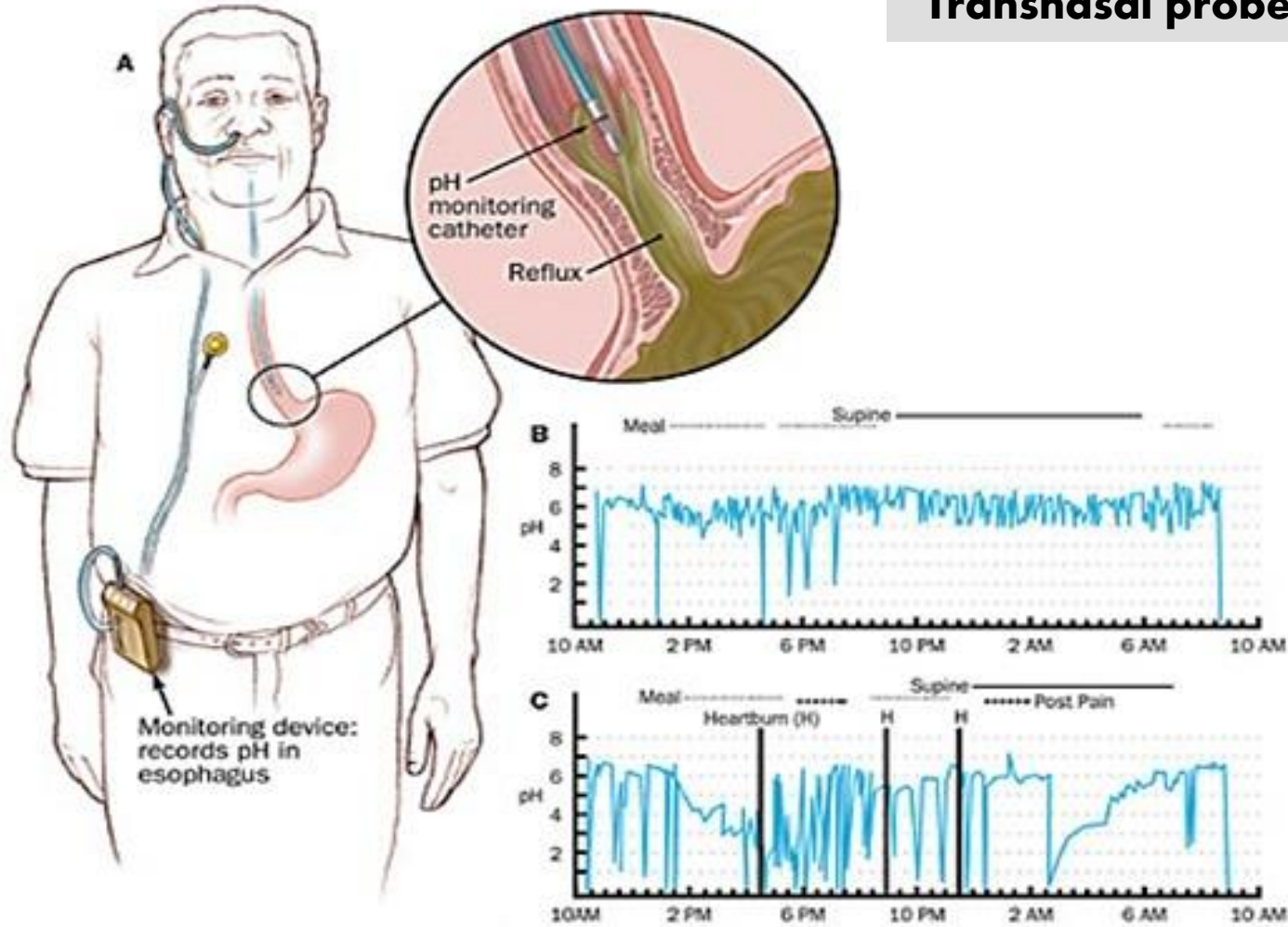
- Used to **confirm** the diagnosis of GERD in those with **persistent symptoms** (whether typical or atypical, particularly if a trial of twice-daily PPI has failed).
- To monitor the **adequacy of treatment** in those with continued symptoms.

A 24-h (impedance-) pH monitoring is considered to be the **gold standard** investigation for the quantitative evaluation of acid exposure in the distal esophagus.

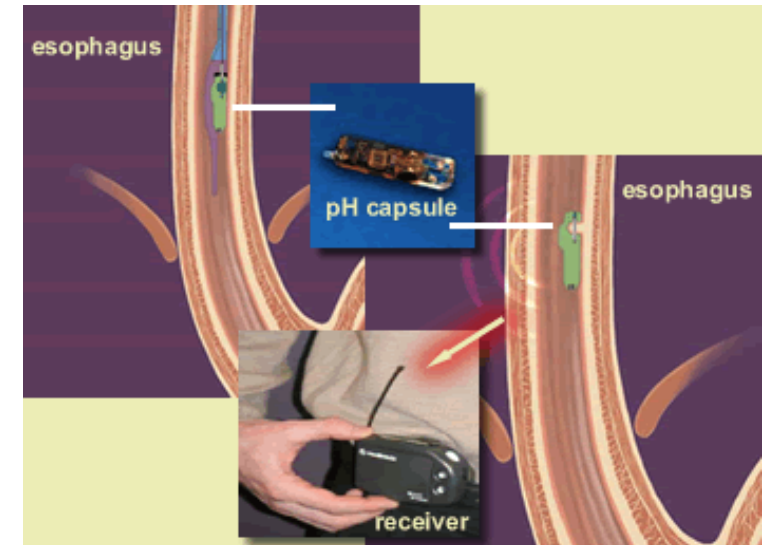
...Can be performed with either a transnasally placed catheter or a wireless, capsule-shaped device that is affixed to the distal esophageal mucosa.



Transnasal probes



Wireless, capsule-shaped device





مرکز اطلاع رسانی دارو و پزشکی ۱۳ آبان
دانشگاه علوم پزشکی تهران



➤ **Therapy**

1. Alleviate symptoms,
2. Promote esophageal healing,
3. Prevent recurrence,
4. Provide cost-effective pharmacotherapy,
5. Avoid long-term complications...



Dietary & Lifestyle Modifications

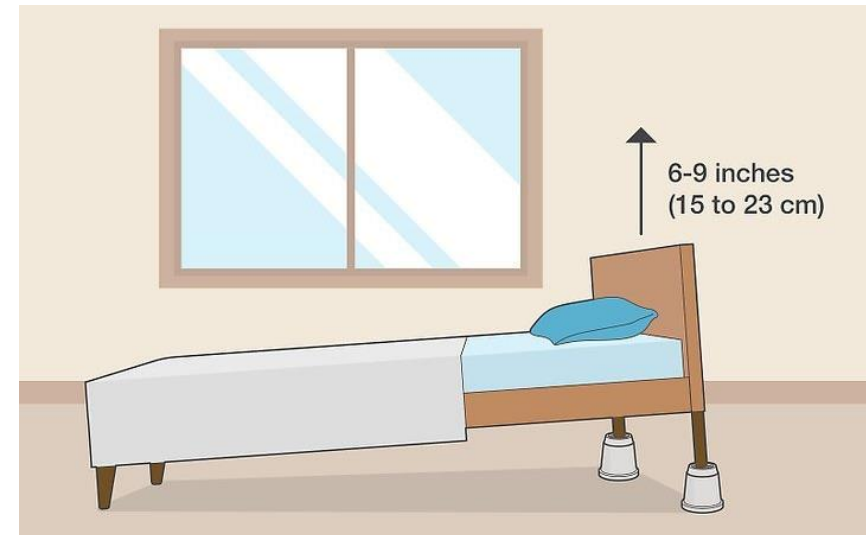
Weight loss :

For patients with GERD who are overweight or have had recent weight gain.



Elevation of the head :

- Elevate the head of bed 6-8 inches,
- Refraining from assuming a supine position after meals,
- Avoidance of meals two to three hours before bedtime.



Selective elimination of dietary triggers :

- Caffeine (coffee, tea)
- Chocolate
- Spicy foods
- Food with high fat content
- Carbonated beverages
- Peppermint

Other :

- Avoidance of tight-fitting garments
- Promotion of salivation through oral lozenges/chewing gum
- Avoidance of tobacco and alcohol





In patients with mild and intermittent symptoms (fewer than two episodes per week)
and
No evidence of erosive esophagitis

Step-up therapy



Lifestyle and dietary modification,

- As needed, low-dose H2RAs,

- Concomitant antacids as needed,

- Increase the dose of H2RAs to standard dose, twice daily for a minimum of **two weeks**,

- Discontinue H2RAs and initiate once-daily PPIs at a low dose and then increase to standard doses if required...



Medication	Low dose (adult, oral)	Standard dose (adult, oral)
H2RAs		
Famotidine	10 mg twice daily	20 mg twice daily
Cimetidine	200 mg twice daily	400 mg twice daily
PPIs		
Omeprazole	10 mg daily	20 mg daily
Lansoprazole	15 mg daily	30 mg daily
Esomeprazole	10 mg daily	20 mg daily
Pantoprazole	20 mg daily	40 mg daily
Rabeprazole	10 mg daily	20 mg daily



In patients with erosive esophagitis,
Frequent symptoms (two or more episodes per week),
and/or
Severe symptoms that impair quality of life

Step-down therapy

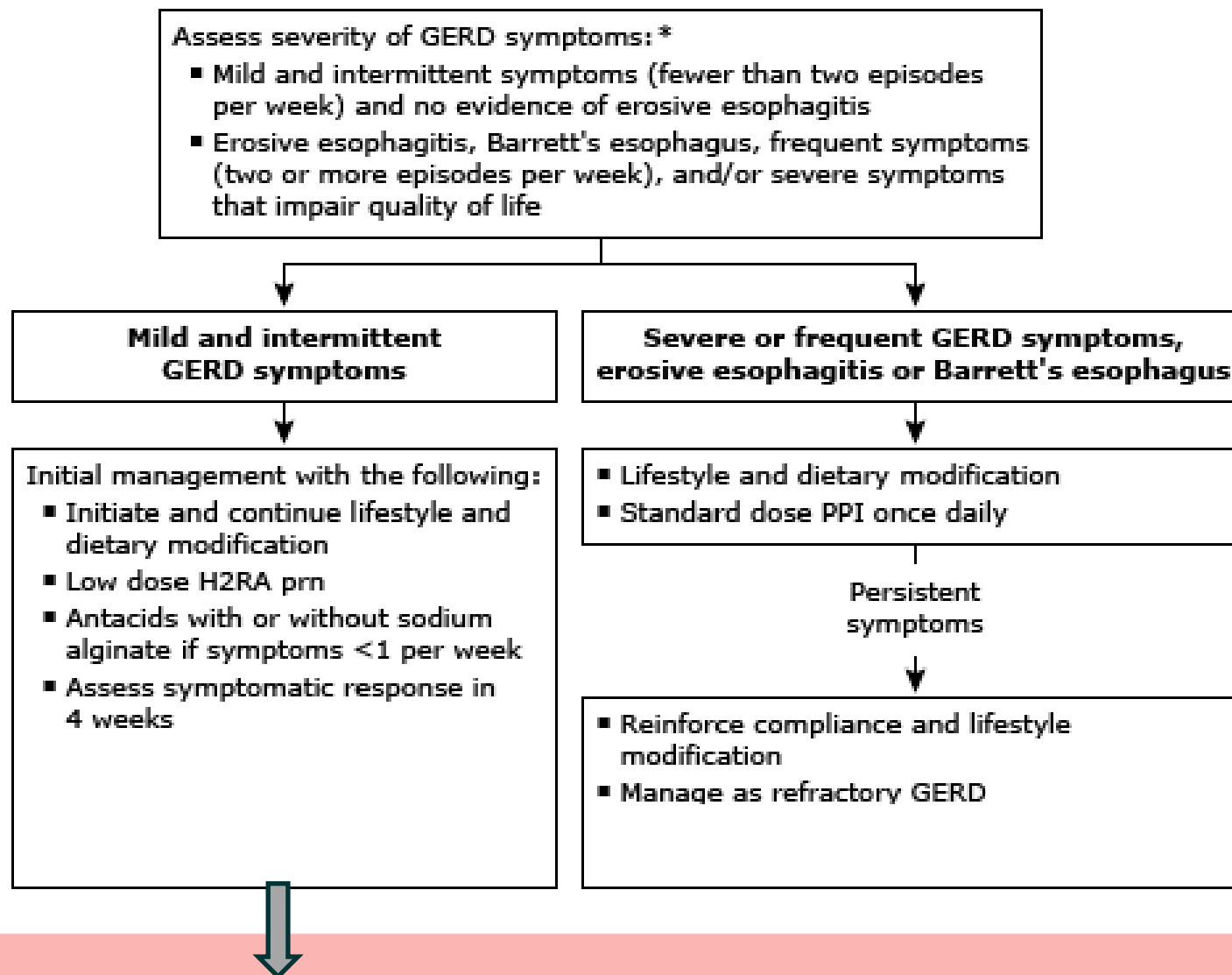


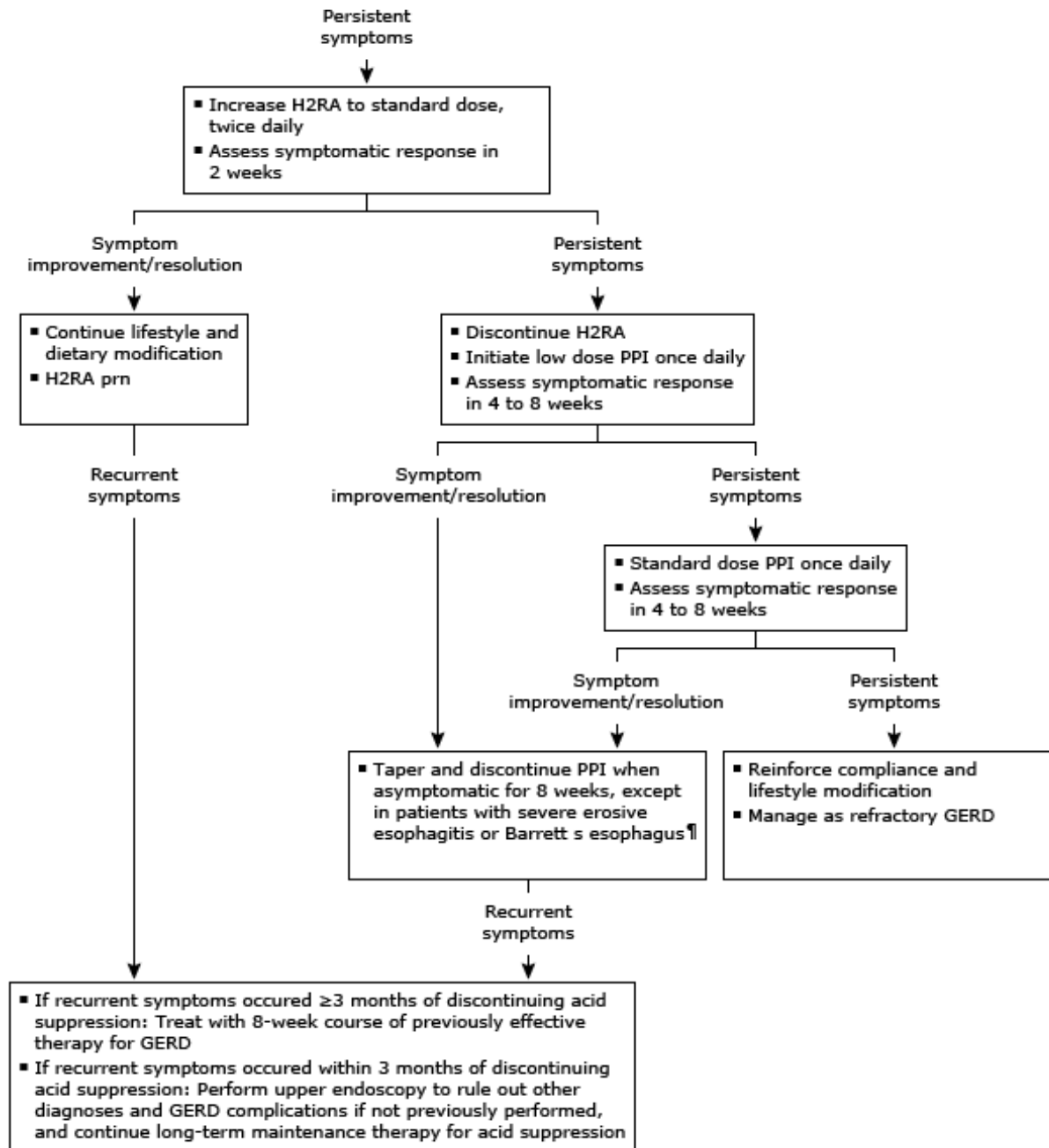
Standard-dose PPI once daily for **eight weeks** in addition to lifestyle and dietary modification

- low-dose PPIs
- H2RAs



Approach to the initial management of patients with GERD







مرکز اطلاع رسانی دارو و پزشکی ۱۳ آبان
دانشگاه علوم پزشکی تهران

GERD during pregnancy





- GERD or heartburn is reported by 40 to 85 percent of women during pregnancy.
- Most studies report an **increasing** prevalence of symptoms from the first to the third trimester, with relief postpartum.
- Gastroesophageal reflux tends to recur in subsequent pregnancies, and similarly affects multiparous and nulliparous women.



- The pathogenesis of GERD during pregnancy involves both **mechanical** and **intrinsic factors** that adversely affect lower esophageal sphincter tone.
- LES pressure is below the lower limits of normal in all trimesters, returning to normal in the postpartum period:
 - ① The enlarging uterus increases intra-abdominal pressure,
 - ② Estrogen and progesterone relax the esophageal sphincter.
- Worsened by **eating, lying down, or bending over**.



- **Initial** management : lifestyle and dietary modification.
- In patients with persistent symptoms, pharmacologic therapy should begin with **antacids** followed by sucralfate.
- Most antacids are considered safe in pregnancy and are compatible with breastfeeding. However, **antacids containing sodium bicarbonate and magnesium trisilicate** should be **avoided** in pregnancy.
- **Sucralfate** is likely safe during pregnancy and lactation because it is poorly absorbed.



- While all **H2RAs** appear to be safe in pregnancy, in patients with continued GERD symptoms on sucralfate, **cimetidine** are suggested as they have the most safety data available.

- Experience with **PPIs** is more limited compared with H2RAs, but suggests that PPIs are probably safe in pregnancy.

In pregnant patients with GERD symptoms despite H2RAs, the use of **omeprazole, lansoprazole, or pantoprazole** is suggested rather than other PPIs, as they have been more widely used in pregnancy.



GERD in infants



Gastroesophageal reflux (GER) :

Refers to the passage of gastric contents into the esophagus.

Gastroesophageal reflux disease (GERD) :

Refers to reflux that has **pathologic consequences**, such as esophagitis, nutritional compromise with weight loss, or respiratory complications.

Regurgitation : Spitting up

Describes **effortless reflux** up to the oropharynx or above.

Vomiting :

Describes **forceful** expulsion.

Rumination :

Refers to **voluntary** regurgitation of stomach contents into the mouth.



➤ Epidemiology

- Extremely common in healthy infants.
- Gastric contents may reflux into the esophagus **30 or more** times daily.
- Declines with increasing age :
decreases toward the end of the **first year** of life and is unusual in children older than 18 months old.



Warning signals of underlying pathology

Gastrointestinal obstruction or disease

- Bilious vomiting
- Gastrointestinal bleeding – Hematemesis, hematochezia
- Consistently forceful vomiting
- Onset of vomiting after six months of life
- Constipation
- Diarrhea
- Abdominal tenderness, distension
- Recurrent pneumonia
- Aspiration



Symptoms or signs suggesting systemic or neurologic disease

- Hepatosplenomegaly
- Bulging fontanelle
- Macrocephaly or microcephaly
- Seizures
- Hypotonia or hypertonia (eg, cerebral palsy)
- Stigmata of genetic disorders (eg, trisomy 21)
- Chronic infections (eg, HIV)

Nonspecific symptoms

- Fever
- **Pneumonia**
- Lethargy
- **Poor weight gain**

➤ Treatment

Lifestyle changes

✓ Avoid tobacco smoke exposure



✓ Breast milk versus formula feeding

Continuation of breastfeeding should be encouraged if practicable.

- Protective effect on regurgitation in infants,
- Differences in gastric emptying,
- Differential exposure of infants with a cow's milk protein intolerance.



✓ Avoid overfeeding

- Because simple reflux is promoted by gastric distention.
- Most relevant for infants who are bottle-fed (with either formula or breast milk).
- Provide smaller but more frequent feedings.





Additional options for infants with problematic GER

Several types of lifestyle changes are suggested for infants with GERD or for those with uncomplicated reflux if the symptoms are distressing to the family.

✓ **Avoidance of cow's milk and soy protein**

Empiric trial of removing all cow's milk from the diet for infants with problematic GER and suspicion for cow's milk protein intolerance, as evidenced by :

- Gross or occult blood in the stool,
- Eczema,
- Strong family history of atopy,
- Poor weight gain.



❑ **Breastfed infants :**

- Can be treated with careful elimination of all cow's milk proteins and beef from the mother's diet.
- Major sources of soy protein may need to be eliminated.
- The response to this change is often more delayed than in formula-fed infants.

❑ **Formula-fed infants :**

- ↓ • Switching to an extensively hydrolyzed formula (often marketed as "hypoallergenic").
- Trial of an amino acid-based ("elemental") formula or elimination of other dietary proteins may be necessary.

Infants who respond to the dietary change are generally maintained on a milk-free diet until **one year** of age.



✓ Thickening feeds

- A trial of thickening feeds is worthwhile for most infants with problematic reflux, except perhaps in infants who are **preterm** or **overweight**.
- Breastfeeding should **not** be stopped for the purposes of thickening feeds.
- By adding **oat** infant cereal, up to one tablespoon of dry cereal per ounce of formula.
- Rice cereal (concerns about possible contamination with arsenic).

Premixed formulas thickened with rice starch are available in some countries (called "**anti reflux**").



✓ Positioning therapy

- Keeping an infant **upright** (eg, on a parent's shoulder) for **20 to 30 minutes** after a feed.
- Semi-supine positioning (in an infant seat) is not helpful, as it increases reflux.

All infants younger than 12 months of age should be placed in the supine position for sleep, even if they have reflux.

((((Elevation of the head of the crib is not recommended, because it has no effect on reflux for infants placed in the supine position.

- Prone & side positioning is associated with an increased risk for SIDS.





Pharmacotherapy

- Acid-suppressing medications have a limited role in the treatment of infants with regurgitation.
- **Not** indicated for infants with uncomplicated reflux.

□ Indications :

limited trial of acid suppression (eg, **2 weeks**) for patients with the following characteristics :

- Infants with mild esophagitis on endoscopic biopsies.
- Infants with significant symptoms suspected to be caused by GERD, such as marked irritability, feeding refusal, or poor weight gain, **and** in whom conservative measures including a milk-free diet have failed.

3- to 6-month course of acid suppression :

- For infants with moderate or severe esophagitis documented by endoscopic biopsies.
↓ Repeat endoscopy



Drug selection

- **PPI** is generally preferred over H2RAs.
- Require higher per-kilogram dosing than older individuals.
- To be most effective, should be taken 30 minutes prior to the first meal/feeding of the day.
- Do not lose efficacy with prolonged use.

Omeprazole, lansoprazole, esomeprazole, and pantoprazole :

have all been studied in young children.

Omeprazole and **esomeprazole** are approved by the **FDA** for use in infants older than one month of age with erosive esophagitis.

- Short-term acid rebound
- Increased risks for diarrhea & possibly pneumonia
- Later development of allergic disease
- Vitamin B12 and iron deficiency
- Increased risk for osteoporosis



Antacids

Not generally useful in the treatment of GER in infants.
Chronic use of antacids in infants can be associated with :

- Aluminum toxicity,
- Milk-alkali syndrome,
- Rickets

Prokinetic agents

- Minimal role
- CNS side effects for metoclopramide,
- Lack of evidence for efficacy and possible safety concerns for domperidone

...Should be considered for use only in carefully **selected** patients after a fully informed discussion with their caregivers, and with appropriate monitoring for concerns and drug interactions.



Monitoring and follow-up

- Because of safety concerns, patients treated with PPIs should be reevaluated on a **regular basis** to determine if ongoing use is necessary.
- Attempt to wean patients from PPIs after **6 months** of treatment and then periodically thereafter, depending on symptom control.
- When stopping therapy after six months, one might consider transitioning to an H2RA for two weeks, followed by tapering, to avoid acid rebound.



مرکز اطلاع رسانی دارو و پزشکی ۱۳ آبان
دانشگاه علوم پزشکی تهران

+ REFERENCES

- **Harrison's Principles of Internal Medicine, 20e**
- **Applied Therapeutics (Koda Kimble and Youngs Applied Therapeutics) 11th Edition**
- **UpToDate, 2021**
- **Management of Gastroesophageal Reflux Disease (Springer Nature Switzerland AG 2020).**



Thank You

For Your Attention