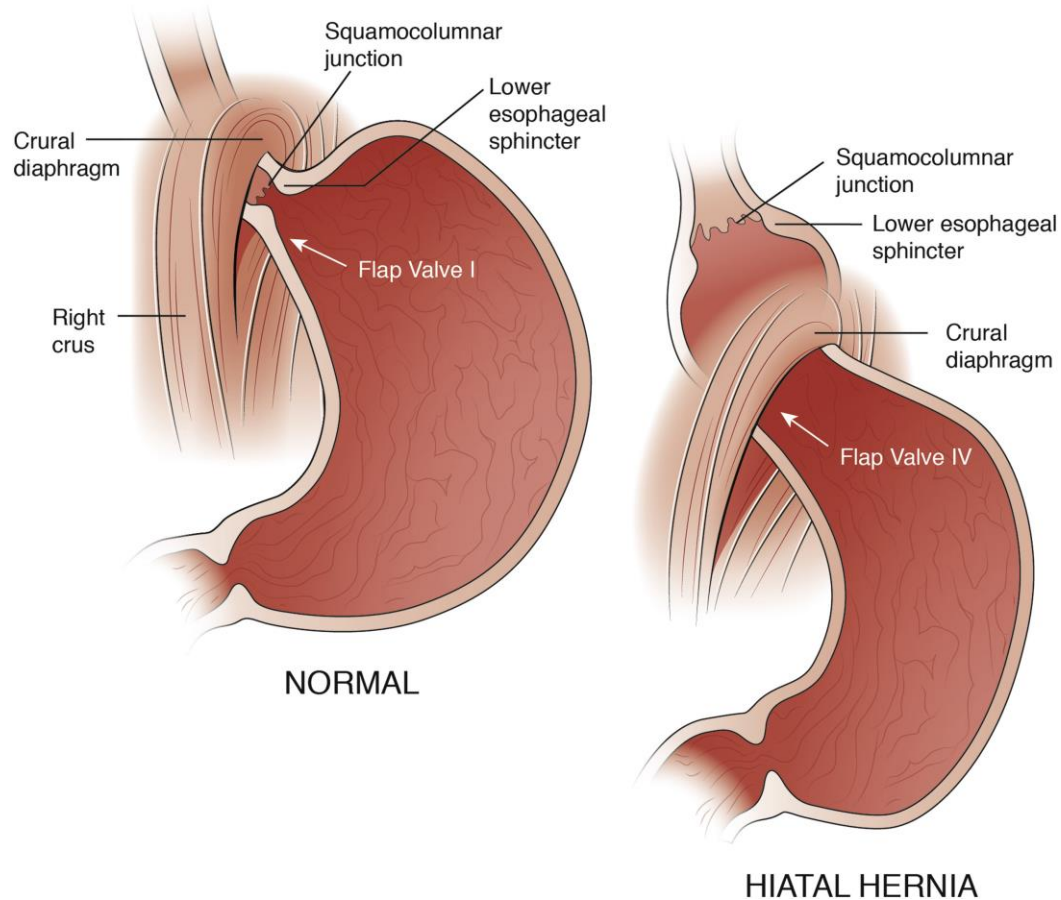
Squamocolumnar junction
Lower esophageal sphincter
Crural diaphragm
Flap Valve I
Right crus
NORMAL
Squamocolumnar junction
Lower esophageal sphincter
Crural diaphragm
Flap Valve IV
HIATAL HERNIA

- The development of gastroesophageal reflux disease (GERD) reflects the balance between injurious and defensive factors (esophageal acid clearance, mucosal integrity).
- The extent of symptoms and of mucosal injury is proportional to the frequency of reflux events, the duration of mucosal acidification, and the caustic potency of refluxed fluid

The three dominant pathophysiologic mechanisms causing gastroesophageal junction incompetence are:

- transient lower esophageal sphincter relaxations (TLESRs), a hypotensive lower esophageal sphincter (LES), and anatomic disruption of the gastroesophageal junction, often associated with a hiatal hernia.

Management

- is based on the :
- Frequency and severity of symptoms and the presence of erosive esophagitis or Barrett's esophagus on upper endoscopy, if previously performed.
- We suggest lifestyle and dietary modification in all patients with GERD
- In patients with mild and intermittent (less than two episodes per week) symptoms of GERD who are naïve to treatment and no evidence of erosive esophagitis or Barrett's esophagus, we suggest as needed low-dose histamine 2 receptor antagonists (H2RAs) Concomitant antacids, and/or sodium alginate can be used if symptoms occur less than once a week. In patients with continued symptoms, we increase the dose of H2RAs to standard dose, twice daily for a minimum of two weeks.

Medication	Low dose (adult, oral)	Standard dose (adult, oral)
Histamine 2 receptor antagonists*		
Famotidine	10 mg twice daily[¶]	20 mg twice daily[Δ]
Nizatidine	75 mg twice daily[¶]	150 mg twice daily
Cimetidine	200 mg twice daily[¶]	400 mg twice daily[Δ]
Proton pump inhibitors		
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
Dexlansoprazole	Not available	30 mg daily
Rabeprazole	10 mg daily[◇]	20 mg daily

- If symptoms of GERD persist, we discontinue H2RAs and initiate once-daily proton pump inhibitors (PPIs) at a low dose (Grade 2B) and then increase to standard doses if required for symptom control (table 1). Once symptoms are controlled, therapy should be continued for at least eight weeks.
- In patients with erosive esophagitis, we recommend initial acid suppressive therapy with standard-dose PPI once daily (table 1) (Grade 1A).

- If symptoms of GERD persist, we discontinue H2RAs and initiate once-daily proton pump inhibitors (PPIs) at a low dose (Grade 2B) and then increase to standard doses if required for symptom control .Once symptoms are controlled, therapy should be continued for at least eight weeks.
- In patients with erosive esophagitis, we recommend initial acid suppressive therapy with standard-dose PPI once daily (Grade 1A).

- In patients with frequent (two or more episodes per week), severe symptoms that impair quality of life or Barrett’s esophagus, we suggest initial therapy with standard-dose PPI once daily (Grade 2B).
- Referral to a subspecialist is warranted for patients who fail to respond to once-daily PPI therapy and patients who cannot tolerate long-term PPIs or want to discontinue therapy.
- We discontinue acid suppression in all patients with GERD whose symptoms resolve completely with treatment with the exception of those with severe esophagitis on upper endoscopy and Barrett's esophagus. (See 'Duration of acid suppression' above.)

- In patients with recurrent symptoms within three months of discontinuing acid suppression, we continue long-term maintenance therapy with a PPI. However, if symptoms occur after three or more months, we use repeated eight week courses of previously effective acid suppressive therapy

- Management of GERD in pregnancy includes lifestyle and dietary modification followed by pharmacologic therapy with antacids and sucralfate.
- Antacids containing sodium bicarbonate and magnesium trisilicate should be avoided in pregnancy. In patients who fail to respond, similar to nonpregnant patients, H2RAs and then PPIs are used to control symptoms.

Medication timing and adherence —

- Poor compliance with proton pump inhibitor (PPI) timing and adherence is an important cause for inadequate acid suppression and refractory GERD .PPIs should be administered 30 to 60 minutes before breakfast for maximal inhibition of proton pumps.

Differences in PPI metabolism —

- CYP2C19 having the dominant role. >10 percent of Asian patients are homozygous for a CYP2C19 mutation (ie, slow metabolizers), potentially leading to greater suppression of gastric acidity.
- However, in wild type homozygotes (rapid metabolizers) the effect of PPIs on gastric acidity is diminished and may contribute to PPI failure.

alkaline reflux (non-acid reflux) —

- occur in the postprandial period as transient lower esophageal sphincter relaxation occurs more frequently following meal-induced gastric fundus distension.

Reflux hypersensitivity —

- Reflux hypersensitivity is characterized by retrosternal symptoms, including heartburn and chest pain associated with non-pathologic acid exposure

- According to the Rome IV criteria, a diagnosis of reflux hypersensitivity requires all of the following criteria be fulfilled for the last three months with symptom onset at least six months prior to the diagnosis

Retrosternal symptoms including heartburn or chest pain

- Normal endoscopy and absence of evidence that eosinophilic esophagitis is the cause for symptoms

- Absence of major esophageal motor disorders (achalasia/esophagogastric junction outflow obstruction, diffuse esophageal spasm, jackhammer esophagus, absent peristalsis)

- Evidence of triggering of symptoms by reflux events despite normal acid exposure on pH or pH–impedance monitoring (response to antisecretory therapy does not exclude the diagnosis)

Alternative diagnoses —

- Other diseases that can mimic symptoms of GERD include achalasia, eosinophilic esophagitis, infectious esophagitis, pill esophagitis, gastroparesis, and rarely esophageal stricture or cancer. Rumination syndrome may also be misdiagnosed as GERD.
- Refractory GERD can be distinguished from these conditions by diagnostic testing.

Bile reflux may have a role in a subset of patients with difficult to manage symptomatic reflux.

Furthermore, in a carefully selected group of patients with symptoms refractory to PPI therapy, baclofen significantly reduced bile reflux exposure and heartburn.

Although these studies suggest a role for measurement of bile reflux in patients with persistent reflux symptoms despite PPI therapy, bile reflux monitoring is not widely available.

Esophageal impedance pH testing —

- Patients who fail twice daily PPI therapy should also undergo esophageal pH monitoring. Esophageal pH monitoring with impedance is preferred to wireless pH capsule and the traditional pH probe, as it has the advantage of detection of non-acid in addition to acid reflux
- Impedance pH testing can be performed while off PPI therapy in patients without typical GERD symptoms to determine if gastroesophageal reflux is the cause of their symptoms. Testing should be performed while on PPI treatment in patients with a partial response to PPIs to determine if there is continued pathological acid or non-acid exposure despite acid suppressive therapy .It can also help predict which patients have acid reflux off PPI therapy

Alginate