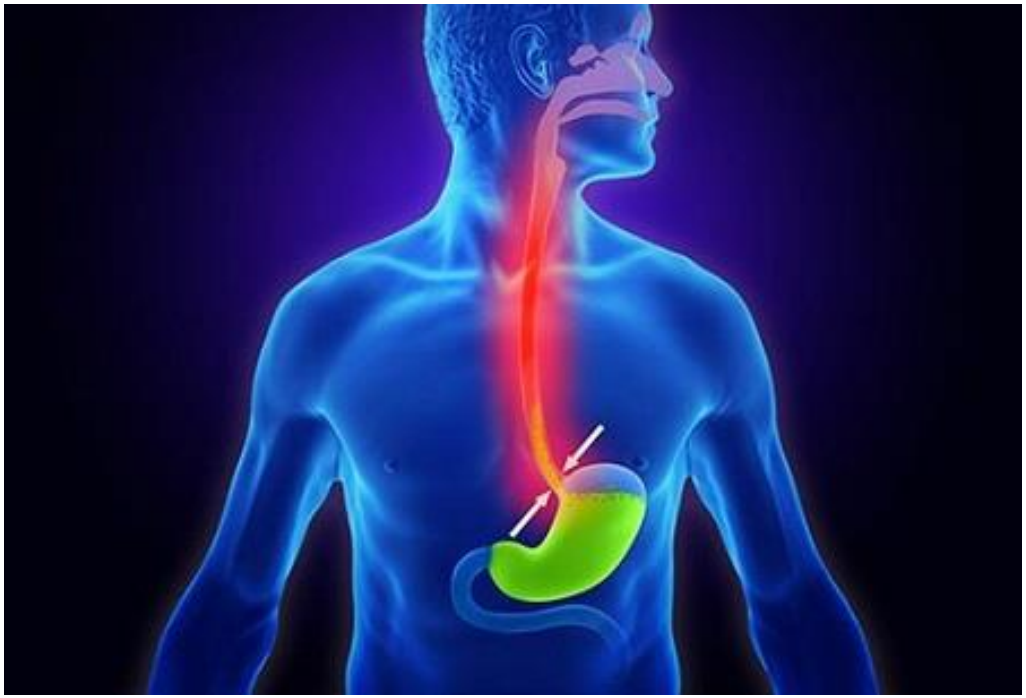
Medical management of GERD

Mohsen Masoodi
Iran University of Medical Sciences, Tehran, Iran.

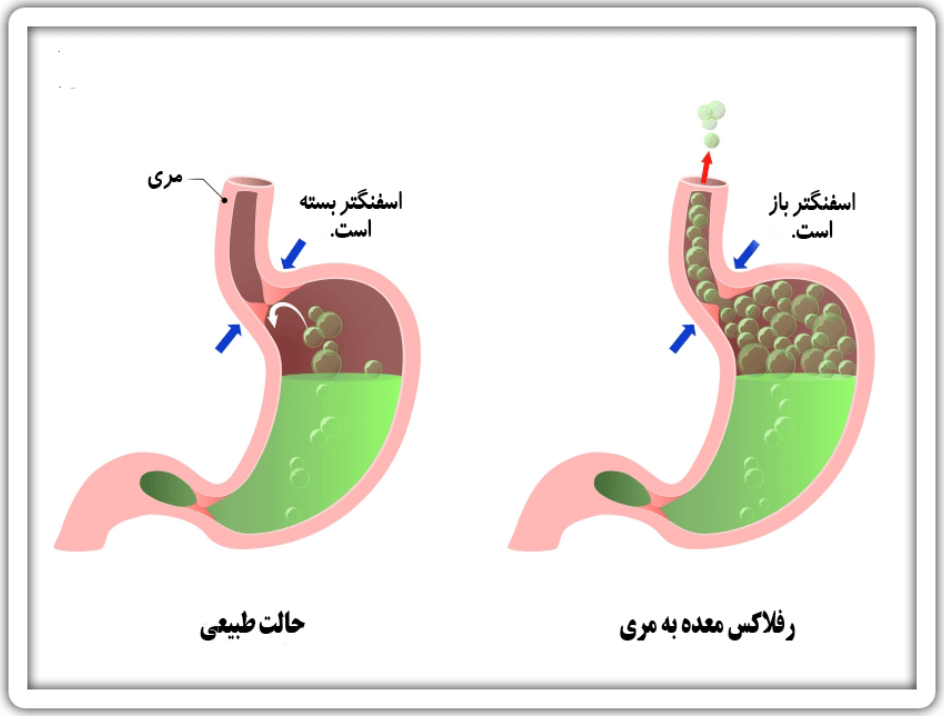


Case 1

- A 43 years old woman complains of mild epigastric discomfort and weekly heart burn.

What is your approach?

Assessment of clinical severity?

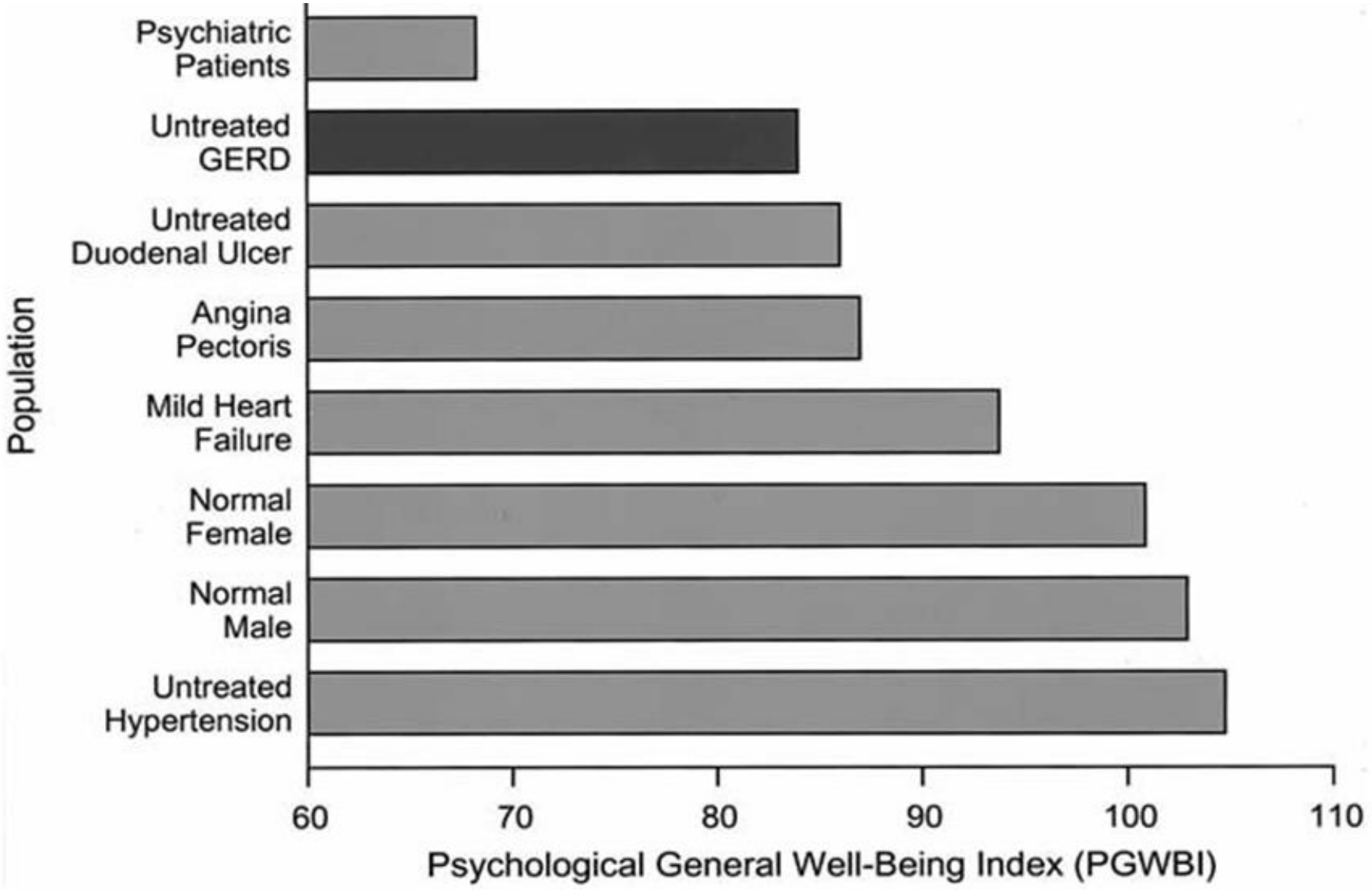


Initial evaluation

- **Assessment of clinical severity**
  - The frequency and severity of symptoms can guide the management of GERD.

    - Mild or moderate/severe based on whether they impair quality of life.

    - Mild and intermittent (<2 episodes per week)
    - Frequent (≥2 episodes per week)


Psychiatric Patients
Untreated GERD
Untreated Duodenal Ulcer
Angina Pectoris
Mild Heart Failure
Normal Female
Normal Male
Untreated Hypertension
Population
60
70
80
90
100
110
Psychological General Well-Being Index (PGWBI)

Initial evaluation

- It is important to consider the regional epidemiology of upper gastrointestinal disease and the pretest probability of GERD relative to other conditions.

History

- Precipitating factors
  - eating, diet (fat), activity (stooping), and recumbence
- Relieving factors
  - bicarbonate, antacids, milk, over-the counter medications
- Nocturnal symptoms
  - impact on sleep, recumbent position, large or late evening meals.
- Treatments and remedies tried
  - symptom improvement with acid-lowering medications including antacids supports a diagnosis of GERD.
- Periodic dysphagia or food bolus impaction
  - may suggest reflux-related esophageal injury, stricture or malignancy, as well as eosinophilic esophagitis or esophageal dysmotility

Current Trends in the Management of Gastroesophageal Reflux Disease. Gut and Liver, Vol. 12, No. 1, January 2018, pp. 7-16

History

- Drug history
  - Aspirin/nonsteroidal anti-inflammatory drugs (NSAIDs), iron, potassium, quinidine, tetracycline, bisphosphonates
  - Zidovudine, anticholinergic agents, alpha-adrenergic antagonists, barbiturates
  - β2-adrenergic agonists, calcium channel blockers, benzodiazepines, dopamine
  - Estrogens, narcotic analgesics, nitrates, progesterone, prostaglandins, theophylline
  - Tricyclic antidepressants, chemotherapy

- In some patients, bloating or constipation may be associated with an increased risk of GERD

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Physical evaluation

- **There are usually no physical signs of GERD**
  - Waist circumference, weight, and BMI are relevant to risk.
  - Peripheral stigmata of scleroderma may, rarely, be present.

- Evaluation and inspection to exclude other medical problems such as asthma, cardiac disease, and cancer:
  - Anemia, weight loss
  - Oropharynx: ulcerations, candidiasis, lesions, masses, lingual dental erosions, caries
  - Neck: nodes, masses
  - Lungs: wheezes, crackles
  - Ears: hearing loss, middle ear effusions (evidence does not support gastroesophageal reflux as a cause of otitis media)
  - Abdomen: masses, tenderness
  - Signs (local or systemic) of malignancy if history and examination are suspicious

When to do endoscopy?

When to do endoscopy?

- EGD is usually performed for new-onset upper gastrointestinal symptoms, almost irrespective of age, in regions where it is available and affordable and where both the frequency of ulcer disease and the concern about malignancy are high.

- If EGD is performed in regions where the prevalence of GERD is low, the majority of GERD patients will have NERD
  - in these circumstances, the sensitivity of EGD for the diagnosis of GERD will be low and the main outcome will therefore be the exclusion of other upper gastrointestinal diagnoses.

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Initial evaluation

- **Are there indications for upper endoscopy?**
  - Upper endoscopy is **not** required in the presence of typical GERD symptoms of heartburn or regurgitation.
  - Indications for upper endoscopy
    1. If the diagnosis of GERD is unclear
    2. Evaluate alarm features or abnormal imaging if not performed within the last three months
    3. Screen for Barrett's esophagus in patients with risk factors
  - Patients with GERD should receive empiric acid suppression therapy, even if endoscopy is indicated.

When to do endoscopy?

- Endoscopy is particularly recommended for patients with alarm features suggestive of GERD with complications or of other significant upper gastrointestinal disease such as dysphagia, bleeding, odynophagia, or weight loss.

- Patients with dysphagia should undergo investigation for a potential complication or for an underlying motility disorder, achalasia, stricture, ring, eosinophilic esophagitis, or malignancy.

Alarm signs

- New onset dyspepsia in patient ≥ 40-60 years
- Evidence of gastrointestinal bleeding
- Iron deficiency anemia
- Anorexia
- Unexplained weight loss
- Dysphagia
- Odynophagia
- Persistent vomiting
- Gastrointestinal cancer in a first-degree relative

- Lymphadenopathy
- Epigastric mass
- Recurrent bronchial symptoms, aspiration pneumonia
- Dysphonia
- Recurrent or persistent cough

When to do biopsy?

When to do biopsy?

- Esophageal biopsies
  - Distal esophageal biopsies are not recommended for diagnosing GERD and should not be taken, unless one is evaluating for complications or eosinophilic esophagitis.

  - Eosinophilic esophagitis

    Biopsies should be taken from the distal and mid-esophagus.

  -BE

    four-quadrant esophageal biopsies

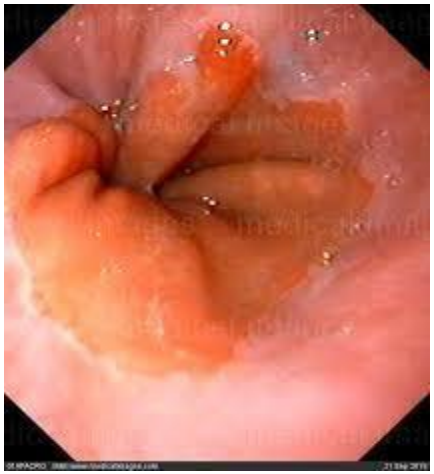
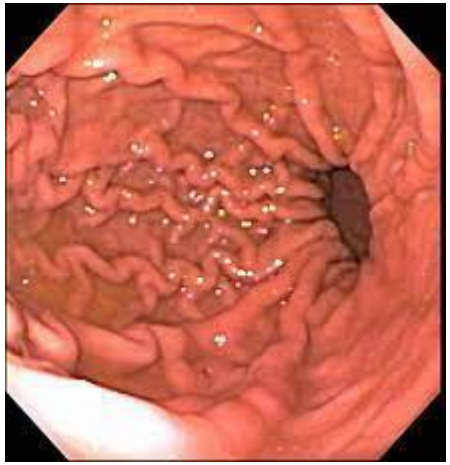
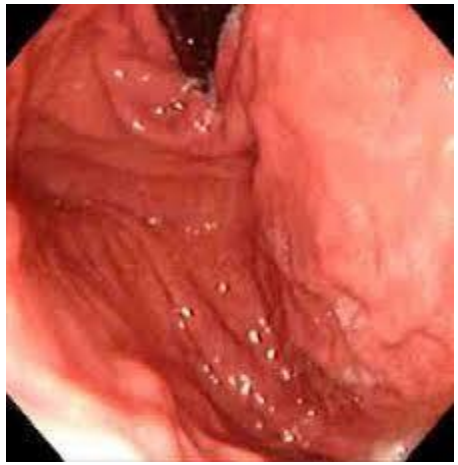
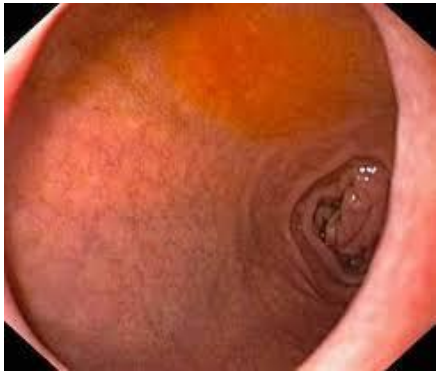
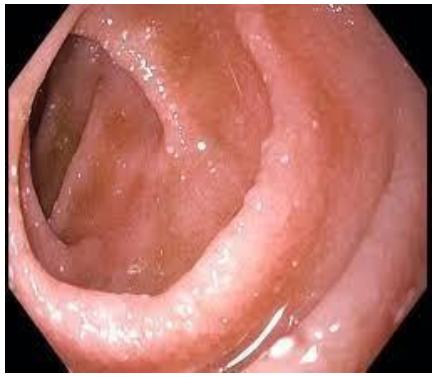
- Gastric biopsies
  - To diagnose H. pylori infection, atrophy, intestinal metaplasia, or dysplasia, even in the presence of erosive esophagitis.

- Duodenal biopsies
  - There is no role for routine biopsies in patients with typical GERD symptoms.

Differential diagnosis of GERD

- Peptic ulcer disease
- Upper gut malignancy
- Functional heartburn
- Schatzki ring, stricture
- Esophageal web
- Achalasia
- Esophageal body motility disorders — scleroderma; diffuse esophageal spasm
- Eosinophilic esophagitis
- Infection — *Candida, herpes simplex, etc.*
- Pill esophagitis
- Cardiac disease— ischemic heart disease, pericardial disease
- Esophageal diverticulum
- Rumination
- Other chest pathology

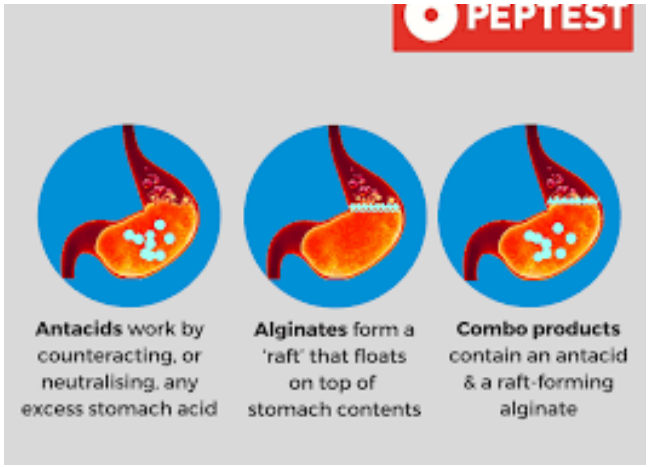
endoscopy

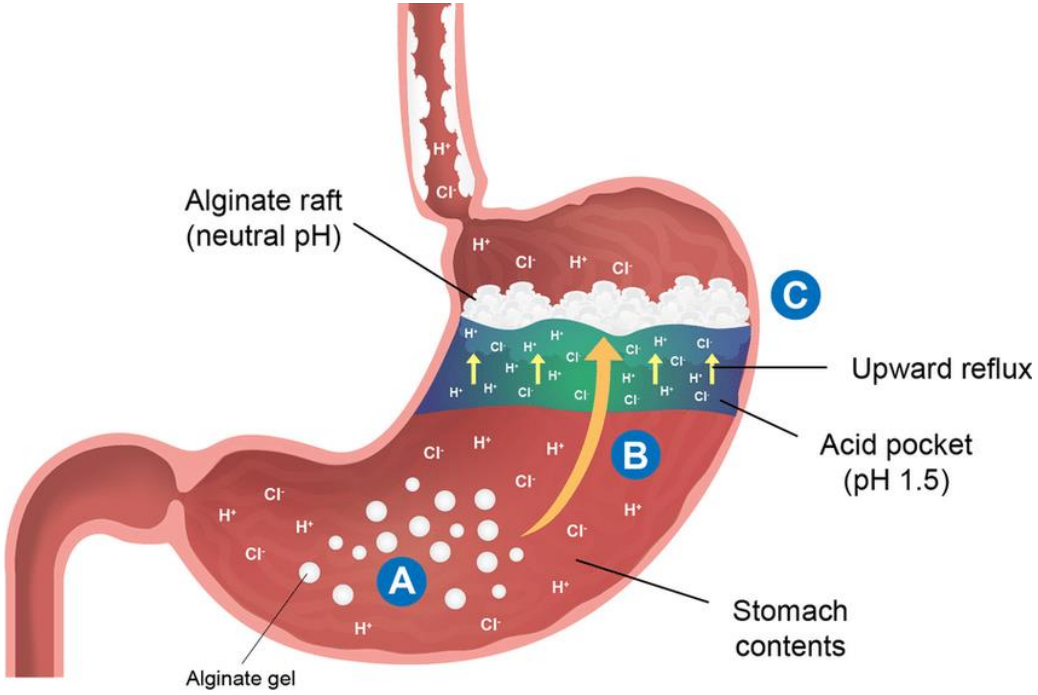






What is your treatment?

- Mild/ intermittent GERD

- Step up therapy
  - Life style and dietary modification
  - Low dose H2RA/PRN
  - Antiacid and Aliginate/PRN
  - Visit in 4 weeks





- Patients with GERD may be managed with a **step-up** or **step-down** approach to therapy.

  - The step-up approach minimizes the use of PPIs and their associated costs and side effects
  - The step-down therapy provides faster symptom relief.

Lifestyle modification

GERD Lifestyle

Chew well, sit straight, raise bed, don't drink with meals, walk after food, manage stress, quit smoking/alcohol, exercise gently, don't eat at bedtime, bend not after food, eat less for dinner, and no pressure on stomach.

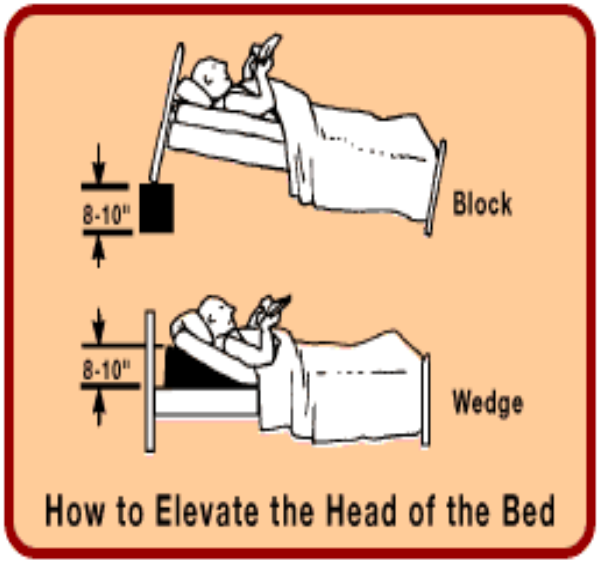












8-10"
Block
8-10"
Wedge
How to Elevate the Head of the Bed

Dietary modification

- limited evidence for the avoidance of
  - alcohol
  - carbonated drinks
  - Caffeine
  - Fat
  - spicy foods
  - chocolate
  - mint
  - Fermentable carbohydrates

Histamine 2 receptor antagonists	Low dose (adult, oral)	Standard dose (adult, oral)
Famotidine	10 mg twice daily	20 mg twice daily Δ
Ranitidine	75 mg twice daily	150 mg twice daily Δ
Nizatidine	75 mg twice daily	150 mg twice daily
Cimetidine	200 mg twice daily	400 mg twice daily Δ

Adverse effects of H2RAs

- **Gynecomastia and impotence -** cimetidine
- **Hematopoietic and immune effects**
  - Long-term H2RA use is also associated with B12 deficiency
  - idiosyncratic cases of myelosuppression, thrombocytopenia, neutropenia, anemia, and pancytopenia
  - polymyositis and interstitial nephritis with cimetidine, an immune complex rash with ranitidine, and fever with both cimetidine and ranitidine
- **Central nervous system (CNS) effects**
  - confusion, restlessness, somnolence, agitation, headaches, dizziness, and, with prolonged therapy, hallucinations, focal twitching, and seizures
  - these symptoms are generally reversible upon discontinuation of the drug,
- **Hepatic effects**
  - H2RAs are metabolized in the liver by the cytochrome P450 system.
  - The clinical presentation of the hepatic injury may be cholestatic, hepatocellular, or mixed with features of both cholestatic and hepatocellular injury
- **Cardiac effects**
  - Sinus bradycardia, hypotension, atrioventricular block, prolongation of the QT interval, and sinus and cardiac arrest have occurred with the rapid infusion of an H2RA
- **Renal effects**
  - Mild increases in serum creatinine have been observed with cimetidine.

H2RA Dose adjustment in Renal Impairment

- CrCl ≥50 mL/minute
  - No dosage adjustment necessary.
- CrCl <50 mL/minute:
  - Oral: 150 mg every 24 hours; adjust dose cautiously if needed (frequency of dosing may be increased to every 12 hours or further with caution).
  - IV: 50 mg every 18 to 24 hours; adjust dose cautiously if needed
- Hemodialysis
  - Adjust dosing schedule so that dose is scheduled to coincide with the end of hemodialysis.

Case 1-cont.

- She is not better with low dose H2RA.

What is the next step?

Case 1-cont.

- Standard dose of H2RA/bid
- Reevaluate after 2 weeks

Case 1-cont.

- She is better

What is the next step?

Case 1-cont.

- Continue life style modifications
- H2RA/PRN

Case 1-cont.

- After 4 months she returns with recurrent symptoms.

What is your plan?

Case 1-cont.

- Treat with standard dose of H2RA /bid for 8 weeks.

Recurrent symptoms

- Recurrent symptoms ≥ 3 months of acid suppression therapy
  - 8 week retreat with the previous effective therapy

- Recurrent symptoms within 3 months of acid suppression therapy:
  - Endoscopy if not done before
  - Continue long term maintenance acid suppression therapy

Case 2

- Patient is a 34 yrs old lady with CC of daily regurgitation and heart burn since last year.

What is your approach?

- Mod /frequent GERD
  - Step down therapy
    - Life style and dietary modifications
    - Standard dose PPI once daily
    - R/O other causes
    - Low dose and if not responding standard dose PPI/d for 8 weeks.

Proton pump inhibitors	**Low dose** (adult, oral)	**Standard dose** (adult, oral)
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

Treatment

- A formal course of PPI therapy, of adequate duration (usually 8 weeks) is required in order to assess the treatment response in GERD patients.

- "PPI trial" (empirical short-term (1–2-week) course of high-dose PPI)
  -It is no longer recommended, it is neither sensitive nor specific.
  -Nonetheless, this is commonly done in practice.

Selecting a PPI?

Selecting a PPI

- Often determined by patient preference and payer coverage.

- No consistent difference in symptom resolution and esophagitis healing rates with different PPIs.

- In patients unable to swallow pills or capsules,
  - oral suspension of lansoprazole
  - powder formulation of omeprazole-sodium bicarbonate

PRETREATMENT CONSIDERATIONS AND MONITORING

- **Magnesium**
  - Prior to starting a PPI in patients who
    - expect to be on long-term (≥1 year) treatment
    - take PPIs in conjunction with other medications associated with hypomagnesemia (eg, diuretics).
  - Periodically in such patients while they are taking a PPI.
  - The frequency of testing is based on the clinical history and the presence of symptoms of hypomagnesemia. As an example, in patients with a history of arrhythmias or QT interval prolongation, we monitor magnesium levels every six months.
- **Vitamin B12**
  - Vitamin B12 levels yearly in patients on long-term PPIs
    - Routinely monitoring vitamin B12 levels is controversial.
- **Bone densitometry**
  - There are insufficient evidence to support routine bone density monitoring or
    calcium supplementation due to proton pump inhibitor use alone .

Dose and timing of administration

- PPIs should be administered 30 to 60 minutes before breakfast for maximal inhibition of proton pumps.

- Polymorphisms in the *CYP2C19* gene, which encodes the cytochrome P450 isoenzyme that metabolizes different PPI preparations, are common in Asian and other populations
  - **slow metabolizer** : prolong the antisecretory effect of PPIs.
  - **rapid metabolizer**: the duration of acid inhibition would be decreased
    - Differences in PPI metabolism might account for incomplete inhibition of acid secretion and a high prevalence of nocturnal breakthrough symptoms in gastroesophageal reflux disease patients.

Principal cytochrome P450 enzymes involved in hepatic metabolism

PPI	Primary pathway	Secondary pathway	Sulfotransferase
Omeprazole Lansoprazole Rabeprazole Pantoprazole Esomeprazole	CYP2C19 CYP3A4	CYP3A4	No
		CYP2C19	No
	CYP2C19	CYP3A4	No
	CYP2C19	CYP3A4	Yes
	CYP2C19	CYP3A4	No

Optimizing PPI treatment

- Improve compliance
- Ensure proper dosing time
- Split the PPI dose
- Swith to another PPI
- Not administered concomitantly with antisecretory agents including:
  - histamine-2 receptor antagonists (H2RAs)
  - analogues of prostaglandin E (eg , misoprostol)
  - somatostatin analogues (eg, octreotide)

Switching between PPIs

- Is a reasonable strategy in patients with side- effects to an individual PPI.

- May be necessary due to cost differences.

- Switching PPIs in patients with well-controlled symptoms may also be associated with increased symptom severity and decreased patient satisfaction

Drug-Drug interactions

Concomitant drug	Omeprazole	Lansoprazole	Rabeprazole	Pantoprazole	Esomeprazole
Warfarin	PT decreased by 10 percent	-	-	-	-
Diazepam	T1/2 increased by 130 percent	-	-	-	Decreased clearance
Phenytoin	T1/2 increased by 27 percent	-	-	-	-
Theophylline	-	AUC increased by 10 percent	-	-	Unknown
Digoxin	AUC increased by 10 percent	-	AUC, Cmax, T1/2 increased	-	Unknown
Carbamazepine	AUC increased by 75 percent	-	-	-	Unknown

Case 2-cont.

- She is back after 2 months of treatment and is better but asks how long she has to continue her PPI?

Discontinuing PPIs?

When patients is asymptomatic for 8 weeks except in erosive esophagitis or Barrett's esophagus

Discontinuing PPIs

- PPIs should be prescribed at the **lowest dose** and for the **shortest duration** appropriate to the condition being treated.

- Rebound gastric acid hypersecretion following discontinuation of PPIs in patients with long-term use (more than 6 months).

  - Standard or high-dose PPI
    - decrease the dose by 50 percent every week.

  - Twice daily dosing
    - decrease the dose to once in the morning to the lowest dose of the medication
      - After one week, discontinue the PPI.

Adverse effects

- **Diarrheal illnesses**
  - Clostridioides (formerly Clostridium) difficile and other enteric infections
  - Microscopic colitis

- **Magnesium malabsorption**
  - due to reduced intestinal absorption
  - Severe forms can associated with QT interval prolongation and torsades de pointes.
  - mainly in long-term use(> one year), but cases have been reported within one year of starting PPI therapy.

Adverse effects

- **Calcium and fracture risk**
  - Hypochlorhydria
    - impact on absorption of
      - » water soluble calcium salts
      - » calcium in dairy products
        - can be overcome by
          - ingestion of a slightly acidic meal
          - use calcium supplements that do not require acid for absorption(calcium citrate).
    - augment osteoclastic activity, thereby decreasing bone density.
      - association between PPI use and bone fracture is plausible, but causality has not been established.
        - » the FDA has mandated revised safety information on all PPIs about a possible increased risk of fractures of the hip, wrist, and spine with the use of these medications.

Adverse effects

- **Vitamin B12 malabsorption**
  - Absorption of oral B12 supplements is not affected.
- **Iron malabsorption**
  - Does not appear to be of clinical significance.
    - exception may be in patients who require oral iron supplementation.
      - higher dose or longer duration of supplementation .
- **Hypergastrinemia**
  - No dysplasia or neoplastic changes have been observed .
  - No increased risk of colon cancer

Adverse effects

- **Atrophic gastritis**
  - the risk of atrophic gastritis is small and, the clinical consequences are uncertain
- **Kidney disease**
  - Acute interstitial nephritis (AIN)
    - not dose-dependent
    - recurrence or exacerbation can occur with a second exposure to the same or a related drug.
  - Increased risk of chronic kidney disease (CKD), CKD progression, and end-stage renal disease
    - it is possible that the weak association observed in these studies is due to methodological limitations (residual confounding)

Adverse effects

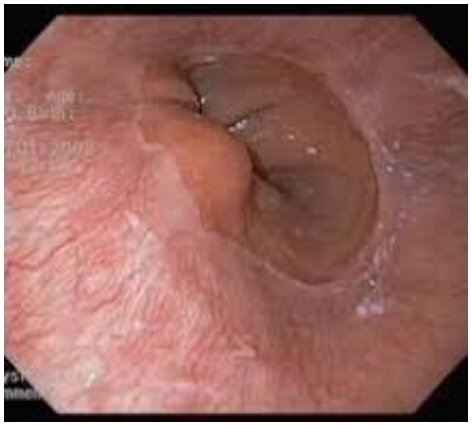
- **Drug-induced lupus**
  - PPI-associated SLE usually occurs days to years after initiating PPI treatment and typically presents with a rash.
  - Most patients improve within 4 to 12 weeks of discontinuation of PPI therapy.
- **Dementia**
  - The association between PPI use and dementia may reflect residual confounding by factors related to both use of PPIs and the development of dementia.
- **Pneumonia**
  - The observed association may be due to confounding such that individuals prescribed PPIs may be more likely to have other unobserved health characteristics that predispose them to pneumonia as compared with nonusers

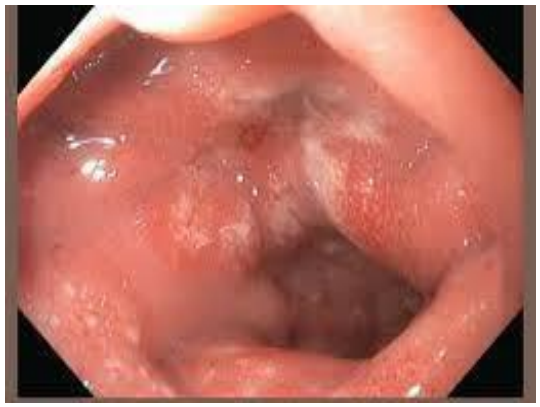
Adverse effects

- **Mortality**
  - Increase in all-cause mortality as compared with H2RA use (HR 1.25, 95% CI 1.23-1.28).
  - Increase in risk of death as compared with individuals without any PPI use and individuals without any acid suppression use (HR 1.15, 95% CI 1.14-1.15; HR 1.23, 95% CI 1.22-1.24, respectively).
  - Among new PPI users, the risk of death increased with the duration of PPI use.

Case 3

- A 48 yrs old man complains of nausea, dysphagia and epigastric pain. An upper endoscopy was done.





Case 3-con

- After HP eradication his pain subsides, but he complains of recurrent heartburn and regurgitation at least 4 times/week with globus sensation.

What is your comment?

- What is the role of HP in GERD?
- When to screen for HP in GERD?

HP and GERD

- H. pylori infection should be sought and eradication therapy given when indicated in accordance with international, national, or local guidelines.

- In many countries with a high prevalence of H. pylori, peptic ulcer and cancer continue to be more common than GERD and cause much greater morbidity and mortality .
  - decision regarding the relative merits of a test-and-treat approach in comparison with esophagogastroduodenoscopy (EGD) to test for H. pylori and related diseases before empirical antireflux therapy.

- Although epidemiological studies show a negative association between the prevalence of H. pylori infection and the presence and severity of GERD, this is not proof of causation.
  - Improving socioeconomic status
    - decline in the prevalence of H. pylori
    - rising prevalence of obesity, sedentary occupations, and altered dietary habits
      - *this may well reflect differing effects of a separate, distinct factor or factors on the two conditions, rather than a causal relationship between H. pylori and GERD.*

HP and GERD

- Physiological studies using pH monitoring have shown that abnormal esophageal acid exposure, which is the hallmark of esophageal reflux, is not influenced by the presence or absence of *H. pylori infection.*

- In most patients, *H. pylori status has no effect on symptom severity, symptom,recurrence, or treatment efficacy in GERD.*

- *H. pylori eradication does not exacerbate preexisting GERD or affect treatment efficacy . Indeed, in patients with H. pylori–positive uninvestigated dyspepsia, eradication therapy has been found to be associated with a lower prevalence of reflux-like symptoms (36%) than control therapy (49%) .*
- • A subgroup of patients infected with more proinflammatory strains of *H. pylori (virulence factors vacA and cagA) may be less likely to have severe esophagitis or BE. This may be because infection in these patients more often causes severe* corpus gastritis with atrophy, resulting in reduced acid output. However, these patients are at much greater risk of developing gastric cancer or ulcer. Eradication therapy in these patients has the potential to reduce the risk of gastric malignancy.

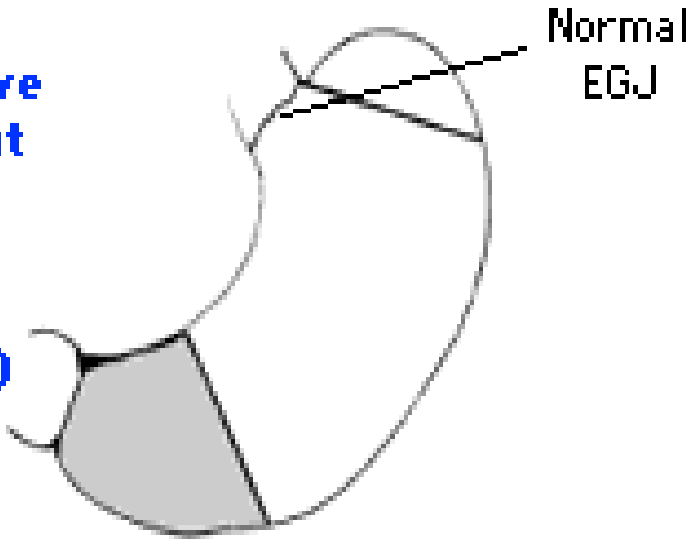
HP and GERD

- It is uncertain whether chronic acid suppression with PPIs increases the risk for atrophic gastritis in patients with *H. pylori*. Therefore, routine screening for *H. pylori* infection and empiric eradication of *H. pylori* are not recommended in patients with GERD .

- However, if *H. pylori* is diagnosed in the setting of GERD, eradication of *H. pylori* has been associated with an improvement of symptoms in patients with antral-predominant gastritis.

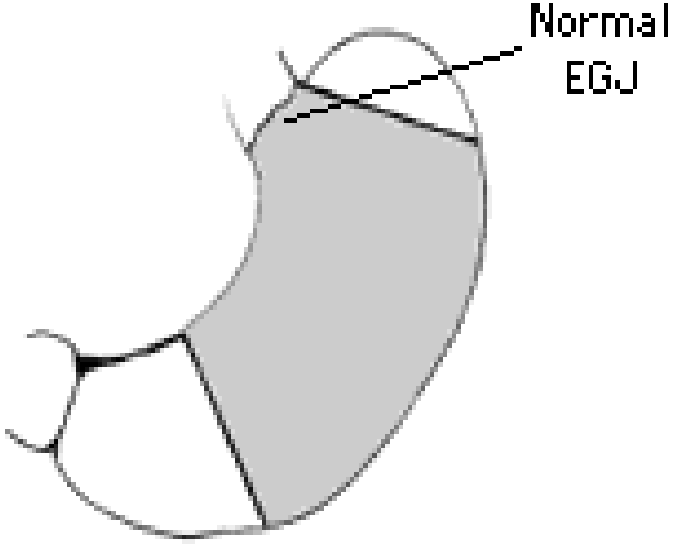
H. Pylori positive patients without GERD (normal EGJ and esophageal acid clearance)

Antral-predominant gastritis



- Acid secretion normal or increased
- 10 percent lifetime duodenal ulcer risk
- H. Pylori eradication:
  - GERD should not develop
  - Reduced recurrence of DU

Corpus-predominant gastritis



- Acid secretion normal or decreased
- 2-3 times risk for gastric cancer
- H. Pylori eradication:
  - May unmask subclinical GERD
  - Decreased PPI efficacy
  - Decreased risk for gastric cancer?

HP and GERD

- **Patients with GERD** — Studying the effects *of H. pylori* eradication in patients with GERD is difficult because these patients necessarily have preserved acid secretion and EGJ compromise. Because they have preserved acid secretion, it is likely that these patients have either antral-dominant gastritis or only mild corpus gastritis. Regardless, eradication should not significantly worsen acid reflux in patients with preexisting GERD and should improve reflux in patients with antral-dominant gastritis. At least three studies support this hypothesis .

- **Effect of H. pylori on PPI therapy** — *H. pylori* infection affects gastric acid secretion in patients treated with proton pump inhibitors (PPIs).
- For example, inhibition of gastric acid secretion with a PPI is greater in patients with *H. pylori* infection compared to *H. pylori*-negative subjects.
- Studies of patients with duodenal ulcers have also demonstrated that the acid suppressing ability of PPIs is augmented in patients who are infected with *H.pylori* .
- Whether or not the demonstrated effect of *H. pylori* on acid suppression with PPIs is clinically important has yet to be determined.
- In one study, PPIs appeared to be more effective in preventing and curing ulcers in patients who are *H. pylori* positive with or without NSAID use. However, in a controlled trial comparing the efficacy of esomeprazole with lansoprazole, healing rates with PPIs were not influenced by *H. pylori* status .

- In combined analysis of three large controlled trials of short- and long-term treatment in patients with reflux disease, *H. pylori* was a weak independent protective factor against relapse .
- In another open-label study that included 971 patients with symptomatic reflux and esophagitis treated with pantoprazole, relief from heartburn and regurgitation and the likelihood of endoscopic healing after four weeks of therapy was significantly greater in *H. pylori*-positive patients compared with *H. pylori*-negative patients (87 versus 76 percent) .
- Long-term studies evaluating maintenance therapy for GERD found no difference in the PPI dose required for *H. pylori*-negative and positive patients. Thus, it appears that although *H. pylori* increases the acid suppressive effect of PPIs, there is no evidence suggesting a need to titrate the dose according to the presence of *H. pylori*.

- Another issue that may be of clinical relevance is acid rebound after discontinuation of PPIs. Studies suggest that it may be more difficult to withdraw PPI therapy in H. pylori negative patients

- The authors speculated that this phenomenon was the result of persistence of corpus gastritis in H. pylori-positive patients.

- **Theoretical risk of long-term PPI therapy** — A major concern regarding long-term PPI therapy has been the suggestion that patients infected by *H. pylori* are at increased risk for the development of atrophic gastritis during long-term therapy with PPIs . A US Food and Drug Administration panel reviewing the data supporting this contention concluded that the findings were flawed and inconclusive.

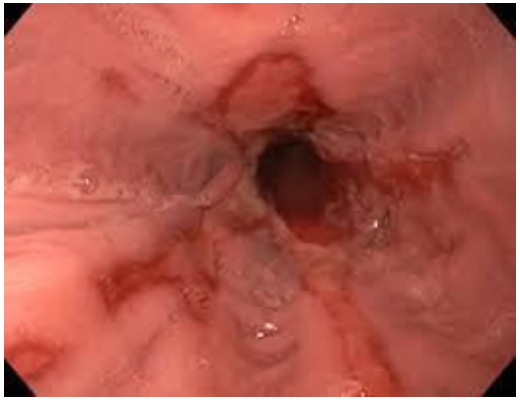
- However, at least two controlled trials have demonstrated that eradication of *H. pylori* in patients with reflux esophagitis receiving long-term acid suppression therapy decreases inflammation and reverses corpus gastritis .
- *PPIs are associated with a worsening of the histological grade of gastritis in H. pylori–infected patients, accompanied by an increased prevalence of gastric mucosal atrophy and intestinal metaplasia that occurs earlier, as well as more frequently, than in H. pylori–infected patients who do not take PPIs.*
- *This risk of gastric mucosal atrophy and intestinal metaplasia is not seen when PPIs are used in uninfected patients or in those who have had successful H. pylori eradication therapy before longer-term PPI use.*

PPIs and H. pylori

- *. As gastric mucosal atrophy and intestinal metaplasia are known to be the major risk factors for the development of gastric adenocarcinoma, most expert guidelines recommend testing and treating for H. pylori before long- term PPI therapy is administered, particularly in younger patients.*
- As a result, European consensus guidelines suggest that *H. pylori* testing be performed in patients receiving long-term acid suppression with PPIs .

Case 4

- A 62 yrs old man visits you because of dysphagia and heart burn since last year. You order an upper endoscopy and this is the result:



- What is your plan?

- Standard dose PPI for 8 weeks
- Re-endoscopy to R/O Barret
- Maintenance of standard dose PPI

Case 5

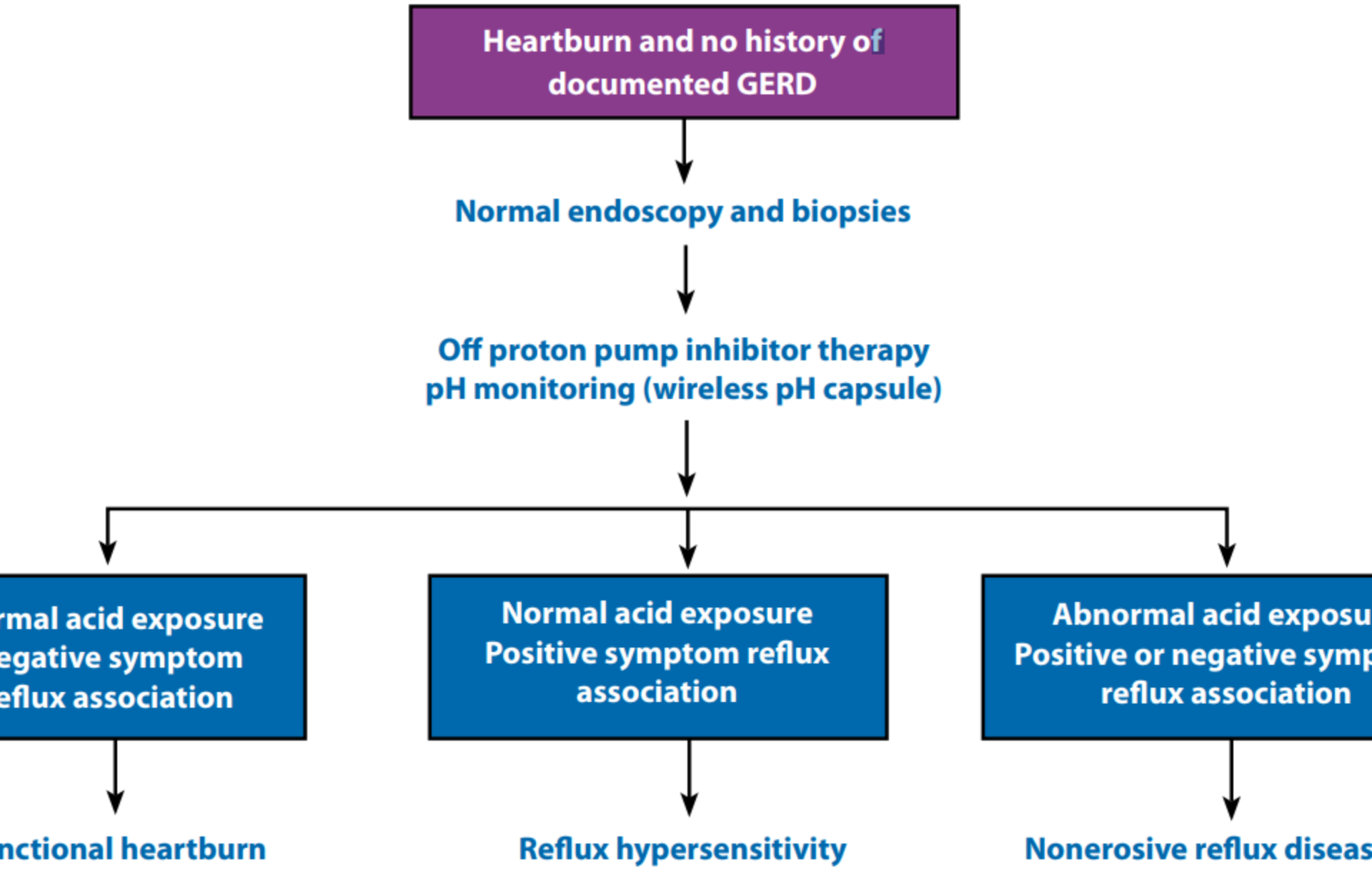
- A 53 yrs old lady visits you because of frequent heart burn and retrosternal pain. Cardiologist consultation was negative.
- You prescribe standard dose of PPI for 8 weeks. On her second visit she is better but still suffers from heartburn at least 3 times a week. What now?

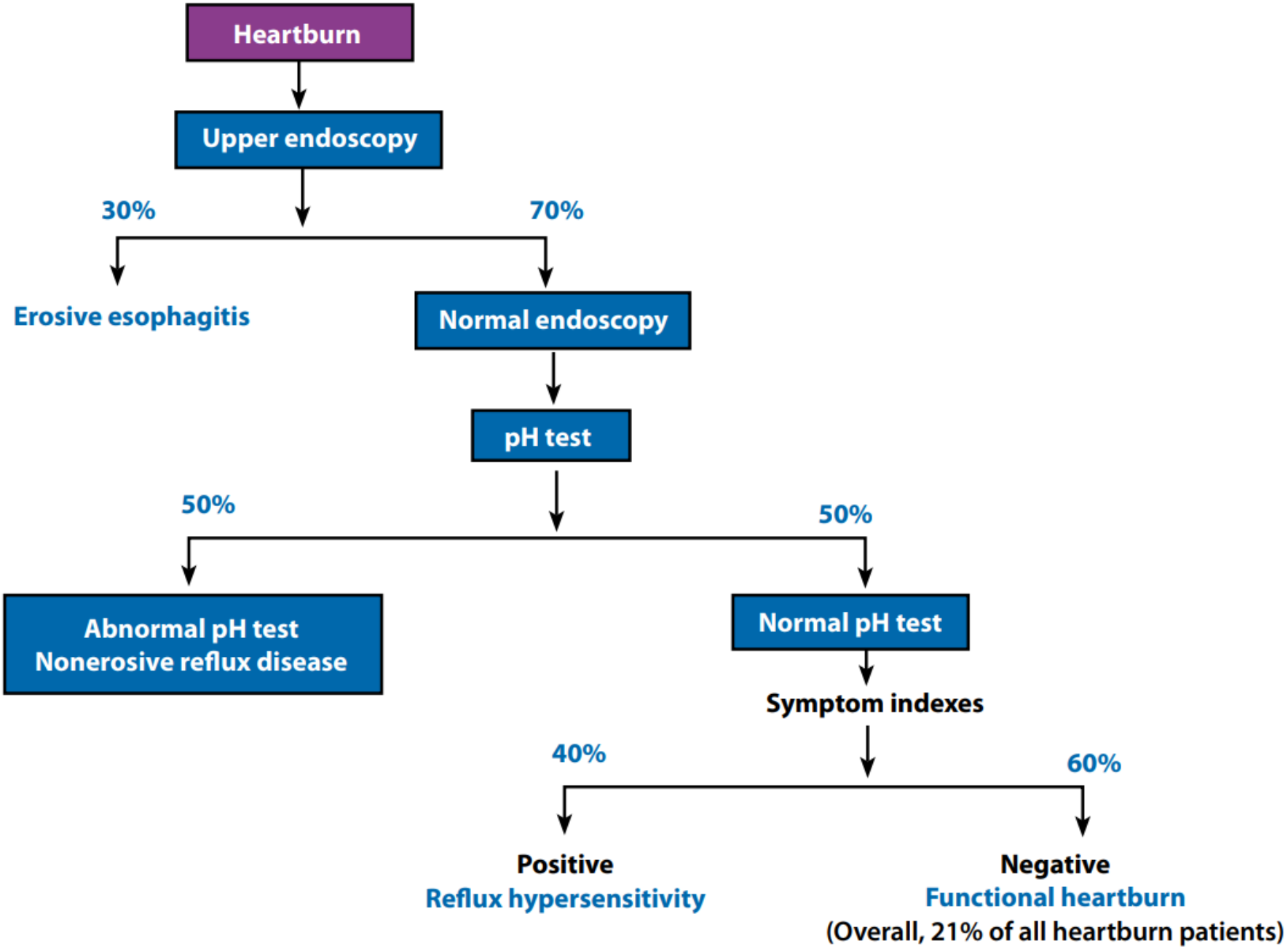
Refractory GERD

- The definition of refractory gastroesophageal reflux disease (GERD) is controversial.
- Patients with GERD who exhibit partial or lack of response to proton pump inhibitor (PPI) twice daily or once a day ?
  - According to most experts, patients with GERD who exhibit partial or lack of response to proton pump inhibitor (PPI) twice daily are considered to have failed PPI therapy . GERD in these patients is termed refractory GERD. However, we suggest that lack of satisfactory symptomatic response to PPI once a day should be considered a failure of PPI therapy.

Etiology of refractory GERD

- Insufficient acid suppression
  - Medication related factors
  - Medication timing and adherence
  - Differences in PPI metabolism
  - Residual acid reflux
- Weakly acidic or alkaline reflux (non-acid reflux)
- Reflux hypersensitivity
- Functional heartburn
- Alternative diagnoses


Heartburn and no history of documented GERD
Normal endoscopy and biopsies
Off proton pump inhibitor therapy
pH monitoring (wireless pH capsule)
rmal acid exposure
egative symptom
eflux association
nctional heartburn
Normal acid exposure
Positive symptom reflux association
Reflux hypersensitivity
Abnormal acid exposu
Positive or negative symp
reflux association
Nonerosive reflux diseas


Heartburn
Upper endoscopy
30%
70%
Erosive esophagitis
Normal endoscopy
pH test
50%
50%
Abnormal pH test
Nonerosive reflux disease
Normal pH test
Symptom indexes
40%
60%
Positive
Reflux hypersensitivity
Negative
Functional heartburn
(Overall, 21% of all heartburn patients)

- GERD can be distinguished from rumination syndrome by impedance pH manometry by detecting gastric straining preceding or during reflux events that extend to the proximal esophagus.

- If alarm signs do endoscopy
- Check for compliance
- High dose PPI for 2 months then go for Change to another PPI
- Split dose

Case 5- con

- Patient returns after 2 months and still complains of regurgitation in month.
  You can not do impedance and PH metery.

- What will you do?

- In patients whose symptoms are primarily regurgitation, we use an empiric trial of **baclofen (TLESR reducer).**
- We initiate baclofen at a low dose (5 to 10 mg twice a day before meals)
- In patients who fail to respond, we make incremental changes and increase the dose by 5 mg every four days to 20 mg three times a day while carefully monitoring for side effects.
- Because baclofen crosses the blood-brain barrier, a variety of central nervous system-related side effects may occur. These include somnolence, confusion, dizziness, lightheadedness, drowsiness, weakness, and trembling.
- We usually continue baclofen for four to eight weeks before stopping if it is ineffective.

Case 5- con

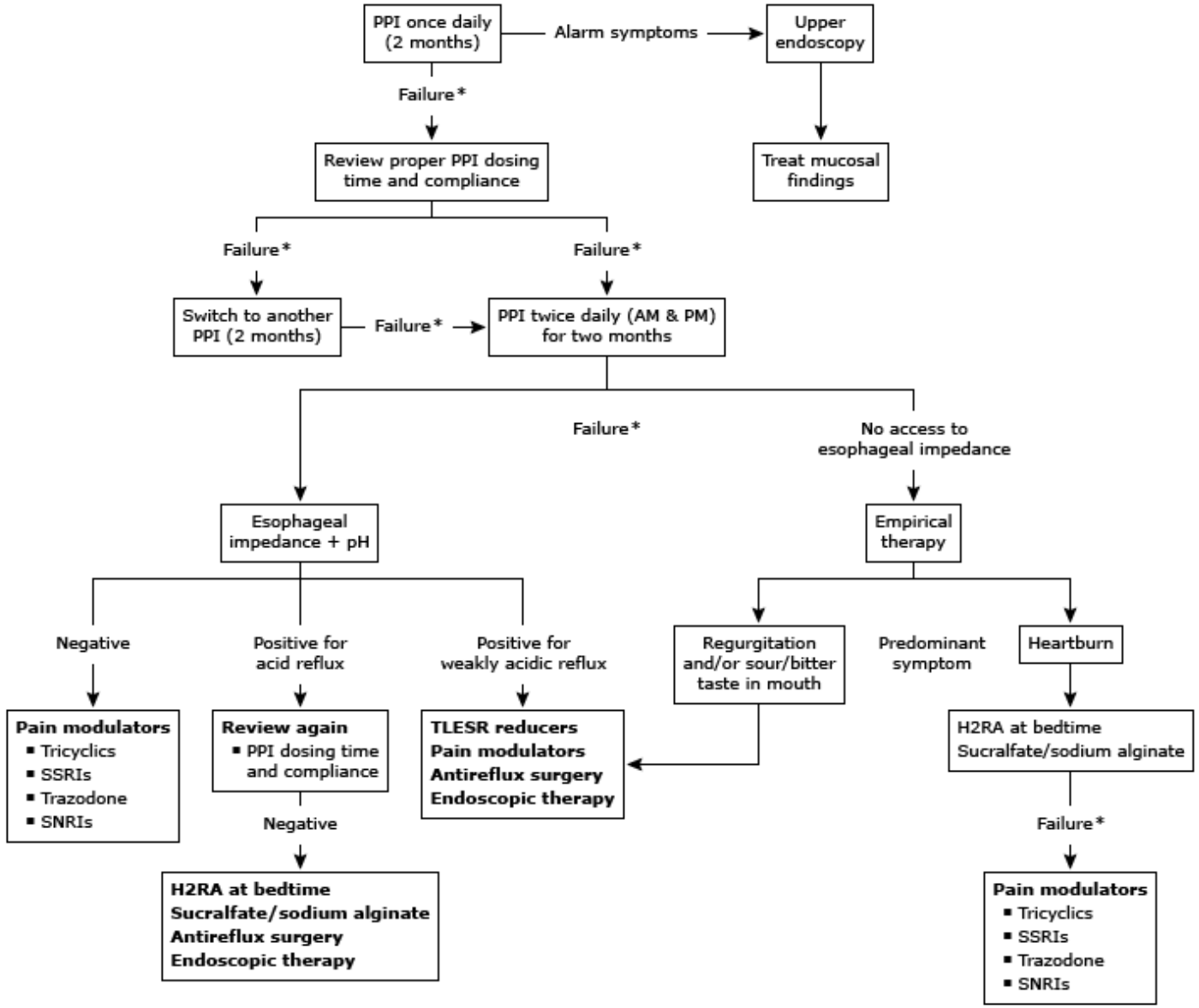
- What if she mainly complained of heartburn?

- H2RA at bedtime
- Sucralfate/alginate

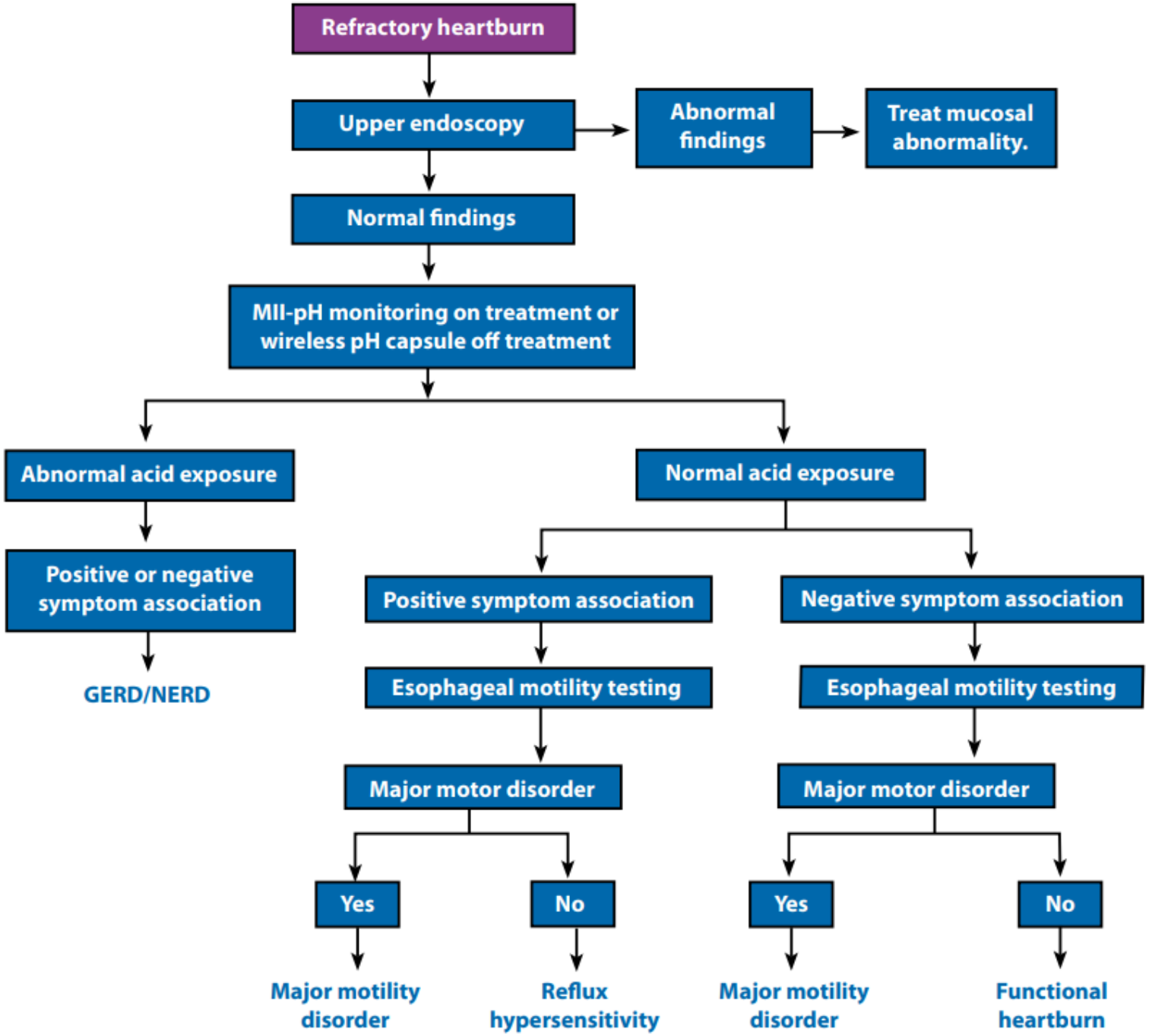
- If did not respond
  - TLESR reducers
  - Pain modulator (Tricyclics, SSRI, Trazodone, SNRIs)
  - Antireflux surgery
  - Endoscopic therapy

- **Prokinetics agents**
  - reserved for patients with refractory GERD and objective evidence of delayed gastric emptying
  - not increase healing of erosive esophagitis or improve esophageal motor performance
  - more likely to experience adverse effects.
- **Bile acid binders**
  - Unclear
- **Acupuncture**
  - significant improvement in regurgitation and heartburn
    - additional studies are needed to define the role of acupuncture in patients with refractory GERD.

Management algorithm of GERD patient who failed PPI once daily



 Management algorithm of gastroesophageal reflux disease (GERD) patient who failed PPI once daily (complete or partial*)


Refractory heartburn
Upper endoscopy
Abnormal findings
Treat mucosal abnormality.
Normal findings
MII-pH monitoring on treatment or wireless pH capsule off treatment
Abnormal acid exposure
Positive or negative symptom association
GERD/NERD
Normal acid exposure
Positive symptom association
Esophageal motility testing
Major motor disorder
Yes
No
Major motility disorder
Reflux hypersensitivity
Negative symptom association
Esophageal motility testing
Major motor disorder
Yes
No
Major motility disorder
Functional heartburn

Treatment options for GERD in pregnancy

Treatment option	Details
Dietary and lifestyle modifications	Frequent (every 3 h), small meals Last oral intake 3 h before bedtime Elevate head of bed
Antacids or sucralfate	Avoid long-term use or high doses of magnesium trisilicate Avoid sodium bicarbonate
H2-receptor antagonists	Use ranitidine: FDA category B Limited data are available for other H2-receptor antagonists, but they are probably also safe
PPIs	Use omeprazole: FDA category B Limited data are available for other PPIs, but they are probably also safe