



Pharmacotherapy I

Dr. Abdallah Abukhalil

# Suggested Readings

- Chapter 32: Gastroesophageal Reflux Disease

# Learning Objectives

Explain pathophysiology and etiologies of GERD

Identify typical, atypical, and alarm symptoms of GERD

List foods and medications that can worsen GERD

Counsel on lifestyle modifications and

medications for GERD

Recommend appropriate therapy for a patient with GERD

Monitor a patient receiving GERD therapy

# Common Abbreviations

GERD –  
Gastroesophageal  
reflux disease

H2RAs – Histamine  
type-2 receptor  
antagonists, AKA  
“H2 blockers”

LES – lower  
esophageal  
sphincter

PPIs – proton  
pump inhibitors

Sx – symptoms

# Introduction

Heartburn: burning feeling begins in substernal area (lower chest) or stomach & spreads up to neck and sometimes the back

Postprandial heartburn: occurs within 2hrs after eating or when bending over or lying down

Nocturnal heartburn: occurs during sleep and usually awakens person

Dyspepsia (bad digestion): consistent or recurrent discomfort in upper abdominal area (epigastrium)

Mainly self-treat

Need to distinguish between who can be self-treated & who need to be evaluated by PCP

# Other Definitions

Episodic heartburn –  
heartburn of low  
frequency or severity

Esophagitis –  
inflammation of the  
lining of the  
esophagus

Erosive esophagitis –  
erosion of the  
squamous epithelium  
of the esophagus

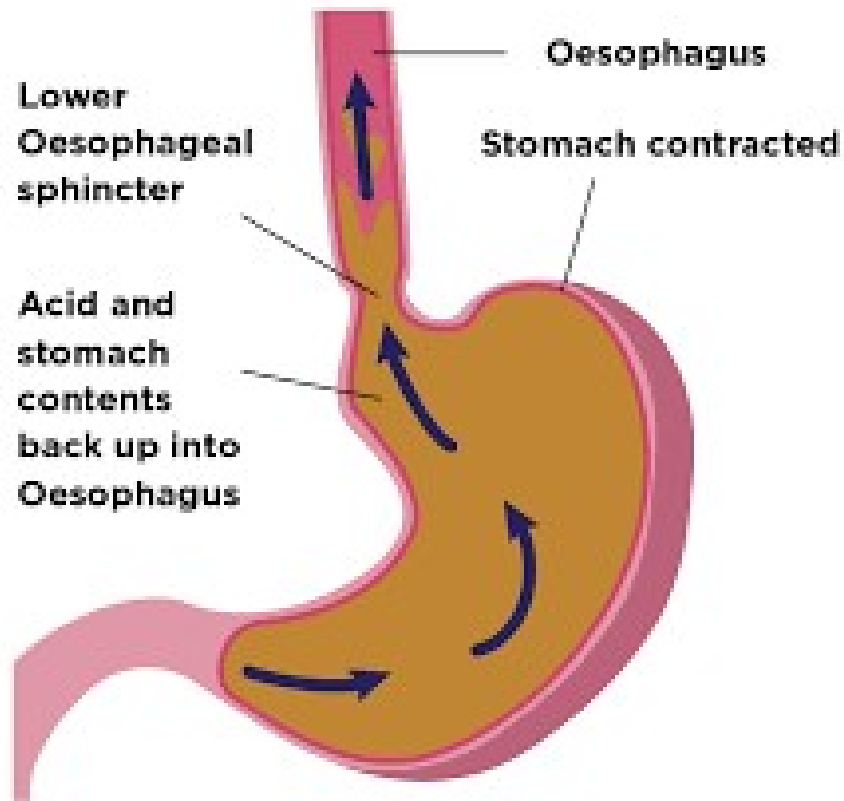
Nonerosive reflux  
disease (NERD) –  
GERD symptoms  
without erosions

## Anatomy and Physiology of the Upper Gastrointestinal System

Esophagus: from pharynx to stomach and closed at both ends by upper and LES

Lower esophageal sphincter (LES): lower end of esophagus, prevents reflux, pass food into stomach, regulates belching

- At rest: LES contracts to prohibit passage of stomach contents into esophagus
- Swallowing: LES relaxes for food to pass into stomach



## Definition of GERD

- Symptoms or complications resulting from the reflux of gastric contents into the esophagus or beyond, into the oral cavity or lung.”



## GERD/Heartburn Pathophysiology

Abnormal reflux of gastric contents into esophagus causing symptoms and/or esophageal mucosal damage

Retrograde flow of gastric contents into esophagus

Signs and symptoms

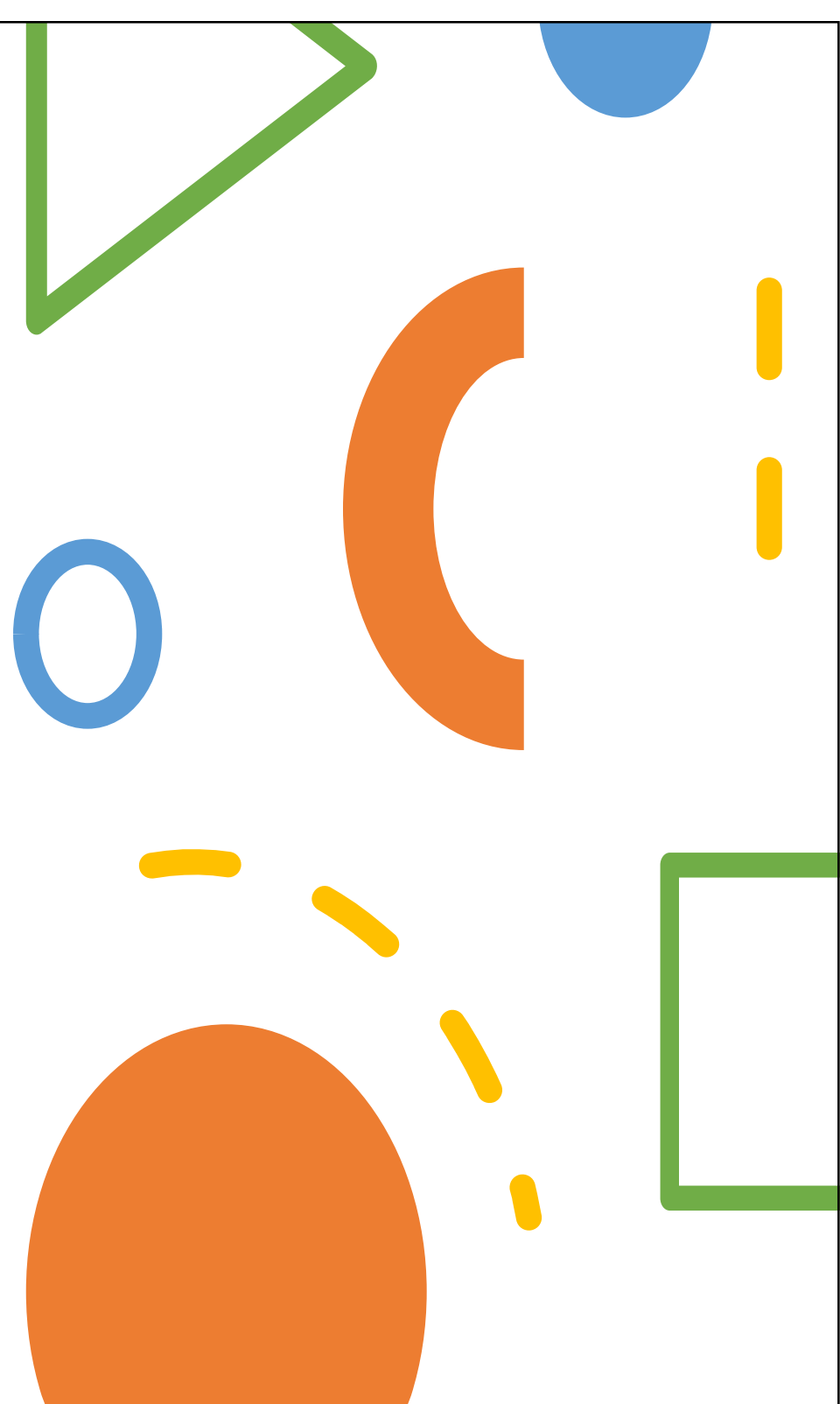
- Esophagus, oropharynx, larynx, & respiratory damage
- (ex: esophageal erosions, ulcers, esophagitis)

# Case Presentation

- AA is a 35 YO WM who comes to your pharmacy Complaining severe heartburn 3 to 4 times per week.
- He wants to know what you recommend for heartburn.
- What questions would you want to ask this patient?

# Pathophysiology

- Common disorder (10-20%)
- Reflux of gastric contents
- Defective lower esophageal sphincter (LES)
- Defective mucosal defense
- Delayed gastric emptying
- Composition of reflux
- Gastric acid
- Pepsin



# What Foods Can Exacerbate GERD?

## Decrease LES pressure

- Carbonated beverages
- Chocolate
- Tobacco

## Increase acid exposure

- Chocolate
- ETOH
- Fatty foods
- Tobacco Others

## Acidic foods

- Citrus, Orange
- Tomatoes

Caffeine, Coffee

Spearmint/Peppermint

Tight-fitting clothes

# What Medications Can Worsen GERD?

## Decrease LES pressure

- Anticholinergics
- Barbiturates
- Calcium channel blockers
- Estrogen
- Progesterone
- Nitrates
- Nicotine
- Theophylline

## Direct mucosal irritant

- Aspirin
- Bisphosphonates
- Iron
- NSAIDs , ASA
- Potassium chloride

# Clinical Presentation

Typical symptoms – heartburn (hallmark), regurgitation, non-cardiac chest pain

- Occurs within 1 hour of meal, lying down, stress, bend over, exercise (cycling, sit-ups), emotional stress

Atypical symptoms – dyspepsia, epigastric pain, nausea, bloating, belching

Extraesophageal symptoms – asthma, chronic cough, laryngitis, Hoarseness, Dental erosions

Severity of symptoms does not always correlate with severity of tissue injury

# Alarm Symptoms

Constant pain

Dysphagia Difficulty swallowing

- could be severe erosive esophagitis,

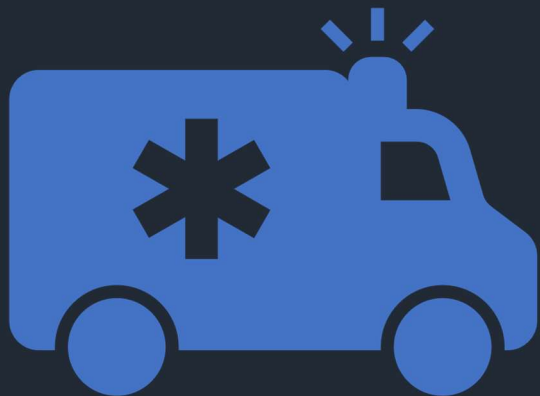
Odynophagia Pain on swallowing

- Due to ulcerative esophagitis, esophageal cancer, pills (tetracycline, ASA,
- NSAID, bisphosphonate, KCL, vitamin C), infection

Unexplained Weight loss

Choking

## Patients Who Should Be Referred



- Any of alarm symptoms
- Heartburn or dyspepsia on recommended doses of OTC PPI, H2RA
- Heartburn or dyspepsia continues after 2 weeks on OTC PPI, H2RA
- Heartburn and dyspepsia when taking RX PPI, H2RA
- Under PCP care for epigastric pain
- Symptoms > 3 months
- Higher than recommended OTC doses for GERD
- Concurrent use of H2RA and PPI
- HB and dyspepsia that is severe and/or long-lasting
- Nocturnal heartburn
- Chronic hoarseness, wheezing, coughing, or choking
- Chest pain with sweating, pain radiating to shoulder, arm, neck, or jaw and shortness of breath
- Adults > 45 YO with new-onset dyspepsia



# Diagnosis of GERD



## Typical symptoms – empiric trial of therapy

- Mild, episodic symptoms (heartburn, regurgitation)
- Most likely do not need invasive esophageal evaluation
- Medication trial and lifestyle modifications → respond → GERD

## Further work-up

- Non-responders to empiric medication
- Require continuous chronic therapy to relieve symptoms
- Alarm symptoms

## Endoscopy (pictures)

## PillCam

## Ambulatory pH monitoring

## Manometry (pressure) – preop eval only

# Endoscopy

Visualize esophageal mucosa, biopsy

Technique of choice to diagnose Barrett's esophagus and GERD complications

Need biopsy to confirm Barrett's epithelium diagnosis and evaluate for dysplasia

Detects esophagitis, Barrett's esophagus (since need biopsy), ulcers, erosions

Specific but not very sensitive (50% for GERD) → in mild GERD mucosa may appear normal but biopsy may have different result

- Symptoms do not predict erosive esophagitis → esophagus

may be normal in ½ patients with GERD (normal endoscopy does not exclude GERD)

# Diagnosis

## PillCam ESO

- Camera-containing capsule swallowed to see esophageal mucosa by endoscopy (esophagus images downloaded through sensors on chest)
- Less invasive
- Less than 15 minutes to perform in office
- Capsule eliminated in stool and cannot obtain biopsy

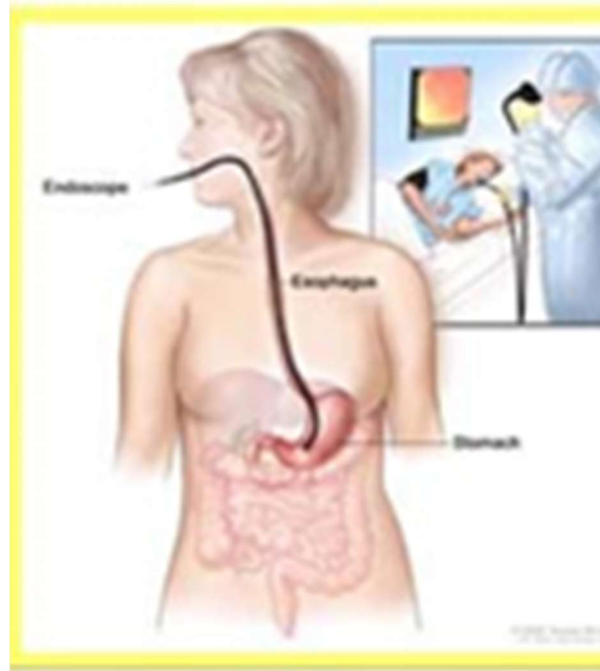
## PPI test

- Empiric use for therapeutic trial
- Especially useful: symptoms but no esophageal erosions, peptic

## ulcers, cancer

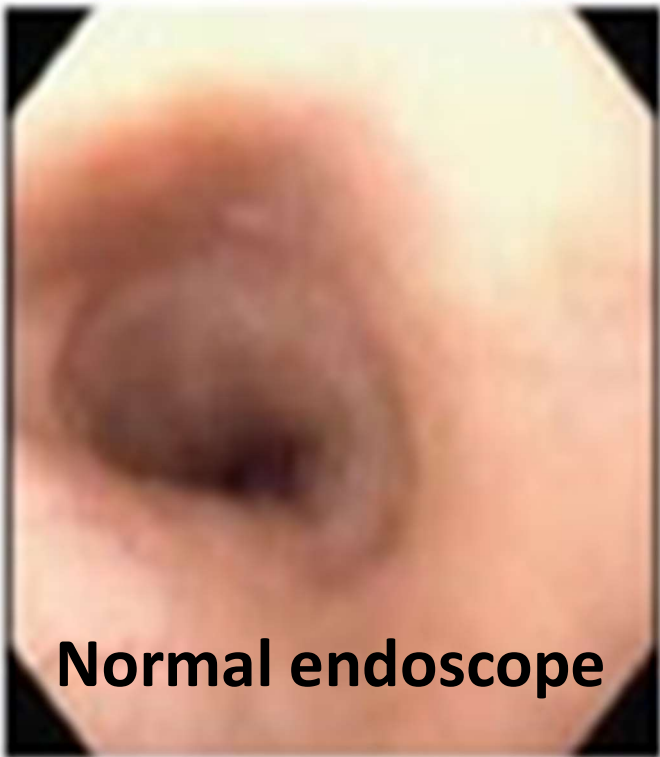
- Problems: no standard dose or duration

## Diagnosis of GERD



- Endoscopy
- Telemetry pH Monitor

# Endoscopy



**Normal endoscope**



**Erosive esophagitis**

# Goals of Treatment

Reduce or  
alleviate

- Reduce or alleviate symptoms

Decrease

- Decrease recurrence of reflux

Promote

- Promote healing of injured mucosa

Prevent

- Prevent complications
- Barrett's esophagus Esophageal strictures Esophageal cancer

# Approaches to Treatment

Lifestyle  
modifications

Patient-directed  
OTC therapy

Rx  
acid-suppressive  
therapy

Antireflux  
surgery

Choose based  
on severity of  
symptoms

# Case Presentation

- AA is a 35 YO WM who comes to your pharmacy Complaining severe heartburn 3 to 4 times per week.
- He wants to know what you recommend for heartburn.
- What lifestyle modifications might you recommend for CP to help with his GERD symptoms?



# Lifestyle Modifications

Lose weight

Elevate head of bed (nocturnal GERD)

Don't eat before bed (nocturnal GERD)

Avoid fatty foods

Avoid peppermint

Avoid spicy foods

Eat small meals

Minimize caffeine

Avoid meds that can worsen GERD

Limit ETOH (not recommended)

May be some benefit in select patients

Do not lie down after meal

## Patient-Directed OTC Therapy

For mild, intermittent  
symptoms

Further evaluation required

- Duration of symptoms > 2 weeks
- Alarm symptoms

Options

- Antacids
- OTC H2RAs
- OTC PPIs

# Antacids



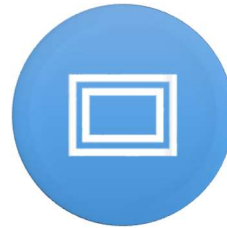
Use for treatment of mild symptoms



Provide immediate relief



Decrease the activation of pepsinogen



Neutralize gastric fluid



Dose PC and HS



May be combined with other therapy

# Antacids

## Types of antacids

- Aluminum
- Magnesium (Phillips Milk of Magnesia<sup>®</sup>)
- Al-Mg combination (Maalox<sup>®</sup>, Mylanta<sup>®</sup>)
- Calcium carbonate (Tums<sup>®</sup>)
- Alginic acid (Gaviscon<sup>®</sup>)

## Considerations

- Adverse effects
  - Constipation (Al)
  - Diarrhea (Mg)
  - Bone issues (Al)

## Calcium content

## Drug interactions

- Tetracycline
- Iron
- Quinolones

## Frequent dosing

## H<sub>2</sub>-Receptor Antagonists (H<sub>2</sub>RAs)

---

Inhibit gastric acid secretion by antagonizing histamine receptors

---

Slower onset, but longer duration of action as compared to antacids

---

Have similar efficacy at equivalent doses

---

Achieve relief of sx in ~ 60%

---

Less effective than PPIs

---

Available OTC

---

## PPIs - Considerations

- Formulation – delayed-release cap or tab to prevent degradation in stomach acid
- For patients unable to swallow pills/caps
- Slow metabolizers - omeprazole, esomeprazole
- Drug interactions

PPI	Suspension	ODT	IV
Esomeprazole	X		X
Lansoprazole	X	X	X
Omeprazole	X		
Pantoprazole	X		X

## H<sub>2</sub>-Receptor Antagonists (H<sub>2</sub>RAs)

### Cimetidine

- Rx: Tagamet generic formulations
- OTC: Tagamet HB 200

### Famotidine

- Rx: Pepcid
- OTC: Pepcid AC, Pepcid AC Maximum Strength, Pepcid Complete (famotidine + Ca and Mg antacid)

### Nizatidine (Axidâ)

### Ranitidine (off the market)

- Rx: Zantac
- Zantac 75 (store brand) or Zantac 150

# H2-Receptor Antagonists (H2RAs)

## OTC Dosing

Intermittent, mild heartburn

Take up to twice daily

- Cimetidine 200 mg
- Famotidine 10 mg
- Famotidine 20 mg
- Ranitidine 75 mg

## Rx Dosing

- Symptomatic relief - mild to moderate GERD

Take twice daily

- Cimetidine 400 mg
- Famotidine 20 mg
- Nizatidine 150 mg
- Ranitidine 150 mg

Continue for 6-12 weeks

Higher doses may be needed for severe sx



# H2RAs - Considerations

Select based on PK considerations, adverse effects, and cost

Generally well tolerated – headache, dizziness, constipation, diarrhea

Renal dosing

Cimetidine - gynecomastia

Cimetidine – drug interactions (inhibits CYP1A2, CYP2C9, CYP2D6, CYP3A4)

- Warfarin, phenytoin, nifedipine

# Proton Pump Inhibitors (PPIs)

Inhibit H<sup>+</sup>/K<sup>+</sup> ATPase enzyme pump

Preferred for symptom relief and healing of erosive esophagitis (8-week course)

Relief of symptoms in ~ 80-85%

Available OTC

- Omeprazole magnesium 20 mg (Prilosec OTC)
- Lansoprazole 15 mg (Prevacid24HR)
- Esomeprazole 20 mg (Nexium24HR)
- Omeprazole + sodium bicarbonate (Zegerid OTC)
- Should not be taken for more than 14 days without notifying a healthcare provider

# Dosing of Rx PPIs

## Take on

- Take on empty stomach 30-60 min before meal
  - Esomeprazole (Nexium®) 20 mg daily
  - Lansoprazole (Prevacid®) 30 mg daily
  - Omeprazole (Prilosec®) 20 mg daily
  - Pantoprazole (Protonix®) 40 mg daily
  - Rabeprazole (Aciphex®) 20 mg daily

## Take

- Take before first meal of the day

## Breakfast

- Before breakfast and before dinner if BID

# Dosing of Rx PPIs

May be taken without regard to meals

- Dexlansoprazole (Dexilant®) 30 mg daily

May be administered at bedtime

- Omeprazole-sodium bicarbonate

Partial responders to PPIs

- Adjust timing of dosage (take on empty stomach or HS)
- Twice daily dosing (esp. nighttime symptoms)
- Add H2RA at bedtime (nighttime symptoms) - tachyphylaxis

Switch to another PPI ??

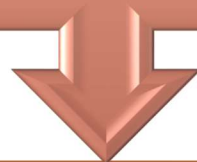
Non-responders - refer

# PPIs – Drug Interactions

Drugs with pH-dependent absorption (all) – ketoconazole, iron salts, protease inhibitor (atazanavir)



Clopidogrel – converted to active metabolite via CYP 2C19; omeprazole, esomeprazole inhibit 2C19; recent meta-analyses do not support an increased risk of CV events



Omeprazole

Inhibits 2C19 and 2C9

warfarin, diazepam, phenytoin

# Case Presentation

- AA is a 35 YO WM who comes to your pharmacy Complaining severe heartburn 3 to 4 times per week.
- He wants to know what you recommend for heartburn.

- Based on this patient's presentation, what initial pharmacotherapy would you recommend?

# Other Therapies for GERD

## Antireflux surgery

- For patients responsive to, but unable to tolerate acid suppressive therapy
- For patients with symptoms despite PPI

## Promotility agents

- Metoclopramide – not recommended unless documented gastroparesis

Sucralfate – not recommended; may be used in pregnant patients

Baclofen – consider for those with symptoms on optimal PPI therapy

# Maintenance Therapy

Required by majority of patients

PPIs are preferred therapy

Titrate to lowest effective dose

Consequences of acid suppression:

Increased incidence of *C. diff* colitis

- Increased risk of hip fracture – use caution in patients with other fracture risk factors
- Increased incidence of community-acquired pneumonia (short- term usage)
- Vitamin B12 deficiency
- Hypomagnesemia



## Case Presentation

- AA is a 35 YO WM who comes to your pharmacy Complaining severe heartburn 3 to 4 times per week.
- He wants to know what you recommend for heartburn.
- Would this patient be a candidate for maintenance therapy? If so, what pharmacotherapy would you recommend?

Case  
Presentation  
– Part 5

- You were so helpful that 2 weeks later CP comes in with his wife. She is having terrible heartburn, too! What can you recommend?



# Special Populations

## Pregnancy

- OTC antacids (esp. those with calcium) – first line
- H2RAs: ranitidine or cimetidine (pregnancy category B)
- PPIs: All pregnancy category B, except omeprazole pregnancy category C (use still supported)
- Sucralfate – pregnancy category B

## Pediatrics

- Smaller feedings, thickened feedings
- H2RAs: ranitidine, famotidine
- PPIs: omeprazole

Elderly - PPIs preferred

# Special populations

---

Pediatrics

---

Smaller feeding, thickened feedings

---

H2R2

---

Famotidine

---

Ranitidine

---

PPI

# Take Home Message

The common symptoms include heartburn, acid brash, regurgitation, chest pain, and dysphagia

Lifestyle modifications – as appropriate

Mild, intermittent heart burn

- OTC antacids, H2RAs, or PPIs as needed

Mild symptomatic GERD

- Trial of once-daily PPI (or BID H2RA)

Moderate to severe GERD/ erosive esophagitis

- PPI preferred

Maintenance therapy

- PPI preferred