Heartburn and Barrett’s Esophagus

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GERD is common in the U.S.

- Heartburn and GERD
- GERD therapy
- Extraesophageal GERD
- Barrett’s esophagus
- Esophageal dysplasia and cancer

Disclosures

- None

GERD is common in the U.S.

Locke GR et al Gastro 1997
GERD has greater impact on QOL than other common diseases

![Graph showing PGWB Index scores for various conditions](Dimenas.jpg)

GERD can present with a number of symptoms

**Typical/Esophageal**
- Heartburn
- Acid regurgitation

**Atypical/Extraesophageal**
- Chest pain
- Laryngitis
- Asthma
- Sinusitis
- Chronic cough
- Aspiration pneumonia
- Tooth decay

Heartburn should be described for the patient

- Pts may not correctly identify the sx of heartburn
- “A burning feeling rising up from the stomach or lower chest up towards the neck”

![Image showing heartburn symptoms](Heartburn.jpg)

Heartburn does not mean GERD

GERD: symptoms or complications resulting from reflux of gastric contents

- +/- Heartburn
- +/- Acid
- +/- Esophagus

![Image showing GERD vs. other diseases](GERD_Diagram.jpg)
A 38 yo woman presents to her primary care provider with 5 months of heartburn. She has symptoms several times per week. She has no dysphagia, emesis or weight loss. Her PMH is notable for migraines, and she takes no medications.

What is the next step?

A. H2 blocker and lifestyle changes
B. PPI daily
C. PPI as needed (on-demand)
D. Endoscopy, then therapy based on findings
E. pH testing, then therapy based on findings
Lifestyle factors have little impact on GERD

- **Weight loss**
- **HOB elevation**
- **Avoid late meals**
- **Avoid tobacco/alcohol**
- **Avoid aggravating foods**

- Correlation when BMI > 30
- Nurses Health Cohort: ↓ BMI 3.5→ ↓ 40% GERD sx

Global elimination **not** recommended

Who needs an endoscopy?

- **Warning signs**
  - Dysphagia, bleeding, emesis
- **Risk factors for Barrett’s esophagus**
  - Male age > 50
  - Sxs > 5-10 yrs
  - **Obesity**
- **Persistent symptoms**

Endoscopic appearance

- **Normal**

Endoscopic Assessment

- **Los Angeles classification:**
  - Grade A: < 5mm, < 2 folds
  - Grade B: ≥ 5mm, < 2 folds
  - Grade C: ≥ 2 folds, < 75%
  - Grade D: ≥ 75%

- Ulcer, stricture, Barrett’s noted separately
Endoscopic appearance

Heartburn severity and esophagitis

No esophagitis

Mild
Moderate
Severe
Heartburn

Smout et al APT 1997

Treat GERD with PPI: Initial therapy

- PPI is treatment of choice
  - Faster, more complete sx relief
  - Superior healing of esophagitis
    (vs H2 blockers)
- ERD responds better than NERD
  - 70-80% vs 60% sx relief
- 8 week course of any PPI, qday, AC

PPI vs H2B for Erosive GERD: Metanalysis

Gastro 1997
Treat GERD with PPI: Initial therapy

- Erosive esophagitis requires PPI
  - Healing at 8 wks: 84% PPI vs 52% H2B
  - Sx response better
    (Chiba et al Gastro 1997)

- Once daily PPI adequate
  - % pts with sx relief: qday = BID
  - If persistent sx, only 20% improve with BID
    (or new PPI) (Fass et al J Aliment Pharm Ther 2000)

Some patients need indefinite PPI therapy

- LA class B/C esophagitis
  - ~ 100% relapse by 6 mos
- Barrett’s esophagus
  - PPI use may decrease dysplasia
- Recurrent sx off PPI
  - 66% have recurrent sx
  - On-demand PPI same sx control as PPI daily
    (Pace et al Aliment Pharm Ther 2007)

Long term therapy for GERD can be symptom based

6-12 months

Continuous

Intermittent

On demand

= symptom recurrence

Our 38 yo woman with 5 mos heartburn without warning signs was given omeprazole once daily.
She took the medication for 2 months and noted only “a little” improvement. You confirmed correct use of the PPI.
An EGD was done and was normal.

What now?
**What now?**

A. Trial of a different PPI  
B. Trial of her PPI increased to BID  
C. Perform barium esophagram  
D. Perform pH/impedance study on PPI  
E. Perform pH study off PPI

**Persistent Symptoms**

- Optimize PPI therapy  
  - 46% refractory GERD pts taking PPI correctly  
  
- Consider PPI change  
  - New or BID: 20% improve  

- Endoscopic evaluation  
  - Biopsy for eosinophilic esophagitis  

- Reflux monitoring

**Reflux monitoring**

- Catheter or wireless pH, impedance-pH  
- Acid vs non-acid reflux vs no reflux  
- Correlate specific sxs with reflux events

**Is chronic PPI use safe?**

- Rebound acid hypersecretion  
- Bone disease  
- Clopidogrel and CV events  
- Enteric infections
Rebound acid hypersecretion can occur

- Omeprazole 40mg/dy X 8 wks
- Omeprazole stopped
- Acid output compared pre- vs post-treatment

Gastro 1999

Rebound acid hypersecretion can last for 8 weeks

- Omeprazole 40mg/dy for 8 weeks
- Omeprazole stopped
- Max acid output after 7, 14, 28, 42 and 56 dys

Gastro 2004

Bone disease

- Hip fracture associated with PPI use in 4 of 5 studies
  - ↑ hip fx IF another risk factor (Corley Gastro 2010)
  - Dose dependent, can occur at 2 yrs
- Bone density not affected: Manitoba data (Targownik et al Gastro 2010)
- PPI-fracture link explained by confounders?
- Ca2+ release vs osteoclast inhibition

**Wean off slowly**
**Clopidogrel and CV events**

- ↑ risk suggested:
  - Competitive inhibition of P450-2C19 (least: pantoprazole)
  - Retrospective studies ([JAMA 2009](https://doi.org/10.1001/jama.2009.903))
  - FDA alert 2009
- No ↑ risk in meta-analysis of 13 studies ([APT 2010](https://doi.org/10.1002/apt.1865))

**ACG Practice Guidelines for GERD 2013**

- “PPI therapy does not need to be altered in concomitant clopidogrel users . . .”
- “Patients with known osteoporosis can remain on PPI therapy. Concern for hip fractures and osteoporosis should not affect the decision to use PPI long-term except in patients with other risk factors for hip fracture.” ([Katz et al AJG 2013](https://doi.org/10.1053/j.ajg.2013.05.020))

**Chronic PPI: Enteric infections**

- Gastric pH < 4.0 rapidly bactericidal
- Colonic microbiome altered by PPI
- Enteric infections ↑
  - *Salmonella*, *Campylobacter*, *C difficile*, others
  - Systemic review: OR 2.05, 95%, CI 1.47-2.85 ([Am J Gastro 2007](https://doi.org/10.1016/j.amjgastro.2007.03.007))
- *C dif* ↑, more severe
  - Nosocomial, community, initial, recurrent

**Is chronic PPI use safe?**

- Rebound acid hypersecretion: YES
- Bone disease: YES
- Kind of . . .
- Clopidogrel and CV events: Probably not
- Enteric infections: YES
- PPI use contributes to . . .
What about surgery for GERD?

- Fundoplication of gastric fundus
- Efficacy similar to chronic PPI use
  - Medical failure predicts surgical failure
- PPI use may still be necessary
  - At 5 yrs, 62% on PPIs
  - Spechler et al, JAMA 2001

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Extraesophageal GERD

- Asthma
- Chronic cough
- Noncardiac chest pain
- Laryngeal symptoms

Controversial association:
- 30-80% lack classic GER symptoms
- 65-90% lack endoscopic changes
- Variable response to acid suppression
Asthma/Chronic Cough

• Reflex vs reflux?
• Esophageal acid → pulmonary vagal activity
  ↗ mucous production, bronchoconstriction
  – Esophago-bronchial cough reflex
  ↗ bronchoreactivity
• Microaspiration
  – Cough, decreases PEF

Prevalence of GER in asthma ~ 50-60%
  – ~ 51% asthmatics have abnl pH tests
  – What causes what?
• Prevalence of GER in chronic cough ~ 20-30%
  – 60% do not have typical sxns
  (Irwin et al Chest 1993)

Laryngeal Symptoms

• Hoarseness
• Throat clearing/globus
• Sore throat
  – Also from smoking, alcohol, allergies, voice abuse, viral
• LPR questionable
  – No benefit with PPI
  – No benefit with fundoplication

Extraesophageal GERD: Testing

• If typical GER sxns, treat
• If no GER sxns, reflux testing
  – Helpful:
    • + symptom-reflux correlation
    • nl study
• EGD not recommended unless typical GER
  – Asthma: EGD abnl in ~ 30% pts
  – Laryngeal sxns: EGD abnl in ~ 25% pts
  (Gut 1992, Aust J Otolaryg 1999)
Extraesophageal GERD: Management

- PPI
  - Daily vs BID
  - Observational, uncontrolled data for BID
- Improvement by 2 mos, resolution by 6 mos
- Laryngeal sx least responsive

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Barrett’s esophagus

Barrett’s: Endoscopic assessment

Prague Criteria:
- C (circumferential) extent
- M (maximal) extent

C2M3
Barrett’s Esophagus: Significance

- First visible step in path to EAC
  - IM $\rightarrow$ LGD/HGD $\rightarrow$ EAC
- Risk of progression varies:
  - ~10% GERD pts have BE
  - Risk of BE $\rightarrow$ HGD: 0.4%/yr
  - Risk of HGD $\rightarrow$ EAC: 1.5%/yr
  (Rees et al Cochrane Database Sys Rev 2010)
- EAC incidence rising, survival rates poor

The definition of Barrett’s esophagus is controversial

- Columnar metaplasia of esophageal mucosa
  - Fundic vs cardia vs intestinal with goblet cells?
  - Most EAC associated with intestinal
- BE is specialized intestinal metaplasia
- Cardia-type has malignant potential
- BSG: BE is “columnar lined oesophagus on histology”

What is Barrett’s esophagus?

Most recent AGA review:
BE is “any extent of metaplastic columnar epithelium that predisposes to cancer development”
(Spechler et al Gastro 2010)
Barrett’s Esophagus: Screening

• No high quality supportive evidence
  – 40% EAC pts have no GERD hx
  – Only 10% EAC pts have BE dx
• GI societies recommend screening:
  – Chronic GERD sx AND
  – One or more EAC risk factors
    • Age > 50, male, white race, tobacco use, obesity
  – If no Barrett’s, no further screening

Barrett’s Esophagus: Surveillance

- Screening EGD/bx shows BE
- No Dysplasia
- LGD
- HGD
- Expert confirmation of path
- EGD every 3-5 yrs
- EGD every 6-12 mos OR Endoscopic eradication

Esophageal adenocarcinoma

Relative Change in EAC Incidence

- Esophagus
- Melanoma
- Prostate
- Lung/Breast
- Colorectal

Rate ratio (relative to 1975)

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Extraesophageal GERD: Management

Other specialities think differently:

- PPI BID trial in asthma
  - If mod/severe asthma (2 inhalers)
  - If GER sx, nocturnal asthma
  - “Success”: 20% ↑ PEF or ↓ po steroid; ↓ sx
- R/DB trial 207 asthmatics, BID PPI
  - ↑ QOL, ↓ flares
  - ↔ PEF, FEV1

(Littner et al Chest 2005)
Barrett’s: Endoscopic Assessment

- Normal squamous esophagus
- GE junction
- Esophageal side
- Gastric side
- Stomach
- Diaphragm
- Hiatal hernia