Brigham and Women's Hospital
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Updates in Upper GI Disorders: GERD, Barrett's Esophagus, and *H. pylori*

Molly Perencevich, MD
Associate Physician
Division of Gastroenterology, Hepatology & Endoscopy
Brigham and Women's Hospital
Assistant Professor of Medicine
Harvard Medical School

CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE

HARVARD MEDICAL SCHOOL
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Molly Perencevich, MD

- Harvard Medical School
- Internal medicine residency @ Brigham and Women's Hospital
- GI fellowship @ Brigham and Women's Hospital
- Associate Physician @ BWH
- Assistant professor @ Harvard Medical School
- Program Director for BWH Fellowship in Gastroenterology, Hepatology & Endoscopy

Disclosures

I have no relevant financial relationships with ineligible companies.

I will discuss the use of medications for non-FDA approved indications

Learning Objectives

GERD

- Recognize the indications for EGD
- Review current and new treatments

Barrett's esophagus

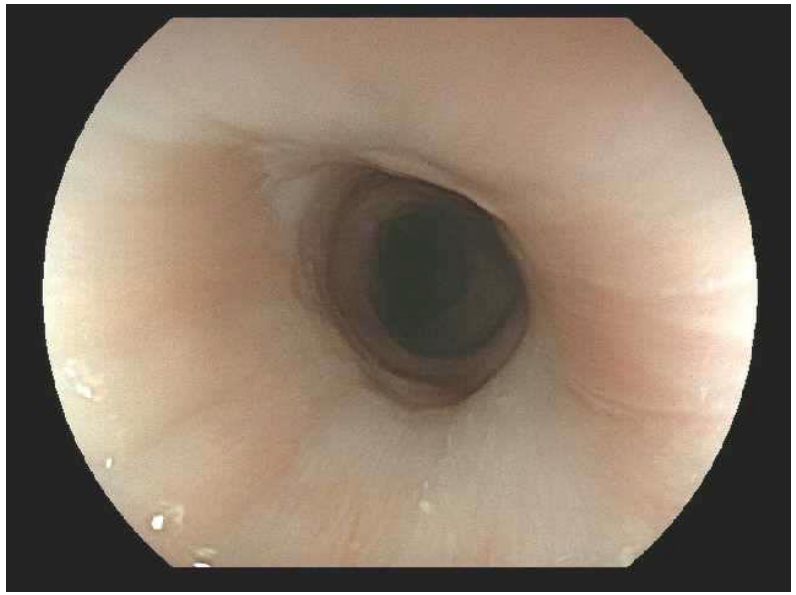
- Discuss screening recommendations
- Summarize treatment options

H. pylori

- Explain current treatment recommendations

Gastroesophageal Reflux Disease (GERD)

Indications for EGD in GERD



Not for diagnosis of GERD

- Most patients will have a normal esophagus

Used to diagnose complications, other causes for symptoms, and evaluate for malignancy

- Erosive esophagitis, Barrett's esophagus, strictures, eosinophilic esophagitis, esophageal cancer

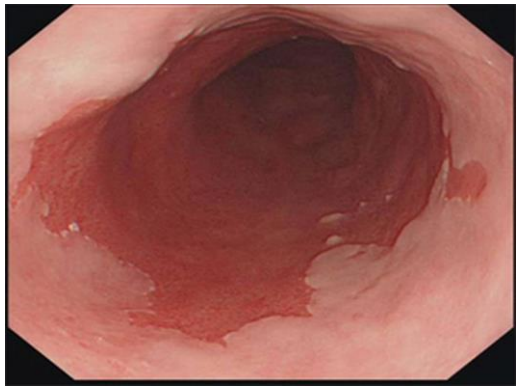
Indications for EGD in GERD

1. Alarm features

- New dyspepsia at age ≥60 years
  - No age criteria for GERD symptoms
- GI bleeding (overt, occult)
- Iron deficiency anemia
- Dysphagia, odynophagia
- Anorexia, weight loss, persistent vomiting
- Family history of upper GI cancer

Indications for EGD in GERD

1. Alarm features
2. GERD symptoms which
   - Do not respond to an 8 week trial of standard-dose PPI (ex. omeprazole 20mg daily)
   - Recur <3 months after stopping PPI
   - [Ideally do the EGD off PPI for 2-4 weeks to see if esophagitis is present]
3. Severe esophagitis (LA Grade C and D)
   - After PPI x 8-12 weeks to assess healing and r/o Barrett's



Katz PO, et al. ACG Clinical Guideline for the GERD. Am J Gastroenterol 2022.

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3. Severe esophagitis (LA Grade C and D)
   - After PPI x 2-3 months to assess healing and r/o Barrett's
4. Screen for Barrett's in patients with multiple risk factors
5. Abnormal upper GI tract imaging

Prescribing Proton Pump Inhibitors (PPI)

Optimal dosing

- 30-60 min before eating (breakfast and/or dinner)
- Avoid giving with H2-blockers (can give H2B at bedtime)

Overprescribed

- Clear indication in only 1/3 of patients

Similar efficacy

- Differences may relate to drug metabolism polymorphisms – can switch if needed

Possible adverse effects

- Most data is retrospective (residual confounding) – need more prospective data
- Few concerns are supported by consistent data demonstrating a causal relationship

Potential PPI Adverse Effects

GI issues

- *C. diff* and other enteric infections
- SBP in cirrhosis
- Small intestinal bowel overgrowth (SIBO)
- Microscopic colitis
- Possible increased risk of IBD
- ↑ gastrin and atrophy – but no clear increased risk of GI cancer

Renal

- AIN – idiopathic
- ? CKD – unclear mechanism

Bone fracture

- ? ↑ osteoclast activity, ↓ Ca absorption (Ca carbonate >> dietary)
- WHI study (2010) – PPI not associated with hip fracture, but was modestly associated with spine, wrist, and total fractures

Potential PPI Adverse Effects

Malabsorption

- Magnesium – check prior to long-term use, esp. if diuretics/elderly or hx arrhythmias/prolonged QTc – then check periodically/yearly
- Vitamin B12 – consider periodic/yearly monitoring
- Iron – no clear recommendation to monitor

Unclear significance

- Dementia
- CV/stroke events
- COVID-19
- Pneumonia

Drug interactions

- CYP2C19 metabolism
  - Omeprazole & esomeprazole the most
  - Pantoprazole the least
- Clopidogrel – no clear evidence of increased adverse effects
- Protease inhibitors – ↓ absorption

Prospective PPI Trial (2019)

- Large, prospective, randomized trial
- PPI (pantoprazole 40mg daily) vs placebo
- 17600 older patients (age >65, 78% men, 23% smokers)
  - Pts with stable CAD/PAD receiving rivaroxaban or ASA
- During median f/u of 3 years
  - No difference in pneumonia, hip fracture, CKD, dementia, COPD, gastric atrophy, or cancer
  - Enteric infections other than *C. diff* were more common in pts taking PPI (1.4% vs 1%, p 0.04)
  - *C. diff* 2x more common in pts taking PPI, but not statistically significant

Moayyedi P, et al. Gastroenterology 2019.

PPI – General Thoughts

- Overall safe and well-tolerated
- Possible safety issues – need more data
- Balance possible risk of PPI with risk of uncontrolled GERD (symptoms, bleeding, strictures, Barrett's)

- Consider discontinuing PPI w/ frequent symptom re-evaluation
- Use lowest dose needed
- Titrate down dose to avoid rebound acid hypersecretion
- Switch to H2-blockers when possible
- Maintenance PPI recommended if severe esophagitis and Barrett's

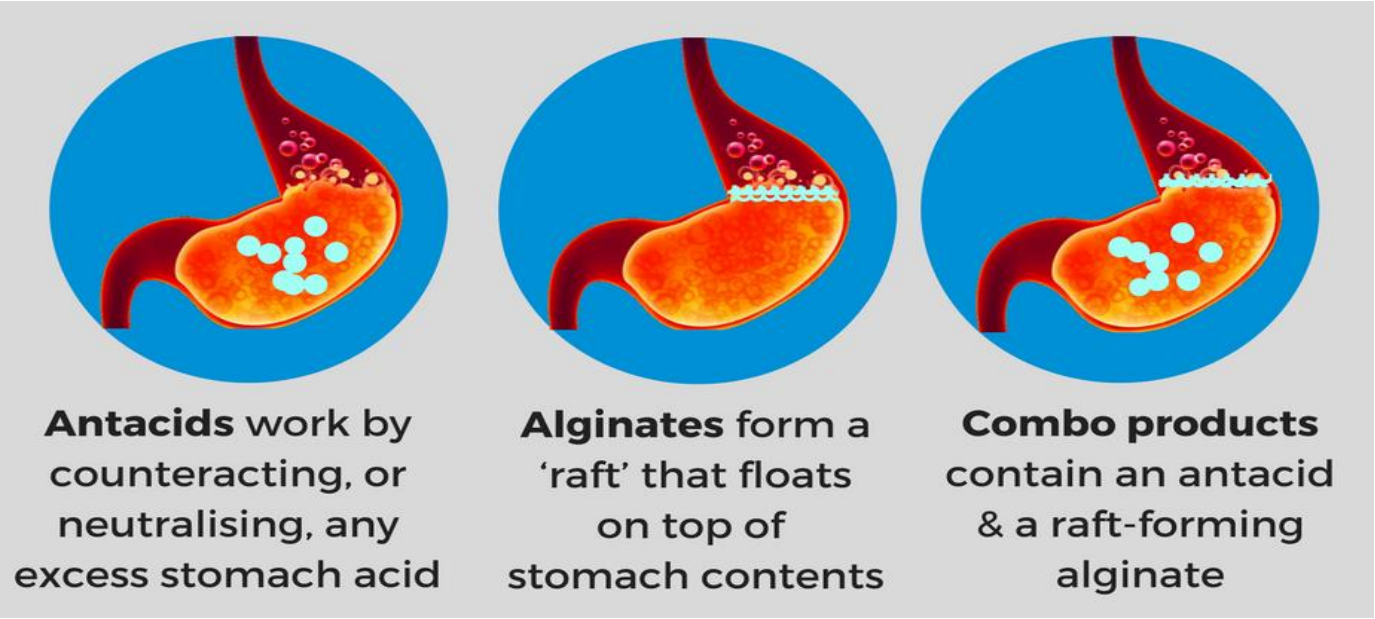
Vonoprazan – New Treatment for GERD

- Potassium-competitive acid blocker (PCAB)
  - May decrease intragastric acidity and maintains it to a greater degree than PPI
  - Rapid onset and dosing independent of meals
- Erosive esophagitis – FDA approval 10/2023
  - RCT PCAB vs PPI (Laine, Gastro 2023)
  - Vonoprazan was noninferior and superior to the PPI lansoprazole in healing and maintenance of healing of erosive esophagitis (esp. more severe erosive esophagitis)
- Non-erosive GERD – FDA approval 7/2024
  - RCT PCAB vs placebo (Fass, Aliment Pharmacol Ther 2023; Laine, Clin Gastroenterol Hepatol 2024)
  - Vonozprazan more effective than placebo
- Adverse events - abdominal pain, dyspepsia, hypertension, UTI
  - Longer terms concerns may be similar to PPI, but less is known at this time
- Insurance coverage and cost still an issue
  - Usually need to document failure of PPI for acid-related reflux

Alginates

- Sodium alginate – polysaccharide derived from seaweed

- Forms a gel that floats above the food/liquid in the stomach
  - Neutralizes the postprandial acid pocket in the proximal stomach
  - Prevent reflux from entering the esophagus



https://www.peptest.co.uk/

Alginates

- Used in
  - Mild GERD
  - Refractory acid reflux (on PPI)
  - Non-acid reflux
- Dosing
  - Liquid, tablet
  - After meals and before bed
- Limited efficacy data
  - Mild GERD > refractory GERD or non-acid reflux
- Minimal side effects

Chiu CT, et al. Aliment Pharacol Ther. 2013.

Barrett’s Esophagus

Screening for Barrett's Esophagus

- Expert opinion, not based on RCT data
- A single screening EGD for patients with chronic GERD symptoms** and 3+ additional risk factors for Barrett's

Male sex	Age >50 years
White race	Obesity
Tobacco smoking	Hiatal hernia?

Family hx of Barrett's/esophageal adenocarcinoma in first- degree relative

** 40% of patients with esophageal adenocarcinoma do not have chronic GERD symptoms

- If initial EGD is negative, repeating EGD for BE screening not recommended
- If EGD reveals severe esophagitis (LA Classification C/D) → repeat EGD after PPI for 2-3 months

Shaheen NJ, et al. Am J Gastroenterol. 2022

Novel Screening Modalities for Barrett's

- Swallowable, non-endoscopic capsule device combined with a biomarker
- Swallowed then withdrawn orally – obtaining esophageal cytology samples
- Can be performed in an office setting without sedation

- May make screening for Barrett's easier and more cost-effective
- More research is needed

New Barrett's Management Recommendations AGA 2025

- Surveillance intervals every 3 years
  - Interval ay be extended to every 5 yrs in patients at lower risk of progression, for instance those with short-segment BE (<3 cm)
- Possible Barrett's esophagus <1 cm, a conditional recommendation was made *against* endoscopic surveillance
- Conditional recommendation for the use of daily proton pump inhibitor therapy compared with no therapy and compared with antireflux surgery to prevent progression in Barrett's

Wani S, et al. Gastroenterology 2025

H. Pylori Treatment

Add H. pylori testing family members?

H. pylori Treatment Guidelines

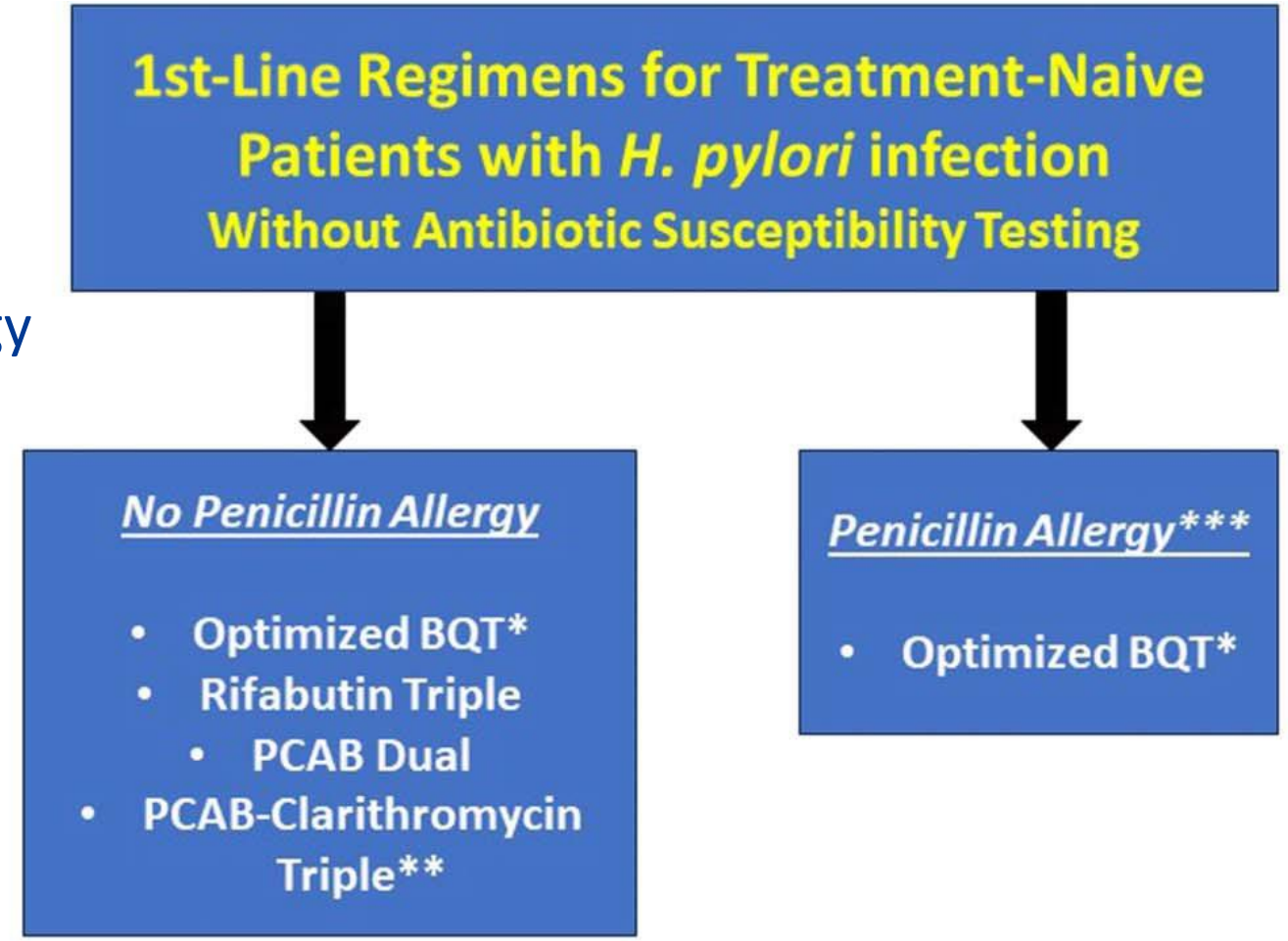
American College of Gastroenterology (ACG) **September 2024**

Bismuth quad therapy (BQT) - metronidazole, tetracycline, bismuth, PPI

Rifabutin triple – rifabutin, amoxicillin, PPI

PCAB dual – amoxicillin (higher dose), vonozopram

PCAB-clarithromycin triple – clarithromycin, amoxicillin, vonozopram
(only if the above are not available and no prior macrolide exposure)



BQT, bismuth quadruple therapy, PCAB, potassium-competitive acid blocker
*Includes appropriately dosed PPI, bismuth, nitroimidazole, and tetracycline (not doxycycline)
** Avoid in those with previous macrolide exposure
*** May require formal allergy testing

All regimens for 14 days

Chey WD, et al. Am J Gastroenterol 2024

First-Line Treatment Summary

- Eradication rates for *H. pylori* in the US have decreased to <80%, mainly due to rising rates of clarithromycin resistance (now up to 30%)

- Bismuth quad therapy (BQT) generally recommended as 1st line (eradication rate approx. 85%)
- Generally avoid clarithromycin-based regimens unless susceptibility is known

Other *H. pylori* Regimens

- In general
  - Clarithromycin, metronidazole, and levofloxacin should not be used again due to concern for resistance
  - Amoxicillin, tetracycline, and rifabutin can often be reused as resistance is rare
- Levofloxacin – resistance a concern given common general use (up to 40%)
  - Levofloxacin, amoxicillin, and PPI BID x 14 days
  - Generally avoid unless documented susceptibility
- Rifabutin (anti-TB drug) – H. pylori resistance rare (eradication rate 84% in US RCT)
  - Rifabutin, amoxicillin, and PPI BID x 14 days
  - ACG 2017 salvage therapy; ACG 2024 consider as first-line
  - Potential concerns
    - Cytopenias (less likely with short course), uveitis/myeloxicity (rare)
    - Drug-drug interactions (similar to rifampin)
    - May increase mycobacteria resistance
- PPI consideration – rapid CYP2C19 metabolizers are at increased risk of failure with standard doses of earlier PPIs
  - Consider esomeprazole and rabeprazole – bypass or are minimally metabolized by CYP2C19
  - Consider higher dose PPI

Consider Penicillin Allergy Testing

- Most patients with a history of penicillin (PCN) allergy do not have true PCN hypersensitivity
  - 5-10% of US population report PCN allergy →
  - 90% have negative skin testing and can tolerate PCN

- Consider referral for allergy testing after failure of a 1st line treatment to see if an amoxicillin-containing regimen can be given

Anti-Acid Therapy for *H. pylori* Treatment?

- Intragastric acid suppression is important for *H. pylori* eradication
  - High gastric pH promotes active replication of H. pylori, making it more susceptible to antibiotics
  - Higher gastric pH promotes stability of acid-labile antibiotics (amoxicillin, clarithromycin) → increases their concentrations in the stomach → may improve eradication
- PPI better than H2-blockers
- New PCAB (potassium-competitive acid blocker) better than PPI?
  - Decrease intragastric acidity faster and maintains to a greater degree than PPI
  - Optimized dosing not impacted by meals (unlike PPI ideally 30-60 min before a meal)
  - Use of this instead of a PPI may improve *H. pylori* eradication rates

Prevent Treatment Failures

- Think about resistance
  - Especially to clarithromycin, metronidazole, and levofloxacin
- Explain regimen & reinforce compliance
- Consider sensitivity testing after 2 failed regimens
  - Culture – requires EGD and special processing, increasingly available via commercial labs
  - Molecular testing – the future, but not widely available and insurance may not cover
- Test and treat household members of patients with *H. pylori* to reduce reinfection rates

Chey WD, et al. Am J Gastroenterol 2024

Confirmation of *H. pylori* Eradication

- Who?
  - Anyone that has been treated, but especially PUD, gastric cancer/MALT
- Which tests?
  - Breath test or stool antigen; not serology
  - EGD if doing for another reasons (e.g. gastric ulcer follow-up, persistent dyspepsia)
- When?
  - Avoid false negatives due to bacterial suppression
    - 4-8 weeks after *H. pylori* treatment
    - Off antibiotics/bismuth for 4 weeks and PPI for 2 weeks

Summary

GERD

- EGD should be performed to diagnose complications, other causes for symptoms, and evaluate for malignancy – and should be repeated after an EGD shows severe esophagitis
- Be mindful about PPI therapy
- Vonoprazan a new possible treatment (instead of PPI) for refractory acid-related GERD

Barrett's esophagus

- Screening can be considered in patients with multiple risk factors
- PPI therapy is generally continued at lowest dose to control GERD symptoms

H. pylori treatment

- Review prior antibiotic exposure, more commonly using quadruple therapy
- Consider penicillin allergy testing to allow use of amoxicillin
- Vonoprazan a new possible treatment (instead of PPI)
- Consider sensitivity testing after 2 failed regimens

Selected References

GERD

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PCAB (Potassium-Competitive Acid Blockers)

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