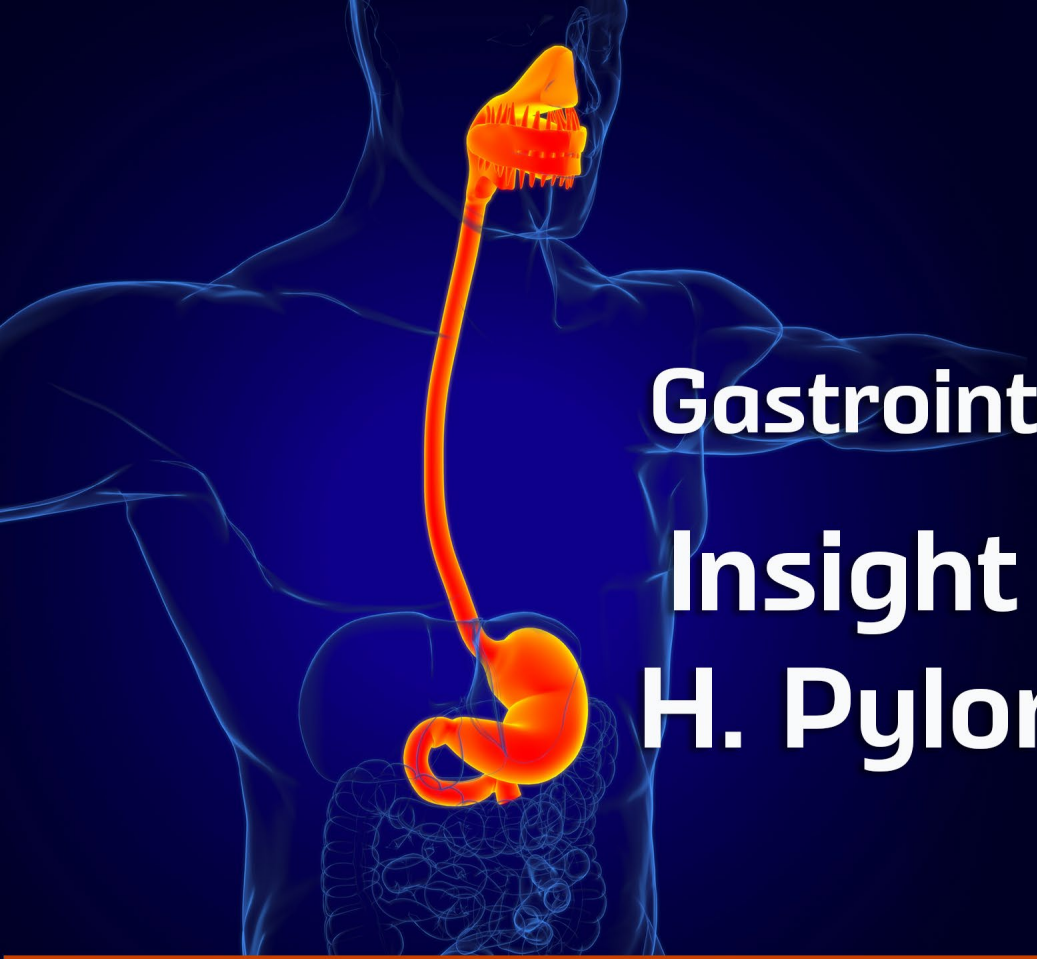

Navigating Gastrointestinal Challenges:

Insight Into GERD and H. Pylori Management

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Learning Objectives

- Describe the natural history and burden of gastroesophageal reflux disease (GERD) and *Helicobacter pylori* (*H. pylori*) infections
- Identify appropriate tests to support decision-making in the differential diagnosis of GERD and *H. pylori* infections
- Individualize therapy in patients with nonerosive or erosive GERD who achieve an inadequate response to proton pump inhibitor (PPI) therapy
- Evaluate the latest evidence-based guidelines for the treatment of *H. pylori* infections, including implementing effective eradication regimens and addressing antibiotic resistance

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Overview of GERD and *H. pylori* Infections

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Burden of GERD

- Global prevalence 2.5% to 30%
- Range of disease from nonerosive to advanced stages of erosive esophagitis (EE)
- Significant associations with morbidity and reduced health-related quality of life
- Can be chronic and progressive disease if left untreated

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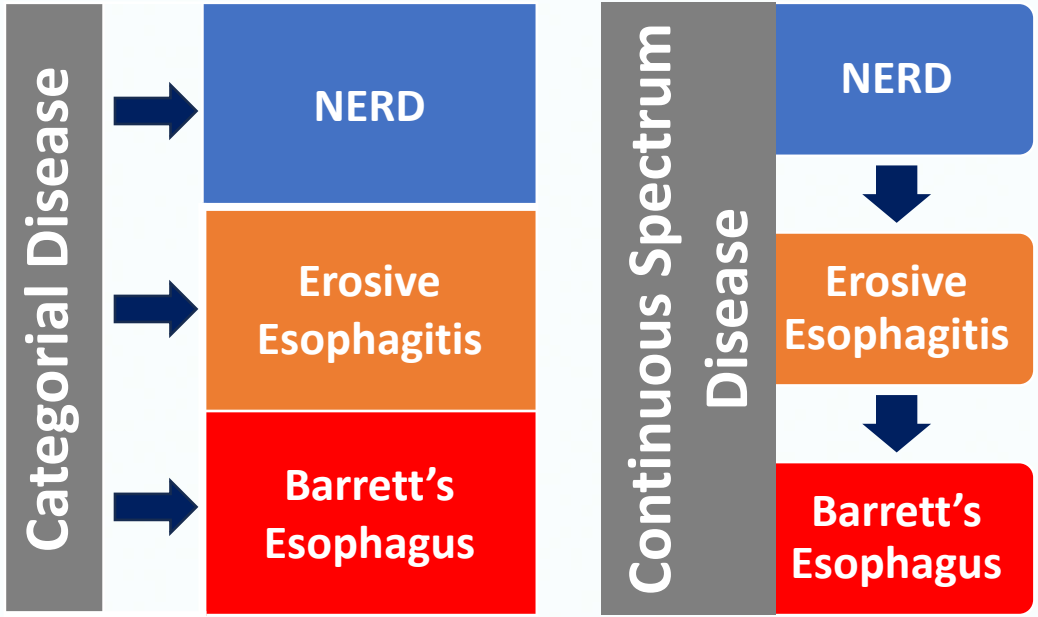
Savarino E, et al. *Dis Esophagus*. 2017;30(2):1-9. Nirwan JS, et al. *Sci Rep*. 2020;10(1):5814. Katz PO, et al. *Am J Gastroenterol*. 2022;117:27-56. Wiklund I. *Dig Dis*. 2004;22(2):108-114.

Natural History of GERD

- Varied patient presentations
  - Classic symptoms – heartburn and regurgitation
- Nonerosive (NERD) and erosive (ERD)
  - 70% vs 30% prevalence
- Complications of disease
  - Barrett's esophagus
  - Esophageal adenocarcinoma



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Pathophysiology of GERD

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Chatila AT, et al. *Disease-a-Month*. 2020;66(1):100848.

Burden of *H. pylori* Infections

- Global prevalence of 43%
  - Affected by many factors, including age, geography, and socioeconomics
- Most infections are acquired in childhood, but persist
- Fecal-to-oral and oral-to-oral transmission are most likely
- Associated with peptic ulcer disease and gastric cancer
- Treatment is hampered by rising rates of antibiotic resistance

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Malfertheiner P, et al. *Nat Rev Dis Primers*. 2023;9:19.
Chey WD, et al. *Am J Gastroenterol*. 2024;119(9):1730-1753.

Natural History of *H. pylori* Infections

- *H. pylori* colonizes the gastric mucosa
- Many patients are colonized with *H. pylori*
- Majority of patients are asymptomatic
- Infections primarily in the antrum of the stomach
- May eventually lead to gastric or duodenal ulcers
- Risk for cancer

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Correa P, et al. *Dig Liver Dis*. 2008;40(7):490-496.
Chey WD, et al. *Am J Gastroenterol*. 2024;119(9):1730-1753.
Malfertheiner P, et al. *Nat Rev Dis Primer*. 2023;9:19.

Diagnosis of Nonerosive GERD, Erosive GERD, and *H. pylori* Infections

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Guideline Directed Evaluation of GERD

- “condition in which reflux of gastric contents into the esophagus results in symptoms and/or complications”
  - Presence of:
    - Mucosal injury seen on endoscopy and/or
    - Abnormal esophageal acid exposure seen on reflux monitoring

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Katz PO, et al. *Am J Gastroenterol*. 2022;117:27-56.
Gyawali CP, et al. *Gut*. 2023;73(2):361-371.

Case

- A 62-year-old male is being seen by his primary care clinician following an emergency department visit last week for severe epigastric and chest pain and vomiting. His ECG was normal at the emergency department with no evidence of cardiac ischemia.
- At his primary care clinician visit, key findings on history and physical examination include chronic cough, hoarseness, and bloating. He describes persistent regurgitation and heartburn.

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Treatment of Nonerosive and Erosive GERD

Module 3

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Guideline-Directed Treatment of GERD

- Lifestyle modifications recommended for all patients, as applicable:
  - Weight loss in patients with obesity
  - Meal avoidance within 2-3 hours of bedtime
  - Smoking cessation
  - Trigger food avoidance
  - Elevating head of bed (optional)

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Katz PO, et al. *Am J Gastroenterol*. 2022;117:27-56.

Guideline-Directed Treatment of GERD (continued)

- Use of proton pump inhibitors (PPIs) over histamine-2-receptor antagonists (H2RAs)
  - For healing and maintenance of healing from EE
- For patients who respond, PPI discontinuation is recommended
- For patients with NERD, on-demand or intermittent treatment
- Long-term PPI use has safety concerns

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Katz PO, et al. *Am J Gastroenterol*. 2022;117:27-56.
Kwok CS, et al. *Am J Gastroenterol*. 2012;107:1011-1019.
Hess MW, et al. *Aliment Pharmacol Ther*. 2012;36(5):405-413.

Safety Concerns With PPIs

- Common adverse events
  - Abdominal pain
  - Diarrhea
  - Headaches
- Potential adverse events:
  - *Clostridium difficile*-associated diarrhea
  - Pneumonia
  - Bone fractures
  - Chronic kidney disease

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Katz PO, et al. *Am J Gastroenterol*. 2022;117:27-56.
Nehra AK, et al. *Mayo Clin Proc*. 2018;93(2):240-246.

Since the Guidelines

- Vonoprazan – a potassium-competitive acid blocker (PCAB) that leads to the inhibition of the H^+,K^+-ATPase-mediated secretion of gastric acid
  - H^+,K^+-ATPase is an enzyme in the parietal cells of the stomach
  - Vonoprazan reversibly binds to the pump and inhibits its production of gastric acid
    - Mechanism of acid suppression is different from PPIs

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Laine L, et al. *Gastroenterology*. 2023;164(1):61-71.

Efficacy and Safety of Vonoprazan in EE

- Randomized, active comparator trial of adults with EE
  - Healing: Vonoprazan 20 mg daily or lansoprazole 30 mg daily up to 8 weeks
    - 514 patients in vonoprazan group and 510 patients in the lansoprazole group
  - Maintenance: rerandomized for those with EE healing
    - Vonoprazan 10 mg daily, 20 mg daily, or lansoprazole 30 mg daily for 24 weeks
      - 291-294 patients in each of the groups

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Laine L, et al. *Gastroenterology*. 2023;164(1):61-71.

Efficacy and Safety of Vonoprazan in EE

- Endpoints were healing as seen on endoscopy
  - At 8 weeks: 92.9% vonoprazan vs 84.6% lansoprazole; noninferiority (difference, 8.3%; 95% CI, 4.5%–12.2%, *P*<0.0001)
    - LA Grade C/D healing was 91.7% vs 72%
  - At 24 weeks: 80.7% vonoprazan 20 mg, 79.2% vonoprazan 10 mg, 72% lansoprazole; noninferiority (*P*<0.0001 for both vonoprazan dosage comparisons)
    - LA Grade C/D maintenance was 74.7-77.2% vs 61.5%

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Laine L, et al. *Gastroenterology*. 2023;164(1):61-71.

Efficacy and Safety of Vonoprazan in EE

- Adverse Events
  - 30%-56% of vonoprazan treated patients across healing and maintenance phases
    - 0.4%-5.7% severe and 0.6%-4.7% serious
  - 29%-50% of lansoprazole treated patients across healing and maintenance phases
    - 0.8%-2.7% severe and 0.6%-2.4% serious
- Most common: diarrhea during healing

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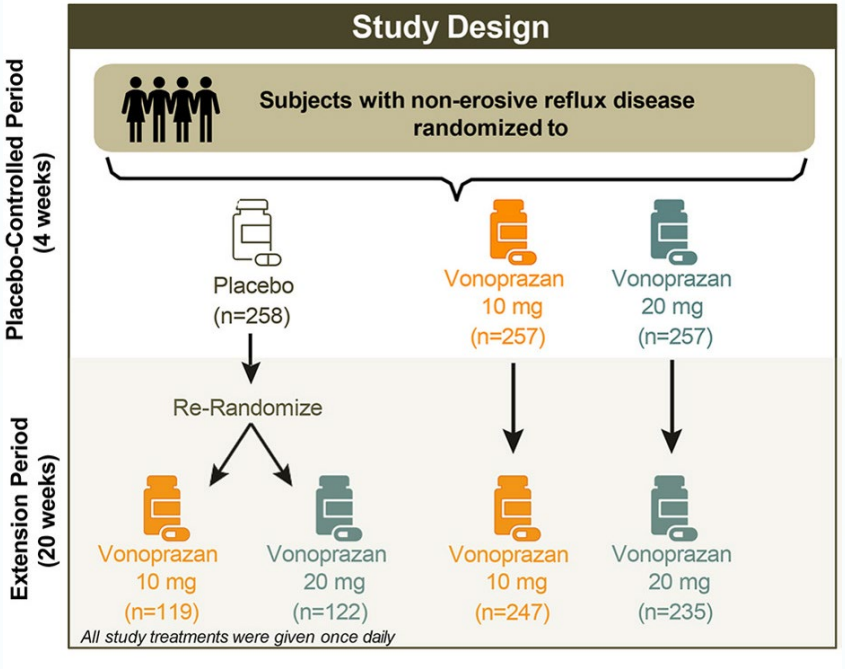
Laine L, et al. *Gastroenterology*. 2023;164(1):61-71.

Efficacy and Safety of Vonoprazan in NERD

- Randomized, placebo-controlled trial of adults with at least 4 days per week of heartburn without EE
  - Treatment: Placebo, vonoprazan 10 mg daily or 20 mg daily up to 4 weeks
  - Maintenance: placebo patients rerandomized to vonoprazan arms for up to 20 weeks
  - Primary endpoint: % of days without daytime or nighttime heartburn



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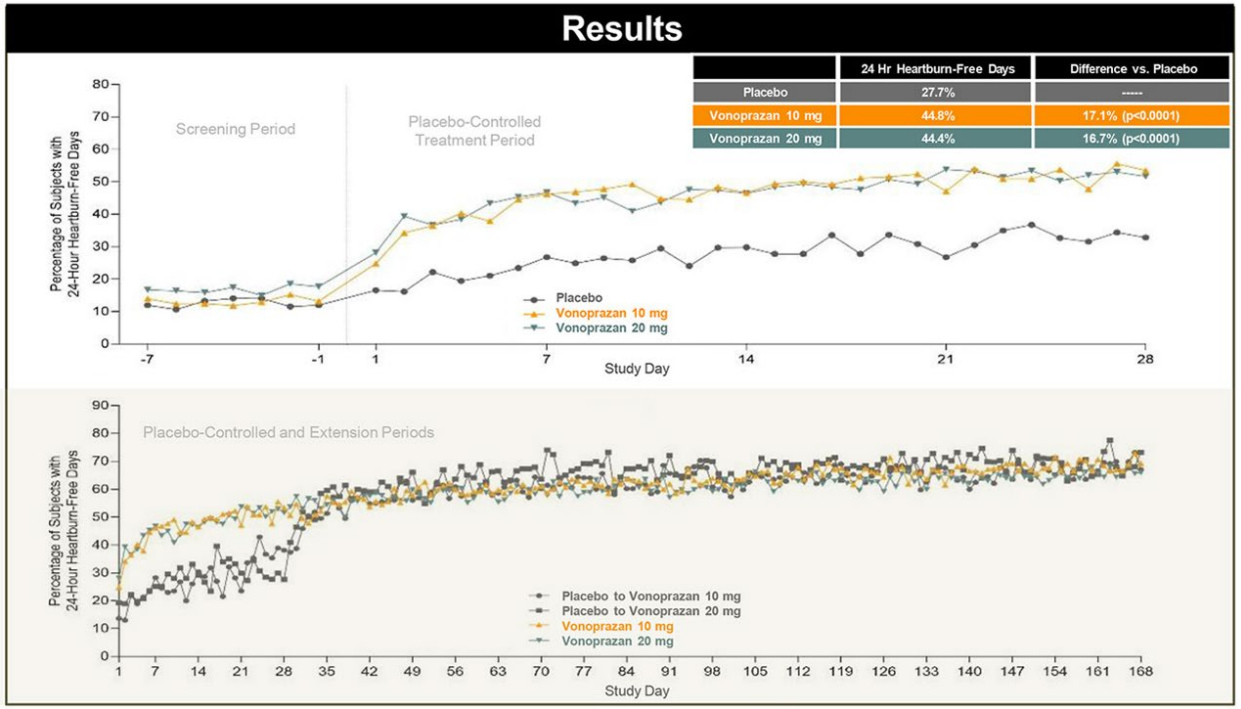
Efficacy and Safety of Vonoprazan in NERD



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Efficacy and Safety of Vonoprazan in NERD

- Adverse events during 4-week period
  - 21.6%-26.1% of vonoprazan-treated patients
    - 0.4%-0.8% serious
  - 16% of placebo-treated patients
    - 0% serious

- Adverse events during 20-week period
  - 31%-33% of vonoprazan-treated patients
    - 1.3%-3.38% serious

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Laine L, et al. *Clin Gastroenterol Hepatol*. 2024;22:2211-2220.

Vonoprazan

- Dosage:
  - EE: 20 mg daily for 8 weeks (healing) and 10 mg daily for up to 6 months (maintenance)
  - Heartburn relief: 10 mg daily for 4 weeks
- Reduced dose recommended in patients with eGFR < 30 mL/min and hepatic impairment for healing of EE
- Drug interactions: some antiretrovirals, clopidogrel (2C19), 3A4 inducers

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Vonoprazan [Prescribing information]. Phathom Pharmaceuticals, Inc.; 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218710s000lbl.pdf -

Case

- A 47-year-old female presents to her primary care clinician for follow-up after an 8-week course of a PPI. She initially presented with symptoms of heartburn and regurgitation, for which an empiric PPI was given without diagnostic testing.

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Treatment of *H. pylori* Infections

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A Quick Note on Diagnosis

- Urea breath test
  - ~90% sensitive and 95+% specific
- Stool antigen assay
  - ~94% sensitive and 97% specific
- Serum antibody testing
  - ~85% sensitive and 79% specific

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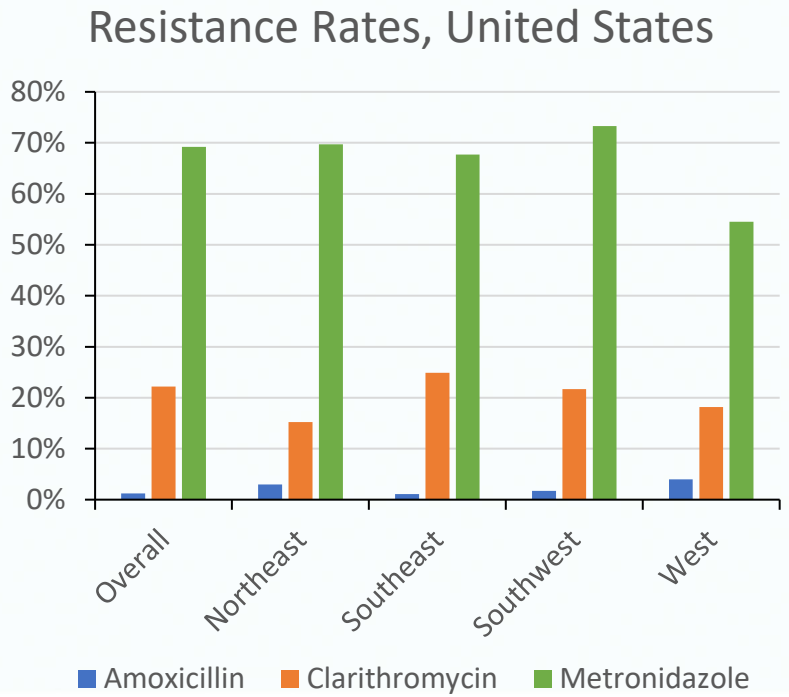
Malfertheiner P, et al. *Nat Rev Dis Primers*. 2023;9(1):19.
Howden CW, et al. *Am J Gastroenterol*. 1998;83(12):2330-2338.
Wu DC, et al. *Diagn Microbiol Infect Dis*. 2006;56(4):373-378.

Changed Landscape of *H. pylori*

- Resistance to clarithromycin, levofloxacin, and metronidazole remains above 30% in some geographical areas
- New antibiotics have been studied
- PCABs have been introduced to *H. pylori* treatment regimens



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Megraud F, et al. *Am J Gastroenterol*. 2023;118(2):269-275.

Guideline-Directed Treatment of *H. pylori*

C, consider when other treatments are not options; R, recommended; S, suggested *Consider for allergist referral	Treatment-Naïve	Treatment-Experienced (Salvage)		Penicillin Allergy
Regimen		Empiric	Proven sensitivity	
Optimized Bismuth Quadruple (PPI, bismuth subcitrate or subsalicylate, tetracycline, metronidazole)	R	S	S	R*
Rifabutin Triple (PPI, amoxicillin, rifabutin)	S	S	S	
Vonoprazan Dual (Vonoprazan, amoxicillin)	S	C	C	
Vonoprazan Triple (Vonoprazan, amoxicillin, clarithromycin)			S	
Levofloxacin Triple (PPI, levofloxacin, amoxicillin or metronidazole)			S	

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Chey WD, et al. *Am J Gastroenterol*. 2024;119:1730-1753.
Megraud F, et al. *Am J Gastroenterol*. 2023;118(2):269-75.

New to the Block

- Vonoprazan + Amoxicillin (DualPak) and Vonoprazan + Amoxicillin + Clarithromycin (TriplePak) were FDA approved in 2022
- Randomized active comparator
  - Vonoprazan/amoxicillin vs vonoprazan/amoxicillin/clarithromycin vs lansoprazole/amoxicillin/clarithromycin
- Vonoprazan regimens were noninferior to lansoprazole in non-clarithromycin/amoxicillin resistant strains, but superior in resistant strains
- Adverse events were largely similar across treatment groups

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Chey WD, et al. *Gastroenterology*. 2022;163:608-619.

Case

- A 46-year-old male presents for evaluation after failure to respond to a PPI-clarithromycin triple therapy course. A urea breath test has confirmed that *H. pylori* infection persists.

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Treatment-Experienced Patients With *H. pylori* Infection[1]

	No Penicillin Allergy	Penicillin Allergy***
Previous PPI-Clarithromycin Triple	• Optimized Bismuth Quadruple* • Rifabutin Triple • High-dose PPI or PCAB Dual?**	• Optimized Bismuth Quadruple*
Previous Nonoptimized Bismuth Quadruple		

[1]Without antibiotic susceptibility testing; PCAB, potassium-competitive acid blocker
*PPI, bismuth, nitroimidazole, tetracycline; **Consider only when optimized BQT or rifabutin triple therapy are not options and antibiotic susceptibility unknown; ***May require allergy testing

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Chey WD, et al. *Am J Gastroenterol*. 2024;119:1730-1753.

Multidisciplinary Care

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Multidisciplinary Care Considerations

- The vast majority of patients with GERD and *H. pylori* infections are initially seen and managed in primary care settings
- Endoscopy referrals may be used as decision points for referrals based on availability of resources
- Consider dietitian support for patients with chronic symptoms
- Post-specialist management surveillance by primary care is important to maintain response to treatment

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Key Concepts

- PPIs are the mainstay of treatment for GERD
- Endoscopy has a key role in the diagnosis of GERD and EE
- Vonoprazan may be considered for EE and NERD
- Optimized bismuth quadruple therapy is the preferred regimen for treatment-naïve patients with *H. pylori* infection

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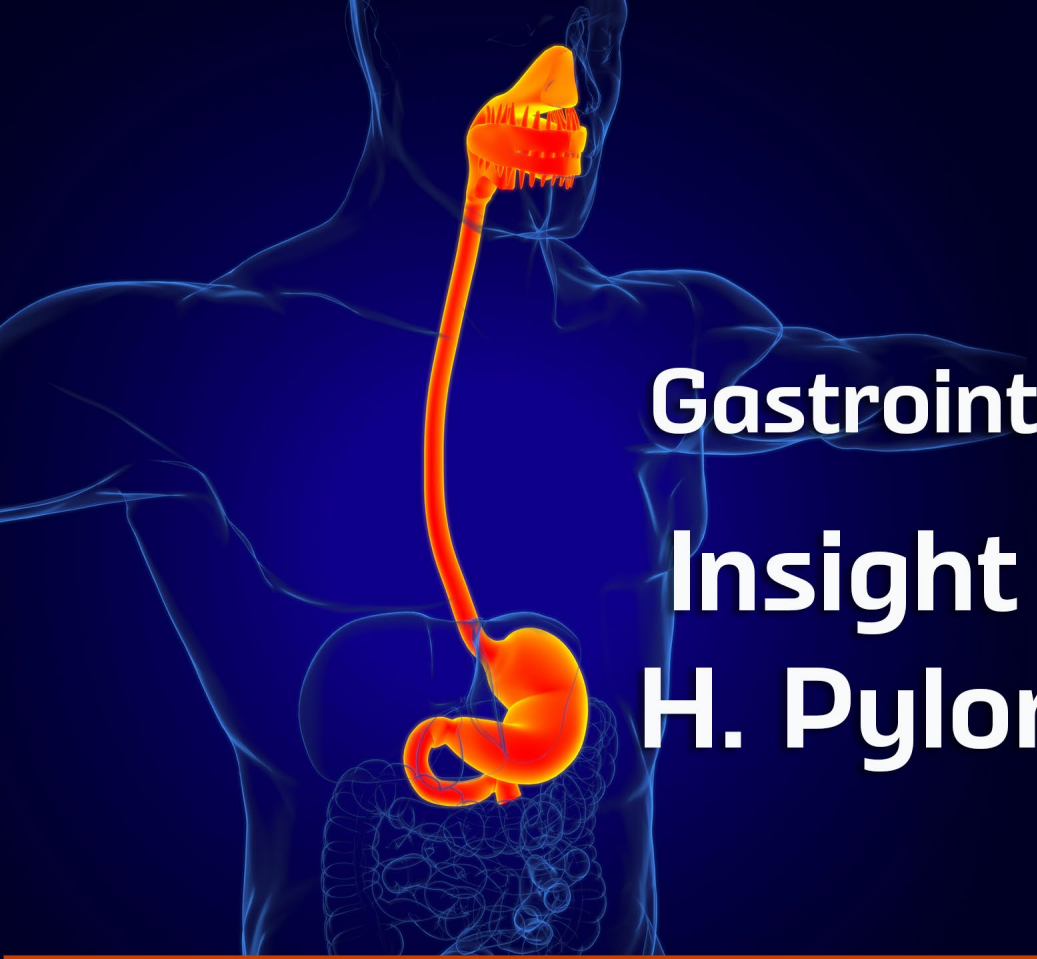

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