Behind the Guidelines: *H. pylori* Management in 2025

An update from the 2024 clinical practice guideline from the American College of Gastroenterology

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Objectives

1

To review the epidemiology and disease associations of *H. pylori* infection

2

To understand the indications for testing for *H. pylori* infection

3

To be able to implement appropriate testing strategies

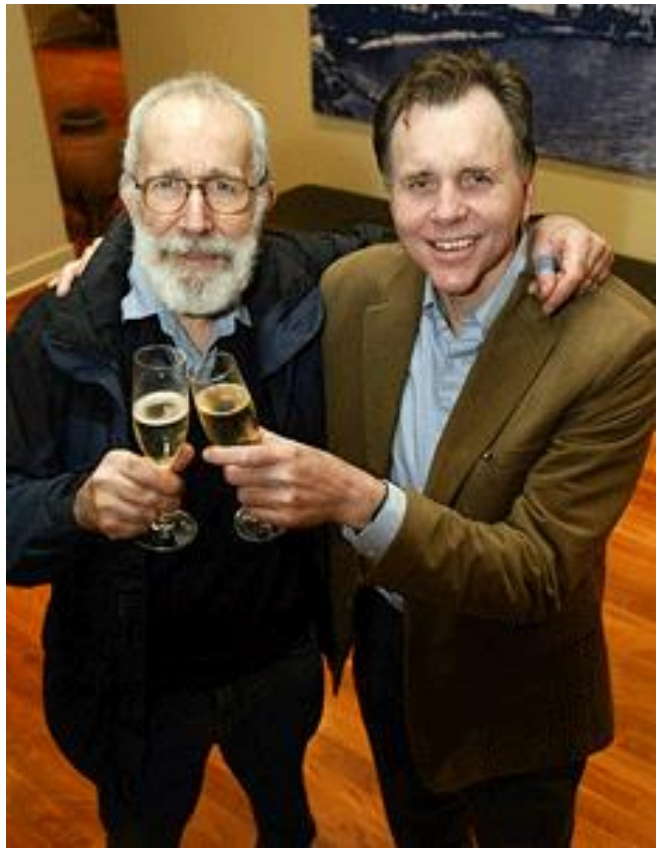
4

To identify appropriate treatment regimens for treatment-naïve and treatment-experienced patients with *H. pylori* infection

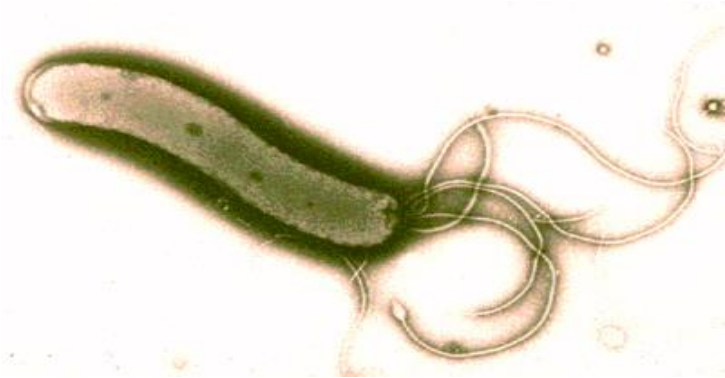
(with reference to a typical patient case)

Epidemiology and Disease Associations

Helicobacter pylori



- Identified (almost accidentally) 1983
- Initial widespread skepticism
- Nobel Prize 2005 for Drs. Robin Warren and Barry Marshall



H. pylori: Common, chronic bacterial infection

- Gram-negative spiral bacterium with unipolar flagella
- Lives on gastric mucosa
- Causes inflammation and can lead to atrophic gastritis, peptic ulcer, or gastric cancer

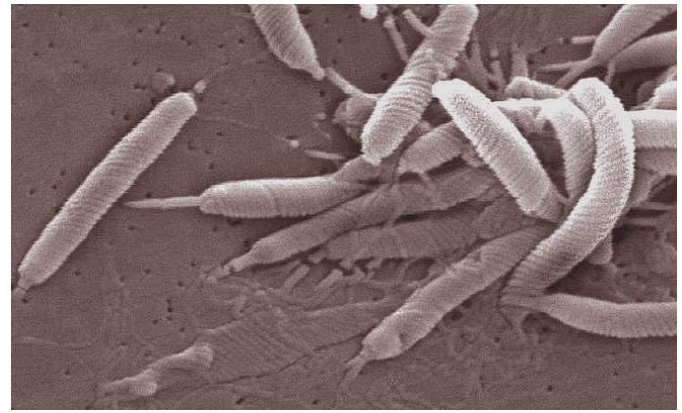


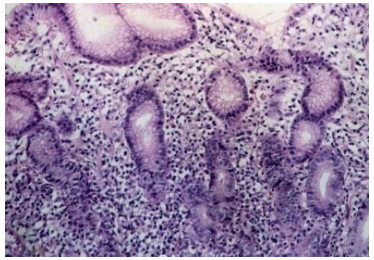
Image: https://www.genengnews.com/news/research-links-specific-h-pylori-strain-with-stomach-cancer-risk/

Epidemiology of *H. pylori* infection

- 36% of U.S. population infected[1]
- Individuals typically infected by 10 years of age[2]
- Duration of infection is usually lifelong
- Prevalence higher in racial/ethnic minorities
  - Including people migrating from high-prevalence countries
- Intrafamilial person-to-person transmission
  - Fecal-oral/gastric-oral
- Risk factors:
  - Living in crowded/poor sanitary conditions

1. Hooi JK, et al. Gastroenterology. 2017;153:420-429.
2. Pacifico L, et al. World J Gastroenterol. 2010;16(41):5181-5194.

Diverse outcomes of *H. pylori* infection



60 YEARS

H. pylori infection

100%

Chronic superficial gastritis

10%

Peptic ulcer disease

60%

Chronic superficial gastritis

Usually asymptomatic

<1%

Lymphoma

30%

Atrophic gastritis

1-2%

Carcinoma

H. pylori and gastric cancer

- *H. pylori* is the #1 risk factor for gastric cancer[1]
- International Agency for Research on Cancer – *H. pylori* is a Group 1 (definite) carcinogen[2]

Study from University of Pennsylvania

- > 370,000 patients with *H. pylori* infection in the VA Health Administration database
- Confirmed eradication of *H. pylori* led to a 75% relative reduction in the risk of gastric cancer[3]

1. National Cancer Institute. (2019). Surveillance Epidemiology and End Results. SEER Stat Fact Sheet: Stomach. Retrieved from http://seer.cancer.gov/statfacts/html/stomach.html.

2. Schistosomes, liver flukes and Helicobacter pylori. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Lyon, 7-14 June 1994. IARC Monogr Eval Carcinog Risks Hum. 1994;61:1-241.

3. Kumar, et al. Gastroenterol 2020;158:257 S

Case presentation

Patient
- Female
- White (non-Hispanic)
- 32 years old

Symptoms
- Upper abdominal discomfort with nausea for 2 years
- No weight change, no vomiting
- Symptoms occur daily – worse after eating

Medication/History
- Has tried OTC omeprazole without improvement
- No regular medicines; denies NSAID use
- No relevant family history
- Physical exam unremarkable

What would you do next?

A. Order *H. pylori* serology

B. Treat her for *H. pylori* infection

C. Order a urea breath test

D. Order a fecal antigen test

E. Refer for endoscopy and biopsy

Testing for *H. pylori* Infection

General testing principles for *H. pylori* infection

- Anyone who is tested and found to be infected should be offered treatment
- Anyone who is treated for the infection should be re-tested after treatment

Who should be tested for *H. pylori* infection?

Patients with:

- Peptic ulcer
- Gastric MALT lymphoma
- Gastric pre-cancerous changes
- Personal or family history of gastric cancer
- Unexplained iron deficiency
- ITP
- Starting long-term NSAIDs/ASA
- Dyspepsia symptoms

Anyone testing positive should be offered treatment

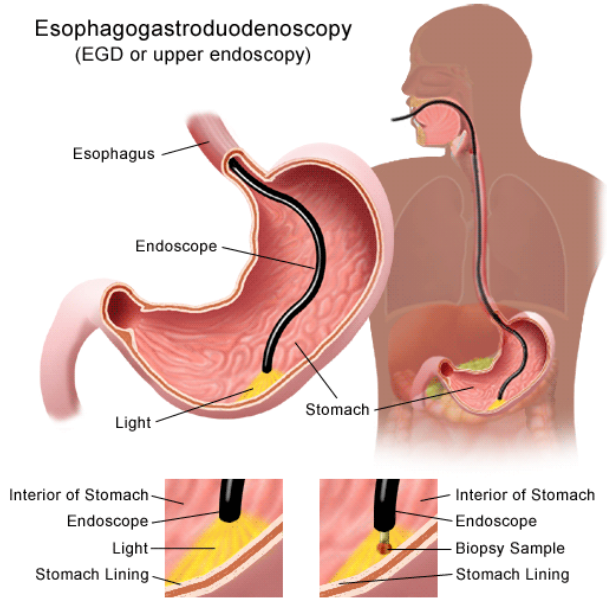
NEW (ACG Guidelines 2024)*

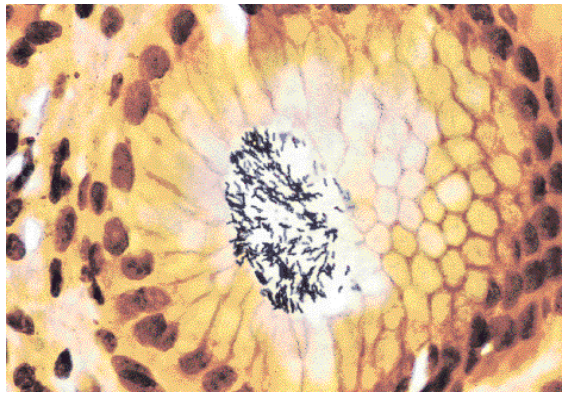
- Adult household member contacts of *H. pylori*-positive individual
- Screen non-white racial/ethnic groups, since they are at increased risk of gastric cancer

*Chey et al, Am J Gastroenterol 2024; 119: 1730

Endoscopic tests for *H. pylori* infection

- Histology
- Biopsy urease test
- Culture
- PCR/next-generation sequencing (NGS)





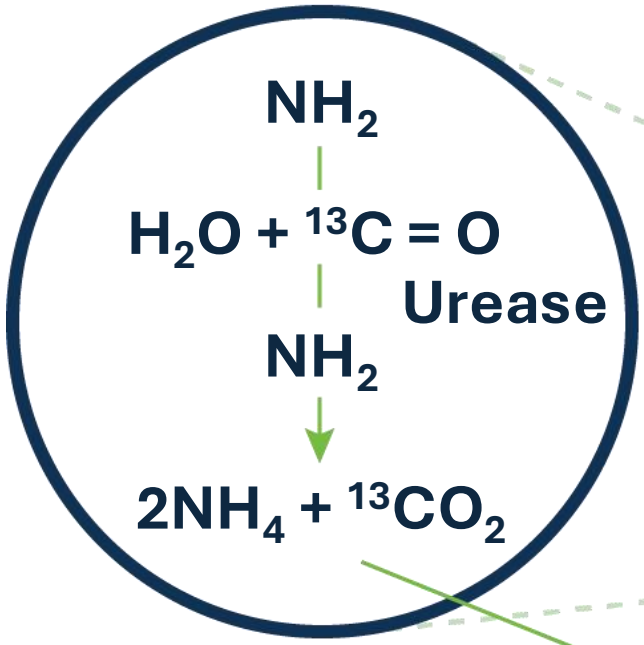
Non-endoscopic tests for *H. pylori* infection

- Urea breath test*
- Stool antigen test*
- Stool PCR/NGS
- Serology for IgG anti-Hp
  - No longer recommended
  - Cannot distinguish past from current infection
  - Poor sensitivity and specificity

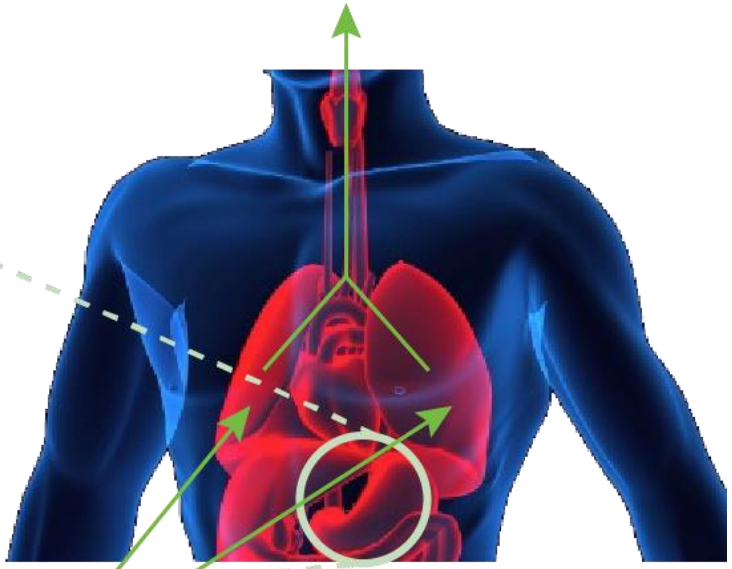
***To avoid FALSE NEGATIVES:**

- no antibiotics/bismuth for 4 weeks
- no PPIs for 2 weeks (H_2RAs OK)

^{13}C-urea breath test



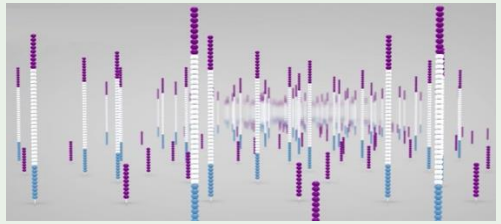
$^{13}CO_2$ in breath



$^{13}CO_2$ in blood

Analyze $^{13}CO_2$ / $^{12}CO_2$ in breath

Testing for antimicrobial susceptibility

1. Standard 	• Endoscopic biopsy → Microbiology lab • Takes 7-10 days • Available mostly in commercial labs • Measures phenotypic resistance • Cultures sometimes fail to yield organisms
2. Molecular (PCR/NGS) 	• Endoscopic biopsy → PCR ± sequencing • Rapid • Can be done in-house or commercially • Detects MUTATIONS underlying antimicrobial resistance (genotypic resistance)
3. Molecular on STOOL (PCR/NGS)   	• Stool sample → PCR ± sequencing • Rapid • Can be done in-house or commercially • Detects MUTATIONS underlying antimicrobial resistance (genotypic resistance) • Not yet widely available • **AVOIDS REPEAT ENDOSCOPY**

Treatment of *H. pylori* Infection

Treatment of *H. pylori* infection: General considerations

- Require a positive test of active infection
- Offer treatment to all who test positive
- Explain the treatment, possible side effects, etc.
- Choice of treatment?
  - Availability of antimicrobial sensitivity testing?
  - History of macrolide/quinolone use?
  - True penicillin allergy?
- Always re-test after treatment
  - Test → Treat → Re-test

Optimized bismuth quadruple therapy (the only STRONG recommendation)

1

Appropriately dosed PPI

- *b.i.d.*, Before meal
- ? Preferably rabeprazole or esomeprazole

2

Bismuth subsalicylate (300 mg) or subcitrate (120-300 mg) *q.i.d.*

- Avoid bismuth subsalicylate if salicylate allergy

3

Tetracycline (NOT doxycycline) 500 mg *q.i.d.*

4

Metronidazole 500 mg *t.i.d.* or *q.i.d.*

All taken together for 14 days

Chey et al, Am J Gastroenterol 2024; 119: 1730

Success rates with different regimens – U.S. “real world” data

Regimen	N	Cure rate
Bi-based quadruple (tetracycline), 14 days	585	87%
Bi-based quadruple (tetracycline), 10 days	135	77%
PPI-clarithromycin-amoxicillin, 14 days	161	79%
PPI-clarithromycin-amoxicillin, 10 days	101	67%
Bi-based quadruple (doxycycline), 14 days	48	70%
Bi-based quadruple (doxycycline), 10 days	16	67%

Alsamman et al, Dig Dis Sci 2019; 64: 2893

Other suggested regimens for treatment-naïve patients

Rifabutin triple (Talicia)[f]	Omeprazole (10mg)[b] Amoxicillin (250 mg) Rifabutin (12.5 mg)	4 capsules t.i.d.	**Each is FDA-approved**	Conditional (low quality of evidence)
PCAB dual (Voquenza DualPak)[g]	Vonoprazan (20 mg) Amoxicillin (1000 mg)	b.i.d. t.i.d.		Conditional (moderate quality of evidence)
PCAB dual (Voquenza DualPak)[h]	Vonozapran (20 mg) Clarithromycin (500 mg) Amoxicillin (1000 mg)	b.i.d.		Conditional (moderate quality of evidence)

Chey et al, Am J Gastroenterol 2024; 119: 1730

1st-Line Regimens for Treatment-Naïve Patients with *H. pylori* Infection

Without Antibiotic Susceptibility Testing

No Penicillin Allergy
- Optimized BQT
- Rifabutin Triple
- PCAB Dual
- PCAB-Clarithromycin Triple**

Penicillin Allergy***
- Optimized BQT

**Avoid if previous macrolide exposure
***May require formal allergy testing

Chey et al, Am J Gastroenterol 2024; 119: 1730

Case continues

- Positive urea breath test demonstrated active *H. pylori* infection
- Prescribed 14-day course of optimized bismuth quadruple therapy
- Completed entire course with minimal side effects

Antimicrobial resistance by *H. pylori*: (Re)-stating the obvious

1

H. pylori infection is usually acquired in childhood

+

2

H. pylori lives in the stomach

=

3

H. pylori has been exposed to every antibiotic consumed by mouth since childhood

Meta-analysis: *H. pylori* resistance rates in US isolates, 2011 – 2021

	Pooled prevalence
Clarithromycin	31.5%
Metronidazole	42.1%
Levofloxacin	37.6%
Amoxicillin	2.6%
Tetracycline	0.9%
Rifabutin	0.2%
CLA + MET	11.7%

Ho et al, Am J Gastroenterol 2022; 117: 1221

Rates of antimicrobial resistance in *H. pylori* isolates from clinical trial patients in US and Europe

- 103 sites across US and 7 European countries
- 907 treatment-naïve patients

	Overall prevalence in US	Range among different regions
Clarithromycin	22.2%	15.2% - 24.9%
Metronidazole	69.2%	54.5% - 73.3%
Amoxicillin	1.2%	1.1% - 4.0%

Similar results were found in Europe

Mégraud et al, Am J Gastroenterol 2023; 118: 269

Case continues

4 weeks later

- Successfully completed optimized bismuth quadruple therapy
- Reported improvement in her abdominal discomfort
- No longer taking omeprazole

What would you do now?

A. Order a urea breath test

B. Order a fecal antigen test

C. Re-check her *H. pylori* serology

D. No further testing

Post-treatment testing for cure

Key Concept

All patients who are treated for *H. pylori* infection should undergo a test of cure with an appropriately conducted urea breath test, fecal antigen test, or biopsy-based test at least 4 weeks after completion of therapy.

Chey et al, Am J Gastroenterol 2024; 119: 1730

Case continues

Post-treatment urea breath test was **positive**

Salvage treatment: General principles

- Confirm that infection has not been eradicated
  - Symptoms do not predict post-treatment status
  - UBT/fecal antigen test – **NOT SEROLOGY**
- Never re-use clarithromycin or levofloxacin
- Emphasize the importance of adherence to treatment and completing the 14-day course
- Discuss potential/expected adverse effects

Salvage Regimens for Treatment-Experienced Patients with Persistent *H. pylori* Infection

Without Antibiotic Susceptibility Testing

Previous PPI-Clarithromycin Triple

No Penicillin Allergy
- Optimized BQT
- Rifabutin Triple
- High-Dose PPI or PCAB Dual?**

Penicillin Allergy***
- Optimized BQT

Previous Nonoptimized BQT

No Penicillin Allergy
- Optimized BQT
- Rifabutin Triple
- High-Dose PPI or PCAB Dual?**

Penicillin Allergy***
- Optimized BQT

List of treatments are meant to present appropriate options but are ***not*** meant to present a treatment hierarchy

**Only if optimized BQT and rifabutin triple unavailable
***May need formal allergy testing

Chey et al, Am J Gastroenterol 2024; 119: 1730

Salvage Regimens for Treatment-Experienced Patients with Persistent *H. pylori* Infection

Antibiotic Susceptibility Testing

Clarithromycin- and levofloxacin-sensitive
- Clarithromycin Triple*
- Optimized BQT**
- Rifabutin Triple
- Levofloxacin Triple

Clarithromycin-resistant, levofloxacin-sensitive
- Optimized BQT**
- Rifabutin Triple
- Levofloxacin Triple

Clarithromycin-sensitive, levofloxacin-resistant
- Clarithromycin Triple*
- Optimized BQT**
- Rifabutin Triple

Clarithromycin- and levofloxacin-resistant
- Optimized BQT**
- Rifabutin Triple
- High-Dose PPI or PCAB Dual?**

**Only if optimized BQT and rifabutin triple unavailable

Chey et al, Am J Gastroenterol 2024; 119: 1730

Case Concludes

- Due to failure of optimized bismuth quadruple therapy, despite apparently good compliance, consider re-treatment with rifabutin triple therapy

Summary

- Chronic infection – potentially serious consequences
- Test for active infection before treating
- Choose treatment regimen carefully
  - Patient's antibiotic history is important
  - Only use clarithromycin if known susceptibility
  - Discuss importance of adherence, possible side effects
- Future availability of antimicrobial sensitivity testing
- Re-test at least 4 weeks after completion of treatment
  - UBT, fecal antigen test, (endoscopy)

Thank you!

Questions?