ACG Clinical Guideline: Treatment of *Helicobacter Pylori* Infection

By Aaron Hein, MD

When to Test?

- ✓ Current or previous peptic ulcer disease
- ✓ MALT marginal zone B-cell lymphoma
- ✓ Dyspepsia in patients <60 years old
- ✓ High-risk populations for gastric cancer (age 45-50)
- ✓ Functional dyspepsia
- ✓ Adult household members of those with + *H. pylori* non-serologic testing
- ✓ Long-term NSAID or aspirin therapy
- ✓ Unexplained iron deficiency anemia
- ✓ Idiopathic thrombocytopenic purpura
- ✓ Gastric premalignant condition (GPMC) or gastric cancer
  - ✓ GPMCs: Atrophic gastritis, gastric intestinal metaplasia, autoimmune gastritis
- ✓ Gastric adenomas or hyperplastic polyps
- ✓ Persons with 1st degree relatives with gastric cancer or others at ↑ risk of gastric cancer

How to Test?

- ✓ Urea breath testing
- ✓ Fecal antigen test
- ✓ Endoscopic histology or biopsy urease test
- ✗ **Avoid** serologic testing

Key point: All patients offered testing should be offered effective treatment for active infection and undergo test-of cure

Class I carcinogen → causal association between gastric cancer and *H pylori* (dominant risk factor with attributable risk of 75 – 89%)

Progression of Gastric Adenocarcinoma (Correa Cascade)

Normal gastric mucosa → *H. pylori* → Chronic gastritis → Atrophic gastritis → Gastric intestinal metaplasia → Gastric dysplasia → Gastric cancer

Recommended First-Line Regimens in Treatment-Naïve Patients

Regimen Name	Medications	Eradication Rates	Comments
Optimized Bismuth Quadruple Therapy (BQT) **(Rec: strong, moderate QOE)**	PPI (standard dose)* BID Bismuth subcitrate or subsalicylate QID Tetracycline 500 mg QID Metronidazole 500 mg TID or QID	10 d – 77% 14 d – 87%	- ✓ if penicillin allergy, ✗ bismuth subsalicylate if salicylate allergy - ✗ substitute doxycycline - Minor GI upset, avoid with alcohol - ✗ in women of childbearing potential (tetracycline)
Rifabutin Triple Therapy (Rec: conditional, low QOE)	Omeprazole 10 mg, amoxicillin 250 mg, and rifabutin 12.5 mg *combination pill (Talicia), 4 capsules TID	14 d – 84–89%	- Very low resistance rates to amoxicillin and rifabutin - Low rates of myelotoxicity given low rifabutin dose, and ↑ intragastric concentration of rifabutin with 50 mg TID compared to 150 mg daily
PCAB Dual Therapy (Rec: conditional, moderate QOE)	Vonoprazan 20 mg BID Amoxicillin 1000 mg TID (Voquenza DualPak)	14 d – 70%	- Vonoprazan can be taken with meals or fasting - ✓ Low pill burden - ↓ rates of adverse effects compared to BQT
PCAB-Clarithromycin Triple Therapy (Rec: conditional, moderate QOE)	Vonoprazan 20 mg BID Clarithromycin 500 mg BID Amoxicillin 1000 mg BID (Voquenza TriplePak)	14 d – 81%	- Use only if H. pylori strain is clarithromycin sensitive - Use in lieu of clarithromycin-PPI triple therapy

Avoid regimens with clarithromycin (resistance rates 22-31%) or levofloxacin (resistance rate 38%) without demonstrated susceptibility

Avoid concomitant therapy with PPI, clarithromycin, amoxicillin and metronidazole given resistance patterns

Avoid omeprazole, lansoprazole, or pantoprazole in those with known rapid/ultrarapid CYP2C19 genotype due to rapid metabolism; **Use** esomeprazole or rabeprazole

Standard Dose PPI
Lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg, rabeprazole 20 mg, or esomeprazole 20 mg

Chey, William D. MD, FACG[1]; Howden, Colin W. MD, FACG[2]; Moss, Steven F. MD, FACG[3]; Morgan, Douglas R. MD, MPH, FACG[4]; Greer, Katarina B. MD, MSEpi[5]; Grover, Shilpa MD, MPH[6]; Shah, Shailja C. MD, MPH[7]. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. The American Journal of Gastroenterology 119(9):p 1730-1753, September 2024. | DOI: 10.14309/ajg.0000000000002968

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Eradication Testing

- **Key Point:** All patients require confirmed eradication testing to avoid serious sequelae of infection.
- Eradication testing options are similar to those for initial testing; **avoid** repeat endoscopy unless there is a specific indication.
- **Key Point:** Avoid false negatives for **all** forms of eradication testing
  - Hold PPI ≥ 2 weeks prior
  - Hold bismuth and antibiotics at ≥ 4 weeks prior
  - No effect on accuracy with H2RA or antacids
- **Avoid** serologic testing for eradication testing
- Recurrence rates after eradication: 1% yearly

Use of antibiotic susceptibility testing: Consider when choice of therapy remains unclear after noting previous treatments of *H pylori*, antibiotic exposure, or penicillin allergy

Probiotics: Insufficient evidence for increased efficacy or tolerability of *H pylori* treatment

Salvage Regimens for Treatment-Experienced Patients with Persistent Infection

Persistent *H pylori* infection: Ongoing infection despite ≥ 1 previous course of eradication therapy

Key Points:
- ✓ Use optimized BQT first in those without prior exposure
- ✓ In those with prior optimized BQT exposure, use Rifabutin Triple

Options in those **without** antibiotic susceptibility testing

		Previous Therapy Receipt	
		Clarithromycin Triple	**Nonoptimized BQT**
Penicillin Allergy	**Yes**	Optimized BQT*	Optimized BQT*
	No	Optimized BQT Rifabutin Triple High-Dose PPI or PCAB Dual	Optimized BQT Rifabutin Triple High-Dose PPI or PCAB Dual

*Consider formal allergy testing in patients with penicillin allergy in whom optimized BQT is not appropriate

Options in those **with** antibiotic susceptibility testing

		Clarithromycin Susceptibility Testing Result	
		Sensitive	**Resistant**
Levofloxacin Susceptibility Testing Result	**Sensitive**	Clarithromycin Triple Optimized BQT Rifabutin Triple Levofloxacin Triple	Optimized BQT Rifabutin Triple Levofloxacin Triple
	Resistant	Clarithromycin Triple Optimized BQT Rifabutin Triple	Optimized BQT Rifabutin Triple High-Dose PPI or PCAB Dual

Levofloxacin Triple Therapy: PPI standard dose, Levofloxacin 500 mg daily, Amoxicillin 1000 mg BID, Metronidazole 500 mg BID

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