HELICOBACTER PYLORI INFECTION: DIAGNOSIS, ERADICATION THERAPY, AND THE CHALLENGE OF ANTIBIOTIC RESISTANCE

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Abstract

Background: Helicobacter pylori is a gram-negative, spiral bacterium that chronically colonizes the gastric mucosa of a large proportion of the world's population and is classified by the International Agency for Research on Cancer as a definite (Group I) human carcinogen. Untreated infection drives a stepwise progression from chronic gastritis to peptic ulcer disease and, in a subset of patients, gastric cancer, while rising global antibiotic resistance increasingly threatens the success of standard eradication regimens.

Methods: This narrative review synthesizes current evidence on the diagnosis, eradication therapy, and antibiotic resistance patterns of H. pylori infection, drawing on the Maastricht VI/Florence Consensus Report and the 2024 American College of Gastroenterology (ACG) clinical guideline.

Results: Diagnostic testing must be selected according to clinical context and recent medication use, since proton pump inhibitors, bismuth, and antibiotics can all produce false-negative results; the urea breath test and stool antigen test are the preferred non-invasive options, while endoscopic biopsy-based testing additionally allows histological assessment and, where available, culture-based susceptibility testing. Rising clarithromycin resistance, now exceeding 15% in many world regions, has rendered standard clarithromycin-based triple therapy unreliable as an empiric first-line choice in high-resistance settings; bismuth quadruple therapy and susceptibility-guided regimens are

increasingly preferred, together with extension of treatment duration to 14 days and mandatory confirmation of eradication.

Conclusion: Antibiotic resistance has fundamentally shifted first-line H. pylori management away from one-size-fits-all empiric triple therapy toward regionally informed, often bismuth-based quadruple regimens, with confirmation of eradication as a routine step. This shift is directly relevant to Uzbekistan and other settings with anticipated high regional clarithromycin resistance and limited access to routine susceptibility testing, where bismuth-based regimens and antimicrobial stewardship offer a practical, high-yield strategy.

Keywords

Helicobacter pylori, eradication therapy, antibiotic resistance, urea breath test, bismuth quadruple therapy, peptic ulcer disease, gastric cancer.

Methods

This work was prepared as a narrative literature review. A literature search was conducted in September 2026 using PubMed, the databases of major gastroenterology societies, and World Health Organization antimicrobial resistance surveillance reports, with the search terms “Helicobacter pylori,” “eradication therapy,” “antibiotic resistance,” “clarithromycin resistance,” and “bismuth quadruple therapy,” combined with filters for publication in English between 1992 and 2026. Priority was given to the Maastricht VI/Florence Consensus Report, the 2024 ACG clinical guideline, global resistance surveillance meta-analyses, and landmark studies of gastric carcinogenesis; case reports and articles without accessible full text were excluded. A total of twelve sources meeting these criteria were selected and synthesized for this review.

Introduction

Helicobacter pylori infects a substantial proportion of the global population, with prevalence generally higher in developing regions and typically acquired in early childhood through person-to-person transmission. Once established, infection persists for life unless actively treated, producing chronic active gastritis in essentially all colonized individuals. A minority of infected patients go on to develop peptic ulcer disease, and a smaller subset develop gastric mucosa-associated lymphoid tissue (MALT) lymphoma or gastric adenocarcinoma, the latter recognized since 1994 by the International Agency for Research on Cancer as a Group I human carcinogen.

For much of the past three decades, standard clarithromycin-based triple therapy served as reliable, near-universal first-line treatment. Rising antibiotic resistance — particularly to clarithromycin, but also to metronidazole and, increasingly, levofloxacin — has eroded the reliability of this empiric approach in many parts of the world, prompting a

shift toward resistance-informed regimen selection, bismuth-based quadruple therapy, and routine confirmation of successful eradication.

The aim of this review is to summarize the clinical significance of H. pylori infection, the principles guiding selection of diagnostic tests, the evidence base for eradication therapy in the context of rising antibiotic resistance, and relevance to gastroenterology practice in Uzbekistan.

Understanding and applying current diagnostic and eradication-therapy principles for H. pylori infection is relevant across several areas of clinical practice, including:

- Gastroenterology (test selection, regimen choice, management of treatment failure)
- Primary care (test-and-treat strategies, appropriate use of non-invasive testing)
- Oncology and cancer prevention (population-level gastric cancer risk reduction)
- Infectious disease and microbiology (antimicrobial stewardship, resistance surveillance)
- Public health (screen-and-treat programs in high-prevalence populations)

Clinical Significance: From Chronic Infection to Gastric Cancer

H. pylori survives the acidic gastric environment through urease production, which locally neutralizes acid, together with flagella-mediated motility that allows penetration of the protective mucus layer. Strain-specific virulence factors, notably CagA and VacA, are injected into or act upon gastric epithelial cells, triggering a sustained chronic inflammatory response. Depending on the anatomical distribution of this inflammation, some patients develop antral-predominant gastritis with increased acid secretion and a predisposition to duodenal ulcer, while others develop corpus-predominant or pangastritis that progresses toward atrophic gastritis.

This latter pathway follows a well-characterized, stepwise sequence — the Correa cascade — progressing from chronic active gastritis to atrophic gastritis, intestinal metaplasia, dysplasia, and ultimately gastric adenocarcinoma in a minority of patients. Critically, the early stages of this cascade are largely reversible with successful eradication, whereas established intestinal metaplasia and beyond carry cancer risk that eradication reduces but does not eliminate, underscoring the value of earlier diagnosis and treatment. This sequence is illustrated in Figure 1.

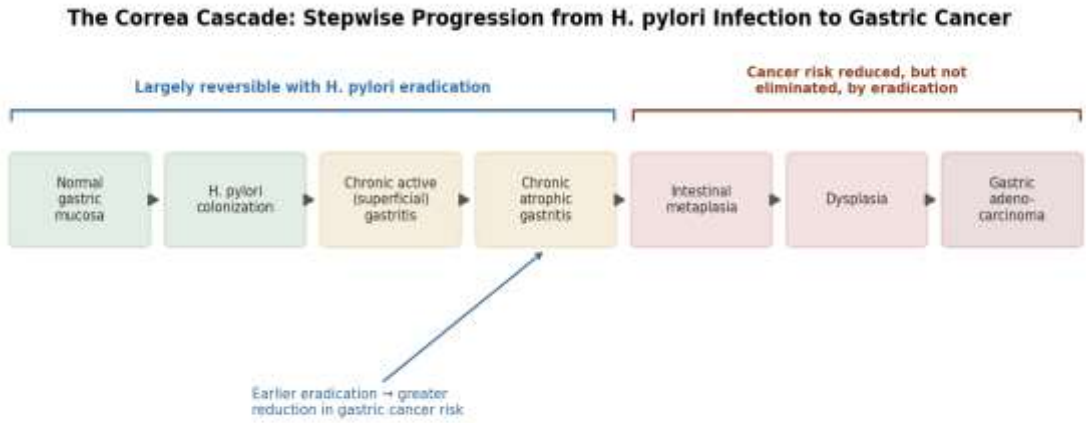

Figure 1. The Correa cascade of gastric carcinogenesis: chronic H. pylori infection progresses stepwise from active gastritis through atrophic gastritis, intestinal metaplasia, and dysplasia to gastric adenocarcinoma in a minority of patients, with earlier eradication associated with greater reversibility and risk reduction.

Diagnostic Testing: Choosing the Right Test for the Clinical Context

Selecting an appropriate diagnostic test requires considering whether endoscopy is independently indicated, recent use of proton pump inhibitors, bismuth, or antibiotics (all of which can suppress bacterial load and cause false-negative results), and whether the goal is initial diagnosis or confirmation of eradication after treatment. Non-invasive tests are generally preferred when endoscopy is not otherwise indicated, while biopsy-based testing during endoscopy additionally allows histological grading of gastritis and, where available, culture-based antibiotic susceptibility testing to guide therapy in cases of prior treatment failure. Key characteristics of the principal diagnostic tests are summarized in Table 1.

Test	Type	Approximate Accuracy	Key Caveats
Urea breath test	Non-invasive	Sensitivity and specificity both >95%	Preferred test for initial diagnosis and eradication confirmation; requires stopping PPIs ≥2 weeks and antibiotics/bismuth ≥4 weeks beforehand

Test	Type	Approximate Accuracy	Key Caveats
Stool antigen test	Non-invasive	Sensitivity and specificity both >90% (monoclonal assay)	Accurate, low-cost alternative to urea breath test; same withdrawal requirements for PPIs/antibiotics apply
Serology (IgG antibody)	Non-invasive	Sensitivity high, but specificity lower and variable by population	Cannot distinguish active from past infection; not recommended to confirm eradication
Rapid urease test	Invasive (endoscopic biopsy)	Sensitivity ~90–95%, specificity >95%	Fast bedside result during endoscopy; false negatives with recent PPI, antibiotic, or bismuth use, or active bleeding
Histology	Invasive (endoscopic biopsy)	Sensitivity and specificity both >95% with adequate sampling	Also allows assessment of gastritis pattern, atrophy, and intestinal metaplasia
Culture with susceptibility testing	Invasive (endoscopic biopsy)	Specificity near 100%; sensitivity limited by fastidious growth requirements	Reference standard for guiding antibiotic choice, but not widely available; molecular resistance testing is an emerging alternative

Table 1. Diagnostic Tests for Helicobacter pylori Infection: Type, Accuracy, and Key Caveats.

Eradication Therapy in the Era of Rising Antibiotic Resistance

Antibiotic resistance is now the single largest determinant of eradication failure. Clarithromycin resistance, driven predominantly by point mutations in the 23S rRNA gene, has risen above the 15% threshold considered the point at which empiric clarithromycin-

based triple therapy becomes unreliable in many regions of the world; metronidazole resistance is even more common but can be partially overcome with higher doses, longer treatment duration, and combination with bismuth; fluoroquinolone resistance, driven by gyrA mutations, is also increasing and limits the reliability of levofloxacin-based salvage regimens. Reflecting this shifting resistance landscape, the Maastricht VI/Florence Consensus and the 2024 ACG guideline both recommend basing first-line regimen selection on local or regional clarithromycin resistance data and prior macrolide exposure whenever susceptibility or reliable molecular resistance testing is not available, extending treatment duration to 14 days, and favoring bismuth quadruple therapy as the preferred empiric choice in most high-resistance settings. Regardless of the regimen chosen, confirmation of eradication with a urea breath test or stool antigen test at least four weeks after completing therapy, and at least two weeks after stopping proton pump inhibitors, is now considered mandatory rather than optional. This decision process is illustrated in Figure 2.

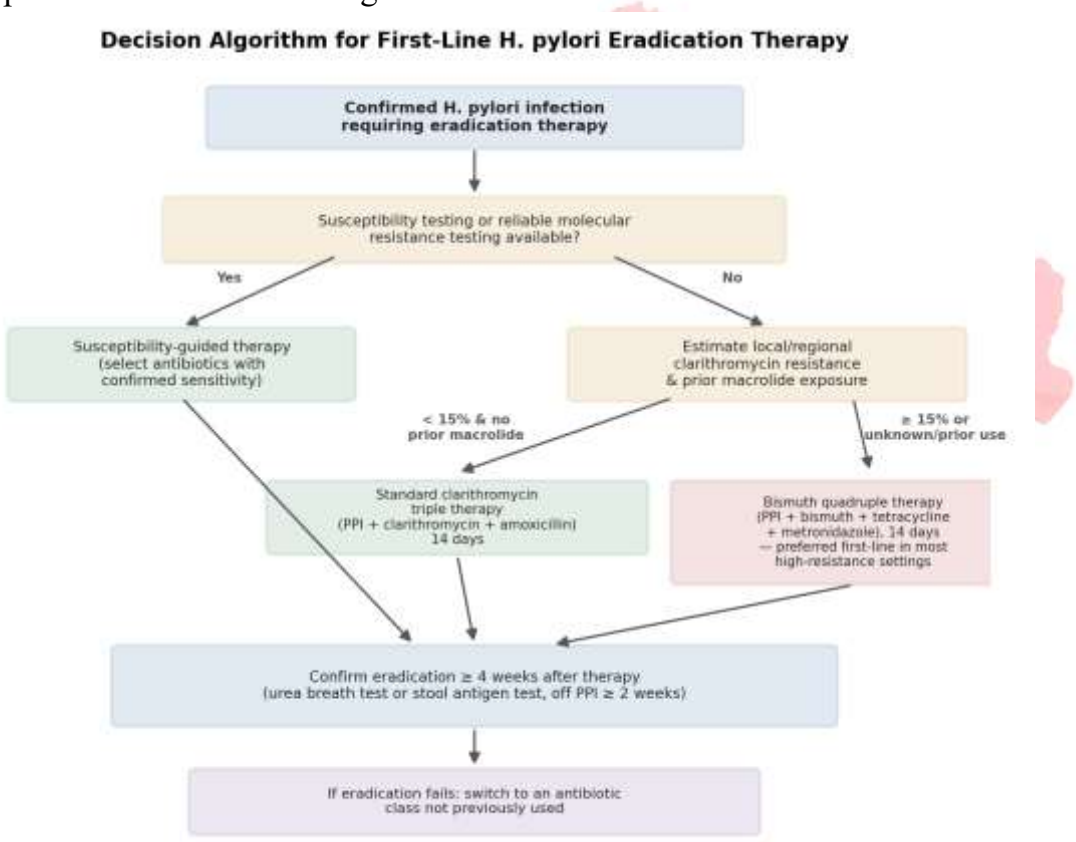

Figure 2. Decision algorithm for selecting first-line H. pylori eradication therapy based on availability of susceptibility testing, estimated local clarithromycin resistance, and prior antibiotic exposure, with mandatory confirmation of eradication and antibiotic-class rotation upon treatment failure.

Conclusion

Helicobacter pylori remains a major, modifiable driver of peptic ulcer disease and gastric cancer worldwide, but rising antibiotic resistance — most notably to clarithromycin — has fundamentally altered the evidence-based approach to first-line eradication therapy. Diagnostic test selection must account for the clinical context and recent medication use, while therapy selection should be guided by local resistance data, prior antibiotic exposure, and, where available, direct susceptibility testing, with bismuth quadruple therapy now preferred over standard clarithromycin triple therapy in most high-resistance settings.

For clinical practice, this translates into two actionable priorities: matching diagnostic test choice to the clinical context and recent medication history, and moving away from a uniform empiric therapy toward a resistance-informed, regionally adapted choice of eradication regimen with routine confirmation of success. Continued application of these principles, adapted to local resource constraints, holds substantial potential to improve eradication success rates and reduce the long-term burden of peptic ulcer disease and gastric cancer, including within the healthcare system of Uzbekistan.

References

[1] Malfertheiner P, Megraud F, Rokkas T, et al. Management of Helicobacter pylori infection: the Maastricht VI/Florence consensus report. Gut. 2022;71(9):1724-1762.

[2] Chey WD, Howden CW, Moss SF, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol. 2024;119(9):1730-1753.

[3] Correa P. Human gastric carcinogenesis: a multistep and multifactorial process. Cancer Res. 1992;52(24):6735-6740.

[4] IARC Working Group. Schistosomes, Liver Flukes and Helicobacter pylori. IARC Monogr Eval Carcinog Risks Hum. 1994;61:1-241.

[5] Hooi JKY, Lai WY, Ng WK, et al. Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis. Gastroenterology. 2017;153(2):420-429.

[6] Savoldi A, Carrara E, Graham DY, Conti M, Tacconelli E. Prevalence of Antibiotic Resistance in Helicobacter pylori: A Systematic Review and Meta-analysis in World Health Organization Regions. Gastroenterology. 2018;155(5):1372-1382.

[7] Megraud F. H pylori antibiotic resistance: prevalence, importance, and advances in testing. Gut. 2004;53(9):1374-1384.

[8] Fallone CA, Chiba N, van Zanten SV, et al. The Toronto Consensus for the Treatment of Helicobacter pylori Infection in Adults. Gastroenterology. 2016;151(1):51-69.

[9] Graham DY, Lee YC, Wu MS. Rational Helicobacter pylori therapy: evidence-based medicine rather than medicine-based evidence. Clin Gastroenterol Hepatol. 2014;12(2):177-186.

[10] Gisbert JP, Calvet X. Review article: non-invasive and invasive testing for Helicobacter pylori infection. Aliment Pharmacol Ther. 2011;34(11-12):1177-1194.

[11] Ford AC, Yuan Y, Moayyedi P. Helicobacter pylori eradication therapy to prevent gastric cancer: systematic review and meta-analysis. Gut. 2020;69(12):2113-2121.

[12] Liou JM, Malfertheiner P, Lee YC, et al. Screening and eradication of Helicobacter pylori for gastric cancer prevention: the Taipei global consensus. Gut. 2020;69(12):2093-2112.