Indications and diagnostic tests for Helicobacter pylori infection in adults

AUTHOR: J Thomas Lamont, MD
SECTION EDITOR: Mark Feldman, MD, MACP, AGAF, FACG
DEPUTY EDITOR: Shilpa Grover, MD, MPH, AGAF

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Sep 2023.**
This topic last updated: **Jul 13, 2023.**

INTRODUCTION

Helicobacter pylori (*H. pylori*) is the most prevalent chronic bacterial infection and is associated with peptic ulcer disease, chronic gastritis, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue (MALT) lymphoma [1-4].

This topic will review the clinical indications for testing for *H. pylori*, diagnostic tests for *H. pylori,* and their interpretation. Our recommendations are largely consistent with 2017 guidelines from the American College of Gastroenterology and the Maastricht V consensus report [5,6]. The epidemiology, pathophysiology, and immune response to *H. pylori* and treatment regimens for *H. pylori* infection are discussed separately. (See "Pathophysiology of and immune response to Helicobacter pylori infection" and "Acute and chronic gastritis due to Helicobacter pylori" and "Association between Helicobacter pylori infection and gastrointestinal malignancy" and "Association between Helicobacter pylori infection and duodenal ulcer" and "Bacteriology and epidemiology of Helicobacter pylori infection" and "Treatment regimens for Helicobacter pylori in adults".)

INDICATIONS FOR TESTING

Testing for *H. pylori* should be performed only if the clinician plans to offer treatment for positive results. Indications for testing include (table 1):

- Gastric marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
- Active peptic ulcer disease or past history of peptic ulcer if cure of *H. pylori* infection has not been documented
- Early gastric cancer

Evidence to support testing for *H. pylori* in individuals with pathogenic variants associated with specific inherited cancer syndromes is discussed in detail, separately. (See "Risk factors for gastric cancer", section on 'Familial predisposition'.)

Other indications for testing for *H. pylori* are more controversial. These indications include [2,7-10]:

- **Uninvestigated dyspepsia in patients <60 years without alarm features** – Patients with dyspepsia who are <60 years of age and do not have any alarm features (table 2) should be tested for *H. pylori* [11,12]. (See "Approach to the adult with dyspepsia", section on 'Patient age <60 years'.)

- **Prior to chronic treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) or long-term, low-dose** aspirin **use** – *H. pylori* infection is a risk factor for the development of ulcers and for ulcer bleeding in patients on low-dose aspirin treatment. *H. pylori* also increases the risk of NSAID-related peptic complications. (See "NSAIDs (including aspirin): Pathogenesis and risk factors for gastroduodenal toxicity" and "NSAIDs (including aspirin): Primary prevention of gastroduodenal toxicity".)

- **Unexplained iron deficiency** – *H. pylori* can cause iron deficiency and iron deficiency anemia by interfering with absorption of oral iron. (See "Causes and diagnosis of iron deficiency and iron deficiency anemia in adults", section on 'Celiac disease/atrophic gastritis/H. pylori' and "Treatment of iron deficiency anemia in adults", section on 'Approaches to lack of response'.)

- **Adults with immune thrombocytopenia** – Limited evidence suggests that eradication of *H. pylori* infection improves platelet counts in some adult patients with idiopathic thrombocytopenic purpura. (See "Initial treatment of immune thrombocytopenia (ITP) in adults", section on 'H. pylori testing'.)

There are insufficient data to support routine testing for *H. pylori* in patients with lymphocytic gastritis, hyperplastic gastric polyps, and hyperemesis gravidarum. (See "Gastric polyps", section on 'Hyperplastic polyps' and "Gastric cancer screening", section on 'Helicobacter pylori eradication'.)

APPROACH TO DIAGNOSTIC TESTING

The choice of test used to diagnose *H. pylori* depends on whether a patient requires an upper endoscopy for evaluation of symptoms or surveillance. Endoscopy is not indicated solely for the purpose of establishing *H. pylori* status. Other important determinants include the recent use of medications that can suppress the bacterial load of *H. pylori* (eg, proton pump inhibitor therapy [PPI], antibiotics, and bismuth), the prevalence of *H. pylori*, test availability, and cost. A suggested approach to initial diagnostic testing in a patient with suspected *H. pylori* is outlined in the algorithm (algorithm 1).

Medications that should be discontinued prior to testing — PPI use within one to two weeks and bismuth/antibiotic use within four weeks of testing can decrease the sensitivity of all endoscopy-based tests and noninvasive tests of active *H. pylori* infection (stool antigen and urea breath test). Patients should be advised to stop PPI therapy one to two weeks prior to testing. If feasible, testing should performed at least four weeks after completion of bismuth/antibiotic treatment.

Patient undergoing upper endoscopy — Among patients undergoing upper endoscopy, the choice of test to diagnose *H. pylori* and extent of testing varies based on the clinical presentation and endoscopic findings.

- **No active peptic ulcer bleeding**
  - **No recent PPI/bismuth/antibiotic use and no indication for gastric biopsy** – In patients without recent PPI/bismuth/antibiotic use who do not require biopsies of the stomach for histology, the diagnosis of *H. pylori* can be established with a biopsy urease test. (See 'Biopsy urease testing' below.)
  - **Recent PPI/bismuth/antibiotic use or indication for gastric biopsy** – In patients with visible endoscopic abnormalities (eg, gastric ulcer, gastropathy), and patients with recent antisecretory/bismuth/antibiotic use, we perform histology to diagnose *H. pylori*. Since recent PPI/bismuth/antibiotic use may diminish numbers of bacteria detected by histology, we perform a urea breath or stool antigen assay to confirm a negative test result once these medications have been held for an appropriate length of time. (See 'Medications that should be discontinued prior to testing' above and 'Histology' below and 'Urea breath testing' below and 'Stool antigen assay' below.)
  - **Prior antibiotic treatment failures** – In patients with *H. pylori* that is refractory to two courses of antibiotic therapy we perform culture and antibiotic sensitivity testing on

gastric biopsies in order to guide treatment. (See 'Bacterial culture and sensitivity testing' below and 'Confirm eradication in all patients' below and "Treatment regimens for Helicobacter pylori in adults".)

- **Active peptic ulcer bleeding** – In patients with bleeding duodenal or gastric ulcer on upper endoscopy, we perform a gastric mucosal biopsy at the time of the initial endoscopy unless it is impractical or difficult, such as with a blood-filled stomach. A negative biopsy result does not exclude *H. pylori* in the setting of an active upper gastrointestinal bleed, and another test (ideally a urea breath test) should be performed to confirm a negative result [13,14].

  If a gastric mucosal biopsy is not obtained at the time of endoscopy, we perform a urea breath test or stool antigen assay to diagnose *H. pylori*.

  Testing for *H. pylori* does not need to be performed immediately, and can be performed once the patient has stopped bleeding and can safely be off PPI therapy for one to two weeks. (See "Peptic ulcer disease: Clinical manifestations and diagnosis", section on 'Exclude Helicobacter pylori (H. pylori) infection'.)

Patients not undergoing upper endoscopy — In patients who do not require endoscopic evaluation, the diagnosis of *H. pylori* should be made with a test for active infection (stool antigen assay or urea breath test). In clinical situations where patients are unable or unwilling to stop PPI therapy one to two weeks prior to testing, positive test results are true positives; negative results may represent false negatives and should be confirmed with repeat testing after stopping PPI therapy for one to two weeks. Serologic testing for *H. pylori* should be avoided altogether. If performed in areas of low prevalence of *H. pylori*, positive results should be confirmed with a test for active infection prior to initiating eradication therapy. (See 'Serology' below.)

DIAGNOSTIC TESTS

Diagnostic testing for *H. pylori* can be divided into invasive (endoscopic) and noninvasive techniques, based upon the use of upper endoscopy. Endoscopy-based tests, the urea breath test, and the stool antigen assay test for active *H. pylori* infection.

Endoscopic testing — The diagnosis of *H. pylori* can usually be established during endoscopy by one of three methods: biopsy urease test, histology, and much less commonly by bacterial culture. (See 'Patient undergoing upper endoscopy' above and 'Confirm eradication in all patients' below.)

Biopsy urease testing — Gastric biopsy specimens are placed in a medium that contains urea and a pH reagent. Urease cleaves urea to liberate ammonia, producing an alkaline pH and a resultant color change. Commercially available urease testing kits differ in the use of medium (agar versus membrane pad) and testing reagents and the time to obtain a final result (1 to 24 hours).

The sensitivity and specificity of biopsy urease testing is approximately 90 and 95 percent, respectively [3]. With the rapid urease testing kits, results are obtained in one hour. One hour sensitivity and specificity of rapid urease tests are comparable (89 to 98 percent and 89 to 93 percent, respectively) to those seen with agar gel tests at 24 hours and superior to agar gel tests at one hour [15-18]. False-negative results can occur in patients with acute upper gastrointestinal bleeding or with the use of PPIs, antibiotics, or bismuth-containing compounds [19]. In such patients it is recommended that samples be taken from the both the gastric antrum and the fundus to increase the sensitivity of the test [20]. Increasing the number of gastric biopsy specimens from one to four also increases the sensitivity of the test [21].

Although biopsy urease kits are inexpensive, the cost is greater than that of a simple diagnostic endoscopy due to the addition of the biopsy and the resultant "upcoding" of the procedure to esophagogastroduodenoscopy with biopsy. Nevertheless, biopsy urease testing is less expensive as compared with histology.

Histology — Gastric biopsies can diagnose of *H. pylori* infection and associated lesions (eg, atrophic gastritis, intestinal metaplasia, dysplasia, and mucosa-associated lymphoid tissue [MALT] lymphoma). Biopsies for histology should be taken from both the antrum and body of the stomach, especially when looking for evidence of multifocal atrophic gastritis (picture 1A-B) and/or intestinal metaplasia. The accuracy of histologic diagnosis of *H. pylori* infection can be improved by using special stains such as Giemsa or specific immune stains [22]. (See "Acute and chronic gastritis due to Helicobacter pylori" and "Metaplastic (chronic) atrophic gastritis".)

The sensitivity and specificity of histology for the diagnosis of *H. pylori* infection are 95 and 98 percent, respectively. The sensitivity of histology may be decreased in patients with acute peptic ulcer bleeding and in patients on PPI therapy due to the proximal migration of *H. pylori* to the corpus from the antrum. Even in the absence of PPI use, the density of *H. pylori* can vary at different sites and interpretation of histologic slides is associated with interobserver variability [23,24]. (See 'Patient undergoing upper endoscopy' above.)

Bacterial culture and sensitivity testing — Biopsies for culture should be obtained before the forceps are contaminated with formalin. The tissue should be placed into a container with a

few drops of saline. This preparation will allow for culture and antibiotic sensitivity testing. While bacterial culture has high specificity, it has low sensitivity as *H. pylori* is difficult to culture. Microcapillary culturing methods and improved transport media may improve sensitivity [25-28]. (See 'Confirm eradication in all patients' below and "Treatment regimens for Helicobacter pylori in adults", section on 'Treatment failure'.)

Noninvasive testing — Noninvasive tests for the diagnosis of *H. pylori* include urea breath testing (UBT), stool antigen testing, and serology. Of these, UBT and stool antigen assay are tests of active infection. *H. pylori* serology can be positive in patients with an active or prior infection.

Urea breath testing — UBT is based upon the hydrolysis of urea by *H. pylori* to produce CO_2 and ammonia. Urea with a labeled carbon isotope (nonradioactive 13C or radioactive 14C) is given by mouth; *H. pylori* liberate labeled CO_2 that can be detected in breath samples. The tests can be performed in 15 to 20 minutes and have similar cost and accuracy. The dose of radiation in the 14C test is approximately 1 microCi which is equivalent to one day of background radiation exposure [29]. Even though this dose of radiation is small, the nonradioactive 13C test is preferred in young children and pregnant women. (See "Radiation-related risks of imaging", section on 'Special populations'.)

The sensitivity and specificity of UBT are approximately 88 to 95 percent and 95 to 100 percent, respectively [30]. Thus, false-positive results are uncommon. False-negative results may be observed in patients who are taking PPIs, bismuth, or antibiotics and in the setting of active peptic ulcer bleeding [19,31]. The sensitivity but not specificity of the UBT is reduced in the setting of an active peptic ulcer bleed (67 and 93 percent, respectively) [13]. It is unclear if the reduction in sensitivity is induced by the bleeding process or by changes in the microenvironment of *H. pylori* to decrease the activity of urease.

The effect of PPIs, which is presumably due to suppression of *H. pylori*, was illustrated in a series of 93 patients who had *H. pylori* infection documented by UBT [31]. Treatment with lansoprazole was associated with a negative result on subsequent UBT in 33 percent of patients. Repeat breath test results 3, 7, and 14 days after stopping lansoprazole were positive in 91, 97, and 100 percent, respectively. In another study of 60 patients with biopsy-proven *H. pylori* infection who underwent UBT testing 7 and 14 days after treatment with lansoprazole false-negative rates with lansoprazole and bismuth were 40 and 55 percent, respectively [32]. It is controversial whether H2RAs affect the sensitivity of the UBT [19,33-35].

Stool antigen assay — The detection of bacterial antigen indicates an ongoing *H. pylori* infection. Stool antigen testing can therefore be used to establish the initial diagnosis of *H.*

pylori and to confirm eradication [3]. Of the available tests, stool antigen testing is the most cost effective in areas of low to intermediate prevalence of *H. pylori* [36]. (See 'Patients not undergoing upper endoscopy' above and 'Confirm eradication in all patients' below.)

The sensitivity and specificity of the laboratory-based monoclonal enzyme immunoassay (94 and 97 percent, respectively) are comparable to the UBT [37-48]. Stool antigen testing is affected by the recent use of bismuth compounds, antibiotics, and PPIs. Although some data suggest that stool antigen test is predictive of eradication as early as seven days after completion of therapy, to reduce false-negative results, patients should be off antibiotics for four weeks, and PPIs for one to two weeks, prior to testing [19,32,40,49,50]. In the setting of active bleeding from peptic ulcers, the specificity of the stool antigen testing may decrease [51,52]. However, the sensitivity of the monoclonal enzyme immunoassay remains high in the setting of a recent peptic ulcer bleed. This was illustrated in a study in which 34 patients underwent inpatient stool antigen testing a mean of 2.8 days (range 0 to 8 days) after hospitalization for a bleeding peptic ulcer. The sensitivity of the monoclonal enzyme immunoassay in this study was 94 percent, significantly higher than a polyclonal enzyme immunoassay and a rapid monoclonal immunochromatographic stool test (74 and 60 percent, respectively). (See 'Patient undergoing upper endoscopy' above and 'Medications that should be discontinued prior to testing' above.)

Stool antigen testing using the polyclonal enzyme immunoassay is no longer used given its low sensitivity. The rapid in-office monoclonal immunochromatographic stool antigen tests has high specificity but its adoption has been limited by its low sensitivity (96 and 50 percent, respectively) [53]. (See 'Confirm eradication in all patients' below.)

Serology — Laboratory-based ELISA test to detect immunoglobulin G (IgG) antibodies is inexpensive and noninvasive. However, serologic tests require validation at the local level, which is impractical in routine practice. In addition, concerns over its accuracy have limited its use. Guidelines recommend that serologic testing should not be used in low prevalence populations as the low accuracy of serology would result in inappropriate treatment in significant numbers of patients [2,3,11].

One meta-analysis that evaluated the performance of several commercially available serologic assays found an overall sensitivity and specificity of 85 and 79 percent, respectively [54]. Inaccurate serologic tests are more common in older adults and in patients with cirrhosis in whom specificity can be decreased [55,56]. Local prevalence of *H. pylori* affects the positive predictive value of antibody testing. In areas where the prevalence of *H. pylori* is less than 20 percent, as in much of the United States, a positive serologic test is more likely to be a false positive. As a result, secondary testing with a stool or breath test to confirm the initial result is

appropriate before initiating treatment. However, a negative test in a patient with a low pretest probability for infection, is helpful to exclude infection. An example would be a young individual with dyspepsia and no evidence of peptic ulcer disease, especially in an area where the prevalence of *H. pylori* is low.

Serology does not reliably distinguish between active and past infection. A quantitative ELISA test is generally used in research settings. It allows for determination of IgG titers of paired sera from the acute and convalescent (three to six months or longer) phase and can confirm eradication of the infection. However, this is not performed in clinical practice.

Other infrequently used tests

- **13C-urea assay** – A serodiagnostic test using a 13C-urea assay is a noninvasive tool for diagnosis of *H. pylori* infection, but is rarely, if ever, used in clinical practice. This test is performed by measuring two serum specimens; one is taken before and the second 60 minutes after ingestion of a 13C-urea-rich meal. The test has a reported sensitivity of 92 to 100 percent and a reported specificity of 96 to 97 percent [57,58].

- **Polymerase chain reaction** – Quantitative polymerase chain reaction (PCR) testing on gastric biopsies can be used to detect low bacterial loads. It can also be used to identify specific mutations associated with antimicrobial resistance. However, the use of PCR based testing is limited by its high cost.

CONFIRM ERADICATION IN ALL PATIENTS

Confirmation of eradication should be performed in all patients treated for *H. pylori* because of increasing antibiotic resistance [2,5]. Eradication can be confirmed with a urea breath test, stool antigen testing, or endoscopy-based testing. The choice of test depends on the need for an upper endoscopy (eg, follow-up of bleeding peptic ulcer) and local availability. Endoscopy with biopsy for culture and sensitivity should be performed in patients with persistent *H. pylori* infection after two courses of antibiotic treatment. Tests to confirm eradication should be performed at least four weeks after completion of antibiotic treatment [5]. PPIs should be held for one to two weeks prior to testing to reduce false-negative results. Serologic testing should not be performed to confirm eradication as patients may continue to have antibodies after eradication [59]. (See 'Biopsy urease testing' above and 'Stool antigen assay' above and 'Endoscopic testing' above and 'Histology' above and 'Bacterial culture and sensitivity testing' above and 'Serology' above.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: *Helicobacter pylori*".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: H. pylori infection (The Basics)" and "Patient education: Gastritis (The Basics)")
- Beyond the Basics topics (see "Patient education: Helicobacter pylori infection and treatment (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Indications for testing** – Testing for *Helicobacter pylori* (*H. pylori*) should be performed only if the clinician plans to offer treatment for positive results (table 1). Indications include:
  - Gastric marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
  - Active peptic ulcer disease or past history of peptic ulcer if cure of *H. pylori* infection has not been documented
  - Early gastric cancer
  - Other indications that are supported by more limited evidence of benefit include:

- Uninvestigated dyspepsia in patients <60 years without alarm features (table 2)
- Prior to chronic treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or long-term, low-dose aspirin
- Unexplained iron deficiency anemia
- Adults with immune thrombocytopenia

- **Testing approach and important pretest considerations** – The choice of test used to diagnose *H. pylori* depends on whether a patient requires an upper endoscopy for evaluation of symptoms or surveillance. Endoscopy is not indicated solely for the purpose of establishing *H. pylori* status. Other important determinants include the recent use of medications that can suppress the bacterial load of *H. pylori* (eg, proton pump inhibitor [PPI] therapy, antibiotics, and bismuth), concurrent peptic ulcer bleeding, the prevalence of *H. pylori*, test availability, and cost (algorithm 1) (see 'Approach to diagnostic testing' above).

  Patients should be advised to stop PPI therapy one to two weeks prior to testing. If feasible, testing should performed at least four weeks after completion of bismuth/antibiotic treatment. (See 'Approach to diagnostic testing' above and 'Medications that should be discontinued prior to testing' above.)

- **Noninvasive testing in patients who do not require upper endoscopy** – In patients who do not require endoscopic evaluation, initial diagnosis of *H. pylori* should be made with a test for active infection (stool antigen or urea breath test). The urea breath test and stool antigen assay both have high sensitivity and specificity for identifying active *H. pylori* infection. (See 'Patients not undergoing upper endoscopy' above and 'Urea breath testing' above and 'Stool antigen assay' above.)

- **Testing for *H. pylori* in patients undergoing upper endoscopy**

  - In patients undergoing upper endoscopy who have no recent PPI/bismuth/antibiotic use and do not require biopsies of the stomach for histology, the diagnosis of *H. pylori* can be established with a biopsy urease test. (See 'Patient undergoing upper endoscopy' above and 'Biopsy urease testing' above.)

  - In patients with visible endoscopic abnormalities (eg, gastric ulcer, gastropathy) and patients with recent PPI/bismuth/antibiotic use, we obtain gastric biopsies for histology to diagnose *H. pylori.* In patients with recent PPI/bismuth/antibiotic use, we perform a urea breath test or stool antigen assay to confirm a negative test result. (See 'Histology' above and 'Urea breath testing' above and 'Stool antigen assay' above.)

- **Limitations of serologic testing** – Serology has low sensitivity and specificity for *H. pylori* and cannot differentiate between active and past infection. Serology should not be performed in areas of low *H. pylori* prevalence. If performed, positive results should be confirmed with a test for active infection prior to initiating eradication therapy. (See 'Noninvasive testing' above.)

- **Confirmation of eradication** – Eradication should be confirmed in all patients treated for *H. pylori* with either a urea breath test, stool antigen assay, or endoscopy-based testing. Tests to confirm eradication should be performed at least four weeks after completion of antibiotic treatment. Endoscopy with biopsy for culture and sensitivity should be performed in patients with persistent *H. pylori* infection after two courses of antibiotic treatment. (See 'Confirm eradication in all patients' above.)

ACKNOWLEDGMENT

The UpToDate editorial staff acknowledges Sheila E Crowe, MD, FRCPC, FACP, FACG, AGAF, who contributed to an earlier version of this topic review.

REFERENCES

1. NIH Consensus Conference. Helicobacter pylori in peptic ulcer disease. NIH Consensus Development Panel on Helicobacter pylori in Peptic Ulcer Disease. JAMA 1994; 272:65.
2. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of Helicobacter pylori infection--the Maastricht IV/ Florence Consensus Report. Gut 2012; 61:646.
3. Chey WD, Wong BC, Practice Parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guideline on the management of Helicobacter pylori infection. Am J Gastroenterol 2007; 102:1808.
4. Laine L. Helicobacter pylori, gastric ulcer, and agents noxious to the gastric mucosa. Gastroenterol Clin North Am 1993; 22:117.
5. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. Am J Gastroenterol 2017; 112:212.
6. Malfertheiner P, Megraud F, O'Morain CA, et al. Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. Gut 2017; 66:6.

7. DuBois S, Kearney DJ. Iron-deficiency anemia and Helicobacter pylori infection: a review of the evidence. Am J Gastroenterol 2005; 100:453.
8. Rostami N, Keshtkar-Jahromi M, Rahnavardi M, et al. Effect of eradication of Helicobacter pylori on platelet recovery in patients with chronic idiopathic thrombocytopenic purpura: a controlled trial. Am J Hematol 2008; 83:376.
9. Parsonnet J, Harris RA, Hack HM, Owens DK. Modelling cost-effectiveness of Helicobacter pylori screening to prevent gastric cancer: a mandate for clinical trials. Lancet 1996; 348:150.
10. Levi F, Lucchini F, Negri E, et al. Trends in cancer mortality in the European Union and accession countries, 1980-2000. Ann Oncol 2004; 15:1425.
11. Talley NJ, Vakil NB, Moayyedi P. American gastroenterological association technical review on the evaluation of dyspepsia. Gastroenterology 2005; 129:1756.
12. Moayyedi P, Lacy BE, Andrews CN, et al. ACG and CAG Clinical Guideline: Management of Dyspepsia. Am J Gastroenterol 2017; 112:988.
13. Gisbert JP, Abraira V. Accuracy of Helicobacter pylori diagnostic tests in patients with bleeding peptic ulcer: a systematic review and meta-analysis. Am J Gastroenterol 2006; 101:848.
14. Gisbert JP, Esteban C, Jimenez I, Moreno-Otero R. 13C-urea breath test during hospitalization for the diagnosis of Helicobacter pylori infection in peptic ulcer bleeding. Helicobacter 2007; 12:231.
15. Laine L, Lewin D, Naritoku W, et al. Prospective comparison of commercially available rapid urease tests for the diagnosis of Helicobacter pylori. Gastrointest Endosc 1996; 44:523.
16. Yousfi MM, el-Zimaity HM, Genta RM, Graham DY. Evaluation of a new reagent strip rapid urease test for detection of Helicobacter pylori infection. Gastrointest Endosc 1996; 44:519.
17. Young EL, Sharma TK, Cutler AF. Prospective evaluation of a new urea-membrane test for the detection of Helicobacter pylori in gastric antral tissue. Gastrointest Endosc 1996; 44:527.
18. Nishikawa K, Sugiyama T, Kato M, et al. A prospective evaluation of new rapid urease tests before and after eradication treatment of Helicobacter pylori, in comparison with histology, culture and 13C-urea breath test. Gastrointest Endosc 2000; 51:164.
19. Gatta L, Vakil N, Ricci C, et al. Effect of proton pump inhibitors and antacid therapy on 13C urea breath tests and stool test for Helicobacter pylori infection. Am J Gastroenterol 2004; 99:823.

20. Weston AP, Campbell DR, Hassanein RS, et al. Prospective, multivariate evaluation of CLOtest performance. Am J Gastroenterol 1997; 92:1310.
21. Siddique I, Al-Mekhaizeem K, Alateeqi N, et al. Diagnosis of Helicobacter pylori: improving the sensitivity of CLOtest by increasing the number of gastric antral biopsies. J Clin Gastroenterol 2008; 42:356.
22. Wright CL, Kelly JK. The use of routine special stains for upper gastrointestinal biopsies. Am J Surg Pathol 2006; 30:357.
23. Genta RM, Graham DY. Comparison of biopsy sites for the histopathologic diagnosis of Helicobacter pylori: a topographic study of H. pylori density and distribution. Gastrointest Endosc 1994; 40:342.
24. Faigel DO, Childs M, Furth EE, et al. New noninvasive tests for Helicobacter pylori gastritis. Comparison with tissue-based gold standard. Dig Dis Sci 1996; 41:740.
25. Mégraud F, Lehours P. Helicobacter pylori detection and antimicrobial susceptibility testing. Clin Microbiol Rev 2007; 20:280.
26. Mégraud F. Rationale for the choice of antibiotics for the eradication of Helicobacter pylori. Eur J Gastroenterol Hepatol 1995; 7 Suppl 1:S49.
27. Osato MS, Reddy R, Reddy SG, et al. Pattern of primary resistance of Helicobacter pylori to metronidazole or clarithromycin in the United States. Arch Intern Med 2001; 161:1217.
28. Li H, Shen Y, Song X, et al. Need for standardization and harmonization of Helicobacter pylori antimicrobial susceptibility testing. Helicobacter 2022; 27:e12873.
29. Leide-Svegborn S, Stenström K, Olofsson M, et al. Biokinetics and radiation doses for carbon-14 urea in adults and children undergoing the Helicobacter pylori breath test. Eur J Nucl Med 1999; 26:573.
30. Howden CW, Hunt RH. Guidelines for the management of Helicobacter pylori infection. Ad Hoc Committee on Practice Parameters of the American College of Gastroenterology. Am J Gastroenterol 1998; 93:2330.
31. Laine L, Estrada R, Trujillo M, et al. Effect of proton-pump inhibitor therapy on diagnostic testing for Helicobacter pylori. Ann Intern Med 1998; 129:547.
32. Bravo LE, Realpe JL, Campo C, et al. Effects of acid suppression and bismuth medications on the performance of diagnostic tests for Helicobacter pylori infection. Am J Gastroenterol 1999; 94:2380.
33. Savarino V, Tracci D, Dulbecco P, et al. Negative effect of ranitidine on the results of urea breath test for the diagnosis of Helicobacter pylori. Am J Gastroenterol 2001; 96:348.

34. Savarino V, Bisso G, Pivari M, et al. Effect of gastric acid suppression on 13C-urea breath test: comparison of ranitidine with omeprazole. Aliment Pharmacol Ther 2000; 14:291.

35. Graham DY, Opekun AR, Jogi M, et al. False negative urea breath tests with H2-receptor antagonists: interactions between Helicobacter pylori density and pH. Helicobacter 2004; 9:17.

36. Vakil N, Rhew D, Soll A, Ofman JJ. The cost-effectiveness of diagnostic testing strategies for Helicobacter pylori. Am J Gastroenterol 2000; 95:1691.

37. Kelly SM, Pitcher MC, Farmery SM, Gibson GR. Isolation of Helicobacter pylori from feces of patients with dyspepsia in the United Kingdom. Gastroenterology 1994; 107:1671.

38. Braden B, Teuber G, Dietrich CF, et al. Comparison of new faecal antigen test with (13)C-urea breath test for detecting Helicobacter pylori infection and monitoring eradication treatment: prospective clinical evaluation. BMJ 2000; 320:148.

39. Trevisani L, Sartori S, Galvani F, et al. Evaluation of a new enzyme immunoassay for detecting Helicobacter pylori in feces: a prospective pilot study. Am J Gastroenterol 1999; 94:1830.

40. Vaira D, Malfertheiner P, Mégraud F, et al. Diagnosis of Helicobacter pylori infection with a new non-invasive antigen-based assay. HpSA European study group. Lancet 1999; 354:30.

41. Wu DC, Wu IC, Wang SW, et al. Comparison of stool enzyme immunoassay and immunochromatographic method for detecting Helicobacter pylori antigens before and after eradication. Diagn Microbiol Infect Dis 2006; 56:373.

42. Veijola L, Myllyluoma E, Korpela R, Rautelin H. Stool antigen tests in the diagnosis of Helicobacter pylori infection before and after eradication therapy. World J Gastroenterol 2005; 11:7340.

43. Makristathis A, Pasching E, Schütze K, et al. Detection of Helicobacter pylori in stool specimens by PCR and antigen enzyme immunoassay. J Clin Microbiol 1998; 36:2772.

44. van Leerdam ME, van der Ende A, ten Kate FJ, et al. Lack of accuracy of the noninvasive Helicobacter pylori stool antigen test in patients with gastroduodenal ulcer bleeding. Am J Gastroenterol 2003; 98:798.

45. Perri F, Manes G, Neri M, et al. Helicobacter pylori antigen stool test and 13C-urea breath test in patients after eradication treatments. Am J Gastroenterol 2002; 97:2756.

46. Calvet X, Sánchez-Delgado J, Montserrat A, et al. Accuracy of diagnostic tests for Helicobacter pylori: a reappraisal. Clin Infect Dis 2009; 48:1385.

47. Shimoyama T, Kobayashi I, Kato C, et al. Comparison of monoclonal antibody-based stool antigen tests to determine the results of Helicobacter pylori eradication therapy. Scand J

Gastroenterol 2010; 45:1431.

48. Gisbert JP, de la Morena F, Abraira V. Accuracy of monoclonal stool antigen test for the diagnosis of H. pylori infection: a systematic review and meta-analysis. Am J Gastroenterol 2006; 101:1921.
49. Manes G, Balzano A, Iaquinto G, et al. Accuracy of stool antigen test in posteradication assessment of Helicobacter pylori infection. Dig Dis Sci 2001; 46:2440.
50. Vaira D, Vakil N, Menegatti M, et al. The stool antigen test for detection of Helicobacter pylori after eradication therapy. Ann Intern Med 2002; 136:280.
51. Lin HJ, Lo WC, Perng CL, et al. Helicobacter pylori stool antigen test in patients with bleeding peptic ulcers. Helicobacter 2004; 9:663.
52. Gisbert JP, Trapero M, Calvet X, et al. Evaluation of three different tests for the detection of stool antigens to diagnose Helicobacter pylori infection in patients with upper gastrointestinal bleeding. Aliment Pharmacol Ther 2004; 19:923.
53. Korkmaz H, Findik D, Ugurluoglu C, Terzi Y. Reliability of stool antigen tests: investigation of the diagnostic value of a new immunochromatographic Helicobacter pylori approach in dyspeptic patients. Asian Pac J Cancer Prev 2015; 16:657.
54. Loy CT, Irwig LM, Katelaris PH, Talley NJ. Do commercial serological kits for Helicobacter pylori infection differ in accuracy? A meta-analysis. Am J Gastroenterol 1996; 91:1138.
55. Liston R, Pitt MA, Banerjee AK. IgG ELISA antibodies and detection of Helicobacter pylori in elderly patients. Lancet 1996; 347:269.
56. Nardone G, Coscione P, D'Armiento FP, et al. Cirrhosis negatively affects the efficiency of serologic diagnosis of Helicobacter pylori infection. Ital J Gastroenterol 1996; 28:332.
57. Cutler AF, Toskes P. Comparison of [13C]urea blood test to [13C]urea breath test for the diagnosis of Helicobacter pylori. Am J Gastroenterol 1999; 94:959.
58. Ahmed F, Murthy UK, Chey WD, et al. Evaluation of the Ez-HBT Helicobacter blood test to establish Helicobacter pylori eradication. Aliment Pharmacol Ther 2005; 22:875.
59. Cutler AF, Prasad VM, Santogade P. Four-year trends in Helicobacter pylori IgG serology following successful eradication. Am J Med 1998; 105:18.

Topic 18 Version 47.0

GRAPHICS

Indications for *Helicobacter pylori* testing

Established indications
Gastric marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
Active peptic ulcer disease or past history of peptic ulcer if cure of *H. pylori* has not been documented
Early gastric cancer
Supported by more limited evidence of benefit
Uninvestigated dyspepsia in patients <60 years old without alarm features*
Prior to long-term treatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and/or low-dose aspirin
Unexplained iron deficiency anemia
Adults with immune thrombocytopenia

* Alarm features include unintentional weight loss, dysphagia, odynophagia, unexplained iron deficiency anemia, persistent vomiting, palpable mass or lymphadenopathy, family history of upper gastrointestinal cancer.

Graphic 141829 Version 1.0

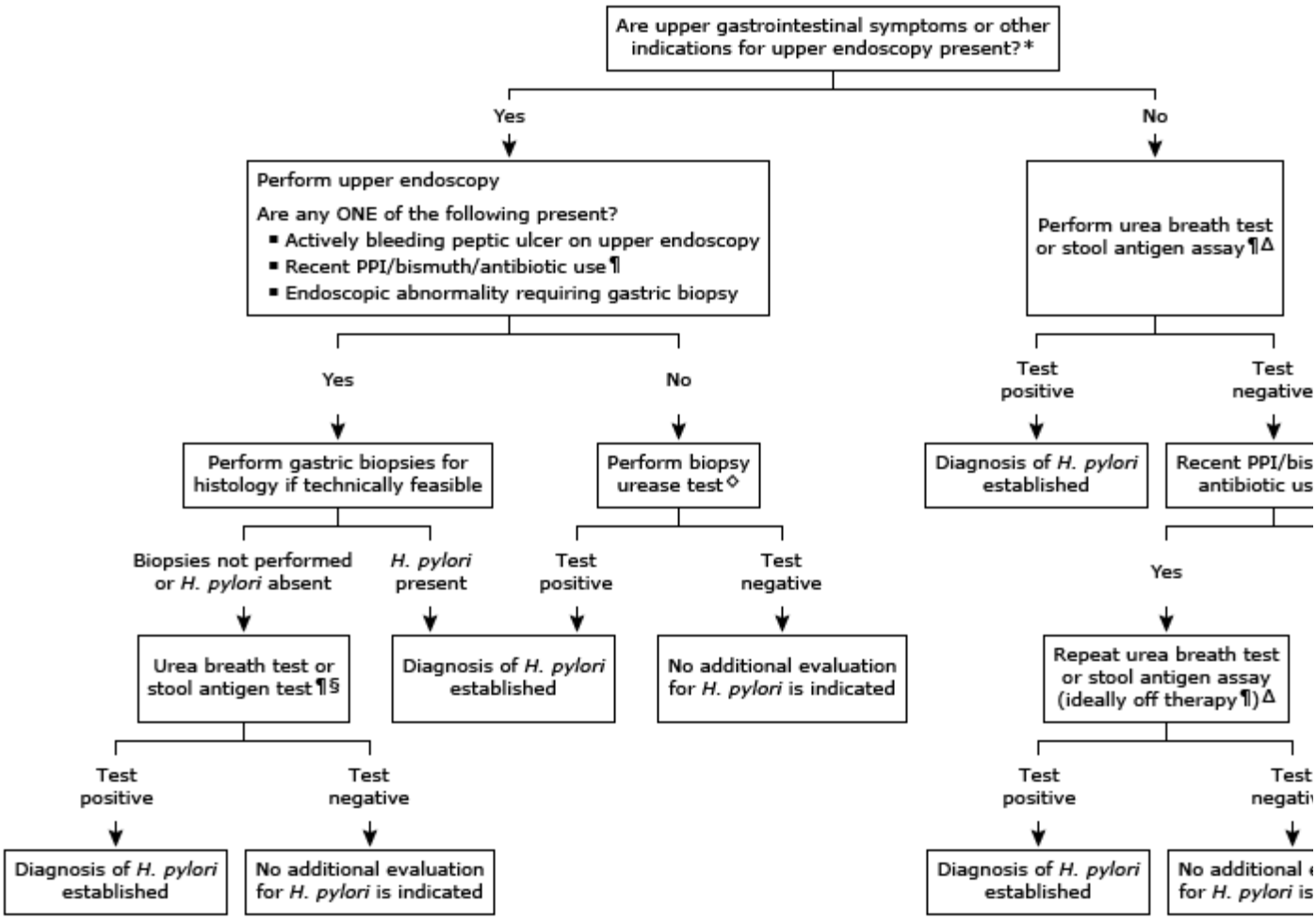
Alarm features in dyspepsia

Unintentional weight loss
Dysphagia
Odynophagia
Unexplained iron deficiency anemia
Persistent vomiting
Palpable mass or lymphadenopathy
Family history of upper gastrointestinal cancer

Adapted from: Talley NJ, Vakil NB, Moayyedi P. American Gastroenterological Association technical review on the evaluation of dyspepsia. Gastroenterology 2005; 129:1756.

Graphic 56585 Version 5.0

Suggested initial diagnostic evaluation in patients with suspected *Helicobacter* infection



* Endoscopy is not indicated solely for the purpose of establishing *H. pylori* status.

¶ PPI use within one to two weeks and bismuth/antibiotic use within four weeks of testing can decrease sen for *H. pylori*. When feasible, PPIs should be discontinued one to two weeks prior to testing and testing shoul performed at least four weeks after last bismuth/antibiotic use.

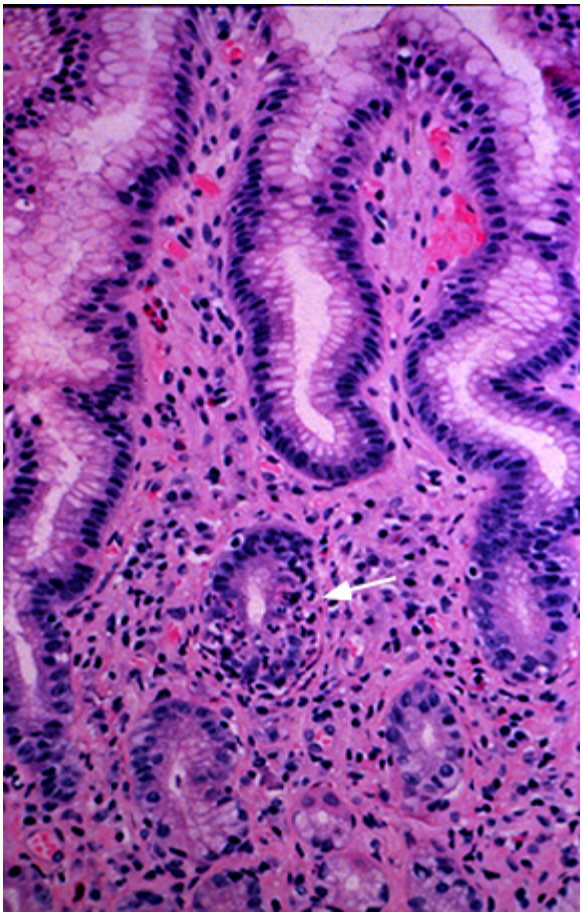
Δ The choice of test depends on local availability. Serologic testing for *H. pylori* should not be performed.

◇ If biopsy urease test is not available, gastric biopsies should be performed for histology.

§ In patients with actively bleeding peptic ulcer on upper endoscopy, testing for *H. pylori* with a urea breath stool antigen can be performed when there is no evidence of ongoing bleeding and PPIs can safely be disco for one to two weeks prior to testing.

Graphic 112677 Version 1.0

Helicobacter pylori gastritis

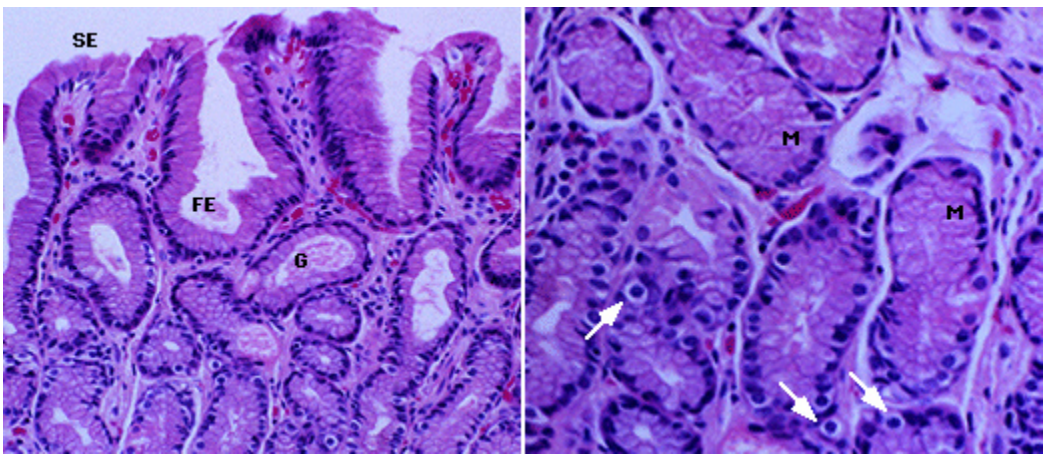


Medium power view of a gastric biopsy obtained at endoscopy shows infiltration of glands with neutrophils (arrow) and increased mononuclear cell infiltration typical of *Helicobacter pylori* gastritis.

Courtesy of Robert Odze, MD.

Graphic 64354 Version 2.0

Normal gastric antrum

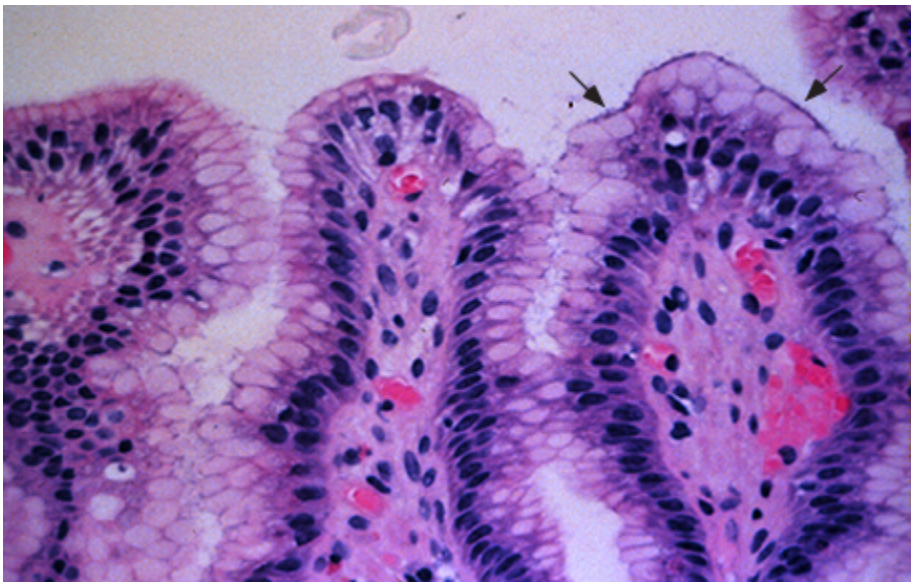


Left panel: Normal surface (SE) and foveolar epithelium (FE) and glands (G). Right panel: Higher power view of the glands shows mucous cells (M) and gastrin-secreting endocrine cells (arrows).

Courtesy of Robert Odze, MD

Graphic 79895 Version 1.0

Helicobacter pylori adherence on gastric surface cells



High power view of surface and foveolar epithelium shows numerous *Helicobacter pylori* organisms lining the surface of the cells (arrows).

Courtesy of Robert Odze, MD.

Graphic 63916 Version 2.0

Contributor Disclosures

J Thomas Lamont, MD Equity Ownership/Stock Options: Allurion [Weight loss]. Consultant/Advisory Boards: Teledoc [Gastrointestinal diseases]. All of the relevant financial relationships listed have been mitigated. **Mark Feldman, MD, MACP, AGAF, FACG** No relevant financial relationship(s) with ineligible companies to disclose. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→