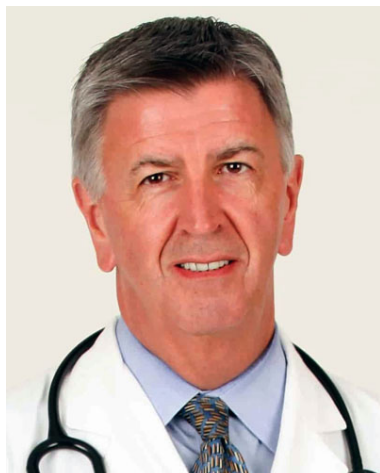


Helicobacter pylori: Current Treatment Options and Challenges

A Q&A With Colin W. Howden, MD



COLIN W. HOWDEN, MD

Hyman Professor of Medicine

Chief, Division of
Gastroenterology

University of Tennessee Health
Science Center

The American Journal of Managed Care® (AJMC®): What treatment options or regimens for *Helicobacter pylori* exist that are not reflected in the 2017 American College of Gastroenterology (ACG) guidelines?

HOWDEN: The most important one that's not present in the 2017 ACG guideline is the triple combination of rifabutin, amoxicillin, and omeprazole, which was approved by the FDA in late 2019. It wasn't included in the 2017 guideline because we didn't have data about its efficacy at that time. Also of note is a clinical trial using the potassium-competitive acid blocker vonoprazan, which is not currently approved in the United States, with either amoxicillin alone or with the combination of amoxicillin and clarithromycin. Top-level results from that should be available shortly. No other established treatments have become available since 2017.

AJMC®: Which treatment regimens are currently used most often to treat *H pylori*?

HOWDEN: I don't know the exact rates at which they are used, but I suspect that the so-called legacy triple therapy (proton pump inhibitor [PPI], amoxicillin, clarithromycin) is still the most widely used regimen in this country. It was endorsed in the 2017 guideline with certain reservations: It should not be used in patients who have previously received a macrolide antibiotic for any reason; it should also not be used unless you know that the patient comes from a region where clarithromycin resistance is below 15%. If people actually followed those recommendations, legacy triple therapy would hardly be used at all, but that's not the case. Bismuth-based quadruple therapy (bismuth, a PPI, tetracycline, and metronidazole) is also widely used. Unfortunately, it can be difficult for patients to take because it contains 4 different medicines and several tablets to be taken daily, so it can be confusing and difficult for patients to follow. The rifabutin-based regimen is a combination capsule. It should be straightforward for patients to take, but I don't have any recent data on how widely it's being used.

AJMC®: What type of information about *H pylori* would be helpful to improving treatment outcomes?

HOWDEN: We still have a lack of information about the prevalence of resistance to commonly used antibiotics for *H pylori* infection. That's why, to some extent, the treatment of the infection is largely empiric. We usually don't know what antibiotics it might be sensitive or resistant to, and we don't know that because we have very limited access to antimicrobial sensitivity testing. If doctors were able to use simpler and more effective regimens that limited the number of antibiotics but were still efficacious in getting rid of the infection, treatment outcomes for patients with *H pylori* infection would be improved. We would also be at less risk of producing resistance among bacteria other than *H pylori*; it would be a win-win situation.

AJMC®: How challenging would it be to adopt and implement antibiotic stewardship principles to *H pylori* treatment? Do you think that clinicians would support a movement toward treating *H pylori* based upon these principles?

HOWDEN: That's difficult to answer because we need to use multiple antibiotics to treat *H pylori* infection. As I indicated, I suspect that the most widely used regimen in this country is still so-called legacy triple therapy. However, its efficacy has diminished recently because of increasing rates of clarithromycin resistance, and that has led people to use a broader combination. Instead of prescribing 3 drugs—a PPI, clarithromycin, and amoxicillin—some have gone to prescribing 4, which would be a PPI, clarithromycin, amoxicillin, and metronidazole. If we knew in advance which of those antibiotics the bug was sensitive or resistant to, based on the availability of reliable pretreatment sensitivity testing, we would be able to practice much better antibiotic stewardship than we currently are. However, we usually don't have that ability. For patients who are using that 4-drug combination, there will inevitably be some who receive an antibiotic unnecessarily. If we're treating a clarithromycin-sensitive infection, we didn't really need to give them metronidazole, and similarly, if we're treating a metronidazole-sensitive infection, maybe we didn't need to give them amoxicillin.

All physicians should be aware of the problems of increasing antibiotic resistance—not just by *H pylori* but by other organisms. I hope that physicians would welcome any chance to improve and limit their use of antibiotics where appropriate. Limiting the number of antibiotics used would simplify things for patients and physicians. Very recent data from the United States suggest that amoxicillin resistance by *H pylori* remains very low. That often comes as a surprise to nongastroenterologists who are used to seeing amoxicillin-resistant urinary and pulmonary infections, but *H pylori* is different. I can't explain why, but *H pylori* appears not to acquire resistance to amoxicillin with anything like the same frequency that some other bacteria do.

AJMC®: Given the challenges of antibiotic resistance that exist and the limited access to antimicrobial sensitivity testing, what treatments are most effective?

HOWDEN: Two regimens do not require antibiotic sensitivity testing because they don't contain clarithromycin. One is bismuth-based quadruple therapy, which consists of a PPI, bismuth, tetracycline, and metronidazole. The other is the triple combination of rifabutin, omeprazole, and amoxicillin. In the case of the rifabutin regimen, we

know from recent US data that resistance to rifabutin and amoxicillin is very low to nonexistent.

AJMC®: How significant is the association of *H pylori* infection and gastric cancer?

HOWDEN: Important developments in recent years show increasing evidence that getting rid of *H pylori* infection in asymptomatic adults is associated with reduced risk of gastric cancer. That's been relatively straightforward to demonstrate in studies conducted in Asia where there's much more *H pylori* infection, and there's probably a greater risk of gastric cancer from it. However, it may also be true in the United States.

Evidence is increasing that eradication of *H pylori* in asymptomatic adults may ultimately reduce the risk of gastric cancer in the United States.

—Colin W. Howden, MD

There was a study published in *Gastroenterology* in 2020 from the University of Pennsylvania¹ that looked at the Veterans Administration database. They found that veterans with *H pylori* infection who were successfully treated for it and had a confirmed posttreatment test of eradication ultimately had a reduced incidence of gastric cancer during follow-up compared with those who weren't treated or weren't successfully treated. There's increasing evidence of the benefits of getting rid of *H pylori*. On a worldwide basis, *H pylori* is probably responsible for more stomach cancers than both hepatitis B and C viruses combined are for hepatocellular cancers. Gastric cancer continues to be either the second or the third most common cause of cancer-related death worldwide. Most of those cancers are due to *H pylori* infection. Evidence is increasing that eradication of *H pylori* in asymptomatic adults may ultimately reduce the risk of gastric cancer in the United States. ♦

REFERENCE

1. Kumar S, Metz DC, Ellenberg S, Kaplan DE, Goldberg DS. Risk factors and incidence of gastric cancer after detection of *Helicobacter pylori* infection: a large cohort study. *Gastroenterology*. 2020;158(3):527-536.e7. doi:10.1053/j.gastro.2019.10.019