Best Practices for *Helicobacter pylori* Management

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**Abstract:** For decades, antimicrobial therapy for *Helicobacter pylori* infection has been given empirically, and the results of therapy (success or failure) have either not been confirmed or when confirmed have not been used to modify prescribing behavior. These practices coupled with increasing antibiotic resistance have resulted in low cure rates overall. Susceptibility testing for *H pylori* has increasingly become available, especially in the United States. Availability of susceptibility-based therapy has encouraged adoption of the principles of antimicrobial stewardship for *H pylori* infection (eg, limiting antibiotic choice to antibiotics for which the infection is susceptible given at optimal doses, formulations, frequency of administration, and duration). Antimicrobial regimens can now be classified as empiric therapies, susceptibility-based therapies, potentially effective therapies requiring optimization, and therapies containing unneeded antibiotics that should not be used. This article describes current best practices and recommendations for integrating culture-based and molecular-based susceptibility testing into *H pylori* therapy.

*Helicobacter pylori* was discovered during investigations of the cause of gastric inflammation.\(^1\,^2\) The focus rapidly expanded from inflammation to the gastritis-associated diseases, peptic ulcer, and gastric cancer.\(^3\) Cure of the infection was subsequently proven to heal or prevent gastritis, peptic ulcers and gastric cancer. Diagnostic tests were developed allowing rapid diagnosis. However therapy remains problematic and largely empiric rather than susceptibility-based as with other infectious diseases (Figure 1).\(^4\) The widespread use of empiric therapies despite increasing antimicrobial resistance has resulted in declining cure rates.\(^1\,^4\) Antimicrobial susceptibility testing (AST) has finally become commercially available especially in the United States,\(^5\) and susceptibility-based therapy is now being integrated into current diagnostic and treatment algorithms.\(^4\) This article focuses on implementing best practices into the routine management of *H pylori* infection.

**Keywords**

*Helicobacter pylori*, susceptibility, diagnosis, antibiotics, antimicrobial stewardship, resistance
Antimicrobial Stewardship

Antimicrobial stewardship focuses on the optimal use of antibiotics to obtain a cure. Successful therapy requires use of antibiotics or antibiotic combinations to which the infection is susceptible given at optimal doses, formulations, frequency of administration, and duration to reliably achieve high cure rates. Ideally, therapy should be tailored specifically for individual patients based on antimicrobial susceptibility data obtained by culture, molecular testing, or by knowledge and local experience to identify reliably and highly effective empiric therapies. Worldwide, the most common locally proven highly effective therapy is bismuth quadruple therapy, although dual therapy with a potassium-competitive acid blocker (P-CAB) plus amoxicillin may provide a second reliable, highly effective, and likely preferred option after undergoing local optimization. Continued use of any therapy is dependent on continuing effectiveness. Thus, treatment outcomes should always be assessed with a test of cure (e.g., urea breath test) to confirm treatment success; treatment failures should be investigated as to the cause of failure.

History of Helicobacter pylori Infection Management

The initial period of learning to treat H pylori infection involved experimentation with a wide variety of antibiotics. In 1990, the first effective therapy consisting of bismuth, metronidazole, and tetracycline (bismuth triple therapy) was identified. Later, metronidazole resistance resulted in a decline in efficacy that often could be restored by the addition of a proton pump inhibitor (PPI), producing what is now known as bismuth quadruple therapy. However, the lack of universal availability of bismuth and associated common side effects of this therapy limited its overall usefulness. When clarithromycin was introduced, its potential role for treatment of H pylori was identified, its potential role for treatment of H pylori was identified. Later, metronidazole resistance resulted in a decline in efficacy that often could be restored by the addition of a proton pump inhibitor (PPI), producing what is now known as bismuth quadruple therapy. However, the lack of universal availability of bismuth and associated common side effects of this therapy limited its overall usefulness. When clarithromycin was introduced, its potential role for treatment of H pylori was identified, its potential role for treatment of H pylori was identified. Although monotherapy was ineffective, a 3-drug therapy that contained an antisecretory drug such as a PPI, clarithromycin, and either amoxicillin or metronidazole appeared especially promising.

The development and approval of clarithromycin triple therapy by the US Food and Drug Administration (FDA) was the result of a joint effort of 2 pharmaceutical companies.

Figure 1. The current and now outdated approach to diagnosis and empiric therapy of Helicobacter pylori for patients with and without alarm features. Alarm features may include weight loss, bleeding, age greater than 50 years, and family history. Adapted from Graham DY.
Importantly, and a harbinger of current issues, resistance to clarithromycin was noted to emerge during therapy and was a common cause of treatment failure.26 This problem was attributed to the high level of *H pylori* in the stomach, which increases the frequency of spontaneous development of resistance (the inoculum effect), resulting in the presence of a mixed population of susceptible and resistant organisms at the start with the resistant organisms remaining undetected because of the low percentage (ie, heteroresistance).27

Although the addition of low-dose amoxicillin to reduce or eliminate the small populations of resistant strains initially proved an effective strategy, clarithromycin resistance developing during *H pylori* therapy has continued to plague its prescribers. Large double-blind studies of omeprazole plus clarithromycin and amoxicillin or omeprazole plus amoxicillin and metronidazole in Europe (the MACH studies) confirmed that both regimens were able to produce excellent results.28-31 Importantly, in the presence of susceptible infections, both PPIs and histamine receptor antagonists produced similar results with clarithromycin triple therapy.32,33

<table>
<thead>
<tr>
<th>Categories of therapy</th>
<th>Agents and frequency</th>
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<tbody>
<tr>
<td><strong>Empiric therapies</strong></td>
<td></td>
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<tr>
<td>Standard bismuth-based quadruple therapy for 14 days</td>
<td>Bismuth subsalicylate 2 tablets QID 30 minutes before meals</td>
</tr>
<tr>
<td></td>
<td>Tetracycline 500 mg QID after meals</td>
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<tr>
<td></td>
<td>Metronidazole 500 mg BID after meals</td>
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<td></td>
<td>PPI BID</td>
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<tr>
<td>Bismuth-based quadruple therapy for 10 or preferable 14 days (generic version available at a reduced price)65</td>
<td>Combination bismuth subcitrate potassium + metronidazole + tetracycline, 3 capsules QID 30 minutes before meals and bedtime</td>
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<tr>
<td></td>
<td>PPI BID</td>
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<tr>
<td>Rifabutin-based triple therapy for 14 days</td>
<td>Rifabutin 150 mg BID after meals</td>
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<tr>
<td></td>
<td>Amoxicillin 1 g TID after meals</td>
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<td></td>
<td>PPI BID</td>
</tr>
<tr>
<td>Branded rifabutin-based triple therapy for 14 days</td>
<td>Combination omeprazole + amoxicillin + rifabutin, 4 capsules after food approximately every 8 hours</td>
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<tr>
<td><strong>Susceptibility-based therapies (do not use empirically unless proven to cure &gt;90% locally)</strong></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin triple therapy for 14 days</td>
<td>Clarithromycin 500 mg + amoxicillin 1 g BID after meals + PPI BID</td>
</tr>
<tr>
<td>Metronidazole triple therapy for 14 days</td>
<td>Metronidazole 500 mg + amoxicillin 1 g BID after meals + PPI BID</td>
</tr>
<tr>
<td>Levofloxacin triple therapyb for 14 days</td>
<td>Levofloxacin 500 mg (am) + amoxicillin 1 g BID after meals + PPI BID</td>
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<tr>
<td><strong>Potentially effective therapies (that remain to be optimized before effective local use)</strong></td>
<td></td>
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<tr>
<td>PPI or P-CABc + amoxicillin dual therapies</td>
<td>In Western societies, these dual therapies are generally ineffective and remain to be optimized before they can be recommended.</td>
</tr>
<tr>
<td><strong>Therapies containing unneeded antibiotics (should not be used)</strong></td>
<td></td>
</tr>
<tr>
<td>All therapies with at least 1 antibiotic that offers no therapeutic benefit and only serves to increase global antimicrobial resistance</td>
<td>Concomitant, hybrid, reverse hybrid, sequential therapies, and vonoprazan + clarithromycin + amoxicillin triple therapy</td>
</tr>
</tbody>
</table>

Adapted from Lee YC, Dore MP, Graham DY.12

BID, twice daily; P-CAB, potassium-competitive acid blocker; PPI, proton pump inhibitor; QID, 4 times daily; TID, 3 times daily.

*PPI dose should at a minimum be 40 mg of omeprazole or equivalent BID (eg, 45 mg lansoprazole, 20 mg of rabeprazole or esomeprazole). If cost is equivalent, 40 mg of rabeprazole or esomeprazole BID 30 minutes before meals should be used.

bThe US Food and Drug Administration recommends fluoroquinolones be used as a last choice because of the risk of serious side effects.

cGenerally, in this era of increased antimicrobial resistance, a high-potency PPI such as esomeprazole or rabeprazole should be used and at high dose (at least 20 mg, preferably 40 mg BID); where available, vonoprazan 20 mg BID should be able to be substituted with approximately the same result.

companies, one that licensed clarithromycin and one that introduced the first PPI, omeprazole, for treatment of acid-peptic disease.26 Importantly, and a harbinger of current issues, resistance to clarithromycin was noted to emerge during therapy and was a common cause of treatment failure.26 This problem was attributed to the high level of *H pylori* in the stomach, which increases the frequency of spontaneous development of resistance (the inoculum effect), resulting in the presence of a mixed population of susceptible and resistant organisms at the start with the resistant organisms remaining undetected because of the low percentage (ie, heteroresistance).27
heavily marketed, and consensus meetings around the world were sponsored (eg, Maastricht I). As predicted based on the development trials, clarithromycin resistance rapidly became a clinical issue and by 2001, meta-analyses confirmed that clarithromycin triple therapies had become generally ineffective in Europe. In 2007, the increasing failure of clarithromycin-based therapy resulted in the Maastricht recommendation to prescribe clarithromycin only if the local resistance was less than 15% to 20%. The lack of susceptibility testing limited the application of that rule. In retrospect, a target such as eliminating its use if cure rates fell below 85% would have been more useful.

One empiric solution to treatment failure related to clarithromycin resistance was to add a third antibiotic to produce a 4-drug combination consisting of a PPI, clarithromycin, metronidazole, and amoxicillin called concomitant therapy. However, this approach violates the principles of antimicrobial stewardship, as it required that all patients receive at least 1 unnecessary antibiotic and overuse of antibiotics promotes the global spread of antimicrobial resistance. For example, concomitant therapy results in administration (misuse) of more than 60 tons of unnecessary antibiotics per million treatments. Despite this problem, concomitant is still recommended by the Maastricht guidelines, and the European registry on H pylori management (Hp-EuReg) reports that concomitant therapy is one of the most commonly used regimens among registry participants.

Both concomitant therapy and clarithromycin triple therapy containing the P-CAB, vonoprazan, which is most commonly used in Japan, contain unneeded clarithromycin (in Japan at least 80% of the clarithromycin in vonoprazan triple therapy is unneeded). Recently, vonoprazan plus clarithromycin triple therapy was tested in US and European studies and was approved by the FDA for use despite poor cure rates and the fact that the majority of patients treated received unneeded clarithromycin. Vonoprazan triple therapy had now joined concomitant therapy on the list of H pylori regimens that should not be used. Nonetheless, the excellent experience in China and Japan with vonoprazan-amoxicillin dual therapy suggests that if vonoprazan-amoxicillin dual therapy can be optimized to produce high cure rates consistently without requiring clarithromycin, it might have a major role as long as amoxicillin resistance remains low.

It is now clear that clarithromycin, metronidazole, and levofloxacain triple therapies should be abandoned in regions still lacking AST unless they are proven, and continually reconfirmed, to remain reliably highly effective. Although vonoprazan has increasingly become available worldwide, the original success in Japan with vonoprazan-amoxicillin dual therapy has not been confirmed in either Thailand or the United States and Europe, consistent with the notion that one should only rely on local or regional results. As noted above, worldwide, where bismuth is available, bismuth quadruple therapy appears to provide good to excellent cure rates. Resistance to tetracycline also remains rare; however, side effects of bismuth quadruple therapy are common, requiring patient education. It is important to note that the term quadruple therapy used in studies may refer to a combination other than traditional bismuth quadruple therapy. For example, in China, a variety of effective quadruple therapies are used in which amoxicillin or furazolidone is employed to replace a locally unavailable drug such as tetracycline.

Current Helicobacter pylori Therapies

The availability of AST makes it possible for H pylori infection to be managed using the same principles as

| Table 2. Laboratories in the United States Offering Helicobacter pylori Susceptibility Testing |

<table>
<thead>
<tr>
<th>Culture-based susceptibility testing</th>
<th>Test ID/name</th>
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</thead>
<tbody>
<tr>
<td>ARUP Laboratories</td>
<td>2006686</td>
</tr>
<tr>
<td>Mayo Clinic Laboratories</td>
<td>HELIS</td>
</tr>
<tr>
<td>Quest Diagnostics</td>
<td>16597</td>
</tr>
<tr>
<td>Labcorp</td>
<td>180885</td>
</tr>
<tr>
<td>Microbiology Specialists Inc</td>
<td>Helicobacter pylori Culture and Susceptibilities</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Molecular susceptibility testing</th>
<th>Test ID/name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo Clinic Laboratories (stool PCR)</td>
<td>HPFREP</td>
</tr>
<tr>
<td>American Molecular Laboratories (NGS of gastric biopsy tissues or stool specimen)</td>
<td>PyloriDx™/PyloriAR™</td>
</tr>
</tbody>
</table>

Adapted from Graham DY, Moss SF. NGS, next-generation sequencing; PCR, polymerase chain reaction.
other infectious diseases.\textsuperscript{12} Therapies can be considered as 4 broad categories (Table 1).\textsuperscript{12} Therapies in the first category are highly effective locally (ie, resistance is low, and effectiveness is high) and they can be used empirically (ie, without susceptibility testing). The second category includes therapies that should only be used as susceptibility-based therapies. All regimens containing clarithromycin and fluoroquinolones (eg, levofloxacin) fall into the susceptibility-based therapy category. The third category consists of potentially effective regimens that have yet to be optimized. The fourth category of therapies contains at least 1 antibiotic that provides no antimicrobial benefit and should not be used.

**Traditional Culture-Based Susceptibility Testing**

Until recently, AST required culture of the bacterium and performance of its antibiogram. This approach can provide susceptibility results for all commonly used antibiotics in a standardized way (Table 2).\textsuperscript{9} The primary limitation to this method is that gastric biopsy (or gastric tissue) is required. Although gastric sampling can be performed using a string, brush, or forceps introduced through the mouth, such methods are not widely used. Currently, sample collection is most often obtained during endoscopy where preferably at least 1 antral and 1 corpus biopsy are taken for culture. A second and practical limitation of endoscopically acquired gastric biopsies is that the clinicians and medical staff who handle the specimens must strictly adhere to the conditions required in order to maintain the viability of the organisms during transport of biopsies.\textsuperscript{9} Biopsies should be placed in specific transport media to avoid desiccation and kept at 4°C or frozen to –70°C or less in transport media to maintain viability and avoid the outgrowth of other bacteria from the gastric microbiota. In the laboratory, proper handling of the samples requires experienced technicians. The final issue is that results often do not become available until several weeks after endoscopy. Realistically, this is a minor issue as the infection has typically been present for decades, and there is no emergency to treat. Although *H pylori* are also present in stools, the bacteria are within the complex fecal microbiota and no longer viable. However, their DNA is present making molecular testing possible.

**Molecular Susceptibility Testing**

Recently, molecular techniques have become available for *H pylori* susceptibility testing.

**Polymerase Chain Reaction Assay**

Polymerase chain reaction (PCR) assays, such as real-time PCR, are based on detection of *H pylori* DNA and the mutations associated with resistance. Clarithromycin resistance mutations occur in 23S ribosomal RNA genes. The real-time PCR method includes fluorescence resonance energy transfer followed by a melting curve analysis or an equivalent. Currently, this approach is practically limited to clarithromycin susceptibility. However, the method is reliable as there are only a few mutations involved in resistance and the correlation with the phenotypic result (antibiogram) is very good.\textsuperscript{49} In the past, many laboratories did not possess a thermocycler to facilitate PCR. Following the COVID-19 pandemic, such an apparatus can be found in almost every laboratory. PCR-based methods have several advantages because DNA is relatively stable and transport conditions are not as strict as for culture. Biopsies used for a rapid urease test can also serve for this purpose, even biopsies that have been stored at room temperature for several weeks.\textsuperscript{50} The results of PCR are rapidly available as the assay can be performed in at most a few hours. Overall, the cost of performing each PCR assay is low, and several kits are commercially available in Europe and Asia. In the United States, there is often a disconnect between cost and price, and it is best to check with the specific vendor for details. Although PCR testing for clarithromycin resistance should theoretically be available in every hospital laboratory in the United States, no test kits have yet achieved FDA approval, and the test available commercially is only for stools (see Table 2).\textsuperscript{9} Currently, PCR testing of stools for clarithromycin resistance is only offered by Mayo Clinic Laboratories.

Importantly, real-time PCR testing can also be performed on stools where fragments of the bacteria (antigens, DNA) are present in low amounts. However, the success of the test requires a DNA extraction method documented to be highly effective with stools, and as noted above, a real-time PCR assay specifically designed for *H pylori* in stools is not yet commercially available for general laboratories to purchase. Because of the difficulties of extraction and the low concentration of *H pylori* DNA in stools, the sensitivity of stool real-time PCR is less than that of gastric biopsies. Finally, real-time PCR can also be performed on formalin-fixed gastric biopsies despite the possible DNA fragmentation following the fixation.\textsuperscript{51} Levofloxacin resistance is currently detected using multiplex PCR with strip hybridization currently available in kit form in Europe (GenoType HelicoDR, Hain Lifescience, Germany).\textsuperscript{52} The kit detects *H pylori* and the mutations associated with both clarithromycin and levofloxacin resistance. This method is required for fluoroquinolones because several mutations not inducing resistance can also be present. Its performance also takes longer than real-time PCR and requires a trained individual to interpret the strip. An alternative to test for
levofloxacin resistance would be an amplification and sequencing of the gyrase A gene.

Next-Generation Sequencing
Next-generation sequencing (NGS) for *H pylori* detection and antibiotic resistance has become commercially available in the United States as well as internationally. NGS has the advantage of providing resistance information for the 6 antibiotics commonly prescribed for *H pylori* infection. This method can also be used on fresh or formalin-fixed gastric biopsy tissues as well as stools. The genes currently tested for their involvement in *H pylori* resistance are shown in Table 3. Results are available in several days. Susceptibility testing using stools provides truly noninvasive testing. NGS has potential as a reflexive stool test, with samples initially evaluated with stool antigen or *H pylori*-specific PCR and negative samples being charged only a minimal fee. Positive samples would automatically be sent for AST (Figures 2 and 3).

Reflexive Molecular Stool Susceptibility Testing
If the full complement of tests becomes universally available in the future, reflexive stool testing will likely become the standard for patients who do not require endoscopy (see Figure 2). Currently, real-time PCR for clarithromycin and NGS for all 6 currently used antibiotics are available as stool tests. In this method, the stool sample is first tested for the presence of *H pylori* using a stool antigen or PCR test, both of which have been confirmed to have good reliability. Stools that test negative are reported as such, and patients are charged only for the diagnostic test. Stools with *H pylori*-positive results reflexly receive molecular testing. Pretreatment AST allows the *H pylori* antibiotic regimen to obtain the highest possible rate of success.

Selection of Antimicrobial Susceptibility Testing
The choice of AST depends on whether an endoscopy is necessary, as culture currently requires endoscopy. The majority of *H pylori*-infected individuals are asymptomatic. Nonetheless, they may be at increased risk for gastric cancer based on ethnicity, family history, physical findings, and age greater than 50 years, or they may have significant symptoms such that endoscopy is frequently indicated. Patients at higher risk typically undergo endoscopy for risk stratification, which involves gastric
mucosal biopsies for histology. Biopsies for culture and/or molecular testing can be obtained at the same time and if culture fails, the formalin-fixed paraffin blocks can still be used for molecular *H pylori* AST. It is generally agreed that a confirmed diagnosis of an *H pylori* infection should be followed by *H pylori* eradication.\(^5,7,8\) When endoscopy is not necessary, noninvasive testing using stool is preferred for AST.

**Practical Aspects of Antimicrobial Susceptibility Testing**

Antimicrobial therapies can be divided into those for which AST is optional and those for which it is required (ie, empiric vs susceptibility-based therapies as shown in Table 1).\(^12\) Empiric therapies are defined as regimens that reliably produce high cure rates locally without prior AST. Currently, the only available therapy that can be empirically used worldwide is bismuth quadruple therapy. As noted earlier, in some areas of China and in Japan, a high-dose, high-potency PPI (eg, 40 mg of esomeprazole) or vonoprazan plus amoxicillin dual therapy has also proven effective.\(^53,54\) In the United States, rifabutin triple therapy is also used empirically given that rifabutin resistance is seldom present. As noted earlier, although the original attempt with vonoprazan triple therapy in United States and Europe produced relatively low cure after optimization (ie, higher doses of vonoprazan), vonoprazan plus amoxicillin dual therapy will likely become the preferred empiric therapy.

**The Critical Role of Optimization**

The goal of optimization is to be able to reliably achieve the highest cure rates (eg, 95% or higher) practically achievable locally.\(^55\) Optimization must include all important parameters, including dosage, duration, and frequency of administration. Few, if any, *H pylori* therapies have been formally optimized. No FDA-approved *H pylori* regimen has been optimized, and in the United States, some *H pylori* regimens are only available as expensive (approximately $1000/course) proprietary-packaged medication, making optimization difficult and expensive. For example, with the traditional bismuth quadruple therapy (bismuth, tetracycline, metronidazole, and a PPI), duration is an important variable with a longer duration (ie, 14 days)

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**Figure 3.** Steps in reflexive stool testing in which positive samples are automatically sent for next-generation sequencing to provide noninvasive susceptibility testing.

Adapted with permission from Graham DY.\(^4\)

PCR, polymerase chain reaction.
preferred in the presence of metronidazole resistance.56 As noted previously, the name bismuth quadruple therapy is given to a wide variety of different formulations. In some regions of the world, 3-in-1 packages of bismuth quadruple therapy are available in which reduction of the pill burden is achieved by having the capsules also containing a second small capsule with metronidazole. Four to 7 days of bismuth quadruple therapy is sufficient in the presence of metronidazole-susceptible strains.57 The branded bismuth quadruple therapy is marketed for 10 days, whereas traditionally the therapy was administered for 14 days.58 In regions where metronidazole resistance is common, or cure rates with branded bismuth quadruple therapy are less than 95% in adherent patients, optimization of the duration could be considered to identify if a longer treatment is advantageous.59

Worldwide there has been a decline in the effectiveness of triple therapies containing a PPI plus amoxicillin and clarithromycin, metronidazole, or levofloxacin (the legacy triple therapies), resulting in them being relegated to the category of susceptibility-based therapies.59,60 With both clarithromycin and levofloxacin resistance, the affected antibiotic drops out leaving only 1 effective drug (ie, amoxicillin), and with triple therapies, producing a PPI or P-CAB plus amoxicillin dual therapy. For a population, the cure rate thus becomes the sum of the 2 remaining therapies (ie, for susceptible infections, a triple therapy, and for resistant infections, a dual therapy).61 This effect can be visualized using an H pylori nomogram (Figure 4).62 Because resistance tends to be high for clarithromycin and levofloxacin, these therapies should currently only be administered as susceptibility-based triple therapies. The cure rates with metronidazole in the presence of resistance are reduced but remain high, and the mechanism for this is not completely understood.

### Need for Routine Testing of Cure

The goals of H pylori therapy are to eradicate the infection, cure H pylori–related peptic ulcer disease, heal gastritis, and halt the progression of gastric mucosal damage to reduce, although likely not eliminate, gastric cancer risk. Cure also eliminates the carrier status of the patient, thus potentially reducing further spread of the infection.

Treatment of H pylori infection should universally be followed by a test to determine whether the therapy was successful. Noninvasive testing is available using the urea breath test or stool antigen test. Either of these tests can be coupled with AST in stools for noninvasive investigation of the possible causes of treatment failure. The susceptibility status both before and after treatment failure is the critical variable required for interpretation of the results. An example is the presence of clarithromycin resistance after therapy for a clarithromycin-susceptible infection. The emergence of resistance during therapy is a typical manifestation of the presence of heteroresistance.63

![Figure 4. H pylori nomogram illustrating the effect of clarithromycin resistance on the effectiveness of a clarithromycin and amoxicillin plus PPI triple therapy 14-day regimen. The population cure rates are high with clarithromycin triple therapy (ie, with only slight differences related to relative PPI potency). In contrast, the ability to suppress acid (PPI potency) is the major determinant of the effectiveness of the amoxicillin plus PPI dual therapy component. OE, omeprazole equivalent; PPI, proton pump inhibitor.](image-url)
In contrast, an infection that is clarithromycin susceptible both before and after therapy would imply that either the drugs were not taken properly or there was a pharmacologic problem with the regimen administered (eg, with the dose, duration, or adherence to the protocol).4

Summary

The science and technology are finally in place to transform the H pylori treatment paradigm to a new standard based on AST that aligns with antimicrobial stewardship and abides by the treatment approach for other infectious diseases. However, actualizing this transformation will require deliberate interventions to improve provider awareness regarding best practices for H pylori management and lay the foundation for susceptibility-guided treatment.58 Indeed, even if H pylori demonstrates unequivocal susceptibility to the prescribed antibiotics, these antibiotics will only be effective if the patient: consumes them; consumes them at the correct frequencies, dosages, and duration; and consumes them while concomitantly achieving appropriate gastric acid suppression (target intragastric pH of at least 6 for amoxicillin-containing regimens). Patient adherence and appropriate antimicrobial treatment (dosage, administration, duration, and intragastric acid suppression) are adjunctive tenets that are critical to successfully executing susceptibility-guided H pylori treatment. Finally, interventions are immediately needed to improve the frequency of H pylori posttreatment test of cure, which is recommended in all persons at least 4 weeks following H pylori treatment owing to rising eradication failure rates. However, the data consistently demonstrate that a nonserologic test of cure is most often not performed. Recent nationwide cohort studies in the United States have reported that as many as 76% of treated individuals have no recorded test.64 Having consistent test-of-cure data available might also facilitate the development of robust H pylori registries to monitor local eradication success rates and practice patterns, which can provide valuable information to facilitate dynamic data-driven modifications to the H pylori therapeutic approach.

Disclosures

Dr Graham is an unpaid consultant for RedHill Biopharma and Phathom Pharmaceuticals regarding novel H pylori therapies and has received research support for the culture of H pylori. He has been a consultant for Janssen Research & Development regarding potential gastrointestinal effects of drugs under development and has collaborated on research projects with American Molecular Laboratories regarding molecular diagnostics for H pylori. He is supported in part by the Office of Research and Development Medical Research Service Department of Veterans Affairs, Public Health

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