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New Guidelines for H. pylori Treatment: 2024 Updates from ACG

Dr. Buch:
Welcome to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today we will be discussing Helicobacter pylori with returning guest Dr. William Chey, lead author of ACG Guidelines' *Treatment of Helicobacter Pylori Infection*, which was published in the *American Journal of Gastroenterology* in 2024. Dr. Chey is the H. Marvin Pollard Professor of Gastroenterology, a Professor of Nutrition Sciences, and Chief of the Division of Gastroenterology and Hepatology at the University of Michigan. Welcome back to the program, Dr. Chey.

Dr. Chey:
Thanks so much for having me on again, Peter.

Dr. Buch:
I'm looking forward to our discussion. Dr. Chey, let's start by discussing how antibiotic susceptibility testing is revolutionizing the treatment of H. pylori.

Dr. Chey:
Yeah, a very important question because there are some seismic changes going on within the realm of antibiotic susceptibility testing. If you think about it, it really hasn't permeated clinical practice, and there's a reason for that. Antibiotic susceptibility testing performed using traditional culture and sensitivity techniques are difficult to conduct, expensive, and not widely available, and for those reasons, they really haven't caught on in a widespread manner in clinical practice in the United States.

Now, enter genetic testing. In the last few years, there's been a move away from traditional culture and sensitivity and more towards molecular testing techniques, like next-generation sequencing, for example, that identifies mutations in the genome of H. pylori that are associated with antibiotic resistance. And the real advantage of next-generation sequencing and other molecular techniques is the fact that you can perform the testing on fresh tissue, paraffin-embedded tissue, or even stool. Any substance, body part, or body product that contains the H. pylori genome, the organism can be used for this molecular testing, so it opens the door to much broader use of antimicrobial susceptibility testing.

Right now, molecular testing isn't widely available, and it's expensive, so for that reason it's still not going to be utilized by everybody in every situation that you're treating H. pylori. But as the price comes down and it becomes more and more available, it could be a real gamechanger in terms of when we use antibiotic susceptibility testing because in the trials that have been conducted so far, the time that antibiotic susceptibility testing is least useful is after patients have failed multiple courses of H. pylori therapy. The time where it appears to be most predictive of treatment outcome, the most useful, is actually as you're offering your first course of H. pylori therapy. So a bit different than we've talked about in the guidelines up to this point, and certainly not quite ready for primetime yet, but clinicians should keep their ear to the ground on this one because times are definitely changing. And as molecular testing becomes more and more available, the paradigm may very well shift towards earlier antibiotic susceptibility testing rather than later—the way we're doing it right now.

Dr. Buch:
Thank you. And moving on to the next question: in bismuth quadruple therapy, why is tetracycline preferred over doxycycline?

Dr. Chey:
Yeah, this is a really controversial area. In the guideline, we come out pretty firmly and say that clinicians should do everything they can to utilize tetracycline and stay away from doxycycline, but if you were in the Far East, they use tetracycline and doxycycline interchangeably in some of the countries. Unfortunately, right now, there are very few direct comparisons between bismuth quadruple

therapy containing tetracycline versus doxycycline. For the studies that do exist, there is a split decision, with some finding that there's no difference in eradication rates and others finding that the doxycycline substitution leads to a roughly 10 percent lower eradication rate, particularly in the salvaged setting compared to traditional tetracycline-containing bismuth quadruple therapy. So for the time being, since we don't have great validation data with doxycycline, we recommend that when using bismuth quadruple therapy, you try as best you can to stay with tetracycline.

Dr. Buch:
Thank you. And moving on to rifabutin triple therapy, could you comment on its effectiveness compared with bismuth quadruple therapy?

Dr. Chey:
Yeah. Rifabutin triple therapy is a real sleeper in my opinion. I think it's one of the most effective therapies that we have at our disposal, and yet it's very rarely used in clinical practice, I think primarily because of the lack of familiarity of most healthcare providers with rifabutin. But particularly at low dose, like the dose that is offered in the commercially available product containing a PPI, rifabutin, and amoxicillin, the commercially available product, the proprietary product contains a 50 mg dose of rifabutin given three times daily. At that low dose, there are very, very few side effects, and there are really no side effects associated with hemolytic anemia or some of the concerns when you're using higher-dose rifabutin. The eradication rates are really quite good with rifabutin triple therapy. In the one randomized controlled trial that was conducted in the United States, the intention-to-treat eradication rate is around 84 to 85 percent. The per protocol eradication rate is closer to 90 percent. So this is a highly effective therapy.

Now, unfortunately, we certainly don't have direct comparative studies between rifabutin triple therapy and bismuth quadruple therapy from western countries like the United States, but the eradication rates in the literature that's available worldwide appears to be fairly comparable between those two treatments. So there's a lot more data for bismuth quadruple therapy, but for the data we have with rifabutin triple therapy, it looks like a very effective alternative option to bismuth quadruple therapy, so to me, it should be viewed on equal footing to bismuth quadruple therapy.

Dr. Buch:
So let's move on. Dr. Chey, how successful is vonoprazan-amoxicillin or vonoprazan-clarithromycin-amoxicillin therapy compared with bismuth quadruple therapy?

Dr. Chey:
Well, I'll tell you, when you look at the worldwide literature on vonoprazan dual or triple therapy, it looks incredibly good. Particularly, studies from the Far East report eradication rates greater than 85 percent, some greater than 90 percent. We conducted the only large randomized controlled trial comparing vonoprazan dual therapy and vonoprazan triple therapy to traditional PPI triple therapy in western Europe and the United States and actually found that in the total study population, the two vonoprazan-based therapies were superior to PPI triple therapy. But it is important to recognize that the eradication rate with vonoprazan dual therapy was in the range of around 80 percent, and that's the intention-to-treat eradication rate. And then the eradication rate with vonoprazan triple therapy was in that range as well, around 81 percent or so. Now, that was a lot better than PPI triple therapy at 68 percent.

And by the way, that's a really important thing for everybody in the audience to take away from that important study—the eradication rate associated with PPI triple therapy when given empirically to patients with H. pylori infection in the United States is now less than 70 percent, so it will work in around two-thirds of patients. Now, it's also important to recognize that for patients that have clarithromycin-resistant H. pylori, the eradication rate is around 30% percent with PPI triple therapy, so it essentially doesn't work. So in today's day and age, in 2024—and this is what the guideline says—you really should not be using PPI/clarithromycin/amoxicillin triple therapy unless you know for certain that the organism that you're treating is sensitive to clarithromycin. You should not be using that regimen in the United States empirically in 2024.

Dr. Buch:
Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Chey about the treatment of H. pylori.

So, Dr. Chey, continuing with that theme, when should we consider vonoprazan-clarithromycin for second-line therapy?

Dr. Chey:
Yeah, that's a really good question as well because we're quite negative about clarithromycin-containing regimens as first-line therapy when treatment is given empirically. But here's the thing. Clarithromycin-containing regimens, whether it be with a PPI or even better with vonoprazan, are highly effective therapies in patients with H. pylori infection that's known to be sensitive to clarithromycin. The good news is amoxicillin resistance in the United States is really low, so you usually don't have to worry about that, but clarithromycin

resistance is probably in the range of 25 to 30 percent—even higher than 30 percent in some parts of the United States, like the South, for example—so clarithromycin resistance is quite common in the United States. And by the way, levofloxacin, quinolone resistance in H. pylori strains is also quite high, probably greater than 25 to 30 percent in the United States as well, so in the guideline, we say you should avoid using clarithromycin- and levofloxacin-containing regimens empirically. Only use those regimens when you know the organism is sensitive to either a macrolide or a quinolone. If you know that, then macrolide- or quinolone-containing regimens are excellent choices.

Dr. Buch:
Thank you. And in the last few moments of our discussion, Dr. Chey, are there other insights you would like to share?

Dr. Chey:
We've hit on most of the highlights. I think it's an exciting time because with the advent of molecular testing, it may very well be that we will be entering more of a precision therapy rather than an empiric treatment choice paradigm. Right now we're still pretty much making our best guess, choosing a regimen for a patient not based on antibiotic susceptibility but really based on our preferences, based on insurance coverage, based upon—and this is an important thing—previous antibiotic use by the patient. And that is actually a very useful thing to do if you're treating empirically, which most of us are, to ask the patient about what antibiotics they previously received. And by the way, that's not just for H. pylori. That's any antibiotics. Because remember that whether you got amoxicillin or clarithromycin for H. pylori or a sore throat, you still took that medication, and your H. pylori infection, if it was not eradicated by the antibiotic, will have a much greater likelihood of being resistant to that antibiotic that you took for whatever reason. So taking a previous antibiotic use history can help you to tailor, to choose the right therapy or the most effective therapy for the individual patient that you're caring for in your practice. So think about that. As time goes on and molecular testing becomes more widely available and less expensive, I think we'll be seeing more liberal use of antibiotic susceptibility testing as a guide to choosing therapy for patients with H. pylori infection.

Dr. Buch:
As that brings us to the end of our program, I want to thank my guest, Dr. William Chey, for sharing this important update on H. pylori treatment. Dr. Chey, it was a pleasure speaking with you again today.

Dr. Chey:
Thanks, Peter. It was wonderful to be on your show.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you next time.