

H. pylori Perspectives - Part 2

Testing Modalities—Pitfalls and Possibilities



PODCAST 53

00:03

Dr. Jane Caldwell

Hi, I'm your host Jane Caldwell. Welcome to the *On Medical Grounds Podcast*, your source for engaging, relevant, evidence-based medical information. As stated in the 2024 American College of Gastroenterology Clinical Guidelines, *Helicobacter pylori* is a gram-negative, spiral-shaped bacterium that has adapted to survive in the harsh, acidic environment of a human stomach.

H. pylori remains one of the most common chronic bacterial infections of humans worldwide and is the leading cause of infection-associated cancer globally. In this OMG interview, we will discuss *H. pylori* testing with Dr. Kileen Shier. Dr. Shier is an independent consultant and the former Senior Science Director of Microbiology and Donor Testing at Quest Diagnostics.

She is a diplomat of the American Board of Medical Microbiology and a certified medical laboratory scientist. Dr. Shier is on the editorial board for both the *American Society for Microbiology Case Studies* and the *Journal of Clinical Microbiology*. Hello, Dr. Shier. Welcome to *On Medical Grounds*.

Dr. Kileen Shier

Hello, thank you so much for having me today.

01:28

Dr. Jane Caldwell

So could you please tell us about your experience with *H. pylori* testing?

Dr. Kileen Shier

H. pylori testing is often performed in the clinical microbiology laboratory, as of course it is a bacterium. And also some of the testing involves stool samples and stool sample testing always ends up in microbiology. So I have experience at three different laboratories, all of which performed *H. pylori* testing in different capacities.

01:59

Dr. Jane Caldwell

Could you name and describe the various tests for *H. pylori*?

Dr. Kileen Shier

Sure, the gold standard test is culture. So when we think of microbiology, we often think of putting samples on media on petri dishes and seeing what grows. And we can do that with *H. pylori*, but it's not easy and it's not fast. So very few laboratories offer this, but because I was in a reference lab setting at my most recent job, we did actually offer that testing. So another test that—and I should mention that that testing uses gastric biopsy samples, and that requires an endoscopy to obtain them. Another test that's performed with

those gastric biopsy samples from the endoscopy is the rapid urease test, but that's actually performed more during the procedure, so it's not something that's usually done in the clinical laboratory. Then we also have stool antigen testing.

So that's where we receive a stool sample from the patient, and we test it for the antigens for proteins from the *H. pylori* as an indicator of the presence of the organism. And then an additional test we offer is somewhat unique. It's a breath test where actually the patients breathe into certain bags. They breathe into a bag first as a baseline, then they drink a special solution, wait the designated amount of time and then breathe into a second bag. And we actually can measure the breakdown of urea because this organism produces an enzyme called urease, and we measure that in the laboratory. And then finally there is a few laboratories that offer a serology test. The serology test really only detects if you have ever had this infection. It doesn't indicate whether you have it right now.

But that can be useful if you're thinking about does this patient have a risk factor for stomach malignancies. But in general, when we're diagnosing active infection, serology is not considered. So that's the whole breadth of testing that we currently have for *H. pylori*.

04:12

Dr. Jane Caldwell

So what are the advantages and also some of the disadvantages of each test?

Dr. Kileen Shier

Alright, so for culture, some of the advantages are you get living organism, and with that you can perform antimicrobial susceptibility testing, which can be very valuable if the patient is not responding to therapy because it guides the physician as to what antimicrobials they can use that would be effective against that patient's particular isolate. But it requires the invasive procedure of an endoscopy and those biopsies.

And the organism, unfortunately, is very fragile. It often dies in transport to the laboratory. And the testing is manual. It's not easy to do. So a lot of laboratories don't perform it, which means they send it to a reference lab, which means it takes even longer to get to the lab. And it's even more likely that the organism will unfortunately die before it gets in the hands of the laboratory. So those are some of the advantages and disadvantages of culture.

That rapid urease test...the same thing in that it detects viable organism but it requires that invasive endoscopy procedure to get the biopsies. But it's very quick. They actually can do it really before the procedure's done, but it does not provide an isolate for antimicrobial susceptibility testing. And you'll hear me list that as a disadvantage for all of, really all of the methods except culture.

When we think about the stool antigen, this is a pretty easy sample to collect. It's stool. However, you've got to get past the yuck factor of it's stool. It can be collected in the home and then taken to a draw station for testing, so for some patients that's a convenience. And it's reasonably stable. It's a very sensitive test. It does remain positive slightly longer than other tests, so it should not be used for test of cure. So, what I mean by test of cure is you don't want to treat a patient and then test them right away with the antigen test because it may still be positive from that initial infection. It doesn't go negative right away.

And then the breath test is also pretty easy to collect. It does require collection in an office or a draw station. I am told that the solution you have to drink is a little chalky and maybe not the most palatable. So, particularly when we're dealing with children who can be picky eaters, it may be a little difficult to convince them to drink this chalky solution in its entirety in a reasonable amount of time so that the test is accurate.

The other thing that is not difficult but sometimes is mistaken, is you do have to properly cap those bags, otherwise, the air leaks out in transit, and there's nothing to test when those bags get to the laboratory.

And then finally, I had mentioned serologies already. Serologies are going to detect if you've *ever* had the infection. Again, that could be useful if you're looking at *H. pylori* infection as a risk factor for other long-term consequences, but it's not useful for diagnosing active infection because it can't tell you, do you have infection now or did you have infection 15 years ago? Either way, a positive just says you've had it at some point in your life.

07:38

Dr. Jane Caldwell

Are there certain patient populations that would benefit from one test over another test?

Dr. Kileen Shier

When we think about our certain patient populations, our pediatric patients, we really like to avoid those invasive procedures where we can. So that's where the *H. pylori* antigen test and the urea breath test can really be an advantage. Now, the breath test that assumes the patient can follow instructions and tolerate drinking that chalky solution that may not be the best tasting. But another test is the stool antigen test, which is generally easy to control the collection for those pediatric patients so that we can then perform accurate testing. However, in patients that have recurrent infections, even pediatric patients, we generally recommend proceeding to the endoscopy and obtaining those gastric biopsy samples so that we can perform culture and obtain an isolate to perform that antimicrobial susceptibility testing, and find out what antimicrobial agents work for this isolate so the patient can be treated and finally get better.

08:45

Dr. Jane Caldwell

Are there situations where you would recommend multiple tests?

Dr. Kileen Shier

In general, no, the one exception is when a patient undergoes an endoscopy, we do recommend they collect multiple gastric biopsy samples and some multiple samples for culture. Because if you're going to put the patient through the discomfort of this procedure, we want to have the best sensitivity possible. So we actually recommend they collect three to five, maybe even six samples, so that even if some of the organism dies in transit, we only need one to be positive.

So it's not so much multiple tests as multiple samples when they perform that culture. But when we think about the urea breath test or the stool antigen, generally there's no need to perform multiple tests. Both are very sensitive and are going to give you the answer you need.

09:38

Dr. Jane Caldwell

Can any of these tests be performed at point of care?

Dr. Kileen Shier

That's great question. So the only point-of-care test is the rapid urease test. So it's actually designed for point of care, which means it's not actually laboratory personnel performing that test, it's going to be other health professionals and they're performing it at or near the patient's bedside. So when the endoscopy is performed and those gastric biopsy samples are obtained, one of those samples can be used to perform the rapid urease test and it has a result in less than an hour.

Now I generally recommend if you've already done the endoscopy and collected those samples, that you send those additional samples for culture so that you get the isolate and can perform susceptibility testing. You've already put the patient through discomfort; you might as well do the full testing. However, a disadvantage of culture is it does take up to 10 days. So it is kind of the opposite of point of care. It is very slow, but it's the only way to perform susceptibility testing.

Then in the middle we have our stool antigen and our urea breath test. Both of those tests take less than an hour to perform, *however*, they have to be transported to the laboratory and laboratories generally don't perform testing one at a time. We perform what's called batch testing, where we gather all of the testing for one day and set it up at the same time. So perhaps our setup time is 10 a.m. So any samples that have come in since 10 a.m. the previous day are then set up and we have all the results by 11 to 12. But if your sample came in at noon, it's got to wait until 10 a.m. the next day, or maybe it's only set up every other day. And so that's why those laboratory tests have more of an experience turnaround time of 1-2 days, even though they only actually take about an hour to perform.

11:32

Dr. Jane Caldwell

Many patients with suspected *H. pylori* are on proton pump inhibitors. Can you explain the test sensitivity risk for those patients if they don't go off these medications prior to testing?

Dr. Kileen Shier

Certainly. Proton pump inhibitors are great because they inhibit the function, if you will, of *H. pylori*. So that decreases your symptoms. The problem is most of these tests rely on functional *H. pylori* to run the test. So many of these tests are looking at, for example, urease production, so producing that urease enzyme that breaks down urea. Well, if we treat a patient with a proton pump inhibitor, that inhibits that enzyme and that process, then our tests may not work. And if we further are inhibiting the growth of that organism, then again our test may not work. Our test may fail to detect it because we are suppressing it for the patient's benefit. So unfortunately for patients, they do have to suffer a little bit of discomfort of being off of their medication before we can perform this testing, because by inhibiting the organism and its functions, we inhibit the ability of the test to detect it.

12:49

Dr. Jane Caldwell

How long does a patient have to be off the proton pump inhibitors?

Dr. Kileen Shier

I've seen various recommendations, anywhere from seven to fourteen days, I would generally recommend at least 10 days. They can take other medications to somewhat manage their symptoms while they are off those proton pump inhibitors, so that they can manage their symptoms and not experience too much discomfort by taking medications that help with their symptoms but don't suppress the function of the organism.

13:25

Dr. Jane Caldwell

During your time in the lab, what kinds of questions were you asked by clinicians about the various tests or their interpretation?

Dr. Kileen Shier

So a couple of the questions that I get, well one was more of a frustration than a question. So oftentimes I would get a call that was a clinician that had done the endoscopy, they collected the gastric biopsy samples, sent them to the laboratory, and the organism had died in transit. So we got a negative culture. And they had seen the culture on pathology slides, the organism. So they knew it was there, but by the time it got to us it had died.

And so in those cases, I would often recommend a urea breath test or a stool antigen as a way to collect samples and detect the organism in a sample type that's more stable than unfortunately those gastric biopsies are. That doesn't solve the problem if they're looking for an isolate for the susceptibility testing, but if they were only looking for a positive or negative, it it would fix that.

The other question I would get is could we perform susceptibility testing if we had done an antigen or urea breath test? And again, unfortunately the answer is no because those tests don't get a culture isolate. We don't grow the bacteria. We're testing for the indicators of the presence of the bacteria. So in those cases, again, where they need an isolate, unfortunately that does require that more invasive procedure. So those were the two most common questions that I received about *H. pylori* testing.

15:00

Dr. Jane Caldwell

So let's talk about antibiotic resistance. What have you seen over the years with antibiotic resistance testing? Is it commonly requested and have you seen any changes?

Dr. Kileen Shier

I see more interest in it. We definitely saw over the last couple of years that I was at a reference laboratory increasing interest in ordering the test with susceptibility testing. Interestingly enough, we did offer the test without susceptibility, but my feeling is if you're going to put the patient through an endoscopy and you're going to perform the culture, why wouldn't you also do the susceptibility testing?

It's like quitting the race right before you cross the finish line. You you're almost there. You might as well finish. So we definitely saw more interest in doing that more test order shifting to our test code that did include that susceptibility testing whenever we got an isolate. And then in terms of patterns, I would refer listeners to a great clinical microbiology newsletter paper published by Azad et al. in 2022, and it actually reported on the susceptibility testing results over the last several years and changes in susceptibility to different antimicrobial agents.

16:19

Dr. Jane Caldwell

That's interesting. We will be sure to add that paper to our references with the transcripts for our listeners. So I'm glad you brought up education. Are there any other areas where you would suggest education for both clinicians and their patients?

Dr. Kileen Shier

I think for patients, it's important for them to understand why we're asking them to go off their proton pump inhibitors before testing. I know as a patient, if you're going to tell me to stop taking a medication that's made my life better and made me feel better, I want a reason why. And so I think it's important for the patients to understand why and for physicians to be able to explain to them here's why we need you to do this. Here's what we can do to manage your symptoms in the meantime.

I think most people can get through discomfort if they know why and the importance of it. It's a lot harder for a patient to comply if they have no idea why they're doing what they're doing.

And then for physicians, I think just being aware of the different options. You know, my personal recommendation with a patient when you first suspect *H. pylori* is to use one of these less-invasive methods. Let's start there. These are easy to collect, they're very sensitive, they're accurate. And then only if the patient is not responding to treatment do we go that next step to the more-invasive procedure. And I think as I interacted with physicians more and more becoming aware of these less-invasive options, it's just reaching physicians who maybe have been in practice for a while and are not familiar with some of these newer methods.

17:55

Dr. Jane Caldwell

Is there anything else that I haven't asked you that you think would be relevant to our listeners?

Dr. Kileen Shier

I think we've all become aware that *H. pylori* is maybe more prevalent than we thought a few decades ago. And laboratory still plays a really important role in being able to detect that infection and then manage our patients. And we're really lucky that we actually have multiple ways to test for this organism. That's not the case with all of the infections we have, all of the bacteria that we test for. But in this case, we have a variety of options so that we can somewhat tailor it to what's best for that individual patient. And I think we're really fortunate to have those options. I'm really grateful to the diagnostic manufacturers who have gone out there and developed these different tests so we can present options to our clinicians and to our patients.

18:47

Dr. Jane Caldwell

Dr. Shier, thank you so much for taking time from your busy schedule to talk to us today.

Dr. Kileen Shier

You're very welcome. Thank you so much for having me. I really enjoyed our talk.

Jane Caldwell

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