

## Things We Do for No Reason™: Serum Serologic *Helicobacter pylori* Testing

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" (TWDFNR) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR series do not represent clear-cut conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

### CLINICAL SCENARIO

A hospitalist admits a 25-year-old woman for evaluation of a 2-day history of intractable vomiting. The patient reports a 6-month history of intermittent dyspepsia. Vital signs include a normal temperature, tachycardia with a heart rate of 115 beats per minute, and a blood pressure of 100/60 mm Hg. Laboratory studies, including a complete blood count, electrolyte panel, and serum lipase, are normal; a pregnancy test is negative. Computed tomography (CT) of the patient's abdomen and pelvis shows no abnormalities. The patient rapidly improves after 2 days with fluid resuscitation and supportive care. A serologic *Helicobacter pylori* test ordered on admission returns positive, prompting the hospitalist to discharge the patient on a course of bismuth quadruple anti-*H pylori* therapy.

### BACKGROUND

*H pylori* infection causes upper gastrointestinal symptoms and progressive gastric damage, which can lead to peptic ulcer disease and gastric cancer. When *H pylori* infection is diagnosed, the current American College of Gastroenterology guidelines recommend eradication of the infection.<sup>1</sup> Even with a waning prevalence in the United States, *H pylori* infects approximately 17% of persons aged 20 to 29 years and 57% of persons >70 years.<sup>2</sup> Widely available noninvasive testing options for detecting *H pylori* include the enzyme-linked immunosorbent assay test for immunoglobulin G antibodies (ie, serology), the stool antigen test, and the urea breath test. Invasive options include upper endoscopy with biopsy. An analysis of diagnostic testing in the United States between 2010 and 2012 showed that approximately 70% of first-time testing was serologic.<sup>3</sup>

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### WHY YOU MIGHT THINK SEROLOGIC *H PYLORI* TESTING IS HELPFUL

Providers often select serologic testing for *H pylori* because of the relative ease of obtaining a blood sample compared to obtaining samples for a stool antigen or urea breath test. Stool antigen and the urea breath tests identify active infections and require a large population of *H pylori* in the stomach. Concurrent treatment with therapies that suppress *H pylori*, such as antimicrobials, bismuth, or proton pump inhibitors (PPIs), reduces the sensitivity of those tests.<sup>4</sup> One study showed that treatment with bismuth reduced the sensitivity of urea breath and stool antigen tests to 50% and 85%, respectively, and that PPIs reduced the sensitivity of the urea breath test and stool antigen test to 60% and 75%, respectively.<sup>4</sup> The use of antibiotics, PPIs, or bismuth, however, does not affect the test characteristics of serology.

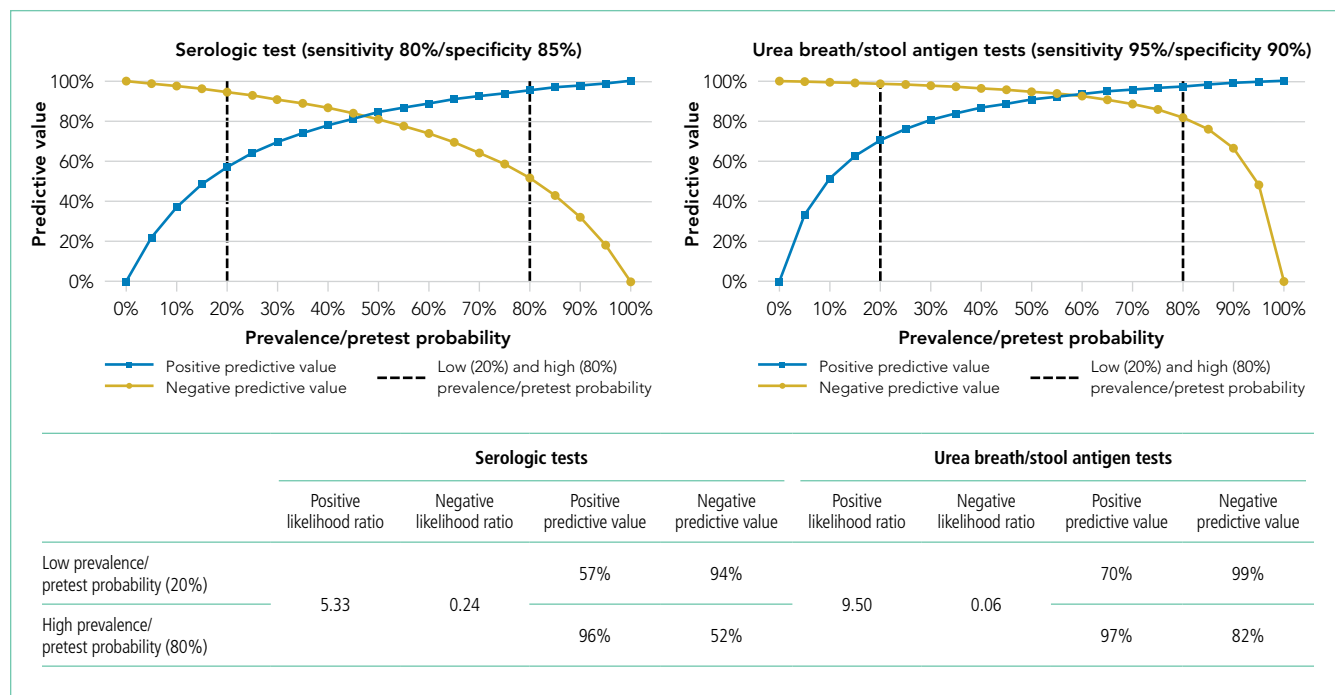
Invasive testing with endoscopy and biopsy may also yield false-negative results. For example, providers often appropriately start PPI therapy in hospitalized patients with suspected bleeding peptic ulcers. Without concurrent treatment with a PPI, the gastric histology should show the histologic hallmarks of *H pylori* (ie, acute-on-chronic inflammation), as well as the organisms. However, PPI suppression of the infection and active bleeding may reduce the sensitivity of endoscopic biopsy.<sup>5,6</sup> In one study, PPI use decreased sensitivity of histology to approximately 67% compared to polymerase chain reaction testing of the biopsy.<sup>6</sup> Bleeding peptic ulcers do not affect the accuracy of serologic testing.

### WHY SEROLOGIC TESTING FOR *H PYLORI* IS NOT HELPFUL

There are three main issues with *H pylori* serology testing: (1) decreased sensitivity of these tests compared to other noninvasive tests, (2) inability of serology tests to distinguish between past and active infection (ie, the test is not specific for active infection), and (3) wide availability and use by commercial laboratories of serologic tests that are not approved by the US Food and Drug Administration (FDA).

A multicenter trial in the United States comparing three different serologic tests for *H pylori* demonstrated sensitivities ranging from 76% to 84%.<sup>7</sup> By comparison, the main stool antigen test for *H pylori* available in the United States has a sensitivity of 93%.<sup>8</sup> A recent meta-analysis showed a pooled sensitivity of 96% for urea breath tests.<sup>9</sup> These studies demonstrate that the stool antigen and urea breath tests generally eclipse the sensitivity of the available serologic tests.

To further illustrate the issues associated with serologic testing, one may consider a population of 1000 people with an



**FIG.** Serologic and Urea Breath/Stool Antigen Testing. Predictive values and likelihood ratios of serologic and urea breath/stool antigen tests assuming serologic test sensitivity of 80% and specificity of 85% and urea breath/stool antigen tests sensitivity of 95% and specificity of 90% are shown. Dotted lines show low (20%) and high (80%) prevalence/pretest probability.

*H pylori* prevalence of 35%, the estimated overall prevalence of *H pylori* in the United States.<sup>10</sup> In this population, a serologic test with an 80% sensitivity would result in 70 false-negative results, whereas a urea breath or stool antigen test with a 95% sensitivity would yield only 18 false-negative results. These numbers change drastically with changing prevalence or pretest probability. In some low-prevalence or low-pretest probability scenarios, serologic tests offer little more than a “coin-flip” chance of detecting active *H pylori* infection (Figure).

Serologic testing offers the benefit of an immediate result, but at the cost of reduced sensitivity and specificity. The superior accuracy of biopsy and urea breath and stool antigen tests is dependent upon cessation of antimicrobials, bismuth, and PPI therapy—something that may be difficult to achieve in hospitalized patients. In the majority of cases, however, there is little evidence equating immediate diagnosis of *H pylori* with improved patient outcomes. The preferred strategy to reduce false-negative results is to defer stool antigen or urea breath testing until patients have been off antimicrobials, bismuth, and PPIs for 4 weeks.

Serologic tests for *H pylori* may remain positive for years, which decreases the specificity of these tests in confirming active or eradicated infection.<sup>11</sup> One study evaluated three different serology tests on 82 patients 6 months after confirmed eradication by urea breath test. In this study, only seven or eight patients tested negative by serology (depending on the serology test)—a specificity of 8% to 10% for active infection.<sup>12</sup> Another study showed that even after 1 year of confirmed eradication, 65% of patients remained seropositive, which equates to a specificity of 35%.<sup>11</sup> These studies illustrate that

serologic testing for *H pylori* has a very poor ability to distinguish between active and past infection.

An additional common misconception is that a positive serologic test in the absence of prior treatment for, or diagnosis of, *H pylori* indicates an active infection. Children and adults can spontaneously clear and become reinfected with *H pylori*.<sup>13,14</sup> Therefore, serologic testing for ascertaining active *H pylori* infection is unreliable.

As noted, the wide availability of non-FDA-approved serologic tests offered by commercial laboratories in the United States creates another problem for serologic testing. Most immunoglobulin A (IgA) and all immunoglobulin M (IgM) tests lack FDA approval and typically have low sensitivity and specificity. One study showed that, compared to stool antigen, IgA and IgM serologic tests had a sensitivity of 63% and 7%, respectively.<sup>15</sup>

### WHEN MIGHT SEROLOGIC *H PYLORI* TESTING BE HELPFUL?

Despite its limitations, serologic testing for *H pylori* may have a role in some situations. Clinical scenarios associated with a high pretest probability of *H pylori* infection (eg, chronic peptic ulcer disease without other risk factors) increase the positive predictive value of *H pylori* infection. In such a situation, a positive serologic test should prompt initiation of treatment, whereas a negative serologic test does not rule out *H pylori* infection (Figure). In contrast, in the presence of lower pretest probability symptoms (eg, dyspepsia), positive serologic testing has such a high false-positive rate that providers must first confirm the result with a stool antigen or urea breath test before initiating treatment.

## WHAT YOU SHOULD DO INSTEAD

For patients with alarm signs and symptoms and an indication for endoscopy (eg, bleeding peptic ulcer, iron deficiency anemia), providers should use endoscopy with biopsy to diagnose *H pylori* infection.<sup>16</sup> For patients with dyspepsia or nonspecific gastrointestinal symptoms (ie, a low pretest probability of *H pylori*) and no indication for endoscopy, providers should diagnose active infection with stool antigen or urea breath test. If possible, serologic testing should be avoided. Except in very high pretest probability clinical scenarios, positive serologic tests should be confirmed via stool antigen or urea breath test before initiating treatment. The stool antigen or urea breath test should only be ordered after patients have stopped antibiotics, bismuth, and PPIs for 4 weeks.<sup>16</sup> For patients requiring antisecretory therapy, providers can substitute histamine-2 receptor antagonists (H2RA) for the PPIs, as H2RAs do not interfere with either the stool antigen or urea breath test.<sup>4</sup> Eradication of *H pylori* infection should be confirmed through biopsy, urea breath test, or stool antigen test 4 weeks after patients have completed treatment.

## RECOMMENDATIONS

- Use stool antigen or urea breath tests to diagnose *H pylori* infection noninvasively in patients without an indication for endoscopy.
- Use endoscopic biopsy with histology to diagnose *H pylori* infection in patients with an indication for endoscopy.
- Delay stool antigen and urea breath testing until 4 weeks after patients have ceased using medications that interfere with test results (eg, antibiotics, bismuth, PPIs); H2RAs do not interfere with testing.
- In cases of a bleeding peptic ulcer with a negative biopsy for *H pylori*, retest with biopsy after the bleeding resolves or retest using stool antigen or urea breath test.
- Confirm a positive serologic test via stool antigen or urea breath test before initiating treatment except in very high pretest probability clinical scenarios.
- Test to confirm eradication with biopsy, urea breath, or stool antigen test in all cases of confirmed *H pylori* infection.
- Do not order or try to interpret *H pylori* IgA and IgM tests as they have no role in the diagnosis or management of *H pylori* infections.

## CONCLUSION

In the clinical scenario, the patient clinically improved with fluid resuscitation and supportive care. The history of unexplained dyspepsia is an indication to assess for *H pylori* infection with either urea breath test or stool antigen test. Given the positive serologic test, the provider should have retested for active infection with a stool antigen or urea breath test prior to initiating treatment.

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Do you think this is a low-value practice? Is this truly a “Thing We Do for No Reason™”? Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other “Things We Do for No Reason™” topics by emailing TWDFNR@hospitalmedicine.org.

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