



TECHNICAL BULLETIN: *Helicobacter pylori*

In the US, acute gastritis is seen in nearly half of the population and *H. pylori* is associated with the majority of those cases. Furthermore, *H. pylori* is the etiologic agent of 95% of duodenal ulcers, 70-80% of gastric ulcers, and is the cause of 60-70% of gastric cancer.¹ Since the beginning of human civilization, *H. pylori* has colonized the stomach of virtually every child and has provided a favorable impact on shaping the immune responses of children in the pre-antibiotic era. In developing countries, the relationship of this bacteria with the human host still exists and, in many ways, is still regarded as symbiotic. However, in developed countries that have improved sanitation and clean (chlorinated) drinking water, *H. pylori* is much less prevalent in the human stomach and is considered a pathogen when detected in patients with symptoms of gastritis.²



The majority of people colonized with *H. pylori* develop subclinical gastritis. Symptomatic individuals will likely consult their physician or they may begin a course of self-medication that includes OTC acid reducers, bismuth preparations, and H₂ receptor blockers such as ranitidine and famotidine. Some of these self-medications can interfere with downstream diagnostic tests (e.g. bismuth containing formulations).^{1,3}

Eradication of *H. pylori* infection is an accepted and effective strategy in treatment of gastric ulcers. Treatment commonly includes clarithromycin in addition to another antibiotic. The increased rate of antibiotic resistance, especially in clarithromycin, resulted in marked decline of the eradication rate achieved with clarithromycin-based regimens.⁴

The diagnosis of *H. pylori* infection is routinely made using one of the diagnostic tests listed in Table 1. These tests are at a disadvantage because they typically require the discontinuation of PPIs, antibiotics, and bismuth preparations for days to weeks before testing to improve the test's sensitivity. Additionally, these testing methods do not provide information regarding the presence or absence of the genetic determinants of antibiotic resistance. Most clinical laboratories do not utilize antimicrobial susceptibility testing due to the slow growth of *H. pylori* as well as the specific requirements for bacterial culture.

Table 1. Diagnostic Tests Used for *H. pylori*²

Urease Detection	Rapid, most positives seen within 2 hours	Increased sensitivity requires longer incubation.
Serology (not reliable in young children)	Non-invasive, rapid, quantitative, inexpensive.	No determination of lesions or pathology, no antimicrobial susceptibility. Not rapidly responsive to therapy. Cannot distinguish past from current infection.
Urea Breath Tests (UBT) (90% sensitivity and specificity)	Non-invasive, relatively rapid, quantitative, rapidly responsive to therapy. Most valuable for assessing response to eradication therapy after 4-8 weeks.	Involves expensive instrumentation and administration of radioisotopes. No determination of lesions or pathology, no antimicrobial susceptibility.
Stool Antigen Test	Non-invasive, EIA format, easy to automate, rapid.	Negative predictive value less than that of UBT. Variation in kits affects both PPV and NPV.
Gastric Biopsy	Invasive procedure performed during an EGD.	High PPV and NPV for <i>H. pylori</i> infection. Also essential to rule out malignancy.

A novel *H. pylori* Test (HP) was developed by Eurofins Diatherix to address limitations of current *H. pylori* diagnostic tests. The Eurofins Diatherix HP Test identifies the presence or absence of the bacteria, *H. pylori*, as well as the presence or absence of the genetic determinants strongly associated with macrolide resistance (mutations in domain V of the *H. pylori* 23S rRNA gene).⁵ The HP Test has proven to be a highly sensitive and specific diagnostic tool that can be used to detect *H. pylori* in stool.

The clinical accuracy of this assay was determined in a recent study comparing *H. pylori* detection by the HP Test vs histopathology in blinded clinical specimens from patients with suspected gastritis (Table 2). *H. pylori* was detected by the HP Test in 15 out of 110 clinical specimens, and histological staining was used to confirm HP Test results. It is important to note that in two of the clinically apparent infections, the histological examination was negative. Discrepancies between the HP Test and histologic findings were resolved using an orthogonal molecular method. Greater than half of the study population was currently taking a PPI or another acid lowering medication at the time on inclusion in the study indicating that the Eurofins Diatherix HP Test is not affected by the same degree of interference as is seen in the other diagnostic tests listed in Table 1.

Currently, there is considerable reliance on the stool antigen test for diagnosing *H. pylori* and confirming eradication. The HP Test has been validated on stool swabs with the goal to assess clinical validity of the test on a non-invasive specimen source. The performance of the Eurofins Diatherix HP Test was comparable to the Meridian ImmunoCard STAT! stool-antigen test with greater than a 100-fold improvement in sensitivity compared to the stool antigen test.

In conclusion, Eurofins Diatherix has developed a laboratory developed test utilizing TEM-qPCR technology that has been validated for stool swabs. Preliminary data suggests a 100x increase in sensitivity using TEM-qPCR as compared to standard stool antigen testing. The HP Test also includes gene targets associated with the genetic determinants of clarithromycin resistance. With some areas of the US reporting resistance in 20% or more cases, the inclusion of the resistance targets should provide increased value for the healthcare provider on whether or not to utilize clarithromycin. The clinical accuracy of this test was determined in a clinical study with an appropriate patient population, and its performance was comparable to histological detection of *H.pylori*.

Table 2. Detection results of *H. pylori* by TEM-qPCR vs histological staining.

		Histology + Molecular Confirmation		
		Detected	Not Detected	
TEM-qPCR <i>H. pylori</i>	Detected	15	0	Sensitivity: 100%
	Not Detected	0	95	Specificity: 100%
				PPV: 100%
				NPV: 100%

Reference:

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5. Nishizawa, N, Suzuki, H. Mechanisms of *Helicobacter pylori* antibiotic resistance and molecular testing. 2014 Front Mol Biosci 1: 1-7