What is the Most *Sensitive* Non-invasive Test for Initial Diagnosis of H.Pylori Infection in Adults?

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Answer: ELISA test that include both IgA and IgG

Level of Evidence: A: Studies comparing noninvasive tests to a gold standard

Search Terms: Helicobacter pylori, diagnosis, laboratory, peptic ulcer disease

Background

H. Pylori infection is common worldwide. In the United States the prevalence of infection is about 10% in adults 18 and 30 years of age and about 50% in those over 60.[1] Within any age group, infection appears to be more common in blacks and Hispanics than in whites or Asians. The risk of acquiring seropositivity is also related to lower socioeconomic status early in life.[2] Most established infections appear to persist until successfully treated.

The current gold standard for diagnosis of H. Pylori infection requires endoscopy with biopsy, an invasive procedure. The primary care physician has a number of non-invasive diagnostic options that are almost as accurate as the gold standard. These include urease-based tests of breath or stool and laboratory and office-based serologic tests.

Current or recent treatment with individual anti-H. Pylori medications, including antibiotics, PPIs, H2-blockers, and bismuth products, will reduce the sensitivity of all urease-dependent tests (urea breath tests, urea stool tests, urease biopsy tests). Patients should therefore be off of these medications for a period of two to six weeks prior to use of these tests. Serologic tests document current or previous infection. Seropositivity generally persists for 6 – 12 months after successful treatment, but it may persist for as long as two years.[3]

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Summary of the Evidence:

Serologic Tests and Urea Breath Test

We found two studies that analyzed the laboratory-based Enzyme-Linked Immunosorbent Assay /ELISA/ serology test, the office-based whole blood test, the urea breath test, and the urea stool antigen test.

The first study compared the whole blood test, urea breath test and an ELISA serologic test to a gold standard defined as a positive result on two invasive tests (histology and urease biopsy CLO™ test) in 136 people with dyspepsia recruited from the offices of 60 primary care physicians in the Netherlands.[4] One-third of the patients were diagnosed with H. Pylori infection based upon the gold standard.

Table 1. First Study Results (Measured % and 95% Confidence Intervals)

	Whole Blood Test (latex agglutination)	ELISA	Urea Breath Test UBT
Sens.	42 (28-58)	100 (94-100)	97 (88-100)
Spec.	93 (87-96)	91 (85-95)	95 (90-98)

A second study analyzed serologic diagnosis of Helicobacter pylori infection in a population with low prevalence of disease. One hundred forty-five dyspeptic patients, 18-45 years of age, were studied in an outpatient setting in Helsinki, Finland.[5] All patients were referred for endoscopy and histological examination including biopsy urease test, histology, and culture /in case of positive biopsy urease test/. Patients also underwent several serologic tests: latex agglutination serum test (Pyloriset Dry), enzyme immunoassay /EIA/(5) for IgG and IgA (Pyloriset EIA-G and EIA-A), and rapid whole blood latex agglutination test (Pyloriset Screen). The results of all three invasive tests, biopsy urease, culture and histological exam, were positive (the gold standard in this study) in 14.5% patients.

Both of the combined (IgG and IgA) EIA tests were highly sensitive and specific. The latex agglutination tests and single immunoglobulin tests were less sensitive.

The positive predictive value for either of the combined (IgA+IgG) EIA tests (in-house or Pyloriset) would be expected to increase with increasing prevalence of H.Pylori infection, ranging from about 80% at a prevalence of 10% to 95% at a prevalence of 50%.

Stool Antigen Test:

The H.Pylori stool antigen test is another non-invasive option. A study conducted in Tokyo clinics in Japan[6] evaluated an H.Pylori stool antigen (HpSA) test before and after H.Pylori eradication therapy. One hundred and thirty six dyspeptic patients (106 men and 30 women; mean age 46 years) underwent gastrointestinal endoscopy with subsequent cultures, histological examinations and rapid urease test (RUT). A urea breath test (UBT) and a HpSA test were also performed in all patients. Patients were considered to have H.Pylori infection if the cultures or both the histology and the RUT were positive. One hundred sixteen of 136 (85.3%) of the patients were H.Pylori positive based on biopsy methods. The HpSA was performed using Premier Platinum HpSA (Meridian Diagnostics, Cincinnati, OH), a polyclonal antigen test. The HpSA was positive in 115. The sensitivity and specificity of the HpSA test before therapy were 98.3% (95% CI: 95.9-100%) and 95% (95% CI: 75.1-99.9%).

Of the 116 test-positive patients, 54 underwent seven days eradication therapy. Six to ten weeks after the therapy, all 54 patients had a second endoscopy with biopsy, histology and cultures as well as urea breath test (UBT) and stool test. Patients were defined as eradicated when all four tests (histology, culture, RUT and UBT) were negative. Data was compared with stool antigen test results. The sensitivity and specificity of the HpSA test after therapy were 90% (95% CI: 55-99.7%) and 97.7% (95% CI: 93.3-100%).

Another study conducted in the United Kingdom provided a comparative evaluation of the performance of several available stool antigen tests, comparing them with gold standard (culture and histology exam).[7] One hundred and twelve adult dyspeptic patients with a mean age of 60 underwent endoscopy. Sixty-four patients were positive for H.Pylori by culture and /or histology. Stool samples of all 112 patients were obtained and stored at -20 Celcius. The Amplified IDEIA HpStAR (monoclonal) kit was more sensitive and specific than the Premier Platinum HpSA (polyclonal) test, sensitivity of 93.8% (95% CI: 88-97%) and 81.3% (95% CI: 73-87%) respectively and specificity 100% (95% CI:97-100%) and 91.7% (95% CI: 85-96%) respectively.

Table 2. Second Study Results (Measured % with 95% confidence intervals)

	Latex Agglutination Tests		
	Pyloriset Screen 10 min	Pyloriset Screen 15 min	Pyloriset Screen Dry
Sens.	62 (38-82)	76 (53-92)	86 (64-97)
Spec.	88 (82-93)	85 (78-90)	96 (91-98)

	Enzyme Immunoassays - ELISA					
	In house EIA-G	In house EIA-A	In house EIA(A+G)	Pyloriset EIA-G	Pyloriset EIA-A	Pyloriset EIA(A+G)
Sens.	95 (76-100)	52 (30-74)	100 (87-100)	90 (70-99)	67 (43-85)	100 (87-100)
Spec.	97 (93-99)	99 (96-100)	97 (93-99)	99 (96-100)	97 (93-99)	96 (91-98)

Conclusion

On the basis of this review, the most sensitive tests are the combined (IgG+IgA) ELISA serologic test. The stool antigen test is a good alternative test for pre-and post-eradication testing. It can be used as early as 6 weeks after eradication therapy. It was suggested that these findings might reflect the delayed clearance of the H.Pylori antigen after eradication therapy.[10] Serologic tests for H.Pylori remain positive for 6 to 12 months after treatment.

References:

1. Smoak BL, Kelley PW, Taylor DN. Seroprevalence of Helicobacter pylori infections in a cohort of U. S. Army recruits. *Am J Epidemiol* 1994; 139:513.
2. Graham DY, Malaty HM, Evans DG, et al. Epidemiology of Helicobacter pylori in an asymptomatic population in the United States. Effect of age, race and socioeconomic status. *Gastroenterology* 1991; 101:1495.
3. Feldman M, Cryer B, Lee E, Peterson WL. Role of seroconversion in confirming cure of Helicobacter pylori infection. *JAMA* 1998; 280(4) 363-365.
4. Weijnen CF, DeWit NJ, Numans ME, et al. Helicobacter pylori testing in the primary care setting: which diagnostic test should be used? *Aliment Pharmacol Ther.* 2001 Aug;15/8/: 1205-10
5. Oksanen A, Sipponen P, Saran S, Rautelin H. Serologic diagnosis of helicobacter pylori infection in outpatients aged 45 years or less. *European Journal of Clinical Microbiology @ Infectious Diseases,* 2001;20 (8):554-7
6. Tanaka A, Watanabe K, Tokunaga K, et al. Evaluation of Helicobacter pylori stool antigen test before and after eradication therapy. *J Gastroenterol Hepatol.* 2003;18(6):732-8.
7. Chisholm SA, Watson CL, Teare EL, et al. Non-invasive diagnosis of Helicobacter pylori infection in adult dyspeptic patients by stool antigen detection: does the rapid immunochromatography test provide a reliable alternative to conventional ELISA kits? *J Med Microbiol.* 2004; 54 (9Pt 7):623-7