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The Chemtrak Hp Chek Fingerstick Whole Blood Serology Test for the Detection of *Helicobacter pylori* Infection

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Objective: **To evaluate a new whole blood serology test (Hp Chek; ChemTrak) that detects IgG antibodies to *Helicobacter pylori*. *Methods:* The study was conducted at 10 sites within the United States. Patients undergoing upper endoscopy for dyspepsia were recruited for enrollment. Those treated for *H. pylori* infection within a year of endoscopy and those who had regularly used proton pump inhibitors, bismuth compounds, or antibiotics within a month of endoscopy were not eligible. During endoscopy, specimens were obtained from the corpus and antrum for histological examination, which was performed by a single experienced pathologist. The Hp Chek was tested using whole blood and serum. Serum was also tested with a reference enzyme-linked immunosorbent assay (ELISA) at a centralized location. Test characteristics for the Hp Chek and ELISA were calculated using histology as the "gold standard." *Results:* Two hundred eighty-seven patients (140 women and 147 men; mean age 53 ± 6 yr) were enrolled. The Hp Chek was easy to perform and yielded results 9 min after inoculation of the test cassette with whole blood or serum. When the Hp Chek used with whole blood was compared with histology as the gold standard, the sensitivity was 88%, specificity 85%, positive predictive value 83%, negative predictive value 90%, and percent agreement 86%. There were no statistically significant differences among the results obtained with the Hp Chek using whole blood, the Hp Chek using serum, or reference ELISA. *Conclusions:* The Hp Chek whole blood serology test was easy to perform and rapid and yielded performance characteristics comparable to those of a reference ELISA or the Hp Chek used with serum. (Am J Gastroenterol 1998;93:16–19. © 1998 by Am. Coll. of Gastroenterology)**

INTRODUCTION

Diagnostic tests for *Helicobacter pylori* can be divided into those that require endoscopy with gastric mucosal biopsy (rapid urease testing, histology, culture) and those that can be performed independently of endoscopy (serology, urea breath testing) (1). Serology is currently the most cost-effective means of testing for *H. pylori* infection (1). The role of *H. pylori* infection in the pathogenesis of dyspeptic symptoms in patients with no evidence of peptic ulcer disease remains poorly defined (2). However, preliminary work using decision analytical modeling suggested that it may be cost-effective to treat patients for *H. pylori* infection without evaluation with upper endoscopy (3). For this reason, it is anticipated that serology testing will become increasingly important in the management of dyspeptic patients, particularly in the primary care setting (4).

The majority of currently available serology tests for *H. pylori* rely upon the identification of specific immunoglobulin G (IgG) antibodies that can be found in saliva (5) and blood (6). Tests for the serodiagnosis of *H. pylori* in blood can be classified as quantitative (enzyme-linked immunosorbent assay [ELISA]) or qualitative. A number of qualitative tests that are easy to perform and inexpensive are now commercially available (7, 8). These tests were originally developed for use with serum, but recently, several companies have introduced products intended for use with whole blood. Unfortunately, the sensitivity of the current generation of whole blood serology tests has been inconsistent (9–12).

We conducted a multicenter trial to evaluate the test characteristics of a new whole blood serology test manufactured by ChemTrak (Hp Chek, formerly the "Accumeter"; Sunnyvale, CA). Results obtained with the Hp Chek were compared with histology and with a reference ELISA.

MATERIALS AND METHODS

Patient population

This study was conducted at 10 geographically diverse sites in the United States. Study sites included seven community gastroenterologists' offices, two university medical centers, and one VA Medical Center. Patients undergoing upper endoscopy for dyspeptic symptoms were recruited for enrollment. Those who had received treatment for *H. pylori*

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infection within a year of endoscopy were not eligible for this trial. Therapy with proton pump inhibitors, bismuth compounds, metronidazole, amoxicillin, or tetracycline within 1 month of upper endoscopy also excluded patients from enrollment. Patients who had undergone previous gastric surgery, except oversewing of a perforation, were not enrolled in this study. All participants provided written informed consent. This protocol was approved by the Institutional Review Board at each participating hospital.

Study protocol

At the time of upper endoscopy, all study patients underwent gastric mucosal biopsy for histological examination (two corpus and two antrum). Biopsy specimens were placed in formalin and transported to a centralized location (Houston VA Medical Center, Texas) for histological evaluation by a single experienced pathologist using the Genta stain (13).

Immediately after upper endoscopy, the patients underwent whole blood serology testing with the Hp Chek test cassette. For this test, a drop of blood obtained by fingerstick was placed directly into the sample well of the test cassette. As sample flowed through the blood separation device in the cassette, red cells were selectively removed. Approximately 1 min after administration of the blood sample, the cassette tab was pulled, initiating the test procedure. Over the next 9 min, a colored front migrated up the testing window, followed by a clear front of wicking reagent. Each test cassette also had an internal positive control containing immobilized human IgG antibodies to *H. pylori*. A positive control indicated that the test cassette operated properly. Test results were read visually and interpreted by the presence of one red line (positive control, negative test = negative study) or two red lines (positive control, positive test = positive study) in the testing window. Operators reported that the test was easy to perform and interpret.

In addition to the fingerstick whole blood serology test, the patients donated 15 ml of whole blood by standard venipuncture. This whole blood sample was centrifuged promptly, and a drop of serum was tested with the Hp Chek using a protocol similar to that described above.

Another aliquot of serum was frozen and sent to the clinical laboratory at ChemTrak (Sunnyvale, CA) for testing with a reference ELISA (HM-CAP; Enteric Products Inc, Stony Brook, NY). Reference ELISA testing was performed according to the manufacturer's package insert by an experienced microbiologist.

Interpretation of data and statistical analysis

Sensitivity (true positive [TP]/TP + false negative [FN]), specificity (true negative [TN]/TN + false positive [FP]), positive predictive value (PPV; TP/TP + FP), negative predictive value (NPV; TN/TN + FN), and percent agreement were determined for the Hp Chek with whole blood and serum and for the reference ELISA using histology as the "gold standard." Test characteristics were also determined for the Hp Chek with whole blood and serum using the reference ELISA as a basis for comparison. Finally, test characteristics are also presented for the Hp Chek using whole blood when discrepent histology results were resolved with the reference ELISA. Test characteristics were compared for statistically significant differences using a 2-way analysis of variance.

TABLE 1

Performance Characteristics of the Hp Chek With Whole Blood or Serum and a Reference ELISA Using Histology as the Gold Standard

	Sensitivity	Specificity	PPV	NPV	% Agreement
Hp Chek (Whole blood)	88%	85%	83%	90%	86%
Hp Chek (Serum)	88%	84%	82%	89%	86%
ELISA*	92%	79%	79%	92%	85%

Sample consists of 287 patients undergoing upper endoscopy for dyspeptic symptoms. PPV = positive predictive value; NPV = negative predictive value; % agreement = percentage of patients who had the same *H. pylori* status as established by the Hp Chek or ELISA and histology.

* HM-CAP; Enteric Products Inc., Stony Brook, NY.

RESULTS

Patient characteristics

Two hundred eighty-seven patients (140 women and 147 men; mean age 53 ± 6 yr) enrolled in this trial. The study population was 72% white, 14% Hispanic, 11% African American, 2% Asian, and 1% other. Histological evidence of *H. pylori* infection was found in 131 patients (46%).

Hp Chek test characteristics

When the Hp Chek used with whole blood was compared with histology as a gold standard, the sensitivity was 88%, specificity 85%, PPV 83%, NPV 90%, and percent agreement 86% (Table 1). The Hp Chek with serum produced similar values for sensitivity, specificity, PPV, NPV, and percent agreement of 88%, 84%, 82%, 89%, and 86%, respectively. Corresponding values for sensitivity, specificity, PPV, NPV, and percent agreement with the reference ELISA using histology as a gold standard were 92%, 79%, 79%, 92%, and 85%. There were no statistically significant differences among the test characteristics obtained with the Hp Chek using whole blood, the Hp Chek using serum, or the reference ELISA.

When the reference ELISA was used as the gold standard, the Hp Chek performed with whole blood had a sensitivity of 87%, specificity of 95%, PPV of 95%, NPV of 87%, and overall agreement of 91%. Test characteristics of the Hp Chek using whole blood and serum relative to the reference ELISA are presented in Table 2. Agreement between Hp Chek results obtained from whole blood *versus* serum was 97%.

When discrepant results with histology were resolved using ELISA, test characteristics of the Hp Chek using whole blood improved to a sensitivity of 93%, specificity of

TABLE 2
Performance Characteristics of the Hp Chek With Whole Blood or Serum Using Reference ELISA as a Basis for Comparison

	Sensitivity	Specificity	PPV	NPV	% Agreement
Hp Chek (Whole blood)	87%	95%	95%	87%	91%
Hp Chek (Serum)	87%	95%	95%	87%	91%

Sample consists of 287 patients undergoing upper endoscopy for dyspeptic symptoms. PPV = positive predictive value; NPV = negative predictive value; % agreement = percentage of patients who had the same *H. pylori* status as established by the Hp Chek and ELISA.

98%, PPV of 98%, NPV of 93%, and overall agreement of 95%.

DISCUSSION

In this age of cost consciousness and practice guidelines, the management of patients with dyspeptic symptoms and no warning signs (such as advanced age, weight loss, evidence of bleeding or anemia, or progressive, unrelenting symptoms) continues to be a topic of heated debate. Using decision analytical modeling, some investigators have suggested that it would be most cost-effective to treat this population empirically for *H. pylori* infection (3). However, it is clear that such a strategy would lead to the unnecessary treatment of the majority of dyspeptic patients, as <50% are infected with the organism (14, 15). In addition, some of the presumptions necessary for such decision analytical modeling were made before the availability of inexpensive, office-based serology kits to detect *H. pylori* infection. The introduction of such tests could have a profound influence on the cost-benefit ratio of identifying infected patients before initiating therapy, particularly in the primary care setting.

Recently, several manufacturers have introduced rapid, office-based serology tests that can be performed using whole blood. There is no dispute regarding the convenience of these tests. However, the published literature addressing the performance characteristics of these tests has yielded inconsistent results (9–12). We report the test characteristics of a new fingerstick whole blood serology test, the ChemTrak Hp Chek. The Hp Chek relies upon the principle of immunochromatography to identify specific IgG antibodies to *H. pylori*. The Hp Chek proved easy to perform and yielded a positive or negative result within 10 min of inoculation with whole blood or serum.

Using histology as a basis for comparison, the Hp Chek yielded a sensitivity, specificity, PPV, and NPV comparable to those of a reference ELISA. Test characteristics of the Hp Chek were at least equivalent and arguably superior to those of other rapid, whole blood serology tests evaluated in recent studies (9–12). Agreement between results obtained with the Hp Chek using whole blood *versus* serum was 97%, suggesting that these two means of performing the test are interchangeable. In addition, we believe that the ethnic and geographical diversity of the patient population studied makes our observations that much more credible. Given the heterogeneity in *H. pylori* strains (16) and differences in the prevalence of infection among patient populations (17), one wonders whether a lack of ethnic and geographical diversity may explain, at least in part, the discrepant results found in previous studies evaluating other whole blood serology tests.

We used histology as the gold standard for this protocol. This method of identifying *H. pylori* infection is certainly not infallible. It is clear that the histological diagnosis of *H. pylori* infection can be negatively influenced by a lack of experience on the part of the interpreting pathologist, the recent use of various drugs (including antibiotics, bismuth-containing compounds, and proton pump inhibitors), and the protocol used to obtain gastric mucosal biopsy specimens (1). We attempted to address each of these variables in the study protocol. First, histological examination was performed by a single experienced pathologist using the Genta stain (13). Second, we excluded patients treated for *H. pylori* within a year of endoscopy and those recently treated with antibiotics or proton pump inhibitors. Finally, we used a standardized biopsy protocol, which included obtaining two biopsy specimens from both the corpus and antrum in each patient at all study sites. Given these precautions, the literature suggests that the sensitivity and specificity of histology would approach or exceed 95% (1, 18, 19).

In conclusion, the Hp Chek is a rapid, easy-to-perform serology test that can be used to examine whole blood or serum for the presence of IgG antibodies to *H. pylori*. The Hp Chek achieved test characteristics similar to those observed with a reference ELISA. This test should provide an accurate means of screening symptomatic patients for *H. pylori* infection in the office setting.

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