The 13C-urea breath test provides accurate, noninvasive diagnosis of active *Helicobacter pylori* infection and can document posttherapy cure. This study evaluated point-of-care testing with onsite sample analysis with the use of a desktop infrared spectrophotometer. Ambulatory patients (N = 320) underwent 13C-urea breath testing, and breath samples were analyzed immediately by clinic staff with no prior breath testing experience. Duplicate samples were sent to a reference laboratory, and the results of both methods were compared. Point-of-care testing was simple, with an overall agreement of 99.1%. Accurate near-patient 13C-urea breath testing is now practical in the primary care setting even when done by inexperienced personnel.

**KEY WORDS** Helicobacter pylori, diagnosis, point-of-care analysis, clinical trial *(J Fam Pract 2002; 51:1030–1033)*

**H**elicobacter pylori infection is etiologically associated with chronic gastritis, peptic ulcer disease, and gastric cancer.1–5 *Helicobacter pylori* infection is also a consideration in the evaluation of uninvestigated or undifferentiated dyspepsia.6,7 The steps in the management of *H pylori* infection include diagnosis, choice of appropriate therapy, and confirmation of cure.8,9 Diagnosis and confirmation of cure require diagnostic testing, and the recent consensus has been in the direction of noninvasive testing.4,5

The urea breath test (UBT) is generally considered the clinical, gold standard, noninvasive test for detection of active *H pylori* infection.9 The intragastric hydrolysis of orally administered urea by *H pylori* urease produces a change in the isotopic ratio (13CO2/12CO2) in the breath.10 The 13C-UBT has been approved by the US Food and Drug Administration for pre- and posttherapy testing.11,12

Recently the 13C-UBT has been shortened and simplified by the use of a citric acid test meal and a tertiary care clinical laboratory site. The study was done between July and September 2001. Consecutive patients were enrolled in the study if they expressed interest in participating and met the inclusion and exclusion criteria. Each site was provided with an infrared spectrophotometer, a breath gas transfer device, and commercially available UBT breath test collection kits (Meretek Diagnostics, Nashville, TN). Each kit contained a 13C-urea solution (125 mg in 75 mL of water), test meal pudding, and a specimen return box containing 4 bar-coded, evacuated 10-mL sample tubes. Before enrollment, all methods have been done in the United States.

This study examined the utility of UBT testing by comparing infrared spectrophotometry with traditional gas isotope ratio mass spectrometry in the primary care environment. Our hypothesis was that the results obtained from the primary care clinics would be as accurate as those obtained from the commercial laboratory or the more experienced hospital-based clinical laboratory.

**METHODS**

This was a multicenter, prospective study designed to compare a new infrared spectrophotometer (UBIT-IR300, Otsuka Pharmaceuticals, Tokyo, Japan) for measuring 13CO2 enrichment in breath with gas isotope ratio mass spectrometry (ABCA, Europa Scientific, Cheshire, UK). Subjects were recruited at the offices or clinics of 4 physicians’ including an indigent care primary care clinic, a hospital-based gastroenterology clinic, a private practice internal medicine office, an academic family medicine clinic, and a tertiary care clinical laboratory site. The study was done between July and September 2001. Consecutive patients were enrolled in the study if they expressed interest in participating and met the inclusion and exclusion criteria. Each site was provided with an infrared spectrophotometer, a breath gas transfer device, and commercially available UBT breath test collection kits (Meretek Diagnostics, Nashville, TN). Each kit contained a 13C-urea solution (125 mg in 75 mL of water), test meal pudding, and a specimen return box containing 4 bar-coded, evacuated 10-mL sample tubes. Before enrollment, all
study personnel received approximately 1 hour of training in the performance of the test and use of the equipment.

Study procedures
Subjects included in the study were medically stable, ambulatory patients between 18 and 75 years old who were asymptomatic or experiencing dyspepsia. Potential subjects were excluded from study participation if they took bismuth preparations, antibiotics (ie, amoxicillin, tetracycline, metronidazole, clarithromycin, or azithromycin) or any anti-ulcer medication in dosages indicated for ulcer disease (ie, proton pump inhibitors, type 2 histamine blockers, or misoprostol) within 2 weeks before the study breath test. Exclusion criteria also included participation in a drug study within 4 weeks, treatment for eradication of H pylori within 4 weeks of the study breath test, or a history of gastric surgery or vagotomy for ulcer disease except simple closure of a gastric perforation.

The protocol was approved by the local Institutional Review Board for Human Studies, and all subjects provided written informed consent. Testing began with a minimum 4-hour fast from solid food. Breath samples were obtained in disposable, balloonlike, breath collection bags designed for use with the infrared spectrophotometer. One sample was obtained immediately before ingestion of the 13C-urea test solution, and the second was collected 30 minutes after substrate ingestion. Paired sample aliquots were taken for separate analyses. Results from local infrared instruments were blinded to the central laboratory.

Statistical analyses
Each primary care site was asked to enroll subjects until 80 positive cases were identified from among all sites. The clinical laboratory site tested a minimum of 30 positive and 30 negative cases. The primary endpoint was the percentage of agreement (overall and within positive and negative cases separately) of results from both methods. Delta-over-baseline (DOB) enrichment values below 2.4 per mil were deemed negative and values greater than or equal to 2.4 per mil were deemed positive. The predicate reference method was gas isotope ratio mass spectrometry. Equivalence was defined by the percentage of agreement for positive and negative cases based on gas isotope ratio mass spectrometry results of at least 95%, and the lower limit of the 95% confidence interval was based on a percentage of agreement of at least 90% for positive cases.

RESULTS
The primary care centers enrolled 258 subjects and the clinical laboratory enrolled 64 subjects, for a total of 320 subjects. Each site enrolled a minimum of 30 positive and 30 negative cases. The overall agreement was 99.1% (95% confidence interval, 97.3–99.7); positive agreement, 98.2% (95% confidence interval, 94.2–99.7); negative agreement, 99.5% (95% confidence interval, 97.3–99.9). Kappa statistic = 0.98.

Table: Comparison of results between IRMS and GIRMS

<table>
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<tr>
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<th>IRMS, %</th>
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</tr>
<tr>
<td>Total</td>
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*Overall agreement, 99.1% (95% confidence interval, 97.3–99.7); positive agreement, 98.2% (95% confidence interval, 94.2–99.7); negative agreement, 99.5% (95% confidence interval, 97.3–99.9). Kappa statistic = 0.98.

GIRMS, gas isotope ratio mass spectrometry; IRMS, infrared mass spectrophotometry.

Graph A highlights data points occurring near the diagnostic cut-off value of 2.4 delta-over-baseline (DOB) and compares results from gas isotope ratio mass spectrometry (GIRMS) with results from infrared mass spectrophotometry (UBiT-IR300). Graph B shows all data for the study population.
enrollment of 322. The subjects’ mean age was 41.5 years (range, 18–70 years), with 88 black non-Hispanics, 106 Hispanics, 92 whites, 32 Asian/Pacific Islanders, and 4 other ethnic groups. There were 215 women and 107 men. Approximately 18% had active or previous gastrointestinal ailments, including previously diagnosed *H pylori* infection (11%) and peptic ulcer disease (3%).

There was excellent agreement between methods (Table), with an overall agreement of 99% (95% confidence interval, 97.3–99.7). Two subjects were excluded from the analysis of the primary and secondary endpoints because 1 or both assay values were missing. The data showed close correlation between methods among all sites (Figure). Evaluation by the personnel who performed the tests and analyses indicated that the office procedure was easy and noninvasive.

There were 3 disagreements between the results obtained with the devices, 1 from the gastroenterology site and 2 from the clinical laboratory site. All results were near the cutoff value.

**DISCUSSION**

13C-urea breath testing is an accurate diagnostic method for the detection of *H pylori* infection12-19-21 and point-of-care assessment of curative therapy. This study confirmed the hypothesis that the infrared instrument is an easy to operate alternative to the original sendout analyses. Rapid turnaround allows for decisions regarding therapy to be made at the time of care. The currently approved UBT in the United States does not require fasting from solid food for longer than 1 hour.

Noninvasive alternatives to UBT include serology and stool antigen testing. Serology assays cannot discriminate between active and recent past infections. Stool antigen testing requires patient compliance with specimen collection and is a sendout test. In general, although studies using pretreatment stool antigen tests have shown sensitivity and specificity comparable to those of histology or UBT, it has become evident that there can be considerable lot-to-lot variation in stool antigen tests.2 The most likely explanation is that the polyclonal serum used for the capture antibody is obtained from rabbits and thus difficult to standardize.25 Stool antigen testing has also proven to be less reliable when used soon after the end of therapy, and it is now generally recommended that one must wait 6 or 8 weeks after therapy when using the stool antigen test to confirm eradication. For example, a recent study had a false negative rate of 12.5% (95% confidence interval, 1.5–33%). Recent recommendations are that the UBT is preferred where available.4

The US Food and Drug Administration recently cleared the UBT-IR300 instrument for use with the commercial 13C-UBT. The costs of the UBT are but a fraction of those of endoscopy, not including indirect patient costs. Office-based testing has a separate reimbursement for testing, and overall the costs appear less than those of the stool antigen test. Economic impact studies comparing the tests are planned. Office-based infrared analysis for 13C makes near-patient or point-of-care UBT and analysis practical and should make accurate diagnosis of active *H pylori* infection readily available.

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**REFERENCES**