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NOTES

Evaluation of a Rapid Urease Test To Detect *Campylobacter pylori* Infection

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Seventy-five consecutive patients referred for upper gastrointestinal tract endoscopy were evaluated for *Campylobacter pylori* infection by pathology, culture, and a biochemical test to detect bacterial urease. Forty-eight patients (64%) had *C. pylori* present based on pathology or culture or both. Thirty-two urease tests were positive after 1 h, all in patients with *C. pylori* detected by the two other methods (specificity, 100%; sensitivity, 67%). After 24 h, 47 urease tests were positive, but only 40 had *C. pylori* present (specificity, 74%; sensitivity, 83%). When read after 1 h, the urease test was highly specific and led to rapid presumptive diagnosis.

A distinct form of spiral-shaped bacilli has been identified as a potential etiologic agent in the pathogenesis of gastritis and ulcers (2, 7). This organism is currently called *Campylobacter pylori*, but may belong to a distinct new genus (16). *C. pylori* can be identified in gastric tissue specimens by culture and histologic staining techniques. Both of these are time-consuming, and a rapid test that can accurately identify *C. pylori*-infected patients would expedite therapeutic decisions. Several investigators have tried to use the strong urease reaction of *C. pylori* by placing fresh antral tissue in Christensen's urea broth and observing it for a change in color, which would indicate the presence of urease (1, 3, 4, 14). However, there are several reports of false-positive results with this technique (4, 5). In some of these studies, the indicator broth was incubated at room temperature (4, 14) and read after 24 h (4, 5, 14). To improve the specificity of the urease test, we investigated a method of combining incubation at 37°C with a 1-h cutoff time for reading.

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Seventy-five consecutive patients referred for upper gastrointestinal tract endoscopy were studied. All patients were symptomatic, mostly with upper abdominal discomfort or pain. Clinical preendoscopic diagnoses included peptic ulcer disease, gastritis, and nonulcer dyspepsia. Two antral biopsies were obtained from each patient for culture and histology. Biopsies were cultured on brain heart infusion agar containing 7% horse blood and 1% IsoVitaleX and incubated in a 10% CO_2 atmosphere (9). Histopathologic specimens were stained with Giemsa stain (10) and observed for presence of characteristic 2.5-μm-long, spiral-shaped organisms as originally described by Marshall (12). An additional fresh biopsy was placed in 0.5 ml of urea broth (Remel, Lenexa, Kans.) containing 2% urea and 0.001% phenol red and was immediately incubated at 37°C. After 1 h, the broth was inspected for a change in color. Yellow was interpreted as negative, indicating absence of urease. Red or pink was interpreted as positive. For comparison, a similar reading of each biopsy was also performed after 24 h. Results of the urease test were compared with culture results and histology. *C. pylori* was considered present if organisms with the previously described characteristic appearance (12) were seen after Giemsa staining or if *C. pylori* was cultured from the biopsy. All positive cultures had oxidase-positive, catalase-positive, and urease-positive organisms with characteristic morphology after Gram staining (9). Tissue sections were interpreted by two independent pathologists who were unaware of the results of the urease test.

Of the 75 patients, 48 (64%) were found to have *C. pylori* in their antral biopsies by either culture (23 of 75 [31%]) or Giemsa staining (47 of 75 [63%]). Of the 23 culture-positive biopsies, 22 were also positive by pathology. One biopsy was positive by culture alone, but it was from a tissue sample with a low number of organisms, which produced only six colonies on the original culture plate. An additional 25 biopsies were positive by pathology alone. There was full agreement between the readings of the two pathologists for all 75 patients. The lack of culture confirmation in 25 of the pathology-positive cases was primarily due to overgrowth of contaminants, which occurred in 16 of these 25 biopsies (64%).

Thirty-two patients had positive urease tests when read after 1 h. All of these 32 patients were among the 48 with *C. pylori* identified by biopsy or culture or both. There were no false-positive urease reactions (Table 1). The urease test specificity was 100%, and the positive predictive value was 100%. The sensitivity after 1 h was 67%, and the negative predictive value was 63%.

When the same urease tests were read after 24 h of incubation, false-positive readings occurred, as previously described by other investigators. Out of 75 patients, 47 had positive tests after 24 h, but only 40 actually had *C. pylori* present according to either culture or Giemsa staining (Table 1). Specificity after 24 h fell to 74% with a positive predictive

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TABLE 1. Urease test results after incubation of antral mucosal biopsies at 37°C for 1 and 24 h

Result of culture or histologic examination or both	No. of results of urease test after incubation for:			
	1 h		24 h	
	Positive	Negative	Positive	Negative
C. pylori present[a]	32	16	40	8
C. pylori absent	0	27	7	20

[a] One positive by culture alone, 25 positive by histology alone, and 22 positive by both methods.

value of 85%. Sensitivity was 83%, and the negative predictive value was 71%.

The goal of our study was to find a rapid test with a high specificity so that patients with *C. pylori* infections could be accurately identified without having to wait up to a week for results of culture or pathology tests. We used a small volume of reagent, 0.5 ml, to achieve a high inoculum/reagent ratio. A temperature of 37°C was used to accommodate postbiopsy urease production in the event that preformed amounts were inadequate. When performed in this manner and read after 1 h, our test had the desired specificity and a positive predictive value of 100%. On the other hand, we found the 74% specificity with the alternative 24-h cutoff time to be too low for the purposes of the test.

This increased rate of false-positive readings could be caused by an instability of the reagent over time or by chemical reactions from autolysis of the tissue. Another possibility is presence of contaminants with a lower urease activity than *C. pylori*, which need prolonged incubation to cause the test to read positive. Contamination of biopsies with oral flora is not uncommon and is one of the reasons selective media are used for primary isolation of *C. pylori*. When sampled, one of our 24-h, false-positive vials did indeed contain a urease-producing contaminant. Only the last three of our late-positive vials were tested in this way, however, and we are therefore unable to estimate how frequently such contamination may occur.

The 100% specificity of our urease test was ideal for rapid identification of patients with *C. pylori* infection. However, the lower sensitivity of 67% means that some infected patients would still be missed on an initial screening. These patients would nevertheless be properly identified when results of culture and pathology tests became available. When dealing with a chronic disease such as *C. pylori*-associated gastritis, we feel that the additional wait of 4 to 7 days for proper diagnosis in these cases would not lead to any significant increase in morbidity.

Improved sensitivity might be accomplished by increasing the number of organisms free to react with the urease broth. Hazell et al. (11) have used a smaller volume of reagent (50 μl) placed in a well of a microdilution tray. With this method, they achieved a 91% sensitivity after 18 h. They did not list specific sensitivity data for readings after 1 h but noted that 75% of their positive biopsies reacted within the first hour, indicating a sensitivity comparable to ours. McNulty and Wise (15) have recommended gently mashing the biopsy with a sterile cotton swab in an attempt to disperse more bacteria into the reagent broth. This method needs further evaluation and may improve the sensitivity.

The advantages of a rapid diagnostic test with 100% specificity are obvious, and it was very satisfactory to find that the urease test performed so well at 1 h. This means that patients infected with *C. pylori* can be identified and given adequate information and instructions before they leave the endoscopy suite. Such instructions may include therapy aimed at eradicating the organism. Bismuth preparations, such as bismuth subsalicylate (Pepto-Bismol), have been shown to be active against *C. pylori* (8, 13, 17). Optimal therapy may, however, be the combination of a bismuth salt and an antibiotic (6, 17). With the help of the rapid urease test, such therapeutic modalities can be quickly and accurately instituted.

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