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Evaluation of Three Commercial Enzyme Immunoassays Compared with the ^{13}C Urea Breath Test for Detection of *Helicobacter pylori* Infection

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The diagnostic significance of the serological detection of antibodies to *Helicobacter pylori* has been established by numerous investigators. Reports of the clinical reliabilities of commercial enzyme immunoassay (EIA) kits available for this purpose vary as a result of the different *H. pylori* antigen sources and reference methods used. The ^{13}C urea breath test (UBT) has been shown to be an extremely accurate and reliable method of detecting *H. pylori* infection. We used the ^{13}C urea breath test as the confirmatory method for *H. pylori* status to evaluate three commercially available EIA kits designed to detect immunoglobulin G antibodies to *H. pylori*. These kits were the HM-CAP EIA kit (Enteric Products, Inc.), the PYLORI STAT EIA kit (BioWhittaker, Inc.), and the G.A.P. kit (Bio-Rad Laboratories/Biomerica, Inc.). The evaluations were performed in a double-blind manner with samples from 473 clinically characterized patients. This group included patients with symptomatic gastrointestinal disorders as well as nonsymptomatic volunteers. The sensitivities of the kits were as follows: HM-CAP, 98.4%; PYLORI STAT, 99.2%; and G.A.P., 100%. The specificities were as follows: HM-CAP, 96.4%; PYLORI STAT, 90.1%; and G.A.P., 26.0%. Although the HM-CAP and PYLORI STAT kits performed comparably, the G.A.P. test yielded significantly more false-positive results and an unacceptably high number of indeterminate results.

The medical importance of a causal relationship between the presence of *Helicobacter pylori* on the gastric mucosa and histologically confirmed gastritis and peptic ulcer disease has been well established. A risk association between *H. pylori* infection and the development of gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma has also been established (10, 23, 25, 31). A National Institutes of Health panel has estimated that peptic ulcer disease affects as many as 10% of people in the United States alone at some time during their lives, and this panel has recommended that all individuals with gastric or duodenal ulcers who are infected with *H. pylori* be treated with specific antimicrobial therapy to cure the infection (23). Fundamental to this recommendation is the requirement for accurate diagnosis of the infection.

A variety of methods are available for detecting *H. pylori* infection. Although biopsy has been referred to as the "gold standard" for the detection of infection, methods requiring endoscopy and biopsy are invasive and costly and can be inaccurate because of their dependence on sampling and technique (2, 18). Noninvasive methods include the ^{13}C- or ^{14}C-labeled urea breath test (UBT) and serological detection of antibodies to *H. pylori*. The UBT has been shown to be an extremely accurate method of detecting *H. pylori* infection because it has the advantage of evaluating the gastric mucosa as a whole, thereby avoiding the sampling errors inherent in biopsy (11, 17, 18, 20, 21, 34). However, the cost, time involved in testing, risk of exposure to radioactive materials, and lack of commercial availability make this method less practical for routine clinical use. Serodiagnostic methods are based on techniques commonly available in clinical laboratories and are significantly less expensive and time-consuming, making them far more practical as a diagnostic tool.

A number of serological enzyme-linked immunoassay (EIA) kits designed to detect immunoglobulin G (IgG) antibodies to *H. pylori* are commercially available. However, the reliabilities of these assays vary, making assessment of the accuracy of serology as a diagnostic tool difficult. The reported performance of these assays may vary as a result of the reference method used to confirm *H. pylori* status, the source of the antigen on which the assay is based, and the reference population studied (3, 7–9, 14, 22, 33). In this study, we evaluated the performance of three commercially available EIA kits, i.e., the HM-CAP kit (Enteric Products, Inc.), the PYLORI STAT kit (BioWhittaker, Inc.), and the G.A.P. kit (Bio-Rad Laboratories/Biomerica, Inc.), compared with the ^{13}C UBT as the reference diagnostic method. In addition, since the reliability of commercial EIAs can also be affected by manufacturing consistency, because of the fact that specific antigen preparations frequently involve a combination of multiple proteins, we evaluated consistency of performance within and between lots of kits for the HM-CAP assay.

The complexity of assay protocols can also affect the accuracy and reproducibility of assay results in the laboratory. These features are compared for the three EIA kits evaluated in this study as well.

MATERIALS AND METHODS

Study population and clinical samples. A total of 473 patients residing in the Houston, Tex., metropolitan area were included in this study. Patients were evaluated at the Texas Medical Center facilities in Houston. This group included 316 asymptomatic volunteers as well as 157 symptomatic patients who had been referred for endoscopy. Enrollment in the study was based on criteria previously described in detail by Graham et al. (12). Each patient provided information on a screening questionnaire, which included demographic information, medical history, frequency of gastrointestinal symptoms, and history of use of medications within the preceding 2 months (specifically, antibiotics, bismuth-containing compounds, or nonsteroidal anti-inflammatory drugs). Subjects were excluded

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TABLE 1. UBT results and population demographics

Patient group	% (no.):		Median age (yr)	% (no.):		Ethnic origin (% African American/ % Caucasian/% other[a])
	UBT positive	UBT negative		Male	Female	
Symptomatic	96 (150)	4 (7)	59	97 (152)	3 (5)	39/52/9
Asymptomatic	29 (93)	71 (223)	40	53 (168)	47 (148)	38/59/3
Total population	51 (243)	49 (230)	44	68 (320)	32 (153)	38/56/6

[a] Hispanic, Asian, or American Indian.

from the study if they used antacids or antibiotics regularly. In addition, asymptomatic volunteers were excluded if they had a history of a peptic ulcer or frequent (defined as more than once a month) symptoms referable to the upper gastrointestinal tract.

Patients belonging to the symptomatic group had been diagnosed by endoscopy as having one of the following conditions: duodenal ulcer, gastric ulcer, use of nonsteroidal anti-inflammatory drugs, or nonulcer dyspepsia. However, patients with ulcer disease were primarily selected, since at the time of the study, blood was routinely drawn only if an ulcer was found on endoscopy.

UBT. The *H. pylori* status of all 473 patients was confirmed by UBT according to methods previously described (12). Results of the test are either positive or negative. The UBT result was positive if the urease activity was $\geq$0.500 μmol kg^{-1} h^{-1}. The test duration was 1 h.

EIA. All patients had blood drawn for serological testing at the time of UBT. The serum was separated, aliquoted, and frozen at −70°C until the time of testing. The samples were forwarded to Enteric Products, Inc., for testing. All samples were coded so that the technicians performing the testing were blinded as to patient *H. pylori* status. EIA testing was performed for all 473 patient serum samples with the HM-CAP, PYLORI STAT, and G.A.P. EIA kits. The three kits are direct EIAs designed to detect IgG-specific antibodies to the following *H. pylori* antigens: high-molecular-weight cell-associated proteins (HM-CAP kit), a urease-enriched antigen preparation (PYLORI STAT), and partially purified *H. pylori* antigens (G.A.P.). For each kit, testing was performed and the results were calculated in strict accordance with the manufacturer's product inserts. In addition, the evaluation of the 473 serum samples was performed a total of three times with the Enteric Products HM-CAP kit. Sera were assayed twice in tandem (run 1) with two different HM-CAP kit lots (lot 1 and lot 2) and again on another day with HM-CAP kit lot 1, in order to evaluate interassay consistency within and between kit lots.

The HM-CAP enzyme-linked immunosorbent assay (ELISA) values and PYLORI STAT index values were extrapolated from linear regression curves generated on the basis of the absorbance of each kit's calibrators. The G.A.P. values (in units per milliliter) were extrapolated from a quadratic curve fit that was generated on the basis of the absorbance of the kit calibrators. High values that could not be interpolated by using a quadratic curve fit were estimated on the basis of a four-parameter curve fit ($r > 0.998$). Assay values thus calculated for each manufacturer's kit were interpreted as positive, negative, or indeterminate according to the manufacturer's instructions.

Cross-reactivity. The HM-CAP, PYLORI STAT, and G.A.P. assays were further evaluated for cross-reactivity with *Campylobacter jejuni*, *Campylobacter fetus*, *Campylobacter coli*, *Escherichia coli*, and *Helicobacter mustalae* according to the indirect procedure of Perez-Perez et al. (26). Cross-reactivity to four strains of *C. jejuni* (ATCC 43464, ATCC 43442, ATCC 43468, and ATCC 33560), three strains of *C. fetus* (ATCC 27374, ATCC 332963, and ATCC 25936), three strains of *C. coli* (ATCC 33559, ATCC 43474, and ATCC 43482), four strains of *E. coli* (ATCC 25288, ATCC 27165, ATCC 35345, and ATCC 4157), and one strain of *H. mustalae* (ATCC 43774) was evaluated. Five strains of *H. pylori* (ATCC 43504, ATCC 43579, ATCC 43526, ATCC 43629, and Baylor stock 8826) were used as positive controls. After culture in tryptic soy broth, the bacteria were collected by centrifugation at approximately 2,000 × *g* for 15 min. Bacteria were washed in phosphate-buffered saline (pH 7.4) and then resuspended in 1 ml of a positive serum pool at a bacterial concentration equivalent to $\geq 10^8$ CFU/ml. This suspension was incubated with gentle shaking for a total of 45 min at 37°C. The absorption was repeated for a total of five absorptions, with an aliquot taken after each absorption. Absorbed serum samples were stored at −70°C until testing.

RESULTS

Study population. A total of 51% of the patients (243 of 473) had positive UBT results, indicating the presence of *H. pylori*. Forty-nine percent (230 of 473) had negative UBT results, indicating the absence of *H. pylori*. The UBT results and population demographics are shown in Table 1. The majority of the symptomatic group were male because this group was drawn from patients referred to a Veterans Administration Medical Center. Ninety-six percent (150 of 157) of symptomatic referrals diagnosed by endoscopy as having gastrointestinal disease were positive for *H. pylori* infection by UBT. Seventy-five percent of UBT-positive symptomatic referrals in this study had a gastric ulcer, and 23% had a duodenal ulcer. The remaining 2% of this group either were diagnosed with nonulcer dyspepsia or were users of nonsteroidal anti-inflammatory drugs.

Twenty-nine percent of asymptomatic volunteers (93 of 316) were positive for *H. pylori* infection by UBT.

EIA. The sensitivities and specificities of the three kits compared with the UBT are shown for the population as a whole in Table 2. The HM-CAP and PYLORI STAT assays had comparable sensitivities, although the HM-CAP assay was slightly more specific than the PYLORI STAT assay. All three evaluations of the HM-CAP EIA kits were consistent, with sensitivities and specificities within 1% of those listed in Table 2. In contrast, the G.A.P. test demonstrated a high sensitivity but an unacceptably low specificity.

Indeterminate results were observed for 1.9 and 3.6% of the study group with the HM-CAP and PYLORI STAT assays, respectively. However, 17.3% of G.A.P. test results fell into the indeterminate range. Four of the nine samples that gave an indeterminate result in the HM-CAP assay also tested as indeterminate with the PYLORI STAT kit. Samples testing as indeterminate with the HM-CAP and PYLORI STAT kits

TABLE 2. Comparison of diagnostic performance of HM-CAP, PYLORI STAT, and G.A.P. assays with UBT as the standard

Assay and serology result	No. of samples:	
	UBT positive	UBT negative
HM-CAP[a]		
Positive	239	8
Negative	4	213
Indeterminate	0	9
Total	243	230
PYLORI STAT[b]		
Positive	241	21
Negative	2	192
Indeterminate	0	17
Total	243	230
G.A.P.[c]		
Positive	241	111
Negative	0	39
Indeterminate	2	80
Total	243	230

[a] Results are for lot 1, run 1. Sensitivity, 98.4%; specificity, 96.4%; positive predictive value, 96.8%; negative predictive value, 98.2%; accuracy, 97.4% (all with indeterminate results excluded).

[b] Sensitivity, 99.2%; specificity, 90.1%; positive predictive value, 92.0%; negative predictive value, 99.0%; accuracy, 95.0% (all with indeterminate results excluded).

[c] Sensitivity, 100.0%; specificity, 26.0%; positive predictive value, 68.5%; negative predictive value, 100%; accuracy, 71.6% (all with indeterminate results excluded).

accounted for only 2 of 82 of the indeterminate results observed with the G.A.P. kit. Ninety-eight percent (80 of 82) of G.A.P.-indeterminate samples were from UBT-negative patients, and these accounted for 35% of the results observed for this group.

The sensitivities of each kit when calculated for the symptomatic and asymptomatic groups separately were within 1% of the sensitivity observed for the study group as a whole. Similarly, the specificities of the three assays when calculated for the asymptomatic group were within 1% of the specificities observed for the group as a whole. Specificities could not be accurately calculated for the symptomatic group because of the low number of UBT-negative patients (4%). Additionally, because of the high rate of UBT positivity in the symptomatic group, virtually all of the false-positive G.A.P. serology results (110 of 111) were observed in the asymptomatic group. The median age of the asymptomatic group was 40 years (Table 1). The median age of those with false-positive G.A.P. results within this group was 35 years and therefore would not be expected to significantly alter the rate of seropositivity.

The frequency histograms of assay results for the HM-CAP and PYLORI STAT assays show well-defined bimodal distributions corresponding to positive and negative UBT results (Fig. 1a and b). A small proportion of the results lies between the positive and negative results and corresponds to the indeterminate range. The frequency histogram of the G.A.P. assay results also shows a bimodal distribution (Fig. 1c). However, the two populations do not correspond to G.A.P. positive and negative ranges. Instead, the UBT-negative population overlaps indeterminate and positive values. In addition, the low point between the two populations, at which UBT-positive and -negative results are relatively evenly represented, is observed in the range of approximately 30.1 to 35.0 U/ml. However, this range does not correspond to the manufacturer's stated indeterminate range. When the positive cutoff for the G.A.P. assay is raised to >35.0 U/ml, with an indeterminate zone of 30.1 to 35.0 U/ml, the specificity of the assay becomes 93.9%, the sensitivity decreases only slightly to 95.9%, but 4.9% of results still fall into the indeterminate range.

PYLORI STAT assay results correlated well with HM-CAP results, with a Pearson product-moment correlation of 0.961. A poor correlation was observed between G.A.P. assay results and HM-CAP assay results (Pearson product-moment correlation of 0.879) and between G.A.P. assay results and PYLORI STAT assay results (Pearson product-moment correlation of 0.895).

In order to determine if the high rate of false positivity observed with the G.A.P. assay compared with the HM-CAP and PYLORI STAT assays was due to cross-reactivity with other gastrointestinal organisms, all three kits were evaluated for cross-reactivity with *C. jejuni*, *C. fetus*, *C. coli*, *E. coli*, and *H. mustalae*. No cross-reactivity with these organisms was observed for any of the assays.

Various assay features for each of the three kits, including reagent preparation and assay protocols, are listed in Table 3. Overall, the HM-CAP protocol was the simplest, requiring no special plate preparation and no additional sample diluent. In addition, the calibrators, conjugate, substrate, and stop solution were all supplied prediluted and ready to use in this kit.

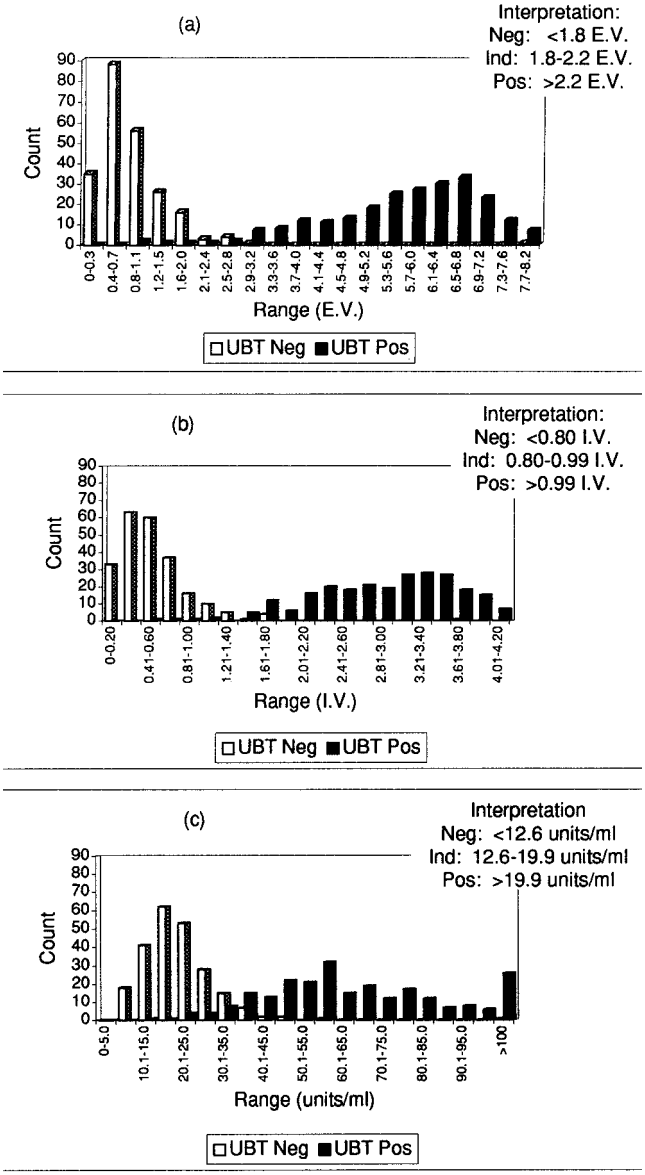

FIG. 1. Frequency distributions of EIA assay results for UBT-positive and UBT-negative patients. (a) HM-CAP assay results; (b) PYLORI STAT assay results; (c) G.A.P. assay results. Neg, negative; Ind, indeterminate; Pos, positive; E.V., HM-CAP ELISA values; I.V., PYLORI STAT index values.

DISCUSSION

Our results demonstrate that both the HM-CAP kit and the PYLORI STAT kit can reliably detect infection with *H. pylori* compared with the UBT. There was a strong correlation between the results observed with the HM-CAP kit and with the PYLORI STAT kit. However, the HM-CAP kit was more specific than the PYLORI STAT kit and gave fewer results in the indeterminate zone. Our data also showed that the HM-CAP kit performance was consistent and demonstrated the same high levels of sensitivity and specificity over time with different lots of kits. Talley et al. also demonstrated consistently accurate performance over time for a group of 76 samples with the PYLORI STAT kit (29).

The G.A.P. kit performance was not as accurate. The G.A.P. kit, although correctly identifying UBT-positive patients as infected with *H. pylori*, incorrectly identified 48% of UBT-negative patients as *H. pylori* positive. The kit also gave an unacceptably high proportion of indeterminate results, most of which were for UBT-negative patient samples.

Our results are in general agreement with those of investigators who reported that the HM-CAP and PYLORI STAT

TABLE 3. Comparison of features of the HM-CAP, PYLORI STAT, and G.A.P. assays

Feature	HM-CAP	PYLORI STAT	G.A.P.
Basic			
Method	96-well EIA	96-well EIA	96-well EIA
Antigen	HM-CAP patented antigen	Urease enriched, patent pending	Partially purified *H. pylori* antigens
Antibody detection	IgG	IgG	IgG
Reference method	UBT	Biopsy	Biopsy
Organisms with no cross-reactivity	*C. jejuni*, *C. fetus*, *C. coli*, *E. coli*	*C. jejuni*, *C. fetus*	*C. jejuni*, *C. fetus*, *C. coli*, *E. coli*
Total no. of tests per kit	93 (1 plate)	178 (2 plates)	89 (1 plate)
Shelf life (mo)	18	12	12
Assay prepn			
Serum vol (μl) required	5	10	25
Serum dilution	Yes (1/100)	Yes (1/20)	Yes (1/200)
Serum diluent	Wash buffer	Serum diluent	Serum diluent
No. of standards	3	5	5
No. of controls	4[a]	2	2
Dilution of standards	None required	Yes (1/20)	None required
Wash buffer dilution	1/20 (1,200 ml)	1/20 (2,000 ml)	1/50 (1,000 ml)
Plate prepn	No additional prepn required	Presoak	No additional prepn required
Conjugate dilution	No additional prepn required	Yes (1/10)	No additional prepn required
Substrate prepn	No additional prepn required	No additional prepn required	1:1 dilution required
Stop solution prepn	No additional prepn required	Dissolve tablets	No additional prepn required
Read wavelength	450	550	450
Special equipment	None required	Plate shaker required	None required
Assay performance			
Incubation temp	Room temp	Room temp	Room temp
Reagent prepn time (min) (excluding sample dilution)	10	30	20
Total incubation time (min)	50	47	100
Total assay time (min)	60	77	125
Data reduction	Linear curve fit	Linear curve fit	Quadratic curve fit or point to point
Special			
Colored reagents	Yes	No	Yes
Microtiter plate format	Breakaway wells	12 × 8 well strips	12 × 8 well strips
Dropper bottles	Yes	No	No
Serum dilution vessel	No	Yes	No

[a] External assayed control panel available from QC Products, Inc.

assays performed well and could accurately detect *H. pylori* infection (6, 8, 19, 29). Those reported sensitivities and specificities in studies performed with a variety of populations around the world were consistent for both the HM-CAP and PYLORI STAT assays. For the PYLORI STAT assay, the sensitivity ranged from 96 to 100% and the specificity ranged from 89 to 94%; for the HM-CAP assay, the sensitivity ranged from 89 to 98% and the specificity ranged from 96 to 100%. The specificity, and therefore the diagnostic accuracy, of the HM-CAP kit was on average slightly higher than that of the PYLORI STAT kit, as was observed in our study. However, reported specificities for the G.A.P. assay ranged from 30 to 89%, and our results are consistent with the results of those investigators who found that the G.A.P. test yielded a lower specificity (1, 4, 15, 19, 27, 28).

Because of the patchy nature of *H. pylori* infection in the stomach, biopsy may be inadequate as a reference method (2, 34). Serological assays which are compared with biopsy as a standard method may appear to have lower specificities. These apparent false-positive serological results compared with biopsy results may simply be a result of the sampling error inherent in obtaining biopsy specimens. The accuracy of biopsy results depends on the biopsy size and the total number of biopsies taken. In this study serological results were compared with those of the UBT, which is not subject to the sampling problems inherent in biopsy and which has been shown to be a highly accurate means of identifying *H. pylori* infection (11, 17, 20, 21). Although the low specificities reported for the G.A.P. kit could possibly be due to inadequate biopsies in studies reporting lower specificities compared with biopsy, our observed specificity was 26.0% compared with UBT, making the reference method alone an unlikely explanation for the low observed specificity.

The sensitivities and specificities of serological assays may also vary with the antigen preparation upon which the assay is based. Crude antigen preparations result in assays which are less specific. This could be as a result of cross-reactivity with antigens of other bacteria as well as possible nonspecific binding of human IgG, resulting in higher background levels in the assays (8, 9, 14, 33). There is evidence that *H. pylori* shares cross-reactive antigens with other gastrointestinal organisms and possibly other nongastrointestinal organisms, such as *Pseudomonas aeruginosa* and *Haemophilus influenzae* (16, 24). The HM-CAP assay is based on the patented high-molecular-weight cell-associated protein antigen (HM-CAP) described by Evans et al. (6). The PYLORI STAT kit is based upon a urease-enriched antigen preparation described by Dunn et al. (5). Partially purified antigen preparations other than HM-CAP have been reported to yield lower specificities relative to the HM-CAP antigen preparation (14). This is consistent with our observation that the PYLORI STAT kit is slightly less specific than the HM-CAP kit. The G.A.P. kit does not specify the antigen preparation used in the assay other than that the kit is based on partially purified *H. pylori* antigens. Although our studies confirmed that the G.A.P. assay was not cross-reactive with four common gastrointestinal pathogens, cross-

reactivity with other organisms and nonspecific background binding of human immunoglobulin cannot be ruled out as causes of the kit's poor performance.

Our study population of 473 UBT-characterized individuals is the largest used to evaluate commercial serological assays. *H. pylori*-positive and -negative patients are equally represented, avoiding error that can occur when diagnostic performance is calculated with populations with a high rate of positivity. A range of ages was represented in the group, such that the population as a whole was not composed primarily of older individuals, in whom a higher incidence of *H. pylori* infection and atrophic gastritis might be expected. It has been suggested that the presence of atrophic gastritis may result in a positive serology (as an indicator of "inactive" or past infection) with a negative biopsy or UBT result (9, 13). Although the mean age of the UBT-positive group was slightly higher than the mean age of the UBT-negative group, the mean age of the group demonstrating false-positive G.A.P. serologies was similar to that of the UBT-negative group. Therefore, the possibility of positive G.A.P. serology due to an inactive or past infection is unlikely. This is confirmed by the fact that both the HM-CAP and PYLORI STAT assays correctly identified the majority of these samples as negative, consistent with the UBT result.

The HM-CAP and the PYLORI STAT assays showed clearly separated distributions of positive and negative results with mean positive and negative values well removed from the cutoff. The distribution of G.A.P. assay results showed that the UBT-negative population had shifted upward and overlapped the UBT-positive population. The observed sensitivity and specificity of a serological assay may vary significantly with the population studied as a result of the types of organisms endemic in that population as well as the population's total antigenic load. When the positive cutoff for the G.A.P. assay is raised, the assay performance becomes acceptable. Investigators and laboratory workers have been cautioned to verify the manufacturer-stated sensitivity and specificity of a serological assay for the population to be tested. It has also been suggested that assay performance in a specific population may be improved by altering cutoff values (8, 32, 33). Although this option may be satisfactory for investigative use, the manufacturer-stated ranges must be strictly adhered to for diagnostic use.

The primary criterion for selection of an assay for clinical use must be diagnostic accuracy. However, once diagnostic accuracy is established, other assay features may contribute to overall reproducibility and accuracy in the hands of the user. Relevant assay features for each kit are listed in Table 3. Features that add not merely to convenience but to the overall accuracy of assay performance include prediluted reagents, ease of assay performance, and data reduction. Prediluted reagents eliminate potential dilution error and run-to-run variability caused by variations in reagent concentration. Ease of assay performance eliminates user error introduced by unintended technical variation in the performance of the assay. In addition, ease of data reduction can also reduce potential error by eliminating potential variability in user-drawn standard curves as well as variability added by standard curve variation from run to run. Linear regression programs are available on most computers and scientific calculators. More complex standard curves, such as the quadratic standard curve fit required by the G.A.P. assay, may require the user to perform a less accurate point-to-point curve fit. In addition, more complex curve fits make evaluation of the effect of alterations in the shape of the standard curve over the dynamic range of the assay more difficult. All three kits offer controls. The G.A.P. and the PYLORI STAT kits each provide two internal controls, a negative and a positive control, with each kit. A four-member assayed external control panel is available for use with the HM-CAP kit, which may be used to verify assay calibration, linearity, and reproducibility over time across lots of kits.

In conclusion, only two of the three serological assays we evaluated, the HM-CAP assay and the PYLORI STAT assay, could be relied upon to accurately diagnose *H. pylori* infection in the population we studied. These results show that not all serological assays for antibodies to *H. pylori* are equivalent and that it is critical for researchers and clinicians to know which assay is being used, and whether the assay has a history of consistent performance in a variety of populations, before it is relied upon as an accurate diagnostic tool. We suggest that serological assays such as the HM-CAP and PYLORI STAT assays are indeed accurate diagnostic tools for the detection of *H. pylori* infection. These methods are noninvasive, simple to perform, and cost-effective and should be the method of choice when screening for infection.

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