Comparison of PCR and Other Diagnostic Techniques for Detection of *Helicobacter pylori* Infection in Dyspeptic Patients

**JUDITH WEISS,†* JAMES MECCA,† ELVIRA DA SILVA,‡ AND DIETER GASSNER‡**

Department of Infectious Diseases, Roche Molecular Systems, Alameda, California 94501,† and
Immunochromatography Division, Roche Diagnostic Systems, Basel, Switzerland CH-4002‡

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A sensitive and specific PCR-based assay to detect the *Helicobacter pylori* 16S rRNA gene present in formalin-fixed paraffin-embedded gastric biopsy specimens has been developed. A total of 95 patients with dyspepsia were evaluated for the presence of chronic active gastritis and an infection with *H. pylori* through the use of diagnostic assays based on biopsy specimens and serology. The "gold standard" for the presence of the bacteria was direct detection in histological sections of biopsy specimens by Giemsa stain. The results obtained with the PCR assay performed on the biopsy specimens (94% sensitivity and 100% specificity) were equivalent to the detection of *H. pylori* immunoglobulin G antibodies by the commercially available second-generation Cobas Core anti-*H. pylori* immunoglobulin G enzyme immunoassay (94% sensitivity and 98% specificity) for the diagnosis of *H. pylori* infection. Urease testing and bacterial culture of the biopsy specimens were inferior (88 and 70% sensitivity and 96 and 98% specificity, respectively). A Western blot (immunoblot) analysis had slightly greater sensitivity (96%), although specificity was reduced to 93%. This research prototype PCR assay was shown to be highly reliable for the detection of infection with *H. pylori* and the presence of chronic active gastritis in the population studied.

The bacterium *Helicobacter pylori* is an etiologic agent for chronic active gastritis and plays a major role in effecting peptic ulcers (2, 9, 28). Colonization of the human stomach and duodenum with this microorganism is widespread throughout the world, although the prevalence in different populations varies. Detection of *H. pylori* in an individual suffering from abdominal dyspepsia can affect the therapeutic course of treatment, since the presence of gastritis and a greater probability of an ulcer can thus be assumed. Thus, a decision to perform an endoscopy may be indicated, as would treatment with antibiotics. Eradication of *H. pylori* in patients with ulcers drastically reduces the chance of recurrence (13).

There are several diagnostic assays for the detection of infection with *H. pylori*. Indirect assays that measure the presence of specific serum anti-*H. pylori* immunoglobulin G (IgG) and/or IgA using various antigen preparations purified to different degrees and serological techniques have been evaluated (8, 31). There have been problems with serological cross-reactivity with some of the antigen preparations leading to a low level of specificity, however, a recent study utilizing several commercial kits has indicated acceptable performances dependent on the population studied (25). Direct demonstration of an *H. pylori* infection in gastric biopsy specimens is possible through the use of culture, histologic examination of biopsy specimens using different stains, and assaying for urease activity. Recently, assays based on the use of the PCR to detect the presence of *H. pylori* DNA using several different gene targets have been described (3, 5, 12, 14, 16, 29, 30, 32, 34). These assays have been tested to date with only limited numbers of gastric biopsy specimens (3, 5, 12, 16, 29, 30, 32); however, the technique looks promising. In this study, a PCR assay to specifically detect *H. pylori* DNA in gastric biopsy specimens was developed. This assay was then tested, and the results were compared with the results obtained by culture of biopsy specimens from 95 dyspeptic individuals, by testing for urease activity, by histologic staining, and by two serologic assays to detect serum anti-*H. pylori* IgG—the commercially available Cobas Core anti-*H. pylori* enzyme immunoassay (EIA) and a Western blot (immunoblot) assay. The sensitivity and specificity of PCR for detecting *H. pylori* infections were compared with those of the other assays.

**MATERIALS AND METHODS**

**Bacterial strains.** The *H. pylori* strains used for sequence determination and design of the oligonucleotide primers and probes were isolated from gastric biopsy specimens from patients at Stanford University Hospital, Stanford, Calif. Additional *H. pylori* isolates were obtained from similar clinical specimens, as well as the American Type Culture Collection (ATCC 43504). Isolates of *Helicobacter cinaedi*, *Helicobacter felineae*, *Helicobacter mustelae*, *Campylobacter coli*, *Campylobacter jejuni*, and *Campylobacter fetus* were obtained from the American Type Culture Collection. All bacteria were cultured on Trypticase-soy agar.

**Clinical specimens.** Patients (age range, 21 to 90 years) with complaints of abdominal pain with a clinical indication for endoscopy of the upper gastrointestinal tract (no treatment with bismuth and/or antibiotics during the last 6 months, no omeprazole therapy, and no gastric injury) were asked to participate in the study. Five biopsy specimens were obtained: two for culture (performed at Institute Viollier, Basel, Switzerland), one for urease testing (*Campylobacter*-like organism test; Delta West, Perth, Australia), and two for histology (formalin-fixed, paraffin-embedded tissue sections stained with modified Giemsa stain for direct demonstration of *H. pylori* and stained with hematoxylin and eosin to grade the severity of gastritis) and PCR. Gastric mucosal biopsy specimens were directly inoculated onto Columbia agar culture plates (BBL Microbiology Systems, Cockeysville, Md.) supplemented with 10% horse blood, vancomycin, and nalidixic acid. Plates were
incubated at 37°C under microaerophilic conditions and inspected after 3, 5, and 7 days. Bacterial colonies were identified as *H. pylori* on the basis of growth characteristics, Gram stain, and positive catalase, oxidase, and urease reactions. A blood sample was obtained at the time of endoscopy, and the serum was separated and stored frozen at −20°C. Dyspeptic patients who tested negative for *H. pylori* by reference methods served as the control group for the PCR and serological assays, rather than individuals without symptoms, since approximately 15% of the adult European population may have an asymptomatic infection.

**Histological analysis.** The degree of gastritis present in the biopsy specimens as determined by hematoxylin and eosin staining was scored from 0 to 4 in accordance with the Sydney System, representing absence of gastritis and minimal, mild, moderate chronic active, and severe chronic active gastritis, respectively (24). Similarly, the direct detection of *H. pylori* bacteria in the Giemsa-stained sections was scored from 0 to 4, representing absence of bacteria, one bacterium, and few, several, and many bacteria, respectively.

**Anti-*H. pylori* IgG EIA.** The second-generation antigen-based Cobas Core anti-*H. pylori* EIA (Roche Diagnostic Systems, Basel, Switzerland) incorporates purified urease into a fast protein liquid chromatography-purified multicomponent antigen preparation free of cross-reacting flagellar proteins and the urease-associated highly conserved 54-kDa heat shock protein. The Cobas Core anti-*H. pylori* EIA was performed as described by the manufacturer. Samples yielding values within the gray zone of ±10% of the cutoff value were redone. The assay was performed on three different occasions, by two different groups, and in a blinded fashion. The serum specimens produced identical results during the multiple runs.

**Western blot.** For immunoblotting, the purified antigen preparation used in the EIA (see above) was electrophoresed on a sodium dodecyl sulfate (SDS)–10% polyacrylamide gel under reducing conditions and electrophotographically transferred onto a nitrocellulose membrane by semidyed blotting. Membrane strips were incubated with a 1:50 dilution of the serum for 3 h at room temperature. Peroxidase-conjugated goat anti-human IgG (Kirkegaard & Perry Laboratories, Gaithersburg, Md.) was used as the conjugate.

**PCR amplification.** The oligonucleotide primers used to amplify a segment of the *H. pylori* 16S rRNA gene were selected to generate a small amplicon since specimens that had been fixed with formalin were the source of the DNA (11). The primers were designed to specifically amplify *H. pylori* DNA and not *C. jejuni* or *Escherichia coli* DNA. A pair of 15-μm-thick sections was cut from the blind-coded formalin-fixed paraffin-embedded specimens, with a control of nonrelevant tissue left after every five sections. For the PCR and Western blot procedures, the sections were individually placed into separate sterile tubes. The tissue sections were deparaffinized with organic solvents (11), and the nucleic acids were solubilized by incubation with 50 μl of lysis buffer (50 mM Tris-HCl [pH 7.5], 1 mM EDTA, 1% Tween 20, 200 μg of proteinase K per ml) at 55°C for 3 h and then at 95°C for 10 min. Amplification was conducted in 100-μl reaction volumes containing 10 μl of solubilized nucleic acid with primer JW21, the upstream primer (5′-GGCAGCTGGTGA ACATTAC 3′; nucleotides 691 to 710), and primer JW22, the downstream primer (5′-CGTATGCTCAGTACTGGAGA 3′; nucleotides 829 to 809). Duplicate reactions were performed for each section. The amplification reaction mixture contained DNA in 10 mM Tris-HCl (pH 8.3)–50 mM KCl–1 mM MgCl2–100 μg of gelatin per ml–5% glycerol–62.5 μM (final concentration) each dATP, dGTP, dCTP, and dTTP–2.5 U of *Taq* DNA polymerase (Perkin-Elmer, Norwalk, Conn.)–50 pmol of each primer. The reaction mixtures were heated to 95°C for 5 min and then subjected to 35 cycles of 95°C for 1 min, 55°C for 1 min, and 72°C for 1 min and a final extension at 72°C for 10 min.

**Detection and analysis of amplified product.** Ten microliters of the amplification reaction mixtures was analyzed by gel electrophoresis in 3% NuSieve agarose–0.5% SeaKem agarose gels in TBE buffer (89 mM Tris-HCl [pH 8.3], 89 mM boric acid, 2.5 mM EDTA). For dot blot analyses, 10 μl of the amplified DNAs was transferred to membranes and hybridized to the 32P-labeled probe as described elsewhere (33). The membrane was hybridized with 2 × 10^6 cpm of 32P-labeled RDR549 probe (5′-CGCTGAATTGCGCGAAA 3′; nucleotides 714 to 729) per ml for 3 h at 52°C in 5 × SSPE (1 × SSPE is 0.18 M NaCl, 10 mM NaH2PO4, and 1 mM EDTA [pH 7.4])–0.5% SDS–0.5% dextran sulfate and then subjected to a stringent wash with 3 M tetramethylammonium chloride solution containing 50 mM Tris-HCl [pH 8.0], 0.1% SDS, and 2 mM EDTA at 51°C. The dried membranes were exposed to X-Omat XAR-5 film with an intensifying screen for 18 h at −70°C. Controls of no DNA and positive control plasmid pH1 DNA (5, 10, or 50 copies) containing the target 16S rRNA gene sequence were subjected to amplification with each series of gastric biopsy control and tissue specimen controls. Individual amplification reactions were scored as positive if the dot blot signal was equal to or greater than that obtained with the positive control of 10 copies of plasmid DNA. All positive reactions were resolved by repeating the analysis. Bioassay specimens were scored as positive only when >50% of the individual amplification reactions from the two sections were positive.

**RESULTS**

A total of 95 patients with complaints of abdominal pain and a clinical indication for endoscopy of the upper gastrointestinal tract were the subjects of the study. Bioassay specimens were taken for culture, for urease testing (*Campylobacter*-like organism test), for direct demonstration of *H. pylori* by modified Giemsa stain, for histological examination, and for detection of *H. pylori* DNA by PCR. DNA and RNA from a blind sample were obtained at the time of endoscopy for testing of the serum for anti-*H. pylori* IgG by the Cobas Core EIA and Western blot analysis. Moderate to severe chronic active gastritis of the antrum was observed in 49 of 95 patients (52%) by histologic examination of the biopsy specimens for inflammation. The biopsy specimens obtained from all 49 of these patients were observed to contain *H. pylori* bacteria by direct staining with Giemsa. However, in most cases, the clinical diagnosis following endoscopy was in contrast to the histologic findings, i.e., the stomach and intestinal linings appeared to be normal. Two patients had other types of gastritis (moderate chemical gastritis and moderate lymphocytic gastritis) without evidence of *H. pylori* infection. Of the eight patients with duodenal ulcers, six showed evidence of antral gastritis as well as *H. pylori* colonization. The other two patients showed no evidence of gastritis or *H. pylori* infection. Four patients exhibited gastric ulcers upon endoscopy; all four had evidence of gastritis and *H. pylori* infection. Of the 26 patients (27%) with minimal to mild gastritis, 25 were diagnostically negative for *H. pylori* infection. A single patient (patient 49) was observed to have *H. pylori* infection by all criteria, except for a finding of only minimal gastritis from the Giemsa-stained section. Eighteen patients (19%) showed no evidence of inflammation of the antral lining, and all were negative for *H. pylori* by direct examination of the biopsy specimens. Due to the excellent agreement between the finding of active chronic gastritis (or its absence)
and the detection of *H. pylori* bacteria in biopsy specimens (or their absence) by histology, the direct demonstration of *H. pylori* in Giemsa-stained biopsy specimens was considered the "gold standard" concerning the status of infection with *H. pylori*. There was only one discrepant result (for patient 49), probably due to the pathologist's interpretation of the level of gastritis. With this gold standard, 50 (53%) of the patients with complaints of abdominal pain were considered to harbor infections with *H. pylori*, while 45 were uninfected. The results obtained by measuring other indicators of *H. pylori* infection were calculated by using this gold standard, and the results are reported below.

**Sensitivities, specificities, and predictive values of the assays.** Sensitivities, specificities, and predictive values of the biopsy specimen-based diagnostic assays and the serological assays calculated for all 95 patients in relation to the direct demonstration of *H. pylori* by Giemsa stain are presented in Table 1. The PCR assay performed on the biopsy specimens was equivalent to the detection of anti-*H. pylori* IgG antibodies by EIA for detecting *H. pylori* infection and superior to the urease and culture assays. Both the PCR assay and the EIA provided excellent sensitivity (94%) and specificity (100 and 98%, respectively) for the detection of *H. pylori* infection in the population of patients examined. The presence or absence of *H. pylori* infection could be predicted by the PCR assay or EIA results with positive predictive values of 100 and 98%, respectively, and a negative predictive value of 94%. Only the Western blot analysis had equivalent sensitivity, although the specificity and positive predictive value were reduced with this assay.

**Results of the 16S rRNA gene PCR assay.** The 16S rRNA gene PCR assay detects the presence of a 139-bp fragment of the *H. pylori* 16S rRNA gene (nucleotides 691 to 829) in DNA present in formalin-fixed paraffin-embedded biopsy specimens following deparaffinization and solubilization of total nucleic acids. The target sequence is amplified by PCR using primers JW21 and JW22 and detected by the use of hybridization with a radiolabeled oligonucleotide probe (RDR549). The assay is specific for *H. pylori* and does not detect *H. cinneedi*, *H. fellellae*, *H. mustelae*, or various *Campylobacter* species (data not shown). When purified DNA was used, the detection limit of the assay was five copies of the target sequence or approximately one bacterium (26). The results of the PCR assay to detect the presence of the *H. pylori* 16S rRNA gene in the coded biopsy specimens in comparison with the results obtained with the gold standard of *H. pylori* infection and the anti-*H. pylori* EIA are presented in Table 2. The biopsy specimens from 47 of 50 patients with *H. pylori* infections contained *H. pylori* DNA as demonstrated by PCR analysis, while all 45 patients without *H. pylori* infections were negative by PCR analysis. The biopsy specimens from three of the patients (patients 59, 60, and 64) resulted in negative results by PCR analysis; however, the panel of results from the other assays was different for each patient. The only indications that patient 59 was infected with *H. pylori* were the finding of a low number of bacteria in the Giemsa-stained biopsy specimen and the finding of chronic active gastritis. The urease and culture assays performed on biopsy specimens from this patient were negative, as were the serological tests. Patient 64 was determined to be infected with *H. pylori* by positive urease, culture, EIA, and Western blot results, as well as the direct demonstration of *H. pylori* in the biopsy sections and chronic active gastritis. One of the gastric biopsy sections from patient 64 was positive by PCR analysis while the other was not, but the algorithm for scoring specimens by PCR classified this specimen as negative for *H. pylori*. Patient 60 was infected with *H. pylori* as indicated by direct detection in the biopsy specimen, urease activity, and Western blot analysis. The result of culture was negative, and the serum from this patient was weakly positive in the EIA. Although DNA of the appropriate size was specifically amplified by PCR from both biopsy sections from this patient, the hybridization probe RDR549 failed to bind to the amplified fragment, and thus the overall score for the patient was negative by PCR analysis. Subsequent analysis of this discrepant sample with a second set of PCR primers and an oligonucleotide probe specific to another region of the *H. pylori* 16S rRNA gene (nucleotides 1090 to 1157) indicated that the biopsy sections did contain authentic *H. pylori* DNA. When the nucleotide sequence of the DNA fragment amplified with primer pair JW21 and JW22 was determined, it was observed to be identical to that of *H. pylori* except for a single nucleotide substitution (C→T) at position 723 in the middle of the probe RDR549-binding region. Under the stringent wash conditions used during the dot blot hybridization analysis, the single-base-pair mismatch was sufficient to prevent probe binding (data not shown) and thus result in a negative score for patient 60.

**Results of the detection of anti-*H. pylori* IgG by Cobas Core EIA and Western blot analysis.** The results of detecting specific IgG in patients' sera by EIA in comparison with the results obtained with the gold standard of detection of *H. pylori* infection, a Western blot analysis, and PCR analysis are presented in Table 2. Of 50 patients with *H. pylori* infections, 47 had anti-*H. pylori* IgG antibodies, as measured by the EIA. EIA results were negative for 44 of the 45 patients without *H. pylori* infection. One patient (patient 17) was weakly positive by the EIA, despite being negative for *H. pylori* by all tests.
performed on the biopsy specimens (culture, urease, PCR, and histologic examination). There was no detectable antral gastritis in this patient. Positive results were obtained with serum in a Western blot analysis, as well as another EIA (Pylori Stat; Whittaker M. A. Bioproducts, Walkersville, Md.), suggesting that this patient may have been previously infected but that the infection had been self-limited or previously eradicated, resulting in only low levels of anti-\textit{H. pylori} IgG. Of the three patients with putative false-negative serum specimens (patients 3, 59, and 89), patient 3 was positive for \textit{H. pylori} by examination of biopsy specimens (urease, culture, and PCR assays) while the serum did not contain anti-\textit{H. pylori} antibodies, as measured by both EIA and Western blot anti-\textit{H. pylori} IgG analysis (including EIA results from Pylori Stat and HMCP [Enteric Products Incorporated, Westbury, N.Y.]), suggesting that this patient had not seroconverted as a result of infection or was immunocompromised. However, serum sample 89, with reproducible gray-zone EIA results, was positive in the Western blot analysis, and the biopsy specimens from this patient were positive by all criteria. Finally, patient 59, classified as infected with \textit{H. pylori} only by the findings of chronic active gastritis and histologic evidence of a single bacterium in the biopsy specimens (see above), was negative by both the EIA (including Pylori Stat and HMCP anti-\textit{H. pylori} EIA) and the Western blot. All of the serum specimens that were negative by Western blot analysis (\textit{n} = 44) were negative by the EIA. Of the 51 serum samples positive by Western blot analysis, two were negative (55 and 88) and one was borderline (sample 89) by EIA. Two of these patients (55 and 88) were negative for \textit{H. pylori} by culture and urease, and histologic evaluation proved the patient to be positive for gastritis.

Results of culture and the urease assay. Biopsy specimens were subjected to a test for urease enzymatic activity (\textit{Campylobacter}-like organism test), and two specimens were cultured for \textit{H. pylori}. All patients with evidence of \textit{H. pylori} infection by culture (\textit{n} = 36) showed histologic evidence of \textit{H. pylori} in the biopsy specimens, with one exception. Patient 95 had a positive culture result, although with only rare growth of bacteria, while all other analyses using the biopsy specimens or serum were negative for \textit{H. pylori} infection. However, biopsy specimens from 15 patients shown to be infected with \textit{H. pylori} did not produce positive cultures, resulting in a 70% sensitivity of the culture method (Table 1). The urease test results for the 95 biopsy specimens were positive for 46 samples, two of which (specimens 8 and 41) were from patients with no other indication of \textit{H. pylori} infection. The biopsy specimens from six patients (patients 22, 25, 32, 59, 80, and 86) with \textit{H. pylori} infections resulted in no detectable urease activity, and the biopsy specimens from five of these patients were also negative by culture.

Discussion

The presence of \textit{H. pylori} bacteria in the upper gastrointestinal tract was directly associated with a histologic demonstration of chronic active gastritis and gastric ulcers in the patients enrolled in this study. The percentage of patients who harbored \textit{H. pylori} infections (55\%) is consistent with the results of other studies of similar populations (8, 10, 15). Importantly, the clinical presentation of the patients and endoscopy did not reveal which patients were infected. The presence of the bacteria and, indirectly, the chronic active gastritis were shown to be readily assessed in this study by several different assays with a high degree of accuracy. We found that a PCR assay that detects DNA encoding the \textit{H. pylori} 16S rRNA gene in formalin-fixed paraffin-embedded biopsy specimens had a high degree of accuracy for demonstrating the presence of the bacteria and chronic active gastritis, as did the Cobas Core EIA performed with patients' sera. Conversely, the presence of normal gastric mucosa was consistent with an absence of bacteria. This is the first study both in which a PCR assay was evaluated for a large number of patients (95) and in which the results were compared with four other diagnostic parameters.

A diagnostic assay that does not require invasive procedures to procure specimens offers an advantage if it can be shown to be highly specific and sensitive for infection. In our study, the second-generation Cobas Core EIA proved to be robust and reproducible when performed multiple times by different laboratories, and the results obtained were highly predictive. This EIA has been shown to be highly specific and sensitive when applied to a similar European population (8, 18, 20). The Western blot assay performed with the same serum specimens yielded several false-positive results. Identical antigen preparations were utilized for these two assays; thus, the discrepancies may be due to differences in binding and adsorption of antigens to plastic and nitrocellulose and due to altered epitope presentation resulting from the denaturation of the antigen used for the Western blot analysis during electrophoresis and transfer to the nitrocellulose membrane. The protein preparation used for the EIA was adsorbed to the plastic in its native state. Nevertheless, a Western blot assay is very labor-intensive, requires more time to complete than an EIA, and is not readily adapted to widespread use.

The research PCR assay for the detection of a \textit{H. pylori} infection assessed in this study utilized specimens that required a biopsy. However, in certain circumstances a PCR-based assay offers distinct advantages over serologic and culture methods of diagnosis. EIA. Early in an infection, prior to seroconversion or when an individual's humoral response is repressed or absent, PCR could indicate an infection while EIA results would be negative (as observed with patient 3). A more widespread use for a PCR-based assay, as an alternative to the $^{13}$C urea breath test, would be to assess the short-term efficacy of eradication of the bacteria with antibiotics. Since the levels of anti-\textit{H. pylori} IgG following antibiotic therapy decline but do not remain significantly lower until 3 to 6 months posttreatment in responders (7, 17), titration of serum antibody levels may be useful for accompanying the long-term course of antimicrobial therapy. Since the levels of specific antibody vary between individuals, quantitative assay formats for IgG may be the most accurate and sensitive method to assess the true eradication of the bacteria. Once the bacteria are detected, the presence of \textit{H. pylori} bacteria in biopsy specimens, the urease test and culture, did not perform as well. There was no discernible pattern as to when these assays failed; a lack of sensitivity when there were low numbers of organisms present was not the problem. In contrast to these findings, culture was found to be equivalent in sensitivity to PCR amplification of DNA from frozen biopsied tissue for the detection of \textit{H. pylori} (30). The poorer performance of culture and the urease test in our study may be due to specimen handling, since the organism is quite fastidious and sensitive to environmental conditions for sustained viability.

The 16S rRNA gene target for the PCR assay utilized in this study is similar to that described by Ho et al. (14); the region amplified by their primers is contained within the ampiclon that we identified in
DNA only from the biopsy specimen of patient 60. Primer Hp2 overlaps both our upstream primer, JW21, and our probe RDRS49. Primers Hp1 and Hp2 used under the conditions described by Ho et al. (14) amplify H. pylori DNA with either the C or the T at nucleotide position 723 with equivalent efficiencies (data not shown). The analytical sensitivities of the two 16S rRNA assays with both versions of the sequence are equivalent (data not shown). The 307 bp of 16S rRNA gene sequence determined for patient 60 indicates that the bacterial sequence was obtained from H. pylori and not from another species of Helicobacter. Additionally, the other diagnostic results indicated that the bacterium behaved as would authentic H. pylori. We found this sequence in only 1 of the 47 PCR true-positive specimens, suggesting that it was a rare occurrence.

It would be interesting to determine if isolates bearing this sequence possess different virulence or biological properties. Other investigators have tested H. pylori assays based on the urease gene target ureA (3, 34). This gene has extensive sequence polymorphism (1, 4, 6); thus, it would not be expected to have adequate clinical sensitivity.

This study examined the performance of a research prototype PCR assay utilizing duplicate reaction mixtures and sections to confirm results. Before it could be widely utilized, it would need to be converted to a nonradioactive format such as the microwell plate assay (19) and validated with a large number of clinical specimens obtained from various populations. However, for the population evaluated it performed excellently, and if the population consisted of patients undergoing antibiotic therapy, the short-term results would be expected to surpass the performance of a serological assay. Recently it has been demonstrated that fecal specimens from individuals with gastritis can contain H. pylori DNA (21), and cultivable H. pylori organisms have been obtained from an infected individual (27). If H. pylori DNA can be detected reliably with PCR from fecal specimens or even saliva supplied by a large number of individuals, this technique could be used more widely in the diagnosis of H. pylori infection and in the monitoring of antibiotic treatment of patients with ulcers. Additionally, there is epidemiologic evidence indicating an association between prior H. pylori infection and an elevated risk for gastric cancer (22, 23). At this point, the additional genetic and/or environmental factors that lead to gastric cancer have not been identified; thus, screening of only limited populations would be warranted.

REFERENCES


