Diagnosis of *Clostridium difficile* Infection

To the Editor—Despite our long-standing interest in earlier tests for *Clostridium difficile* toxin [1], we believe that polymerase chain reaction (PCR) technology should simply replace other algorithms for the diagnosis of *C. difficile* infection, as recently outlined in *Clinical Infectious Diseases* by Kufelnicka and Kirn [2].

We studied 122 consecutive specimens submitted for *C. difficile* testing by enzyme immunoassay (EIA; Premier Toxins A&B EIA kit, Meridian Bioscience, Cincinnati, Ohio) and PCR (Xpert *C. difficile*, Cepheid, Sunnyvale, California). Clinical indications, as determined by the submitting physicians, included ≥1 and usually ≥2 of the following: new onset diarrhea, abdominal discomfort, fever, and leukocytosis. We did not require that the sample submitted be an unformed stool sample, although it nearly always was so. The study was designed to inoculate every sample that was positive for *C. difficile* toxin to cycloserine-cefoxitin fructose agar, *Brucella* sheep blood agar with vitamin K1, and CDC anaerobic sheep blood agar with phenyl ethyl alcohol (Becton Dickinson, Franklin Lakes, New Jersey). *Clostridium difficile* was identified with the RapID-ANA II system (Remel, Lenexa, Kansas), and all isolates were cultured in broth and tested for toxin production by standard cytotoxicity assay.

The results showed that, of 122 specimens, 13 (10.7%) were positive by EIA; all of these were also positive by PCR. An additional 6 samples that were negative by EIA were positive by PCR. Every sample for which the PCR was positive was shown by culture to contain toxin-producing *C. difficile*.

These results suggest that (1) in a substantial proportion of patients, *C. difficile* infection is not detected by EIA, and (2) the presence of *C. difficile* in these samples can be detected by PCR without false-positive results. Because all patients were symptomatic, the issue of colonization is moot. We cannot, of course, exclude the possibility that another, unrecognized cause of acute diarrhea appeared in a patient who was simply colonized with *C. difficile*.

Based on these findings, our hospital has replaced EIA for *C. difficile* toxin with PCR. We felt that clinicians could not be satisfied with a test that failed to diagnose *C. difficile* infection in >40% of cases. Although, on the basis of recommendations developed early in the EIA era, clinicians often send multiple samples from an individual patient, we only study 1 specimen in any given 7-day period [3]; thus, the increased expense for PCR reagents is partially mitigated by the elimination of repeated testing. The suggestion that samples first be tested for glutamate dehydrogenase and that positive samples be further studied by PCR involves 2 steps, takes additional time (which translates into problems in clinical management and isolation of patients [4]), and has been shown to provide false-negative results [5, 6]. As a result, we, along with others [7], have chosen to work exclusively with PCR as the diagnostic test for *C. difficile* infection.

**Note**

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