Microbiology and Infectious Disease / Laboratory Diagnosis of CDI

Laboratory Testing for *Clostridium difficile* Infection

Light at the End of the Tunnel

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**Key Words:** *Clostridium difficile* infection; Laboratory testing; Rapid diagnostics

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**Abstract**

*Clostridium difficile* infection (CDI) is changing as evidenced by increasing virulence, rising incidence, unresponsiveness to metronidazole therapy, and worse outcomes. Thus, it is critical that CDI diagnosis be accurate so ongoing epidemiology, disease prevention, and treatment remain satisfactory. We tested 10 diagnostic assays, including 1 commercial real-time polymerase chain reaction (qPCR) test for the laboratory detection of toxigenic *C difficile* on 1,000 stool samples. Sensitive culture for toxigenic *C difficile* using 2 types of media with broth enrichment defined the reference standard. For the study, 1,000 tests were performed on samples from 919 patients. Of the samples, 146 contained evidence for toxigenic *C difficile* and represented the true-positive results. Only the US Food and Drug Administration–cleared qPCR assay (Becton Dickinson, Franklin Lakes, NJ) and 1 glutamate dehydrogenase test (TechLab, Blacksburg, VA) were not statistically inferior to culture in sensitivity. The common enzyme immunoassay tests all had sensitivity values less than 50%. Clinical laboratory professionals need to seriously consider their diagnostic testing and use the assays that perform best for the detection of CDI.

*Clostridium difficile* infection (CDI) is a costly health care–associated disease,1 which seems to be increasing in virulence2,3 and incidence4-6 and worsening in response to traditionally accepted metronidazole therapy.7 CDI is caused by toxigenic *C difficile* that usually produces 2 major toxins, toxin A, an enterotoxin, and toxin B, a potent cytotoxin.8-12 Recently, it has been shown that toxin B is the main virulence factor for disease.13

The clinical standard for suspecting CDI is significant diarrhea, defined as 3 or more loose stools per day14 for 1 to 2 days.15 Because there is no assay for the actual determination of *C difficile* infection, the role of the laboratory is to accurately detect the presence of virulent (eg, toxigenic) *C difficile* by recovering a toxin-producing strain using culture or via detection of toxin(s) or toxin gene(s) in the stool sample. One of the challenges is that the organism itself has changed over the years. A decade ago, reports appeared of a toxin A–negative, toxin B–positive strain capable of causing disease,16 and this observation led to the development of enzyme immunoassays (EIAs) targeting both toxins. Because these assays provided results rapidly and offered ease of use, they soon dominated laboratory testing so that by 2008, EIAs accounted for more than 90% of all CDI testing in the United States.17,18 The worsening performance of EIAs has led to uncertainty in testing choice for CDI.19,20 Therefore, we evaluated a battery of 10 diagnostic tests for the detection of toxigenic *C difficile* compared with sensitive anaerobic culture. The purpose of this research was to critically assess the current testing available for CDI and define the tests with sufficient sensitivity and specificity for routine clinical use.
Materials and Methods

Specimen Selection and Testing

Excess unformed stool specimens submitted for *C. difficile* analysis from patients with a clinical suspicion of having CDI that were of sufficient quantity for all testing were included in the study. Samples were obtained at the time of arrival in the laboratory after ensuring there was sufficient material for diagnostic testing and were deidentified before being transferred to the research laboratory. The EIA-1 (defined in the next section) was performed in the clinical laboratory, and all other work was done in the research laboratory. Testing was done by 2 teams of research laboratory personnel and began within 24 hours of specimen receipt. One team performed real-time PCR (qPCR) testing and culture, and the other team did the remaining assays. Test results were not shared between the 2 teams until all assays were complete. Culture was the last test to be finalized owing to the slow turnaround time associated with this method. All stool samples were stored at refrigerator temperature (4°C-6°C) until tested and then frozen at –80°C.

CDI Testing Methods

All samples were tested by 4 toxin EIAs, 2 glutamate dehydrogenase (GDH) tests, a lactoferrin assay, 2 qPCR assays, stool tissue culture cytotoxin analysis, and a sensitive culture protocol for toxigenic *C. difficile*. All testing and result interpretation were performed according to the manufacturer’s recommendation. The immunoassays represent the majority (70%) of assays in use in US laboratories. The EIAs were as follows: EIA-1, C DIFFICILE TOX A/B II (TechLab, Blacksburg, VA); EIA-2, ImmunoCard Toxins A&B (Meridian Bioscience, Cincinnati, OH); EIA-3, Premier Toxins A&B (Meridian Bioscience, Cincinnati, OH); and EIA-4, C. DIFF QUIK CHEK COMPLETE (TechLab). GDH is an antigenic enzyme specifically reactive to *C. difficile* (toxigenic and nontoxigenic). The assays tested were the TechLab C. DIFF QUIK CHEK COMPLETE (GDH-1), which is linked to EIA-4 in the same assay, and the Wampole C. DIFF CHEK-60 (GDH-2; TechLab). Lactoferrin was tested using the LEUKO EZ VUE assay (TechLab), which is an immunochromatographic test for the qualitative detection of fecal lactoferrin.

The cell culture cytotoxicity assay was performed with the *C. difficile* Toxin/Antitoxin Kit (TechLab). For direct stool specimens, approximately 0.5 mL of stool was added to 1.5 mL of minimum essential medium broth (ViroMed Laboratories, Minnetonka, MN). Stool suspensions were vortexed and then centrifuged at 10,000g for 10 minutes. The supernatant was filtered through a 0.45-μm Costar Spin-X centrifuge tube filter (Corning, Corning, NY). For cytotoxin testing on isolated *C. difficile* colonies, 2 to 3 mL of the anaerobic chopped meat glucose broth (Becton Dickinson, Franklin Lakes, NJ) suspension was centrifuged at 4,000g for 10 minutes and then filtered through a 0.45-μm Spin-X filter.

Toxigenic culture was done by plating a small aliquot of stool to a pre-reduced cycloserine-cefoxitin-fructose agar (CCFA-VA formulation) media. Plates were incubated anaerobically at 35°C for up to 5 days before a final negative interpretation. A swab dipped into the stool was also inoculated into cycloserine cefoxitin mannitol broth with taurocholate, lysosome, and cysteine (CCMB-TAL; Anaerobe Systems, Morgan Hill, CA) and held for 4 days at 35°C to perform an enriched culture if the original culture was negative. Enriched cultures were sub-cultured by plating an aliquot of the CCMB-TAL broth onto pre-reduced *Brucella* agar with 5% sheep blood, hemin, and vitamin K1 (Becton Dickinson) and incubated. Yellow, spreading colonies were confirmed as *C. difficile* by Gram stain, aerotolerance, and a Pro Disc test (Key Scientific, Stamford, TX). All *C. difficile* isolates were tested for toxigenicity by growing the isolate in anaerobic chopped meat glucose broth (Becton Dickinson) and testing as described in the preceding paragraph. The flow of culture testing for the primary agar is shown in Figure 1A.

One qPCR was done using an in-house–developed assay performed as previously described. The other was a commercial assay, the BD Diagnostics CdFF qPCR test (Becton Dickinson), in which a sterile swab was dipped into the stool specimen and broken off into a sample buffer tube and processed following manufacturer’s recommendation. Control samples were *C. difficile* (American Type Culture Collection [ATCC] 43255 and ATCC 700057) strains in each run.

“Gold Standard” for Assay Comparison

Any specimen that grew toxigenic *C. difficile* in the original CCFA solid agar culture was considered a true-positive. If any specimen grew toxigenic *C. difficile* in culture and no other test was positive, a second culture method, as described by Stamper et al., was done on the original specimen to confirm positivity (to eliminate the possibility of in-laboratory contamination). This second culture method was also performed whenever the original CCFA test was negative but the non–culture-based tests were positive. The workflow for this approach is shown in Figure 1B. For any specimen negative in both culture methods but positive by multiple other tests, including qPCR, a medical record review was done to determine if the patient was receiving oral metronidazole or vancomycin; if that were the case, the specimen also was considered a true-positive.
Approvals and Statistical Analysis

The NorthShore University HealthSystem Research Institute Institutional Review Board (Evanston, IL) approved this research study. Two of us (L.R.P. and A.R.) performed the statistical analysis. Differences in test performance were determined by using the McNemar test.

Results

There were 1,000 stool samples tested from 919 patients. Overall, 146 samples were considered positive; 136 were based on recovery of toxigenic *Clostridium difficile* and 10 on multiple tests (other than culture) for toxin being positive when patients were receiving oral metronidazole or vancomycin.
Of the samples, 23 (16.9%) were positive only on the second 

\(C\) difficile\) agar medium used, and 18 (13.2%) were positive only after broth enrichment despite the use of 2 agar media for all samples. Thus, 41 stool samples (31.1%) were positive as a result of the additional testing beyond a single CCFA-based culture for \(C\) difficile.

Of the 81 patients with repeated tests, 7 had 3 samples, 1 had 4 samples, and 73 had 2 samples. For these 81 patients, 8 were considered to have a positive result for CDI and 73 to have a negative result. Of the 8 with positive results, 3 had negative results on the first sample, and the other 5 had all positive stool samples. No patient contributed more than 2 positive tests. Overall, these patients contributed 9 additional positive stool samples and 81 excess negative samples. Removal of duplicate tests did not alter the results, so they remained in the final analysis. The performance of all the evaluated tests is shown in Table 1 and Table 2 with the statistical analysis of these assays compared with the samples considered positive for \(C\) difficile infection in Table 3. Table 3, when read column by column, indicates the overall performance of each test as represented by the number of bolded entries in each column (eg, the more bolded entries the better the test performance when compared with the assay at the left of the table). If read row by row then the entries with better test performance are underlined when compared with the test at the top.

Overall, Table 3 shows that all of the commonly used EIA tests available in the United States have significantly inferior performance compared with culture for toxigenic \(C\) difficile and with the commercial and in-house–developed qPCR assays, the 2 evaluated GDH test kits, and even the nonspecific lactoferrin test that measures inflammation (leukocytes) in stool. All but the EIA-1 were also significantly inferior to direct cytotoxicity testing of stool for the detection of toxin B. The commercial qPCR assay and the GDH-1 test, when used as a standalone result, even though it is combined with an EIA for toxin A/B (EIA-4), were the only 2 tests not inferior to toxigenic culture. Regarding specificity, the direct cytotoxicity and EIA-4 tests were the best performing assays. As expected, the 2 GDH tests and the lactoferrin assay had the worst specificity. All toxin-specific tests had better performance, with specificities ranging from 96.5% to 99.8% (Table 2).

We also determined the rate of nontoxigenic \(C\) difficile recovered from the samples. There were a total of 169 \(C\) difficile isolates recovered, with 33 of them being nontoxigenic, for a rate of 19.5%. If one considers the 10 additional patients whose culture was negative presumably due to therapy at the time of sample collection, the rate of nontoxigenic \(C\) difficile recovered was 18.4% (33/179).

### Discussion

The recently published US guideline for CDI concluded that for diagnosis “Polymerase chain reaction testing appears to be rapid, sensitive, and specific and may ultimately address testing concerns. More data on utility are necessary before this methodology can be recommended for routine testing.”20 The European Union guideline similarly indicates that only molecular assays and toxigenic culture have sufficient sensitivity to be reliably used for diagnosis of CDI, but that more data are needed on molecular diagnostic testing.23 Our goal with this report is to supply sufficient data on existing test methods in common use so that a rational recommendation on laboratory testing for CDI can be made.

qPCR tests have been developed and investigated that address the problem of providing high sensitivity and rapid turnaround time. Our initial study, in which patients were prospectively interviewed, on an in-house–developed assay found sensitivity and specificity values for qPCR of 93.3% and 97.4%, respectively.15 Shortly thereafter, Sloan and colleagues24 reported the results of their investigation of another in-house qPCR assay in which the reference standard used for comparison was toxigenic culture. They found the

### Table 1

<table>
<thead>
<tr>
<th>Lactoferrin</th>
<th>EIA-1</th>
<th>EIA-2</th>
<th>EIA-3</th>
<th>EIA-4</th>
<th>GDH-1 (With EIA-4)</th>
<th>GDH-2</th>
<th>Cytotoxicity</th>
<th>BD qPCR</th>
<th>NorthShore qPCR</th>
<th>Culture</th>
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<tr>
<td>True-positive</td>
<td>110</td>
<td>65</td>
<td>68</td>
<td>65</td>
<td>66</td>
<td>128</td>
<td>122</td>
<td>73</td>
<td>138</td>
<td>122</td>
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<tr>
<td>False-negative</td>
<td>36</td>
<td>81</td>
<td>78</td>
<td>88</td>
<td>80</td>
<td>18</td>
<td>23</td>
<td>73</td>
<td>8</td>
<td>24</td>
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<tr>
<td>False-positive</td>
<td>338</td>
<td>11</td>
<td>8</td>
<td>20</td>
<td>2</td>
<td>47</td>
<td>55</td>
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<td>10</td>
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<tr>
<td>True-negative</td>
<td>515</td>
<td>843</td>
<td>846</td>
<td>834</td>
<td>852</td>
<td>807</td>
<td>799</td>
<td>852</td>
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<td>844</td>
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<td>0</td>
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BD, Becton Dickinson, Franklin Lakes, NJ; EIA, enzyme immunoassay; GDH, glutamate dehydrogenase; NorthShore, NorthShore University HealthSystem, Evanston, IL; qPCR, real-time polymerase chain reaction.

* For this analysis, there were 146 true-positive and 854 true-negative test results. The EIA and GDH assays were as follows: EIA-1, 2 DIFFICILE TOX A/B II (TechLab, Blacksburg, VA); EIA-2, ImmunoCard Toxins A&B (Meridian Bioscience, Cincinnati, OH); EIA-3, Premier Toxins A&B (Meridian); EIA-4, 2 DIFF QUIK CHEK COMPLETE (TechLab); GDH-1, 2 DIFF QUIK CHEK COMPLETE (TechLab), which is linked to EIA-4 in the same assay; and GDH-2, the Wampole C. DIFF CHEK-60 (TechLab).
the present study, for which Stamper and colleagues22 found gene. One is the BD Diagnostics Cdiff assay, also studied in peer-reviewed journal. The first 3 target the toxin B (tcdB) gene. One is the BD Diagnostics Cdiff assay, also studied in well-done anaerobic culture (44 positive samples). In this study, the assay showed sensitivity and specificity for qPCR to be 86% and 97%, respectively, compared with a range of sensitivities and specificities for 4 EIAs equaling 32% to 48% and 84% to 100%, respectively.24

At present, there are 4 commercially available qPCR assays for the direct detection of toxigenic C difficile in stool samples, and the performance of all has been published in a peer-reviewed journal. The first 3 target the toxin B (tcdB) gene. One is the BD Diagnostics Cdiff assay, also studied in the present study, for which Stamper and colleagues22 found a sensitivity of 84% compared with toxigenic culture from 61 positive specimens. Another test is the Xpert C difficile PCR assay (Cepheid, Sunnyvale, CA) that was found to be 94% sensitive and 96% specific on 72 positive specimens.7 The real-time PCR assay significantly outperformed a GDH assay, a toxin A and B enzyme immunoassay, and a cell culture cytotoxicity neutralization assay, regardless of whether the other tests were considered alone or in combination.25 Stamper and colleagues26 also evaluated the Prodesse TaqMan PCR assay (Prodesse, Waukesha, WI). They found a sensitivity of 83% compared with the recovery of toxigenic C difficile on well-done anaerobic culture (44 positive samples). In this study, the assay showed sensitivity and specificity for qPCR to be 86% and 97%, respectively, compared with a range of sensitivities and specificities for 4 EIAs equaling 32% to 48% and 84% to 100%, respectively.24

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<th>NS qPCR</th>
<th>Culture</th>
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<tr>
<td>Sensitivity</td>
<td>75.3 (67.4-81.9)</td>
<td>44.5 (38.4-53.0)</td>
<td>46.6 (39.3-55.0)</td>
<td>39.7 (31.8-48.2)</td>
<td>45.2 (37.0-53.6)</td>
<td>87.7 (81.0-92.3)</td>
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<tr>
<td>Specificity</td>
<td>80.4 (77.0-83.7)</td>
<td>98.4 (97.6-99.3)</td>
<td>98.1 (98.1-98.6)</td>
<td>97.7 (96.3-98.5)</td>
<td>99.6 (99.1-100.0)</td>
<td>94.5 (92.7-96.0)</td>
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<tr>
<td>PPV</td>
<td>24.6 (20.7-28.9)</td>
<td>85.5 (75.2-92.2)</td>
<td>89.5 (79.8-95.0)</td>
<td>74.0 (63.0-83.3)</td>
<td>97.1 (88.8-99.5)</td>
<td>73.1 (65.8-79.4)</td>
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<tr>
<td>NPV</td>
<td>93.5 (91.9-95.3)</td>
<td>91.2 (89.2-93.0)</td>
<td>91.6 (89.5-93.2)</td>
<td>90.5 (88.3-92.2)</td>
<td>91.4 (89.4-93.1)</td>
<td>97.8 (96.5-98.7)</td>
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* Boldface type, the test at the top of the column was superior to the test listed at the left side of the row; underlined type, the test at the left side of the row was superior to the test listed at the top of the column; no color, no statistically significant difference between tests. Differences in test performance were determined by using the McNemar test. The EIAs and GDH assays were as follows: EIA-1, C. DIFFICILE TOX A/B II (TechLab, Blacksburg, VA); EIA-2, ImmunoCard Toxins A&B (Meridian Bioscience, Cincinnati, OH); EIA-3, Premier Toxins A&B (Meridian); EIA-4, C. DIFF QUIK CHEK COMPLETE (TechLab); GDH-1, C. DIFF QUIK CHEK COMPLETE (TechLab), which is linked to EIA-4 in the same assay; and GDH-2, the Wampole C. DIFF CHEK-60 (TechLab).
The second study evaluated 42 positive samples from a series of 284 stool samples and found the sensitivity of qPCR (Cepheid Xpert) and a combined EIA plus GDH assay (C. DIFF QUIK CHEK COMPLETE) to be 100% with specificities for both also approaching 100%.29 The authors suggested that using the C. DIFF QUIK CHEK COMPLETE assay was sufficiently reliable if one performed qPCR to resolve any assays for which the EIA plus GDH assay did not have concordant results. However, again, the authors did not perform toxigenic culture on all specimens, which causes the apparent sensitivity of other assays to improve.19

In the third study, Eastwood and colleagues30 investigated the performance of 9 commercial assays for detecting C. difficile toxin, toxigenic culture, and tissue culture cytotoxin on 600 stool samples from patients with suspected CDI. The sensitivity of the toxin assays, based on 125 samples containing C. difficile by culture, ranged from 60% to 86%, which is somewhat higher than we found, but there was no broth enrichment performed for recovery of C. difficile; as demonstrated in our current report, not enriching the C. difficile culture lowers the sensitivity of culture by some 31%, which in turn falsely raises the sensitivity of other assays being compared.30

The implications of CDI diagnostics are broad, ranging from how we accurately identify individual patients with disease (and patients without it) to how we understand the biology of this seemingly ever-changing infection. An illustration of how imprecise diagnostics impacts understanding the biology of CDI is evidenced in reports linking the development of CDI to gastric acid suppressants and disassociating the disease from antibiotic prescription.31,32 The investigators for these studies queried large databases to determine risk factors for CDI based on inpatient or outpatient disease classification codes rather than test results. The first study found that CDI risk factors included the use of proton pump inhibitors and H2-receptor antagonists,31 a finding we could not confirm when actual testing using reliable assays was used.15 The second such study determined that nearly half of the patients with the diagnosis of CDI had no history of antimicrobial agent exposure,32 long considered a mainstay of CDI risk.14 However, in a scenario in which physicians frequently repeat tests to ascertain CDI diagnosis and with multiple testing leading to a near equal number of true- and false-positive results,19 it is not difficult to conceptualize that 50% of the included patients may not have had CDI and that the patients not only were treated for the wrong disease, but also lacked the expected antibiotic exposure.

The use of poor diagnostic methods will impair the understanding of risks for CDI, particularly when this handicap from how we accurately identify individual patients with disease (and patients without it) to how we understand the biology of this seemingly ever-changing infection. An illustration of how imprecise diagnostics impacts understanding the biology of CDI is evidenced in reports linking the development of CDI to gastric acid suppressants and disassociating the disease from antibiotic prescription.31,32 The investigators for these studies queried large databases to determine risk factors for CDI based on inpatient or outpatient disease classification codes rather than test results. The first study found that CDI risk factors included the use of proton pump inhibitors and H2-receptor antagonists,31 a finding we could not confirm when actual testing using reliable assays was used.15 The second such study determined that nearly half of the patients with the diagnosis of CDI had no history of antimicrobial agent exposure,32 long considered a mainstay of CDI risk.14 However, in a scenario in which physicians frequently repeat tests to ascertain CDI diagnosis and with multiple testing leading to a near equal number of true- and false-positive results,19 it is not difficult to conceptualize that 50% of the included patients may not have had CDI and that the patients not only were treated for the wrong disease, but also lacked the expected antibiotic exposure.

The use of poor diagnostic methods will impair the understanding of risks for CDI, particularly when this handicap is combined with the inherent errors of disease coding in health care reporting.33 Misunderstanding the biology of CDI can lead to unnecessary testing of patients without appropriate risk factors for infection and waste health care resources. Such database inquiries continue,34,35 and when testing has
sensitivity and positive predictive values approaching 50% to 70%, there is no assurance that the conclusions reached have any biologic meaning.

Our study has limitations. One concern raised regarding the qPCR test is that it may be “too sensitive” (ie, like toxigenic culture, it will detect small quantities of non–CDI-causing C difficile organisms). However, simply using a less sensitive test will not mitigate this problem; it has never been demonstrated that cases detected by less sensitive tests are more likely to represent actual C difficile disease. Furthermore, the colonization of persons in acute care facilities today may be considerably lower than that found in the past in which a longer stay was more common. In August 2007, we conducted a point prevalence survey in one of our hospitals, performing qPCR for C difficile on rectal and perianal swabs of 303 patients. Only 5 of 303 patients had positive qPCR results for C difficile, for a colonization rate of 1.7% (unpublished data, L.R.P. and A.R.). In addition, the performance of all tests other than the commercial qPCR and 1 GDH assay was at the low range of prior reports, including that of our in-house–developed molecular assay, perhaps suggesting some errors in testing. For the present study, we used an exhaustive culture testing approach that included broth enrichment, not done in our prior study, and 2 approaches to enhance culture recovery of toxigenic C difficile (Figure 1), which will comparatively lower the sensitivity of all but the most robust test(s).

Some may argue that immunoassays have always been suboptimal for diagnosis, but in their critical review of published data, Planche et al found no EIA with sensitivity less than 75%, even with toxigenic culture as the reference standard, which is clearly higher than what we currently report. It is important to note that Tenover and colleagues recently demonstrated that concurrent with the changing biology of C difficile, EIAs are unable to detect some newer CDI strains, including epidemic clones, further explaining the waning performance of EIAs. Finally, our data may have been biased if testing were done during the presence of an outbreak that could have favored a single strain type. However, we recently reported the prevalence of CDI in our patients during several years of using an electronic surveillance system that demonstrated no outbreaks of CDI. We continue to use the same surveillance system, and there were no CDI outbreaks detected through the end of 2010.

Improved testing for CDI clearly has positive implications for correct diagnosis, but it also will likely impact an organization’s infection control program. Based on our presented data, changing laboratory testing from an EIA to qPCR could initially seem to double the number of CDI cases by using a test with nearly double the sensitivity of current assays. The long-term expectation would be that improved detection of CDI cases will lead to better deployment of contact precautions to reduce the spread of this pathogen in the healthcare environment, but only future studies will address that important issue.

There is now consensus that CDI is an evolving disease. To clearly understand this evolution, we suggest that the accurate diagnosis of CDI is critical and it should be based on the appropriate clinical manifestation of significant diarrhea, which is 3 or more loose stools in a 24-hour period for most patients, plus a positive result on a reliable diagnostic assay for toxigenic C difficile consisting of pseudomembranes seen at colonoscopy (for colitis) or toxin B (or toxins A and B) detected in the stool by using a sensitive test to detect toxin or toxin genes. At present, qPCR seems to be the only single, rapid test method available with sufficient sensitivity and specificity for directly detecting virulent C difficile.

An alternative choice would be to use a 2-step algorithm that includes GDH antigen testing followed by qPCR of positive samples. However, the cost of this strategy is not insignificant, with the manufacturer’s suggested retail price for reagents of the only adequately performing GDH test being $17.73; reimbursement by the Centers for Medicare & Medicaid Services for this test is $17.18. Furthermore, the delay involved in needing to perform 2 tests would require contact isolation for patients with suspected CDI until the testing is complete (eg, preemptive isolation), which adds expense amounting to $30 or more per hospitalization day. Perhaps most important, this 2-step algorithm is significantly less sensitive than toxigenic culture, making the strategy inferior to qPCR testing alone as a testing approach. With the manufacturer’s suggested retail price for commercial qPCRs assays in the range of $25 to $50 and reimbursement from the Centers for Medicare & Medicaid Services for bacterial detection using amplification being $50.27, the most cost-efficient and reliable approach for the detection of virulent C difficile seems to be qPCR. In considering CDI diagnostic testing, the goal of the laboratory should be rapid, reliable detection of toxigenic C difficile in a patient’s stool sample so that the treating physician can rely on the results of a positive or negative test. After decades of facing the challenge of what test to use for the laboratory diagnosis of CDI, molecular testing finally offers that opportunity for confidence.

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References


