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Use of a Rapid Antigen Test, *C. DIFF QUIK CHEK*®, as a Screening Test for *C. difficile* Disease

Authors: A. H. Lewis[1], M. V. Goodykoontz[1], **D. E. Link[1]**, D. M. Lyerly[1], C. R. Hill[2], L. R. Henry[2]; [1]TECHLAB, Inc., Blacksburg, VA, [2]Carilion Consolidated Laboratories, Roanoke, VA

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ABSTRACT: *C. DIFF QUIK CHEK*® (TECHLAB®) is a rapid test for detection of glutamate dehydrogenase (GDH) in fecal specimens. GDH is produced by all strains of *Clostridium difficile*, which causes nosocomial and community-acquired infections, most often following antibiotic therapy. Some *C. difficile* strains are nontoxigenic while toxigenic strains cause gastrointestinal problems ranging from diarrhea to colitis through the production of toxin A, an enterotoxin, and toxin B, a cytotoxin. Diagnosis of *C. difficile* disease relies on patient symptoms and toxin detection. Tissue culture, which is highly sensitive and specific for toxin detection, requires special equipment and 48 hours before a specimen can be reported as negative. ELISA toxin tests are more rapid but not as sensitive. Screening with *C. DIFF QUIK CHEK*® would allow samples negative for GDH, and therefore *C. difficile*, to be reported out immediately. Positive samples could then be confirmed for toxin by additional testing. 200 fresh fecal specimens were tested using *C. DIFF QUIK CHEK*®, *C. DIFF CHEK-60*™, and tissue culture *TOX-B TEST*. Compared to tissue culture, *C. DIFF QUIK CHEK*® had a sensitivity, specificity, predictive negative value, and correlation of 95%, 78%, 98%, and 82%, respectively. Compared to *C. DIFF CHEK-60*™, the sensitivity, specificity, and correlation were each 94%. The *C. DIFF QUIK CHEK*® is a rapid test that is simple to use with a quick (<30 minutes) turn-around time for reporting samples as negative when no GDH is detected. *C. DIFF QUIK CHEK*® correlates well with the ELISA antigen test, *C. DIFF CHEK-60*™. With high sensitivity and high predictive negative values compared to tissue culture, it is an effective way to screen samples and reduce the workload and cost of diagnosing *C. difficile* without sacrificing patient care.

BACKGROUND: *C. DIFF QUIK CHEK*® (TECHLAB®) is a rapid test for detection of glutamate dehydrogenase (GDH) in fecal specimens. GDH is produced by all strains of *Clostridium difficile*, which causes nosocomial and community-acquired infections, most often following antibiotic therapy. Some *C. difficile* strains are nontoxigenic while toxigenic strains cause gastrointestinal problems ranging from diarrhea to colitis through the production of toxin A, an enterotoxin, and toxin B, a cytotoxin. Diagnosis of *C. difficile* disease relies on patient symptoms and toxin detection. Tissue culture, which is highly sensitive and specific for toxin detection, requires special equipment and 48 hours before a specimen can be reported as negative. ELISA toxin tests are more rapid but not as sensitive. Screening with *C. DIFF QUIK CHEK*® would allow samples negative for GDH, and therefore *C. difficile*, to be reported out immediately. Positive samples could then be confirmed for toxin by additional testing.

SPECIMENS: Two hundred patient specimens were included in this study. Patient ages ranged from 74 days to 96 years. One hundred eighteen (59%) female; eighty two (41%) male. Hospital inpatients comprised 51% of the patients, outpatients = 30%, and nursing home patients = 19%.

METHODS: With *C. DIFF QUIK CHEK*®, the specimen, diluent, and conjugate are mixed, added to a cassette containing immobilized anti-GDH antibodies, and incubated for 15 minutes. The membrane is washed and substrate is added. Reaction development occurs during a subsequent 10-minute incubation. 200 fresh fecal specimens were tested using *C. DIFF QUIK CHEK*®, *C. DIFF CHEK-60*™, and tissue culture *TOX-B TEST*.

RESULTS: Compared to tissue culture, *C. DIFF QUIK CHEK*® had a sensitivity, specificity, predictive negative value, and correlation of 95%, 78%, 98%, and 82%, respectively. Compared to *C. DIFF CHEK-60*™, the sensitivity, specificity, and correlation were each 94%. The predictive negative value was 98%.

ANALYSIS OF THE *C. DIFF QUIK CHEK* ® VERSUS TISSUE CULTURE

(N=200)	TISSUE CULT	
	Pos	Neg
C. DIFF QUIK CHEK ® -pos	41	35
C. DIFF QUIK CHEK ® -neg	2	122
Sensitivity	95% (95% CI 83% - 99%)	
Specificity	78% (95% CI 70% - 84%)	
Pred Neg Val	97% (95% CI 94% - 100%)	
Correlation	82% (95% CI 77% - 86%)	

NOTE: The Predictive Positive Value was not determined because the *C. DIFF QUIK CHEK* ® detects the presence of both toxigenic and nontoxigenic strains whereas the tissue culture assay detects only toxigenic strains. Thus, PPV is not an accurate indication of test performance.

ANALYSIS OF THE *C. DIFF QUIK CHEK* ® VERSUS *C. DIFF CHEK-60*™

(N=200)	*C. DIFF CHEK-60*™	
	Pos	Neg
C. DIFF QUIK CHEK ® -pos	68	8
C. DIFF QUIK CHEK ® -neg	4	120
Sensitivity	94% (95% CI 86% - 98%)	
Specificity	94% (95% CI 88% - 97%)	
Pred Pos Val	89% (95% CI 80% - 95%)	
Pred Neg Val	97% (95% CI 91% -99%)	
Correlation	94% (95% CI 92% - 95%)	

C. DIFF QUIK CHEK ®

Negative Result

C. DIFF QUIK CHEK ®

Positive Result

DISCUSSION: Our study was undertaken to evaluate a new rapid antigen screen for *C. difficile*, the *C. DIFF QUIK CHEK*®. Our results showed the following:

- The test exhibited a high predictive negative value (>98%) for the detection of stool specimens that were negative for *C. difficile* toxin. This screen allows laboratories that use the tissue culture assay to focus on performing this more complicated test only on specimens that are antigen-positive. In our study involving 200 specimens, 159 specimens (ca. 80%) would not have required further testing, although 2 would have been missed upon initial testing.
- The test provided results in less than 30 minutes. This rapid turn-around time allows the physician to know quickly whether the patient is infected with *C. difficile*. This information allows the necessary precautions to be implemented rapidly and efficiently.
- The performance of the test, which uses a new membrane format, correlated closely (94%) with an ELISA format (the *C. DIFF CHEK-60*™) that is specific for glutamate dehydrogenase.
- A limitation of the test is that it does not distinguish between toxigenic and nontoxigenic strains. In our study, 54% of the *C. DIFF QUIK CHEK*®-positive specimens were positive by tissue culture assay. We did not determine whether antigen-positive, tissue culture-negative specimens represented true nontoxigenic strains or contained levels of toxin that were too low to be detected by tissue culture assay. Our results show, however, that GDH, which is expressed constitutively by all strains of *C. difficile*, is an excellent marker for determining the presence of the organism.

CONCLUSIONS: The *C. DIFF QUIK CHEK*® is a rapid test that is simple to use with a quick (<30 minutes) turn-around time for reporting samples as negative when no GDH is detected. *C. DIFF QUIK CHEK*® correlates well with the ELISA antigen test, *C. DIFF CHEK-60*™. With high sensitivity and high predictive negative values compared to tissue culture, it is an effective way to screen samples and reduce the workload and cost of diagnosing *C. difficile* without sacrificing patient care.

TECHLAB®

TECHLAB®, Inc.
2001 Kraft Drive, Blacksburg, VA, 24060
540-953-1664, techlab@techlab.com, www.techlab.com