

FLETCHER ALLEN HEALTH CARE

PATHOLOGY & LABORATORY MEDICINE

TEST UPDATE: CLOSTRIDIUM DIFFICILE TOXIN PCR

ASSAY INFORMATION:

This molecular amplification assay utilizes real time polymerase chain reaction (PCR) technology.

The test will be performed in the Clinical Microbiology Laboratory once daily Monday – Saturday. It replaces an enzyme immunoassay for toxin A/B. This molecular assay provides a more sensitive and specific method for detection of the toxin than the enzyme immunoassay.

CLINICAL APPLICATION:

Clostridium difficile infection is one of the most important and difficult hospital associated infections in most hospitals; Fletcher Allen Health Care is no exception. Prompt recognition of the infection and institution of infection control methods is essential to control of the disease. In recent years new genotypes of the bacterium, which produce more serious disease, have appeared in many countries, including the United States and Canada. The essential steps to making an accurate diagnosis of *C. difficile* disease have been defined clearly^{1,2}

1. Limit testing to patients at risk; i.e. those who have received antimicrobial therapy
2. Limit testing to patients who have had ≥ 3 loose stools for one to two days
3. Use a laboratory test with high sensitivity, such as PCR
4. Do NOT repeat a negative test. The yield will be minimal and the chances of a false positive test will be increased

METHOD:

The test is performed on the Cepheid GeneXpert system, which is a real time PCR instrument. The Xpert® *C. difficile* assay contains probes for the *tcdB* gene, which codes for cytotoxin B, the most important marker of *C. difficile* infection. The sensitivity and specificity of recently marketed PCR assays far exceed other commonly used methods, such as enzyme immunoassay. The Xpert® *C. difficile* assay was compared against an enriched reference culture method. Culture is the most sensitive assay, but requires several days for completion, greatly reducing its clinical relevance. The following data from a large study in institutions with a prevalence of disease similar to that at Fletcher Allen Health Care are³

Sensitivity	93.49%
Specificity	94.02%
Positive Predictive Value	72.98%
Negative Predictive Value	98.82%
Prevalence	14.72%

Note that the Xpert® *C. difficile* assay is not FDA-cleared for testing of formed stool (stool that maintains its shape and does not conform to the container). If there are clinical factors that suggest the need for testing (eg., documented pseudomembranous colitis or toxic megacolon), please consult the pathology resident on call for Microbiology for approval.

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In summary, the Xpert® *C. difficile* provides for the first time a highly sensitive and very highly specific assay that can be performed in a clinically relevant timeframe. It is a major advance both for antimicrobial chemotherapy and for institution of infection control measures. The **sensitivity** of the PCR assay (93%) contrasts starkly with a reported sensitivity of 32%-72% for commercially available enzyme immunoassays.¹ The **specificity** of the assay approaches 100%, obviating the need for repeat testing⁴ For this reason the Microbiology Laboratory will not honor requests for repeat testing within one week of the original specimen. If there is a significant change in clinical status, consult the pathology resident on call for consideration of an additional assay.

TEST INFORMATION:

Test Name: Clostridium difficile PCR

Test Code: CDPCR*

Sample Requirements: Collect soft or liquid stool (takes shape of container) in a sterile container; formed stools not acceptable without pathologist approval.

Days performed: Monday – Saturday

Analytical Time: Report available within 24 hours.

Expected Value: Negative for *C.difficile* toxin by PCR.

Patient Price: Call Laboratory Customer Service for pricing Information (847-5121 or 1-800-991-2799).

Effective Date: October 19, 2009

* This test replaces *C. difficile* Toxin (FECT) and Confirmatory test for *C. difficile* (CCDIF).

References:

1. Peterson, LR, Robicsek A. Does my patient have *Clostridium difficile* infection? Ann. Intern. Med. 151:176-179, 2009.
2. Peterson LR, et al. Detection of toxigenic *Clostridium difficile* in stool samples by real-time polymerase chain reaction for the diagnosis of *C. difficile*-associated diarrhea. Clin. Infect. Dis. 45:1152-60, 2007.
3. Cepheid Corporation. Package insert for Xpert® *C. difficile* assay.
4. Aichinger E, et al. Nonutility of repeat laboratory testing for detection of *Clostridium difficile* by use of PCR or enzyme immunoassay. J. Clin. Microbiol. 46:3795-7, 2008.