June 15, 2011

To: Chiefs of Service, Attending Physicians, Housestaff, Nurses and Other Concerned Personnel

From: Barbara Haller, MD, PhD
Division Chief, Microbiology

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Director, Clinical Laboratory

Re: New Molecular Assay for Clostridium difficile (C. difficile) Toxin B Gene

Effective June 21, 2011, the SFGH Clinical Laboratory will discontinue use of an enzyme immunoassay for detection of C. difficile toxin A/B and will implement use of a PCR assay, the Cepheid GeneXpert C. difficile Toxin B gene assay, which detects the presence of the toxin B gene in stool specimens.

There are important changes in laboratory procedures, specimen acceptance and rejection criteria, and clinical use for the new molecular C. difficile PCR assay.

A. CLINICAL USE

1. Only patients with diarrhea (3 or more unformed stools per day) should be considered for testing for C. difficile infection.

B. LABORATORY ACCEPTANCE AND REJECTION CRITERIA

1. Only soft or liquid stool specimens that take the shape of the container are acceptable. Formed stools are not acceptable.

2. Not acceptable: Stool specimens collected with preservatives, with swabs, or during colonoscopy

3. Not acceptable: Stool specimens from patients less than two years of age (not validated for children or neonates).

4. Because of the high sensitivity and specificity of the PCR assay for the toxin B gene, testing one stool specimen is inadequate.

5. Since most patients do not have a clinical indication for re-testing, repeat testing will be limited:
   a. If PCR assay is negative, repeat testing will be allowed on day 5 or later
   b. If PCR assay is positive, no repeat testing is necessary. DO NOT test for cure. Send another stool specimen only if patient has relapse diarrhea or diarrhea after 14 days of therapy.

   Repeat testing of specimens from patients with PCR positive results will only be performed on day 15 or later.
c. If PCR assay is invalid, another specimen may be submitted for testing if clinically indicated.
d. To have the test approved for C. difficile testing outside of these repeat guidelines, i.e. if the patient has fever, increased WBC, and non-resolving diarrhea or suspected toxic megacolon, contact the Microbiology Lab Medicine Resident (206-5699, pager 443-1438).

C. RESULT REPORTING AND TEST AVAILABILITY

1. Testing will be performed by the Clinical Laboratory twice a day, seven days a week.

2. Results will be reported as:
   a. Positive for Clostridium difficile toxin B gene
   b. Negative for Clostridium difficile toxin B gene
   c. Invalid. Presence or absence of Clostridium difficile target DNA cannot be determined.
      Resubmit if clinically indicated.

D. TEST PERFORMANCE

In the SFGH Clinical Microbiology Laboratory, a comparison of the GeneXpert PCR assay with the enzyme immunoassay was performed on 70 patient stool specimens sent for C. difficile testing using the C. difficile Cytotoxin Cell assay as the “gold standard” test. In this study, the PCR assay was 100% sensitive and 95% specific with a positive predictive value of 77% and negative predictive value of 100%. These performance characteristics are comparable to studies in the literature where the GeneXpert C. difficile PCR assay reportedly demonstrated sensitivities of 90-95% and specificities of 95-98%.

E. CLINICAL MANAGEMENT

Clinical management of the patient will not be changed. Special Contact Isolation is still required and may be initiated based upon clinical presentation of the patient. If there is a question regarding the cause of diarrhea, then ordering isolation may wait until laboratory confirmation is received. Refer to Hospital Administration Policy 3.10 Clostridium difficile: Management of the Patient and Environment.

More information about this test is available in the online SFGH Clinical Laboratory Manual (http://labmed.ucsf.edu/sfglab/data/testlist.html#cc).

For questions or concerns contact Barbara Haller, MD, PhD (206-3595); the Microbiology Lab Medicine Resident (206-5699, pager 443-1438); or Marguerite Roemer, Sr. Microbiology CLS Supervisor (206-3597).

For questions or concerns regarding patient management contact Elaine Marie Dekker, RN, CIC (206-8451); the ID Fellow (pager 443-BUGS); or the Infection Control Practitioner (pager 443-1566).