

Clostridium difficile Diarrhea and Colitis

Laboratory policy is:

1. Only liquid stools (assumes the shape of the container) will be accepted for testing.
2. Issue written reports, but not phone results.
3. Only retest patients with previously positive results after 14 days.

There are two types of anaerobic *Clostridium difficile* bacteria which can inhabit the gastrointestinal tract. One type is a toxin producing strain which can cause gastrointestinal illness, while the other is a non-toxin producing strain which is not responsible for disease. Both of these strains can be carried in the gastrointestinal tract of people who do not have diarrhea or who have diarrhea or colitis due to other causes such as ischemia, inflammatory bowel disease or malabsorption. Therefore the diagnosis of *Clostridium difficile* associated disease should initially be suspected based on clinical findings.

The majority of patients with *C. difficile* associated disease will have two major clinical criteria present. These are prolonged (2-3 days) profuse watery diarrhea and exposure to antibiotics or antineoplastic agents usually within 8 weeks of presentation. Other symptoms may include an increased white cell count, fever, abdominal pain and tenderness.

There are a number of laboratory tests available as an aid to diagnosis. Our laboratory offers a two-step testing algorithm in order to provide a rapid, accurate and cost effective laboratory results. The first test performed is a very sensitive enzyme immunoassay (EIA) screening test for the presence of *C. difficile* bacteria. This test screens for the presence of glutamate dehydrogenase (GDH) which is a protein produced in large amounts by *C. difficile* bacteria. It is not equivalent to the EIA test which detects Toxin A and/or B. The EIA toxin test is relatively insensitive and because of this, it is not used in our laboratory. Testing is done twice daily and negative results are generated rapidly. However positive results must be confirmed with a second test. We use a molecular PCR assay which detects the presence of the *C. difficile* toxin B gene which correlates well with actual cytotoxin production. This test is one of the most sensitive and rapid tests available for confirmation. The results are reported as positive or negative for the presence of *C. difficile* cytotoxin when the test is complete, generally within a few hours.

The specificity of *C. difficile* toxin testing varies with the type of patient tested. Patients who do not meet the clinical criteria for *C. difficile* associated disease may have a positive result on testing due to carriage of the organism. A number of studies of asymptomatic carriage rates have been done in the following populations:

Children, <2 years	7-60%
Cystic fibrosis patients	up to 50%
Children >2years	<4%
Healthy Adults	<4%
Healthy Adults given antibiotics	up to 49%
Hospitalized Adults after 4 weeks in hospital	50%
Elderly in chronic care	21%
Elderly, acute care	14%

Asymptomatic carriage is probably 2 to 5 fold more common than the disease itself. This fact creates difficulty with interpretation of lab test results if the colonized patient develops diarrhea due to another cause. The patient most at risk for *C. difficile* disease is the hospitalized elderly patient on antibiotics.

Guidelines for use of the *C. difficile* toxin assay:

- *Test only diarrheal stool (assumes the shape of the container)
- *Tests of cure should not be performed; cure is cessation of symptoms as *C. difficile* tests can remain positive for long periods after treatment
- *Test only specimens from patients who are older than one year of age, due to the high carriage rate in this age group
- *Diarrhea that develops after 3 days of hospitalization should be tested for *C. difficile*. Stool for culture and ova and parasites are not recommended because of the low yield. Other stool tests should be ordered as clinically indicated.

Guidelines for management of diarrhea and colitis associated with *C. difficile* infection:

- *Discontinue implicated antibiotic if possible (20-25% of patients will respond to this alone)
- *Use supportive measures
- *Follow infection control policies on hospitalized patients
- *Treat with Metronidazole orally for 10 days, 500 mg 3 times daily (children orally 30 mg/kg/day, 4 times daily) when:
 - Diarrhea is severe
 - There is evidence of colitis
 - Diarrhea persists despite discontinuation of implicated antibiotic
 - There is a need to continue treatment of original infection with implicated antibiotic
 - Intravenous route may be used if oral route can't be tolerated
- *Vancomycin can be used orally at 125 mg, 6 times daily for 10 days (children orally 40 mg/kg/day, 4 times daily) when:
 - Patient is pregnant
 - Intolerant or allergic to Metronidazole
 - No response to Metronidazole
- *Patient has severe disease or is critically ill because of *C. difficile*-associated diarrhea or colitis.
In these cases, a infectious disease consult is recommended.

What to do if tests for *C. difficile* are negative and patient has persistent symptoms:

- *Repeat *C. difficile* test
- *Expand diagnostic evaluation to include other causes
- *Treat empirically for *C. difficile* disease

If patient fails to respond to Metronidazole therapy and tests remain negative, the patient probably does not have disease. Rare patients may present with an ileus without prior diarrhea. This may be secondary to antiperistaltic agents or opiates which have been given postoperatively. Making the diagnosis is difficult in these cases and often may require endoscopy. An Infectious Disease or Gastroenterology consult is available if additional help with diagnosis is desired.

REFERENCES:

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