As the incidence of *C. difficile* infection (CDI) increases both in community and inpatient settings, so do the number of asymptomatic carriers of *C. difficile*. Routine diagnostic tests for CDI do not distinguish between active disease and colonization. Since treatment of asymptomatic carriage is discouraged due to lack of benefit and potential long-term harm, it is important to be judicious in choosing which patients to test for *C. difficile*.

Which patients are at risk for *C. difficile* colonization? Colonization of healthy adults is uncommon and very few patients without previous hospital exposure have *C. difficile* in their stool at the time of hospital admission. Up to 20%, however, become symptom-free carriers after just one week in the hospital and nearly 50% have *C. difficile* in their stool by the end of a four week stay. Long term care facility residents also have a higher likelihood of *C. difficile* colonization, ranging from 4% to 20% in the absence of a recognized outbreak.

Carriage of *C. difficile* is also common in healthy neonates for the first year of life.

Do *C. difficile* tests detect colonization in the absence of active disease? All commercially available laboratory tests for diagnosing CDI have the potential to detect asymptomatic carriage. The two most commonly encountered diagnostic tests are the quantitative polymerase chain reaction (PCR; utilized by Multicare and Franciscan Health Systems) and enzyme immunoassay (EIA). The PCR assay has a sensitivity >90%, but is far more likely to detect colonization than the EIA. A study comparing the PCR assay with an EIA for toxin A and B revealed 18-PCR positive samples that were negative by toxin EIA.

Repeated testing after a negative result is discouraged unless there is a high index of suspicion for CDI and the results of repeat testing will alter treatment. This is due to the low increase in yield and a significantly increased number of false-positive results detected on repeat testing. Repeat testing is also discouraged following successful treatment, as patients may continue to shed *C. difficile* toxin in the stool for many weeks.

<table>
<thead>
<tr>
<th>Description</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Potential Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR Toxin regulator genes (tcdB)</td>
<td>&gt;90%</td>
<td>&gt;97%</td>
<td>False Positives</td>
</tr>
<tr>
<td>EIA Toxins A &amp; B</td>
<td>70-80%</td>
<td>&gt;97%</td>
<td>False Negatives</td>
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Which patients should I test? Limit *C. difficile* testing to patients with a reasonable probability of having active disease. Test those with prior antibiotic exposure and clinically significant diarrhea, defined as ≥3 loose stools per day for at least 1–2 days (it is reasonable to test patients with septic presentation and <3 stools/24 hours if suspicion for CDI is high). Diarrheal stools should be interpreted within the context of the patient. Review baseline bowel habits, as those with chronic loose stools and/or diarrhea should have a significant change from baseline before stool testing is ordered. Likewise, review the medication profile for recent use of any laxatives, stool softeners or enemas.

What is the harm in treating asymptomatic colonization? Asymptomatic carriers are thought to be a reservoir for transmission of the organism to susceptible patients, however treating these patients in the absence of active diarrheal illness does not
consistently reduce the risk of transmission. Several studies have explored the treatment of colonized patients and have observed the following trends:

1. Asymptomatic *C. difficile* colonization can be protective against subsequent active CDI. This benefit has been observed in patients colonized with both toxigenic and non-toxigenic *C. difficile* who have received antimicrobial therapy and remained symptom-free.\(^3,7\) This does not include patients who have remained culture positive after successful treatment of active CDI. The mechanism for this protection is thought to be related to host immunity (e.g., higher immunoglobulin A levels) or the colonization of a specific intestinal niche by a *C. difficile* strain that does not cause active disease and protects against more pathogenic strains.\(^1\)

2. Treating asymptomatic *C. difficile* may abolish the observed protective effect. Patients are thought to be continually at risk of exposure to *C. difficile* throughout a hospitalization.\(^2\) Treating a patient who has remained asymptomatic and eliminating a *C. difficile* strain that has not caused active disease will not only further alter the normal intestinal flora, but may also allow for a new, more virulent *C. difficile* strain to be introduced.\(^7\)

3. Treatment of colonized patients with metronidazole does not work. Metronidazole achieves negligible levels in the colon in the absence of significant diarrhea and treatment of asymptomatic individuals provides no benefit.\(^1,2\)

4. Treatment of colonized patients with oral vancomycin has produced mixed results and is not recommended. While one study in 1987 in a leukemia unit showed a reduction in overall *C. difficile* disease from 16.6% to 3.6% after treating all carriers with oral vancomycin, data since this time has failed to show a benefit and even suggested possible harm from this approach.\(^5\) In one study, vancomycin was initially effective (asymptomatic carriage rate reduced to 10% in the vancomycin arm versus 80% for placebo at the end of treatment), but significantly increased the likelihood of reacquiring *C. difficile* compared to those in the placebo group at the two-month follow-up.

### References

4. Litvin, et al. Identification of a pseudo-outbreak of *Clostridium difficile* infection (CDI) and the effect of repeated testing, sensitivity, and specificity on perceived prevalence of CDI. Infect Control Hosp Epidemiol 2009;30(12):1166-71