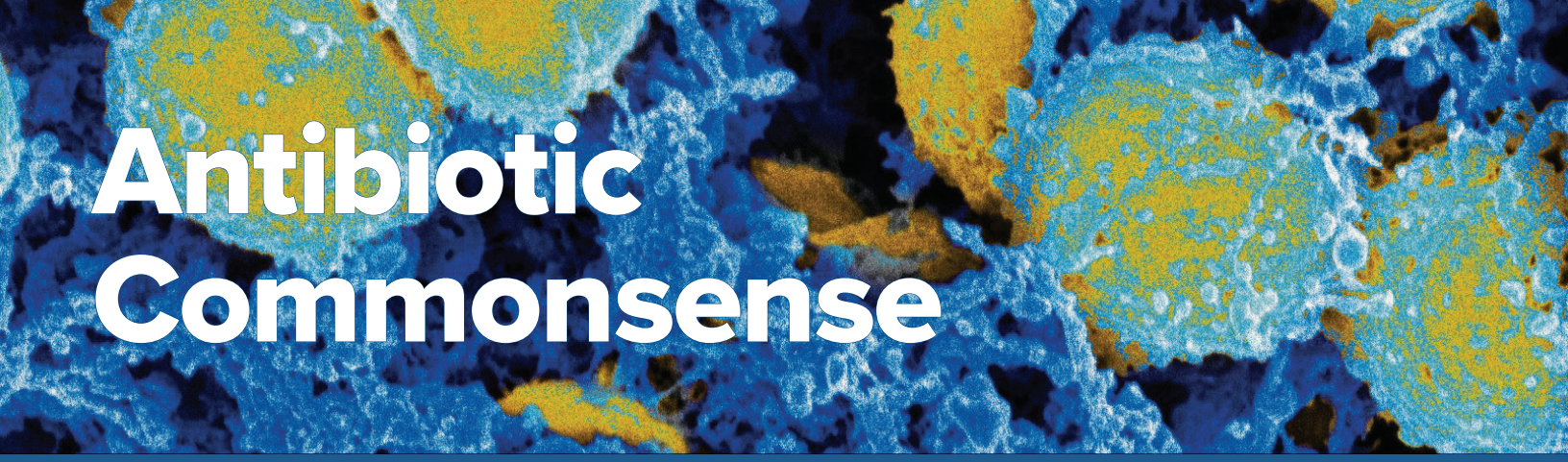

Clostridioides difficile Infection vs. Colonization: Who do I test?

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Actions

- Limit *C. difficile* testing to patients reasonably likely to have active disease.
- Avoid repeat testing within seven days of a negative result—unless you highly suspect infection.
- Avoid testing children younger than two years—asymptomatic carriage is very common.
- Do not perform test of cure.
- Do not treat patients with asymptomatic colonization.

Background

As the incidence of *C. difficile* infection (CDI) increases, so does the number of asymptomatic carriers. Routine tests for CDI do not distinguish between active disease and colonization. Treating asymptomatic carriers can cause long-term harm and provides few benefits. It is important to be judicious when choosing which patients to test.

Which patients are at risk for colonization?

Colonization of healthy adults is uncommon. Very few previously unhospitalized patients have *C. difficile* in their stool when admitted to a hospital. Yet up to 20% become asymptomatic carriers after one week in a hospital. Nearly 50% have *C. difficile* in their stool after a four-week stay.[1]

Long-term care facility residents also have a higher likelihood of *C. difficile* colonization—4% to 20%.[2,3] Carrying *C. difficile* is also common in healthy infants and children younger than two years.[4,5]

Do *C. difficile* tests detect colonization in the absence of active disease?

All CDI tests can potentially detect asymptomatic carriage. The most common tests are polymerase chain reaction (PCR) and enzyme immunoassay (EIA). MultiCare and Franciscan Health Systems use PCR. It has greater than 95% sensitivity but is more likely to detect colonization. In contrast, EIA has high specificity but lacks sensitivity—so false negative results are possible. Recent developments in ultrasensitive *C. difficile* toxin detection may provide a solution for more accurate diagnosis in the future.[6,7]

Test	Target	Sensitivity	Specificity	Potential Problem
PCR	Toxin regulator genes (*tcdB*)	>95%	>97%	False positive
EIA	Toxins A and B	60%-70%	>97%	False negative

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What is the harm in treating asymptomatic colonization?

Treating asymptomatic carriers does not consistently reduce the risk of transmission to others. Several studies have explored the treatment of colonized patients and observed the following.

1. **Asymptomatic colonization can protect against later active CDI.**

   This benefit was observed in patients colonized with both toxigenic and non-toxigenic *C. difficile* who received antimicrobial therapy and remained symptom-free.[8,5] (This does not include patients who 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 strain that does not cause active disease and protects against more pathogenic strains.[2]

2. **Treating asymptomatic colonization may stop the protective effect.**

   Patients are at risk of exposure to *C. difficile* throughout a hospitalization.[9] Treating a patient who has remained asymptomatic will further alter normal intestinal flora and may allow for a new, more virulent strain to be introduced.[5]

3. **Treating colonized patients with metronidazole does not work.**

   Metronidazole achieves negligible levels in the colon in the absence of significant diarrhea. Treating asymptomatic individuals provides no benefit.[2,9]

4. **Treating colonized patients with oral vancomycin has produced mixed results and is not recommended.**

   A 1987 study in a leukemia unit showed reduction in overall *C. difficile* disease after treating all carriers with oral vancomycin. However, data has since failed to show a benefit—and even suggests possible harm from this approach.[10] In one study, vancomycin was initially effective—asymptomatic carriage was reduced to 10% in the vancomycin arm vs. 80% for placebo at the end of treatment—but significantly increased the likelihood of reacquiring *C. difficile* compared to the placebo group at the two-month follow-up.[9]

Which patients should I test?

Limit *C. difficile* testing to patients reasonable likely to have active disease. Test those with prior antibiotic exposure and clinically significant diarrhea—defined as three or more loose stools per day for at least one to two days. It is reasonable to test patients with less than three loose stools in 24 hours if they present with sepsis, ileus or megacolon, and you highly suspect CDI.

Interpret diarrheal stools within the context of the patient. Those with chronic loose stools or diarrhea should have a significant change from baseline before you order stool tests. Likewise, look for recent laxative or enema use.

Often, *C. difficile* testing should not be done. Staff education, standardized patient screening and test order algorithms can reduce inappropriate testing and treatment of colonized patients.[11,12]

If you decide to test

Do not repeat test within seven days of a negative result unless you highly suspect CDI and the repeat test result will alter treatment. Repeat tests detect significantly more false-positives.[13] Do not repeat test following successful treatment. Test of cure is not recommended, as patients may continue to shed *C. difficile* for many weeks.

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