

Management of *Clostridium difficile*-associated diarrhea: Guidelines for Long Term Care and Rehabilitation Facilities

Developed by the Colorado Medical Directors Association and the Colorado Department of Public Health and Environment

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1. Antibiotic-associated diarrhea (AAD)

"Although in recent years discussions of AAD have centered on *Clostridium difficile*-associated diarrhea, only 10%-20% of all AAD cases are positive for toxigenic *C. difficile*"¹. *Clostridium difficile* may produce toxins [an enterotoxin (toxin A) or a cytotoxin (toxin B)] that are responsible for antibiotic-associated colitis, but other mechanisms by which antibiotics cause diarrhea include disturbances in the function of normal bacterial flora (such as altered colonic bacterial carbohydrate metabolism and decreased metabolism of bile acids) and direct effects of antibiotics leading to increased intestinal motility. Other reported infectious causes of AAD include *Clostridium perfringens*, *Klebsiella oxytoca*, and *Candida* species. The antibiotics with the greatest risk for causing *Clostridium difficile*-associated diarrhea (CDAD) are clindamycin, ampicillin, amoxicillin, and cephalosporins.

2. Epidemiology and transmission of *Clostridium difficile*-associated diarrhea (CDAD)

The incidence of community-acquired CDAD is low, but the risk of acquiring *C. difficile* increases in direct proportion to the length of hospital stay. There is a high incidence of asymptomatic carriers in hospitals. Even the most virulent strains of *C. difficile* produce asymptomatic colonization more often than CDAD. There is little data to support the widespread belief that *C. difficile* is part of the normal, endogenous intestinal flora which proliferates because of the suppression of other flora in the presence of antibiotics. Instead, the data indicate that *C. difficile* is exogenously acquired and a variety of clinical outcomes occur following acquisition. One model for the pathogenesis of CDAD is that hospitalized patients acquire the organism and become colonized; when asymptomatic carriers are subsequently exposed to antibiotics, the risk of CDAD is increased. An alternative model, for which there is supportive data, is that hospitalized patients given antibiotics are subsequently exposed to toxigenic *C. difficile*; of these patients an additional factor, such as host susceptibility or virulence of the *C. difficile* strain, determines whether the patient remains asymptomatic or develops CDAD after a brief incubation period. In this model, if and when asymptomatic colonization is established, the patient is at decreased risk of CDAD.

The two major reservoirs of *C. difficile* are infected humans and contaminated inanimate objects. Patients with CDAD are more infectious than asymptomatic carriers. Health care workers probably transmit the organism from patient to patient through transient hand carriage, and they may develop hand carriage directly from patients or from inanimate objects in the vicinity of symptomatic patients. Environmental contamination is enhanced by the persistence of *C. difficile* spores, which may be resistant to disinfectants and usual cleaning. Objects such as commodes, rectal thermometers, and telephones have been implicated as potential sources. The epidemiology of *C. difficile* is similar to that of vancomycin-resistant enterococci.

3. Clinical definition of *Clostridium difficile*-associated diarrhea (CDAD)

Diarrhea, defined as watery or unformed stools, occurring ≥ 3 times a day for several days, usually associated with abdominal cramping, fever, dehydration, white blood cells in the stool, and peripheral leukocytosis; pseudo-membranes seen at lower gastrointestinal endoscopy (because pseudo-membranes are detectable in only 50%-55% of cases, their absence does not exclude CDAD); and no other recognized etiology for diarrhea.

Either a history of treatment with antimicrobial or antineoplastic agents within the previous 2 months or a history of onset of diarrhea within 72 hours of hospitalization is present in virtually all patients. A response to specific therapy for CDAD is suggestive of the diagnosis.

4. Laboratory tests for *Clostridium difficile*-associated diarrhea

The proper laboratory specimen for diagnosis is a single watery, unformed or loose stool specimen (not rectal swabs). The specimen should be submitted in a clean, watertight container (special anaerobic or transport media are not necessary). Submitting multiple specimens does not increase the likelihood of finding a positive by a significant percentage and is not cost-effective for routine practice, but may be useful when the laboratory tests are negative but the diarrhea persists. Testing stools of asymptomatic patients is not clinically useful and is not recommended.

The specimen should be tested for *C. difficile* toxins by cytotoxicity or immunoassay and should be cultured. To interpret laboratory results properly, it is useful to ask the laboratory what is the sensitivity and specificity of the particular test it is using. The stool culture is the most sensitive test for CDAD (89%-100%), whereas stool cell cytotoxicity (toxin B) is the most specific assay (85%-100%); for maximum diagnostic sensitivity and specificity, performance of both tests is recommended. Some laboratories may offer a rapid latex test for *C. difficile* protein, but this is not recommended for routine laboratory detection of *C. difficile* (sensitivity is 58%-92% and specificity is 80%-96%). Other methodologies may be in use (e.g., counterimmunoelectrophoresis for stool toxins) or new methodologies are under development (e.g., PCR).

5. Screening for *Clostridium difficile* in the long term care or rehabilitation setting

Surveillance cultures of asymptomatic residents or screening cultures of new admissions for *C. difficile* are not routinely indicated, even if the resident has fecal incontinence.

6. Treatment of *Clostridium difficile*-associated diarrhea (CDAD)

CDAD will resolve in 15%-25% of patients within 2-3 days of discontinuing the offending antibiotic without any other specific intervention. Specific treatment for CDAD incurs a risk of recurrence (5%-30%) 1 or 2 weeks following treatment that is either due to the original organism or infection by another strain of *C. difficile*.

Oral metronidazole (10 day course, 250mg q.i.d., 375mg t.i.d., or 500mg t.i.d.) is considered the best initial drug of choice for uncomplicated CDAD. Oral vancomycin (10 day course, 125mg q.i.d.) has also been extensively used, but is **not** the recommended first choice because of higher cost and concern about spread or promotion of vancomycin-resistance among other organisms such as enterococci. *If the diarrhea resolves by the conclusion of treatment, there is no need for follow-up laboratory cultures or toxin assays.*

For patients who experience diarrhea recurrence following treatment, most (>90%) will respond to a second course of treatment with the same initial therapy. For those patients with two or more recurrences, alternative treatment strategies designed to re-establish the normal colonic flora should be considered. Such approaches include treatment with vancomycin and rifampin in combination, metronidazole followed by lactobacillus, and vancomycin followed by cholestyramine. Antimotility agents such as diphenoxylate and loperamide are contraindicated for the treatment of *C. difficile* colitis.

Infrequently, *C. difficile* infection may result in toxic megacolon or ileus, and the patient may paradoxically have no diarrhea, but instead have atypical symptoms suggesting an acute surgical abdomen. In these instances, medical management may be attempted before surgical intervention unless there is suspicion of colonic perforation.

It is the right of individuals in LTC facilities to refuse treatment of their particular medical problem. If a resident (or guardian) refuses treatment, their wishes should be respected. It is then the responsibility of the facility to maintain appropriate infection control to protect staff and other residents.

7. Infection control recommendations for patients with CDAD

Patients should be placed in a private room, if available, or semi-private room cohorted with other patients with the same infection. Highest priority for a private room should be patients who are fecally incontinent or who cannot practice good handwashing hygiene. Because of environmental contamination, persons with CDAD should share toilets only with other CDAD patients.

An infected patient may be moved to a non-private room and/or cohorting may be discontinued and may resume all communal activities when the diarrhea ceases. Follow-up stool cultures are not necessary to release from enteric precautions or private room/cohorting.

Health care workers should employ appropriate barrier precautions, i.e. enteric (stool) isolation, and handwashing when caring for such patients. This includes *gloves and gowns* for any significant patient contact. (Insignificant contact would occur if a staff member briefly entered the room to leave a tray of food and had no other interaction with the patient.) Handwashing must be performed after gloves are removed. Since objects may be involved in transmission of *Clostridium difficile*, common use equipment such as thermometers and stethoscopes should not be shared with uninfected or non-cohorted patients.

Disinfection of the room and potentially contaminated objects should be performed using common household bleach in a 10% solution, i.e. diluted 1 part bleach to 10 parts water. The disinfection should include environmental surfaces, such as bedside tables, bed rails, and objects that may be reused, such as stethoscopes.

8. Transfer of residents from long term care or rehabilitation facilities to acute care facilities and vice versa.

If detected, colonization with *Clostridium difficile* should not prevent the transfer of an individual between facilities if the transfer is medically indicated. Patients should not be held in a facility waiting for colonization to clear if the *Clostridium difficile* colonization is the only reason to hold the patient.

9. "Decolonization" of patients.

Treatment of asymptomatic carriers with either metronidazole or vancomycin with the intention of eradicating the infection has little effect on fecal excretion.

10. Use of rectal thermometers

The use of rectal thermometers is discouraged in all patients whether or not the person is infected with *Clostridium difficile*. Oral or electronic tympanic thermometers are recommended for routine use unless there are special circumstances.

11. Outbreaks of CDAD in LTC facilities

An outbreak of CDAD is defined as: three (3) or more cases of clinically significant, facility acquired CDAD occurring in the same general area within a period of seven (7) days. In this instance, the Medical Director should be notified. If feasible, there should be cohorting of infected residents, and staff should not crossover to uninfected residents. Once there is clinical resolution of the infection after treatment, no reculture is needed to remove from cohort.

An outbreak is likely to be caused by the transmission of organisms by staff and a breakdown in the use of standard precautions. Therefore, an intense education program for staff should ensue with rigorous supervision of handwashing and use of gloves and gowns. If after these procedures are done and there continue to be new cases of clinically significant

CDAD, an epidemiologist in the state or local health department should be notified.

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References:

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3. Gerding DN, Johnson S, Peterson LR, Mulligan ME, and Silva J. Clostridium difficile-associated diarrhea and colitis. Society for Healthcare Epidemiology of America position paper. *Infection Control and Hospital Epidemiology* 1995; 16:459-477.