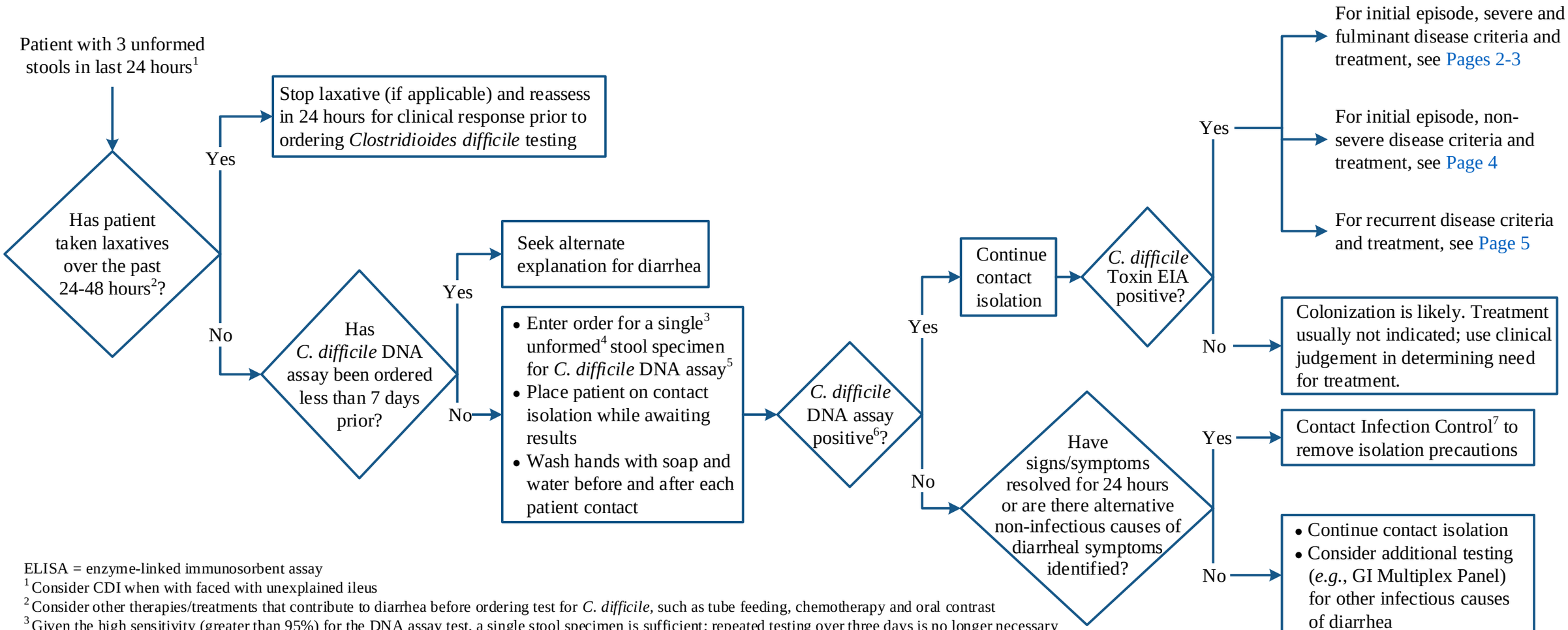
# Assessment and Management of *Clostridioides difficile* Infections (CDI)

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care.*

**PRESENTATION** | **ASSESSMENT** | **INTERVENTION**




ELISA = enzyme-linked immunosorbent assay

[1] Consider CDI when with faced with unexplained ileus

[2] Consider other therapies/treatments that contribute to diarrhea before ordering test for *C. difficile*, such as tube feeding, chemotherapy and oral contrast

[3] Given the high sensitivity (greater than 95%) for the DNA assay test, a single stool specimen is sufficient; repeated testing over three days is no longer necessary

[4] See Appendix A for Bristol Chart

[5] Reflective ELISA for *C. difficile* toxins A and B will be performed on all positive DNA assays. Use clinical judgement in interpreting significance of DNA positive, ELISA negative results.

[6] Do not retest within 7 days, regardless of result

[7] Infection Control (IC): Phone: (713) 792-3655 | Email: INFECTIONCONTROL@mdanderson.org



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## DISEASE SEVERITY

**Initial episode, severe disease**

- Presence of visualized pseudomomembranes on endoscopy, able to take oral medications **and/or**
- Any two of the following:
  - Adult patients age greater than 60 years
  - WBC greater than 15 K/microliter or ANC less than 0.5 K/microliter
  - Serum creatinine (SCr)
    - Adults: greater than 1.5 mg/dL
    - Children: less than 2 years, SCr greater than 0.5 mg/dL; 2-8 years, SCr greater than 0.7 mg/dL; 9-18 years, SCr greater than 0.9 mg/dL
  - Albumin less than 2.5 g/dL
  - GI graft versus host disease (GVHD)
  - Fever greater than 38.3°C
  - Abdominal cramping/pain
  - CT finding with colonic thickening, ascites, or pneumatosis
  - Greater than 10 episodes of diarrhea per day
  - Concomitant chemotherapy or immunosuppression (including corticosteroids)

## TREATMENT[1]

<u>Adult:</u>

- Vancomycin 125 mg oral solution[2] PO every 6 hours for 10 days[3] **<u>or</u>**
- Fidaxomicin 200 mg PO twice daily for 10 days[4]

<u>Pediatric:</u>

- Vancomycin 40 mg/kg/day oral solution[2] PO divided every 6 hours for 10 days (maximum dose of 2 g/day)

**Note**: Carefully review concomitant antimicrobials and stop any that are not absolutely necessary

## REASSESSMENT

Reassess symptoms after 3 days

Improvement?

Yes

- Complete course of therapy
- For adult patients, use bezlotoxumab[5] if institutional criteria met

No

Obtain Infectious Diseases and Gastroenterology consultations

For patients who do not meet criteria for **severe** or **fulminant disease**, see Page 4 for **non-severe disease** treatment

[1] Refer to Appendix B for supportive care considerations
[2] May substitute with capsules if oral solution not available
[3] Concomitant antibiotic therapy for another infection is no longer needed
[4] Concomitant antibiotic therapy for another infection is needed
[5] Refer to Appendix C for institutional use criteria

# Assessment and Management of *Clostridioides difficile* Infections (CDI)





| DISEASE SEVERITY | TREATMENT[1] | REASSESSMENT |
|---|---|---|
| **Initial episode, fulminant disease**<br>• Presence of any of the following:<br>◦ Admission to the ICU<br>◦ Septic shock<br>◦ Toxic megacolon<br>◦ Peritonitis<br>◦ Ileus<br>◦ Perforation<br>◦ Unable to take oral medications | Adult:<br>• Metronidazole 500 mg IV every 8 hours **and**<br>◦ Vancomycin 500 mg oral solution[2] PO or via NGT every 6 hours **or**<br>◦ Fidaxomicin 200 mg PO or via NGT every 12 hours<br>• Consider use of vancomycin retention enema [500 mg in 100 mL normal saline (NS) per rectum every 6 hours] if patient not neutropenic<br>Pediatric:<br>• Metronidazole 30 mg/kg/day IV divided every 8 hours (maximum dose of 2 g/day) **and**<br>• Vancomycin 40 mg/kg/day oral solution[2] PO divided every 6 hours (maximum dose of 2 g/day)<br>• Consider use of vancomycin retention enema dosed every 6 hours if patient not neutropenic<br>◦ 1-3 years: 250 mg in 50 mL NS<br>◦ 4-9 years: 375 mg in 75 mL NS<br>◦ Greater than and equal to 10 years: 500 mg in 100 mL NS<br>All patients:<br>• Consider Surgery, Infectious Diseases, and Gastroenterology consultation(s) | • Continue treatment for 10-14 days of therapy<br>• Reassess appropriateness of therapy continuously based on the patient's clinical status<br>• Obtain Infections Diseases and Gastroenterology consultations for possible fecal microbiota transplant (FMT)[3] |

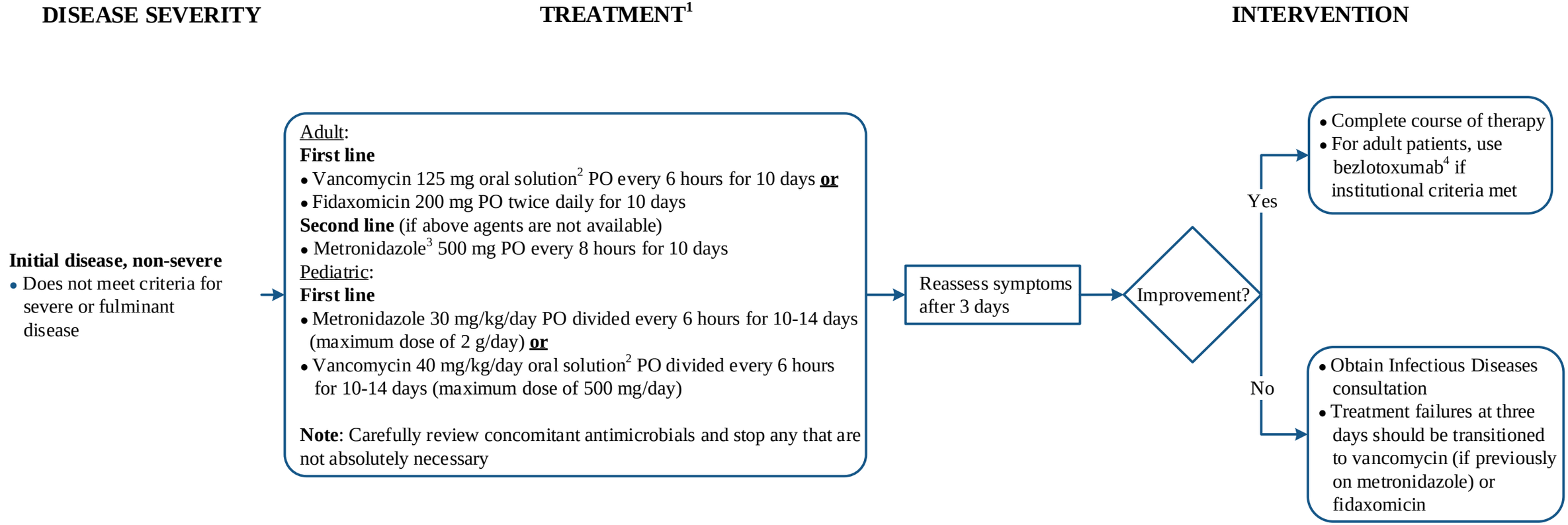
For patients who do not meet criteria for **severe** or **fulminant disease**, see Page 4 for **non-severe disease** treatment

[1] Refer to Appendix B for supportive care considerations
[2] May substitute with capsules if oral solution not available
[3] Refer to Appendix D for fecal microbiota transplant indications

# Assessment and Management of *Clostridioides difficile* Infections (CDI)








[1] Refer to Appendix B for supportive care considerations
[2] May substitute with capsules if oral solution not available
[3] Avoid concomitant use of busulfan due to higher risk of sinusoidal obstruction syndrome (SOS)
[4] Refer to Appendix C for institutional use criteria

# Assessment and Management of *Clostridioides difficile* Infections (CDI)





**Note:** Avoid use of unnecessary antibiotics[1]

## RECURRENCE[2]

Diarrhea due to CDI (patient must have completed 10-14 days of effective therapy and have no symptoms for 48 hours after treatment has ended)

## TREATMENT

First recurrence →

Adult:
- Vancomycin 125 mg oral solution[3] PO every 6 hours for 10 days if metronidazole was used for the first episode **or**
- Fidaxomicin 200 mg PO twice daily for 10 days if vancomycin was used for the first episode **or**
- Vancomycin tapering/pulse treatment if vancomycin or fidaxomicin was used for the first episode:
  - 125 mg oral solution PO every 6 hours for 14 days, then every 12 hours for 14 days, then once daily for 7 days, then every other day for 4 doses, then every third day for 5 doses, then off
  - Some patients may require chronic suppression thereafter
- For all regimens, use bezlotoxumab[4] if institutional criteria are met and not previously administered

Pediatric: See Page 6

→ Reassess symptoms after 3 days → Improvement?

Yes → Consider fecal microbiota transplant (FMT)[5,6] if first two episodes were associated with hospitalization or significant morbidity

No → Consider Infectious Diseases and Gastroenterology consultations for additional work up and possible FMT[5,6]

Second and subsequent recurrences → See Page 7

[1] Clindamycin and fluoroquinolones are associated with the highest risk of CDI. Whenever possible, avoid these agents and all other unnecessary antibiotics, particularly those with anaerobic activity such ampicillin/sulbactam, piperacillin/tazobactam, and carbapenems.
[2] Refer to Appendix E for prevention considerations
[3] May substitute with capsules if oral solution not available
[4] Refer to Appendix C for institutional use criteria
[5] Refer to Appendix D for fecal microbiota transplant indications
[6] Refer to Infectious Disease Clinic at (713) 792-2340 or Gastroenterology at (713) 794-5073



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# Assessment and Management of *Clostridioides difficile* Infections (CDI)





**Note:** Avoid use of unnecessary antibiotics[1]

**RECURRENCE[2]** **TREATMENT**

First recurrence →

Pediatric:

- Vancomycin 40 mg/kg/day oral solution[3] PO divided every 6 hours for 10 days if metronidazole was used for the first episode **or**
- Fidaxomicin[4] if vancomycin was used for the first episode
  - Age 6 years to less than 18 years: 200 mg tablets PO twice daily for 10 days **or**
- Vancomycin tapering/pulse treatment (for children under 18 years) if vancomycin or fidaxomicin was used for the first episode:
  - 10 mg/kg/dose oral solution PO every 6 hours for 14 days, then every 12 hours for 14 days, then once daily for 7 days, then every other day for 4 doses, then every third day for 5 doses, then off

→ Reassess symptoms after 3 days → Improvement?

- Yes → Consider fecal microbiota transplant (FMT)[5,6] if first two episodes were associated with hospitalization or significant morbidity
- No → Consider Infectious Diseases and Gastroenterology consultations for additional work up and possible FMT[5,6]

Second and subsequent recurrences → See Page 7

[1] Clindamycin and fluoroquinolones are associated with the highest risk of CDI. Whenever possible, avoid these agents and all other unnecessary antibiotics, particularly those with anaerobic activity such ampicillin/sulbactam, piperacillin/tazobactam, and carbapenems.
[2] Refer to Appendix E for prevention considerations
[3] May substitute with capsules if oral solution not available
[4] Fidaxomicin is not FDA approved in patients less than 18 years of age but there is phase IIa data to support use in recurrent disease
[5] Refer to Appendix D for fecal microbiota transplant indications
[6] Refer to Infectious Disease Clinic at (713) 792-2340 or Gastroenterology at (713) 794-5073

# Assessment and Management of *Clostridioides difficile* Infections (CDI)

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**Note:** Avoid use of unnecessary antibiotics[1]

## RECURRENCE[2]

## TREATMENT

Second and subsequent recurrences →

Adult:

- Vancomycin course[3] followed by tapering/pulse treatment:
  - 125 mg oral solution PO every 6 hours for 14 days, then every 12 hours for 14 days, then once daily for 7 days, then every other day for 4 doses, then every third day for 5 doses, then off
  - Some patients may require chronic suppression thereafter

**or**

- Fidaxomicin[4] 200 mg PO twice daily for 10 days
- Consider Infectious Diseases consultation
- For all regimens, use bezlotoxumab[5] if institutional criteria met and not previously administered. If previously administered, consider use on case-by-case basis.
- Consider FMT[6,7]

Pediatric:

- Fidaxomicin[4] if vancomycin was used for the first episode
  - Age 6 years to less than 18 years: 200 mg tablets PO twice daily for 10 days **or**
- Vancomycin tapering/pulse treatment (for children under 18 years) if vancomycin or fidaxomicin was used for the first episode:
  - 10 mg/kg/dose oral solution PO every 6 hours for 14 days, then every 12 hours for 14 days, then once daily for 7 days, then every other day for 4 doses, then every third day for 5 doses, then off
- Some patients may require chronic suppression thereafter

→ Reassess symptoms after 3 days → Improvement?

- Yes → Monitor recurrence[8]
- No →
  - Consider alternate causes such as post-infectious diarrhea
  - Consider FMT[6,7]

[1] Clindamycin and fluoroquinolones are associated with the highest risk of CDI. Whenever possible, avoid these agents and all other unnecessary antibiotics, particularly those with anaerobic activity such ampicillin/sulbactam, piperacillin/tazobactam, and carbapenems.
[2] Refer to Appendix E for prevention considerations
[3] May substitute with capsules if oral solution not available
[4] Fidaxomicin is not FDA approved in patients less than 18 years of age but there is phase IIa data to support use in recurrent disease
[5] Refer to Appendix C for institutional use criteria
[6] Refer to Appendix D for fecal microbiota transplant indications
[7] Refer to Infectious Disease Clinic at (713) 792-2340 or Pediatric Infectious Disease at (713) 792-6610 or Gastroenterology at (713) 794-5073
[8] Consider continuing prophylaxis in selected patients and those awaiting FMT (consult Gastroenterology and Infectious Diseases)



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# Assessment and Management of *Clostridioides difficile* Infections (CDI)



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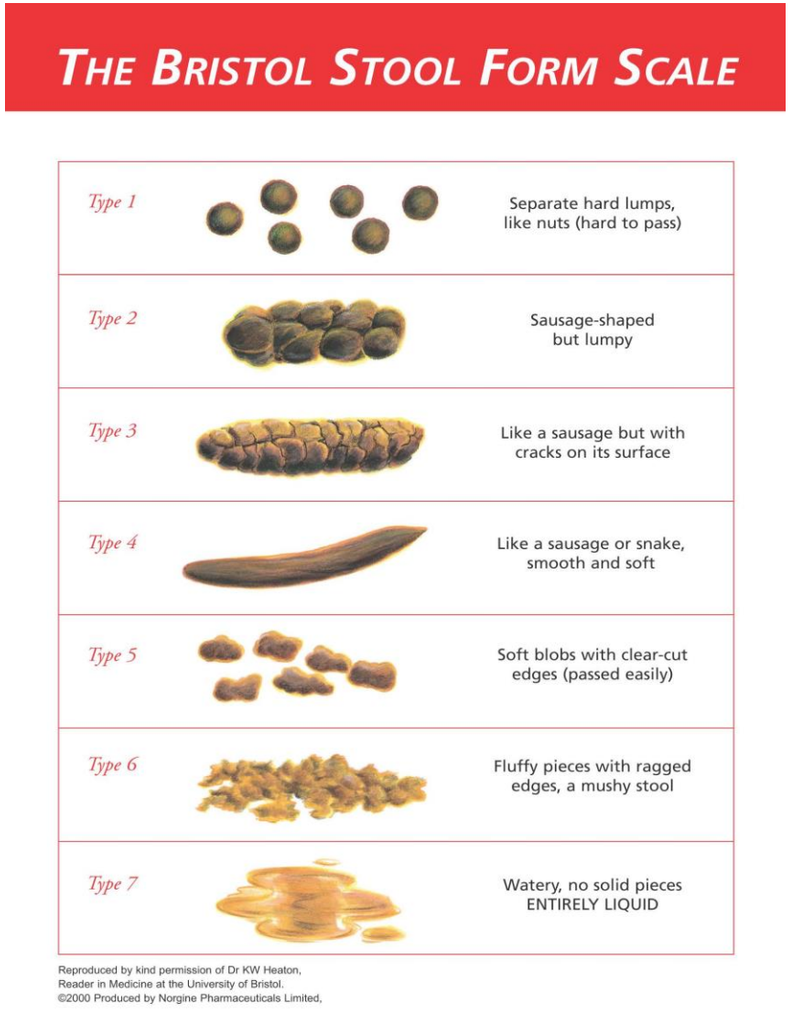
## APPENDIX A

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## APPENDIX B: Supportive Care Considerations

- Supportive care with hydration, avoidance of anti-motility agents, opiates and bile salts binding agents.
- Probiotics are not recommended in cancer patients with CDI. There are no randomized, peer reviewed studies to support the use of probiotics for the prevention or treatment of CDI in cancer patients. Cases of bacteremia (*Lactobacillus*) and fungemia (*Saccharomyces*) have been described in immunosuppressed patients receiving probiotics.
- For patients with a high index of suspicion for severe CDI and negative diagnostic studies, and if not contraindicated, consider diagnostic colonoscopy to examine for pseudomembrane formation. The decision for therapy in these patients is left at the discretion of the treating physician, consider Infectious Diseases consultation.

## APPENDIX C: Institutional Bezlotoxumab Use Criteria (Adults Only)

- Restricted to outpatient use only, with an exception for inpatients with an extended hospitalization that would not allow outpatient administration during concomitant antibacterial treatment for *C. difficile* infection (anti-CDI therapy)
- Must have a positive stool *C. difficile* nucleic acid amplification test AND a positive toxin by enzyme-linked immunosorbent assay (ELISA)
- Must be receiving concomitant anti-CDI therapy (e.g., vancomycin, fidaxomicin, metronidazole)
- Presence of at least one of the following risk factors for recurrent CDI:
  - Age greater than or equal to 60 years
  - At least one prior episode of CDI
  - Compromised immunity: currently receiving immunosuppressants, neutropenia (*i.e.*, ANC less than 0.5 K/microliter), and/or lymphopenia (*i.e.*, ALC less than 0.2 K/microliter)
  - Clinically severe CDI (*i.e.*, Zar score greater than 2)
  - Patient expected to continue non-CDI antibiotics greater than or equal to 3 days beyond end of anti-CDI therapy

## APPENDIX D: Fecal Microbiota Transplant Indications

- Recurrent or relapsing CDI (all CDI must be diagnosed by positive stool test for *C. difficile*):
  - Three or more episodes of mild-to-moderate CDI and failures of a 6-8 week taper with vancomycin with or without an alternative antibiotic (*e.g.*, rifaximin, nitazoxanide, or fidaxomicin).
  - At least two episodes of CDI resulting in hospitalization and associated with significant morbidity.
- CDI not responding to standard therapy (vancomycin or fidaxomicin) for at least a week.
- Severe (even fulminant CDI) with no response to standard therapy after 48 hours.

## APPENDIX E: Prevention Considerations

- Prolonged courses of perioperative antibiotic prophylaxis beyond a single dose is discouraged except in selected circumstances.
- The use of prophylactic antibiotics in patients receiving chemotherapy is discouraged. Exceptions are in patients with neutropenia associated with leukemia and HSCT.
- Continued use of antibiotics during therapy for *C. difficile* increases risk of failure and recurrence. Discontinue concomitant antibiotics as soon as possible following diagnosis of *C. difficile.*
- Empiric therapy while awaiting diagnostic testing results is discouraged except in cases of suspected severe CDI (e.g., toxic megacolon, ileus, severe colitis) or when a pseudo membrane is identified on endoscopy.
- Given the high rates of asymptomatic colonization (3-8%), the detection of *C. difficile* nucleic acid test (NAT) by itself is not sufficient to justify specific therapy unless there is a high index of clinical suspicion (e.g., clinically significant diarrhea and no confirmed alternative causes).
  - Routine testing for *C. difficile* infection in children under 2 years of age with diarrhea not recommended
- Follow infection control measures including:
  - Initiate contact isolation for suspected CDI while awaiting test results.
  - Wash hands with soap and water prior to entering and exiting the room. Wear a gown and gloves. The use of hand sanitizer is insufficient to kill *C. difficile* spores.
  - Clean shared patient care items with a hospital approved bleach product, according to manufacturer's instructions.
  - Do not re-test for CDI for the sole purpose of removing isolation. Patients who are no longer passing unformed stools will be re-evaluated by an infection preventionist prior to discontinuation of isolation. Only an infection preventionist has the authority to remove patients from isolation.
- Preferably delay chemotherapy until CDI treatment has been completed and diarrhea has resolved.
- Consider delaying radiation therapy until GI symptoms have resolved.

HSCT = hematopioetic stem cell transplant

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## DEVELOPMENT CREDITS

This practice consensus statement algorithm is based on majority opinion of the Infection Control, Infectious Disease, and Pediatrics experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

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Sherry Cantu, MPH, CIC (Infection Control)[Ŧ]
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