Assessment and Management of Clostridium difficile Infections (CDI) - Adult

This practice algorithm has been specifically developed for MD Anderson using a multidisciplinary approach and taking into consideration circumstances particular to MD Anderson, including the following: MD Anderson’s specific patient population; MD Anderson’s services and structure; and MD Anderson’s clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers.

1. **Patient with 3 unformed stools in last 24 hours**
   - Has patient been taking laxatives over the past 24-48 hours?
     - Yes
       - **Stop laxative and reassess in 24 hours for clinical response prior to ordering Clostridium difficile testing**
       - Enter order for a single unformed stool specimen for C. difficile DNA assay
       - Place patient on contact isolation while awaiting results
       - Wash hands with soap and water before and after each patient contact
     - No
       - **Continue contact isolation**

2. **C. difficile DNA assay positive?**
   - Yes
     - **C. difficile Toxin EIA positive?**
       - Yes
         - Colonization is likely. Treatment usually not indicated; use clinical judgement in determining need for treatment.
       - No
         - Contact Infection Control to remove isolation precautions
     - No
       - **Have signs/symptoms resolved for 24 hours or are there alternative non-infectious causes of diarrheal symptoms identified?**
         - Yes
           - Continue contact isolation
           - Consider additional testing (e.g., GI Multiplex Panel) for other infectious causes of diarrhea
         - No
           - **ELISA = enzyme-linked immunosorbent assay**

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1. Suspect 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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Department of Clinical Effectiveness V2
Approved by the Executive Committee of the Medical Staff on 05/29/2018
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### DISEASE SEVERITY

**Initial episode, severe disease**
- Presence of visualized pseudomembranes on endoscopy, able to take oral medications and/or one of the following:
  - Age greater than 60 years of age
  - WBC greater than 15 K/microliter or ANC less than 0.5 K/microliter
  - Serum creatinine greater than 1.5 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 or ascites
  - Greater than 10 episodes of diarrhea per day
  - Concomitant chemotherapy or immunosuppression
    (including corticosteroids)

**Initial episode, fulminant disease**
- Presence of any of the following:
  - Admission to the ICU
  - Septic shock
  - Toxic megacolon
  - Peritonitis
  - Ileus
  - Unable to take oral medications

For patients who do not meet criteria for **severe** or **fulminant disease**, see Page 3 for **non-severe disease** treatment.

### TREATMENT

#### Initial episode, severe disease
- Vancomycin 125 mg oral solution every 6 hours for 10 days or Fidaxomicin 200 mg PO twice daily for 10 days
- Carefully review concomitant antimicrobials and stop any that are not absolutely necessary

#### Initial episode, fulminant disease
- Metronidazole 500 mg IV every 8 hours and
  - Vancomycin 500 mg oral solution every 6 hours or Fidaxomicin 200 mg PO or via NGT every 12 hours
- Consider use of vancomycin retention enema (500 mg in 100 mL normal saline per rectum every 6 hours)
- Consider surgery, infections diseases, and gastroenterology consultation(s)

### REASSESSMENT

- Reassess symptoms after 3 days
- Improvement?
  - Yes
  - Complete course of therapy
  - Use bezlotoxumab if institutional criteria met
  - Obtain infectious diseases and gastroenterology consultations
  - Continue treatment for 10-14 days of therapy
  - Reassess appropriateness of therapy continuously based on the patient’s clinical status
  - Obtain Infectious Diseases and Gastroenterology consultations for possible fecal microbiota transplant (FMT)

- No
  - Obtain Infectious Diseases and Gastroenterology consultations
  - Carefully review concomitant antimicrobials and stop any that are not absolutely necessary
  - Metronidazole 500 mg IV every 8 hours
  - Vancomycin 500 mg oral solution or via NGT every 6 hours
  - Fidaxomicin 200 mg PO or via NGT every 12 hours
  - Consider use of vancomycin retention enema (500 mg in 100 mL normal saline per rectum every 6 hours)
  - Consider surgery, infections diseases, and gastroenterology consultation(s)
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**Disease Severity**

**Initial disease, non-severe**
- Does not meet criteria for severe or fulminant disease

**Treatment**

- **First line**
  - Vancomycin 125 mg oral solution^2^ PO every 6 hours for 10 days **or**
  - Fidaxomicin 200 mg PO twice daily for 10 days

- **Second line** (if above agents are not available)
  - Metronidazole^3^ 500 mg PO every 8 hours for 10 days

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

**Intervention**

- Reassess symptoms after 3 days

  - Improvement?
    - Yes
      - Complete course of therapy
      - Use bezlotoxumab^4^ if institutional criteria met
    - No
      - Obtain Infectious Diseases consultation
      - Treatment failures at three days should be transitioned to vancomycin (if previously on metronidazole) or fidaxomicin

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^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
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**Note:** Avoid use of unnecessary antibiotics.

**RECURRENCE**

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)

- Vancomycin 125 mg oral solution 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
  - 125 mg oral solution PO every 12 hours for 14 days, then
  - 125 mg oral solution PO once daily for 7 days, then
  - 125 mg oral solution PO every other day for 4 doses, then
  - 125 mg oral solution PO every third day for 5 doses
- Some patients may require chronic suppression thereafter
- For all regimens, use bezlotoxumab if institutional criteria are met and not previously administered

**TREATMENT**

1. **First recurrence**
2. **Second and subsequent recurrences**

Reassess symptoms after 3 days

- Improvement?
  - Yes
  - Consider fecal microbiota transplant (FMT) if first two episodes were associated with hospitalization or significant morbidity
  - Consider Infectious Diseases and Gastroenterology consultations for additional work up and possible FMT

- No
  - Reassess symptoms after 3 days

**References**

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 as 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
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 as ampicillin/sulbactam, piperacillin/tazobactam, and carbapenems. 

1. Vancomycin course\(^1\) followed by tapering/pulse treatment:
   - 125 mg oral solution PO every 6 hours for 14 days, then
   - 125 mg oral solution PO every 12 hours for 14 days, then
   - 125 mg oral solution PO once daily for 7 days, then
   - 125 mg oral solution PO every other day for 4 doses, then
   - 125 mg oral solution PO every third day for 5 doses
   - Some patients may require chronic suppression thereafter or
   - Fidaxomicin 200 mg PO twice daily for 10 days
   - Consider Infectious Diseases consultation
   - For all regimens, use bezlotoxumab\(^4\) if institutional criteria met and not previously administered. If previously administered, consider use on case-by-case basis.
   - Consider FMT\(^5,6\)

Reassess symptoms after 3 days

Improvement?

- Yes
  - Monitor recurrence\(^7\)

- No
  - Consider alternate causes such as post-infectious diarrhea
  - Consider FMT\(^5,6\)

\(^1\) 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 as 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 microbialota transplant indications

\(^6\) Refer to Infectious Disease Clinic at (713) 792-2340 or Gastroenterology at (713) 794-5073

\(^7\) Consider continuing prophylaxis in selected patients and those awaiting FMT (consult Gastroenterology and Infectious Diseases)
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APPENDIX A

THE BRISTOL STOOL FORM SCALE

- **Type 1**: Separate hard lumps, like nuts (hard to pass)
- **Type 2**: Sausage-shaped but lumpy
- **Type 3**: Like a sausage but with cracks on its surface
- **Type 4**: Like a sausage or snake, smooth and soft
- **Type 5**: Soft blobs with clear-cut edges (passed easily)
- **Type 6**: Fluffy pieces with ragged edges, a mushy stool
- **Type 7**: Watery, no solid pieces ENTIRELY LIQUID

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

- 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).
- 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 = hematopoietic stem cell transplant
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SUGGESTED READINGS


Continued on next page
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SUGGESTED READINGS - continued


SUGGESTED READINGS - continued


UTMDACC Institutional Policy #CLN0432 - Isolation Policy


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

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DEVELOPMENT CREDITS

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

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Further information can be found in the original document.