Abstract # 243

Platform Category A1

Evaluation of St. Peter's Health *Clostridioides Difficile* Testing and Treatment Procedures

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Helena, MT
June 30th, 2024

IRB Status: Exempt

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DISCLOSURES

- Keenan Douglas
- Potential conflict of interest: None
- Sponsorship: None
- Proprietary information or results of ongoing research may be subject to different interpretations
- Presentation is educational in nature and indicates agreement to abide by the non-commercialism guidelines provided
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LEARNING OBJECTIVES

By the end of this presentation, you will be able to:

- Identify risk factors and confounders associated with *Clostridioides Difficile* (*C. difficile*) diagnosis and treatment
- Identify when to order stool labs, interpret stool panel results, and when to initiate antibiotic therapy.

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ST. PETER'S HEALTH

- Rural community hospital
- Located in Helena, Montana
- 123 total staffed beds
- Facility acts as a regional referral center for central Montana
  - Laboratory is utilized by Helena and surrounding areas

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PRETEST ASSESSMENT QUESTION #1

- A patient presents to the emergency department with complaints of diarrhea, abdominal pain, and nausea for the last few days. The patient reports having 5-6 loose stools a day. They have tried Lomotil and Pepto-Bismol with no success. They have a history of ulcerative colitis, for which they are receiving treatment. A GI panel was ordered, which resulted in a positive *C. difficile* DNA, so a toxin assay was ordered and came back negative. Should this patient be treated for *C. difficile*?

A. Yes
B. No

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PRETEST ASSESSMENT QUESTION #2

- Based on current guidelines for an initial episode of *C. difficile* infection (CDI), which would be the preferred treatment option?
- A. Vancomycin 125 mg PO QID x10 days
- B. Metronidazole 500 mg PO TID x10 days
- C. Fidaxomicin 200 mg PO BID x10 days
- D. Vancomycin 125 mg PO QID x10-14 days, tapered vancomycin 125 mg BID x7 days, then QD x7 days, then every 2-3 days x2-6 weeks.

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PRETEST ASSESSMENT QUESTION #3

- A patient presents to their PCP for follow-up. They just finished a course of fidaxomicin 200 mg BID x10 days for treatment of *C. difficile* 2 weeks ago. The patient reports that they are no longer having frequent episodes of loose stool. Should a *C. difficile* PCR and toxin assay be ordered to assess efficacy of therapy?

A. Yes

B. No

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STUDY OBJECTIVE

- To evaluate SPH *C. difficile* testing and treatment practices and compare against most current literature and *C. difficile* guidelines.

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BACKGROUND

- *C. difficile* is an anaerobic, toxin-producing, spore-forming, gram-positive bacillus spread by the fecal-oral route. It is the leading cause of healthcare-associated infections and is responsible for 15-25% of antibiotic-associated diarrhea cases.[1]
- *C. difficile* infection is associated with high clinical, social, and economic burdens and has been classified by the Centers for Disease Control and Prevention (CDC) as an urgent health threat that requires urgent and aggressive action.[1]
- In 2017, there were an estimated 223,900 cases in hospitalized patients alone, with approximately 12,800 deaths in the United States.[1]
- *C. difficile* infections result in significant morbidity, loss of productivity, and decreased quality of life.[2]

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BACKGROUND

- *C. difficile* can naturally colonize the large intestine in humans. Adults and children with healthy immune systems can be asymptomatic carriers of the bacteria.[4]
- Diarrhea and colitis are the primary manifestations of *C. difficile* infections caused by clostridial glycosylation exotoxins, Toxin A and Toxin B.[5,6]
- Patients who present with new onset of three or more loose unformed stools in 24 hours without any other reasonable etiology and with *C. difficile* risk factors are recommended to receive testing for *C. difficile*.[5,6]

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BACKGROUND

- St. Peter's Health (SPH) revised *C. difficile* testing and treatment practices in 2018 following release of updated guidelines.
  - Since that time, two additional guidelines have been published prompting need for review of testing and treatment practices.

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BACKGROUND

- When to test for *C. difficile*
  - Unexplained and new-onset ≥ 3 unformed stools in 24 hours.
    - Stool needs to take the shape of container and have no solid pieces.
  - Consider risk factors
    - Exposure to broad-spectrum antibiotics (while on therapy to 3 months after therapy), exposure to the organism through admission to health care facility (duration of hospitalization), immunosuppression, advanced age, severe underlying illness.
  - Consider confounders
    - Underlying disease states (cancer with ongoing chemotherapy or IBD), history of GI surgery, other medications that can cause diarrhea (laxatives in the past 48 hours or chemotherapy known to cause diarrhea), enteral feeding, older age.

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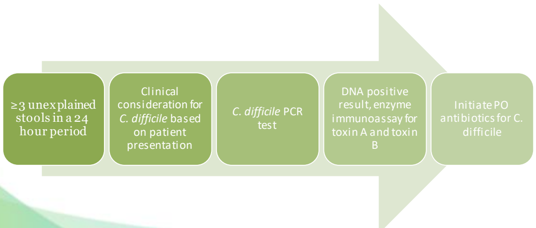
MULTISTEP STEP ALGORITHM



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BACKGROUND

2021 SHEA/IDSA Guidelines

	Recommended	Alternative	Strength
Initial CDI	Use of fidaxomicin over standard course of vancomycin	Vancomycin standard course	Conditional recommendation, moderate certainty
Recurrent CDI	Fidaxomicin standard unless used for initial course*	Vancomycin tapered and pulsed regimen or vancomycin standard course for a first CDI recurrence	Conditional recommendation, low certainty evidence
Recurrent CDI Co-intervention	Use of bezlotoxumab as a co-intervention along with SOC antibiotics for recurrent CDI episode within the last 6 months for patients with high risk factors		

Johnson S, Lavergne V, Skinner AM, Gonzales-Luna AJ, Garey KW, Kelly CP, Wilcox MH. Clinical practice guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 focused update guidelines on management of Clostridioides difficile infection in adults. Clinical infectious diseases. 2021 Sep 1;73(5):e1029-44.

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METHODS: STUDY DESIGN

- Retrospective, single center
- Observational
- Comparison of SPH *C. difficile* testing and treatment practices against current *C. difficile* guidelines

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METHODS: STUDY DESIGN

- A retrospective chart review was performed on 472 patients from January 1, 2019, through December 31, 2023, who had either a GI panel or *C. difficile* PCR ordered.

Variables assessed			
Documentation or reporting of diarrhea consisting of ≥3 unexplained stools in a 24 hour period.	Systemic antibiotic exposure within 2 weeks of symptom onset.	Medications or disease states contributing to diarrhea.	Imaging demonstrating colitis.
Exposure to a healthcare setting 30 days prior to symptoms.	*C. difficile* PCR and toxin assay results.	Treatment used for *C. difficile* infections/recurrent infections.	

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INCLUSION CRITERIA

- Adult patients (≥ 18 years).
- Admitted at SPH during the time of *C. difficile* treatment, or treated for *C. difficile* through SPH facilities.

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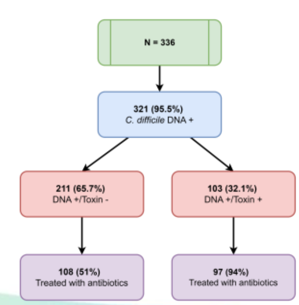
RESULTS



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RESULTS

- There were 9 documented consults with an infectious disease physician.
- One patient received a fecal microbiota transplant.
- Nine patients received bezlotoxumab.

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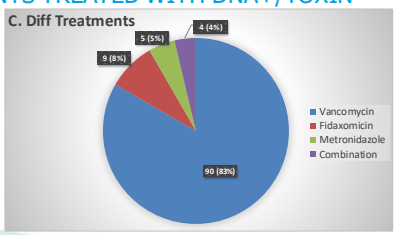
PATIENTS TREATED WITH DNA+/TOXIN-



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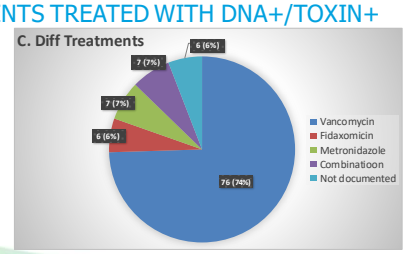
PATIENTS TREATED WITH DNA+/TOXIN+



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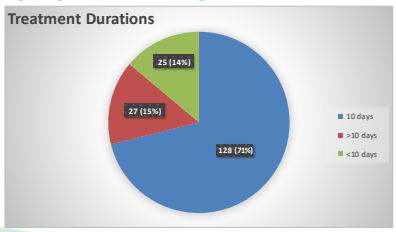
DURATION OF THERAPIES



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CONCLUSION

- Fifty-one percent of the patients with a DNA+/Toxin- result were started on some form of *C. difficile* treatment.
- Ninety-four percent of the patients with a DNA+/Toxin+ result were started on *C. difficile* treatment.
- Vancomycin was predominantly used for the treatment of *C. difficile* regardless of toxin result.

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DISCUSSION

- This study looked at historical data from 2019 to the end of 2023. Previous guidelines recommended vancomycin as the preferred treatment, which is reflected in the results.
- Despite being a first line treatment option, cost barriers to fidaxomicin resulted in preference of vancomycin for first line treatment.
- There were instances where patients were initiated on treatment in the presence norovirus, adenovirus, and patients with a history of ulcerative colitis or Crohn's disease.
- Documentation of diarrhea episodes weren't always quantified making the assessment of criteria for testing challenging.

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STRENGTHS AND LIMITATIONS

Strengths

- Large sample size
- Data from differing SPH facilities and a variety of providers
- Lab submission criteria for stool sample

Limitations

- Study included only 1 site
- Retrospective in nature
- Data collection span was between 2 guideline updates
- Data was collected from 2 different EHR

FUTURE DIRECTIONS

- Implementation of a standardized testing and treatment of *C. difficile*.
  - This will allow for more consistency based on criteria of when labs should be ordered and who antibiotics should be initiated based on results.
  - With a standardized system-wide approach, we hope to reduce costs from unnecessary testing and antibiotic usage.

PROPOSED TREATMENT AND TESTING GUIDELINE

Clostridioides difficile Infection Management at St. Peter's Health
Developed January 2024

Diagnosis
Consider Clostridioides difficile infection (CDI) in patients with new onset diarrhea with at least 3 unformed/watery stools in 24 hours without alternative explanation* AND at least one of the following:

- Fever
- Unexplained WBC elevation
- New onset abdominal pain and/or distention with diarrhea

*Alternative explanations of diarrhea should be evaluated prior to consideration of CDI testing. Evaluate for:

- Antibiotic-associated diarrhea
- Recent chemotherapy
- Use of stool softeners/laxatives
- Other gastrointestinal infections
- IBD/IBS flare
- Use of low-fiber tube feeds

If patient meets any of the above, recommend stopping causative agent (if possible) and monitoring for resolution of diarrhea before considering CDI testing.

Risk factors for CDI:

- Recent antibiotic exposure
- Recent hospitalization
- Advanced age
- Immunocompromising conditions

Testing
If CDI testing is pursued, unformed stool is the only acceptable specimen and non-liquid stool will not be processed. Liquid stool samples will be evaluated in a step-wise approach.

1st step = molecular assay to test for C. difficile toxin A and B genes (not testing for the toxin itself)

- Represents presence of C. difficile in the GI tract, but does not evaluate for colonization vs infection

2nd step = if molecular assay is positive for C. difficile genes, will auto-reflex the C. difficile Immunoassay which tests for actual toxin production

- Toxin A/B positive – probable infection
- Toxin A/B negative – probable colonization

If a patient is PCR positive but toxin negative, strongly consider other diagnoses as this likely represents colonization.
If a patient is PCR and toxin positive, initiate treatment per the table below.

Re-Testing: Repeat C. diff testing is not recommended following completion of treatment or in the 30 days following. Patients will often remain colonized and tests may show false positive results for up to 30 days after symptoms have resolved.

- Re-testing may complicate clinical care and result in inappropriate additional therapy courses.

Disease Severity	Treatment
Initial CDI episode, non-fulminant	• Vancomycin 125 mg PO q6h for 10-14 days* *given the high cost of fidaxomicin and difficulties with insurance authorization, PO vancomycin should be utilized for all initial non-fulminant CDI episodes at SPH.

Recurrent CDI episode, non-fulminant	• Fidaxomicin 200 mg PO q12h for 10-14 days (if vancomycin was used for initial episode)
	OR
	• Vancomycin 125 mg PO q6h for 10-14 days (if fidaxomicin was used for initial episode)
	  ○ Consider pulse/taper regimen in patients with immunosuppression or high risk for recurrence (see next section for pulse/taper regimen)
	
	Bezlotoxumab
	• Consider use of outpatient* bezlotoxumab as an adjunctive treatment in patients if recurrence is within 6 months and who meet ≥2 of the following criteria:
	  ○ Age ≥ 65
	  ○ Meets criteria for severe CDI
	  ○ Immunocompromised host
	• Bezlotoxumab dose = 10 mg/kg IV x1 dose, administered at any time during antimicrobial therapy
	  ○ Use with caution in patients with CHF
	
	*restricted to outpatient use due to cost/reimbursement. Insurance authorization is required before pharmacy will order the medication from the supplier.

Second/Subsequent CDI recurrence, non-fulminant	• Vancomycin PO in a pulse/taper regimen
	
	Pulse/taper dosing = 125 mg PO every 6 hours for 14 days → every 12 hours for 7 days → once daily for 7 days → every other day for 4 doses → every 3rd day for 10-14 doses
	
	Fecal Microbiota Transplant (FMT):
	If CDI recurs after vancomycin taper therapy, consider FMT
	• OpenBiome derived FMT via colonoscopy no longer available at SPH
	• Consider use of outpatient Vowst™ (Fecal microbiota spores, live-brpk):
	  ○ Orally administered fecal microbiota product indicated to prevent the recurrence of CDI following antibacterial treatment for recurrent CDI.
	    ▪ Dosing: 4 capsules PO daily x3 days, beginning 2-4 days after completion of CDI treatment regimen
	  ○ Caveats: expensive, must be obtained directly from a specific specialty pharmacy on a case-by-case basis

Fulminant* disease (initial or recurrence)	• Vancomycin 500 mg PO q6h PLUS metronidazole 500 mg IV q8h for 10-14 days, followed by vancomycin PO in a pulse/taper regimen ○ There is currently insufficient data to recommend use of fidaxomicin in this patient population. • In patients with evidence of ileus, consider use of rectal vancomycin (500 mg q6h as a retention enema, retained for as long as possible) *Criteria for fulminant disease include any of the following: • Admission to ICU • Toxic megacolon • Ileus • Septic shock • Peritonitis • Hypotension • Perforation

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ASSESSMENT QUESTION #1

- A patient presents to the emergency department with complaints of diarrhea, abdominal pain, and nausea for the last few days. The patient reports having 5-6 loose stools a day. They have tried Lomotil and Pepto-Bismol with no success. They have a history of ulcerative colitis, for which they are receiving treatment. A GI panel was ordered, which resulted in a positive C. difficile DNA, so a toxin assay was ordered and came back negative. Should this patient be treated for *C. difficile*?

A. Yes
B. No

ASSESSMENT QUESTION #2

- Based on current guidelines for an initial episode of C. difficile infection, which would be the preferred treatment option?
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- D. Vancomycin 125 mg PO QID x10-14 days, tapered vancomycin 125 mg BID x7 days, then QD x7 days, then every 2-3 days x2-6 weeks.

ASSESSMENT QUESTION #3

- A patient presents to their PCP for follow-up. They just finished a course of fidaxomicin 200 mg BID x10 days for treatment of C. difficile a couple 2 weeks ago. The patient reports that they are no longer having frequent episodes of loose stool. Should a C. difficile PCR and toxin assay be ordered to assess the completion of therapy?

A. Yes

B. No

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Questions?

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