



- *Clostridium difficile* is the most common cause of healthcare-associated diarrhea and recurs in anywhere from 12 to 64% of patients.
- Active CDI is defined as diarrhea (> 3 unformed stools per day) and other symptoms of CDI with a positive stool PCR for *C. difficile* toxin. See OSUWMC guideline for [Prevention and Management of Clostridium difficile Infection](#).
- *Clostridium difficile* infection (CDI) is usually managed with antibiotics; however, severe disease may be refractory to medication therapy necessitating colectomy. Fecal microbiota transplant (FMT) has been evaluated as an alternative treatment modality in the management of severe medication-refractory and recurrent CDI (RCDI).

## Indications

- A FMT could be considered for CDI patients meeting any of the following criteria:
  - RCDI after ≥ 2 episodes of mild-to-moderate CDI **and** failure to respond to appropriate antimicrobial treatment regimens.
    - See **Appendix A** for definition of CDI and appropriate treatment regimens.

**OR**

  - ≥ 2 episodes of severe CDI resulting in hospitalization and significant morbidity within 1 year.

**OR**

  - Severe first episode of active CDI requiring hospitalization and non-responsive to maximal medication therapy
    - See **Appendix A**.
- A second FMT may be considered by ID/Gastroenterology in patients who failed the first.
- In patients with multiple potential etiologies for diarrhea, a *C. difficile* cell cytotoxin assay could be obtained by ID or GI to confirm active CDI.

**NOTE:** FMT for the management of inflammatory bowel disease and other conditions is currently under investigation and requires an IND application. Does not require ID consult.

## Contraindications

- Patients with the following should **NOT** be considered for FMT:
  - Toxic megacolon.
  - Anatomic contraindication to NGT and colonoscopy.
  - Pregnancy.
- Exercise caution when considering an FMT for patients with:
  - A suppressed immune system.
  - Other severe comorbid conditions.
  - The need for broad spectrum antimicrobials immediately post-FMT is considered a relative contraindication to FMT. FMT may be pursued in such patients at the discretion of ID/GI.

## Risks of FMT

- The most common side effects of FMT include:
  - Belching.
  - Nausea/vomiting.
  - Abdominal cramps.
  - Diarrhea.
  - Constipation.
- The risk of infection transmission, colonic perforation, aspiration pneumonia, and death cannot be excluded.
- Data are lacking regarding long term safety risk.

## Recipient Selection

- In CDI cases where FMT is being considered, the following consultations **MUST** be obtained regardless of inpatient or outpatient setting:
  - Infectious Diseases.
  - Gastroenterology.
  - Nutrition (*may occur pre- or post-FMT*).
- Once both the infectious diseases and gastroenterology specialists have documented agreement with FMT in IHIS, the patient's attending physician must place the order for FMT for a date/time at which GI is available to perform the procedure.

## Recipient Preparation

- Gastroenterology or Infectious Diseases will advise patients on the proper discontinuation of antimicrobial treatment (generally 2 days prior to the planned procedure).
  - For critically ill patients, GI and ID should discuss appropriate timing of *C. difficile* antimicrobial therapy discontinuation.
- Patients should follow colonoscopy preparations if that is the intended route of fecal microbiota instillation.
  - [Patient education](#)
  - [Two Day Bowel Prep with Miralax and Dulcolax](#)

## FMT Procurement

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- Frozen fecal microbiota from pre-screened donors is now commercially available and is advantageous from a cost perspective as compared to using a known donor.
  - Please see **Appendix B** for donor selection and the required screening process if frozen fecal microbiota from a pre-screened donor is **not** used.
- 24-48 hours prior to a sample being needed for inpatient or outpatient use, the OSUWMC Pharmacy Department must be contacted to aid in delivering the product to the Endoscopy suite on the day of the procedure.
- In the event of an emergency case on a weekend, contact the pharmacy administrator on call.

## Sample Handling

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- In order to prepare the sample for use, the fecal microbiota must be thawed according to the [instructions](#) provided.
  - Thawing should be performed by the Endoscopy suite staff.
  - The thawing process should **NOT** begin until the date/time of the FMT has been confirmed.
  - Once thawed, the sample is only stable at room temperature up to 4 hours and refrigerated/on ice up to 8 hours.

## Instillation of Fecal Microbiota

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- Administration of fecal microbiota is restricted to gastroenterology attending physicians/fellows.
- The sample volume required varies based on the mode of instillation:
  - 250 ml for colonoscopy instillation.
  - 30 ml for NG administration.
- **At OSUWMC, the preferred route of FMT is colonoscopy** due to risk for aspiration and long-term bacterial overgrowth in the small intestine following NG administration.
  - Please [see this article](#) for information on risks associated with NG administration.

## Electronic Medical Record (EMR) Documentation

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- The following items must be documented in/scanned into the patient's EMR:
  - Patient consent specific to FMT.
    - See back of guideline for patient consent form.
  - FMT date/time in the procedure note.
  - Donor screening results.
  - Document FMT on patient problem list.

## Post-procedural Care

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### Immediate Post-FMT Period Care

- *C. difficile* antimicrobials should **not** be administered.
- One dose of loperamide after the procedure.
- Bed rest while lying on the right side in order to decrease chance of an early bowel movement.
  - Outpatients: 2-3 hours bed rest
  - Inpatients: 4-5 hours bed rest
- Drink water only (no sugary or caffeinated drinks) for 8 hours following the procedure.
- Resume normal diet 8 hours after the procedure.
- Contact GI to report symptoms.

### Long-Term/Discharge Care

- Follow-up with GI by phone one week following the procedure and by office appointment one month following the procedure.
  - Given that FMT is not FDA approved, any adverse reaction must be [documented and reported accordingly to the FDA](#) through MedWatch.
    - For instructions on how to report adverse events to OpenBiome, [please click here](#).
- Long term diet instructions including fruits, vegetables, low fat, and no red meat.
- Physical exercise 120-180 minutes / week if tolerated.
- Avoid NSAIDs if possible.
- No smoking.
- Avoid antibiotics after the procedure for as long as possible (ideally 12 months).
  - In particular, clindamycin, fluoroquinolones, and cephalosporins should be avoided and alternative therapies considered if possible.
  - For additional recommendations on antibiotic use post-FMT, please [see this article](#).

## Quality Measures

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- Patient volume.
- Percent of patients with serious adverse reaction to FMT with 30 days of instillation:
  - Colonic perforation.
  - Aspiration pneumonia.
- Percent of patients who required second FMT within 6 months of initial procedure.
- Percent of patients who required repeated doses of oral vancomycin or fidaxomicin for treatment of *C. difficile* within 6 months of FMT completion.
- Percent of patients requiring colectomy for recurrent *C. difficile* infection.

## References

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## Guideline Approved

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**Disclaimer:** Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC's guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.

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## Appendix A. Antimicrobial Treatment Options for *C. difficile* Infection

Clinical Definition	Recommended Treatment	Supportive Clinical Data
Initial episode, mild or moderate	Metronidazole 500 mg 3 times per day orally for 10-14 days	Metronidazole is not recommended for the treatment of CDI in severely immunocompromised patients such as those who have received an allogeneic stem cell transplant or who have graft vs. host disease (GVHD).*
Initial episode, severe  <b>Consider consulting Infectious Diseases and Colorectal Surgery.</b>	Vancomycin 125 mg 4 times per day orally for 10-14 days  <b>OR</b> Fidaxomicin** 200 mg 2 times per day orally for 10 days (Consider for patients on concomitant antimicrobials)	See <b>Appendix A</b>
Initial episode, severe, complicated  <b>Consider consulting Infectious Diseases and Colorectal Surgery.</b>	Vancomycin 500 mg 4 times per day orally*** <b>PLUS</b> Metronidazole 500 mg every 8 hours intravenously  <b>OR</b> Fidaxomicin** 200 mg 2 times per day orally for 10 days <b>PLUS</b> Metronidazole 500 mg every 8 hours intravenously  Consider for patients on concomitant antimicrobial therapy.  If complete ileus, consider adding rectal instillation of vancomycin 500 mg every 8 hours.	Hypotension or shock, ileus, megacolon
First recurrence****	Fidaxomicin** 200 mg 2 times per day orally for 10 days  <b>OR</b> Same as initial episode (Metronidazole 500 mg 3 times per day orally <b>OR</b> vancomycin 125 mg 4 times per day orally)	---
Second recurrence****	Fidaxomicin** 200 mg 2 times per day orally for 10 days  <b>OR</b> Vancomycin in a tapered regimen (125 mg four times per day orally for 10-14 days, 125 mg two times per day orally for 7 days, 125 mg once per day orally for 7 days, 125 mg one time every 2 or 3 days orally for 2-8 weeks)	---

\* Based on evolving data specific to immunocompromised hosts and CDI and expert opinion.

\*\* Fidaxomicin requires **prior approval** between 8 am - 5 pm, 7 days a week. Orders received between 8 am - 5 pm must have an authorization code obtained from an **Infectious Diseases Consult** or the **Antimicrobial Stewardship Program (ASP)**, on-call pager # 9394.

\*\*\* Based on improved outcome in those with recurrences and higher vancomycin dose and less *C. difficile* recovered in stool (McFarland LV, 2002); and consensus national recommendations (Cohen SH, 2010).

\*\*\*\* Recurrence is defined as the patient having  $\geq 3$  unformed watery stools in a 24-hour period,  $> 2$  weeks and  $< 8$  weeks of completing CDI therapy.

**Note:** Cholestyramine, colestipol, and other anion-exchange resins bind vancomycin, so should not be used in the management of *C. difficile* infections. Metronidazole is not recommended for the treatment of CDI in immunocompromised patients..

## Appendix B. Donor Selection and Screening for Fecal Microbiota Transplant (FMT)

Prior to FMT, the fecal microbiota donor must be screened to mitigate the risk of infection transmission to the recipient. This screening process is costly in both time and money.

### Donor Selection

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- Donors must first complete a screening questionnaire with the Infectious Diseases Division.
- Donors should **not** have:
  - History of incarceration.
  - Received a tattoo or piercing in past 6 months.
  - Known exposure to communicable disease.
  - Use of immunosuppressants or antibiotics within past 6 months.
  - History of high-risk behaviors such as illicit drug use, unprotected sexual activity or sexual activity with multiple partners.

### Donation Screening

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Baseline screening should include the following:

- Blood tests:
  - HIV Antibody (EIA).
  - Syphilis antibody (EIA).
  - Hepatitis A IgM.
  - Hepatitis B surface antigen and core antibody.
  - Hepatitis C antibody.
  - Strongyloides antibody.
- Stool tests:
  - Stool culture including *E. coli*.
  - Comprehensive ova and parasite exam.
  - Cryptosporidium/Entamoeba/Giardia antigens (parasite antigen screen).
  - Microsporidia stain.
  - *C. difficile* PCR.
  - *H. Pylori* antigen (only if FMT is to be performed via NGT route).
- Psychiatric evaluation:
  - Psychiatric evaluation and screening at the clinical discretion of the provider based on history and/or presenting signs and symptoms.



**PATIENT NAME:** \_\_\_\_\_

**DIAGNOSIS/CONDITION:** \_\_\_\_\_

**DATE OF PROCEDURE:** \_\_\_\_\_

I hereby authorize Dr. \_\_\_\_\_ and/or such assistant as may be selected by him to perform the following operation/procedure: Fecal Microbiota Transplantation (FMT)

**RISKS OF PROPOSED OPERATION/PROCEDURE**

\_\_\_\_\_ (physician/provider) has discussed with me the above procedure, the anticipated benefits (to date, the reported success rate for FMT in the treatment of chronic or recurrent *C. difficile* disease is close to 90%), material risks, alternative therapies, potential problems during recuperation and likelihood of achieving my goals. This authorization is given with the understanding that any procedure and recuperation involves some risks and hazards. The more common risks include infection, nerve injury, blood clots, heart attack, allergic reactions, and severe blood loss. I have been made aware of certain risks and consequences that are associated with this particular procedure. These include:

Donors are screened and undergo testing for many common communicable diseases to ensure that the procedure is done as safely as possible, but that it is not possible to test donors for all possible organisms and some infections may be undetectable. I understand that a solution of donor stool is infused into the colon. Patients critically ill with severe *C. difficile* have a high risk of dying from this condition regardless of what treatment is used and fecal transplant may not be successful. Potential risks include:

- Transmission of infectious organisms (bacterial, viral, fungal, parasitic) contained in the stool;
- Missed polyp, cancer or other lesion (infusing donor stool interferes with visualization of colonic mucosa);
- Allergic reaction to antigens in donor stool;
- Enhanced colitis activity in patients with underlying inflammatory bowel disease;
- Theoretical increased risk of developing disease which may be related to donor gut bacteria (obesity/metabolic syndrome, autoimmune conditions, allergic/atopic disorders, neurologic disorders, malignancy).

I understand that this is NOT a complete list, and that unforeseen risks do exist which may not have been discussed with me. Complications may occur even when a procedure is properly performed. Treatment of major complications may require hospitalization, surgery (rarely including colostomy, a bag on the abdomen to collect waste), and blood transfusion.

**RECUPERATION**

Recuperation from FMT is generally complete within a few hours following the procedure. Most individuals can return to typical activities and diet at that time. Because the effects of sedation on memory, coordination and judgment may linger however, activities such as driving, operation of machinery, vigorous physical exertion or activities requiring full mental attention, coordination or recall should not be resumed until the following day if sedation is provided. Increasing abdominal pain, bleeding, fever or other signs of illness could be signs of complication of FMT, sigmoidoscopy colonoscopy or of your sedation, and should be reported promptly to the on call



Digestive Health physician. You will be provided with written instructions on discharge telling you how to contact us in the event of a problem after the procedure.

**ADDITIONAL PROCEDURES**

I understand that other problems/conditions may develop in the course of a procedure that cannot be reasonably foreseen. It is also possible that my physician/provider may discover a different, unsuspected condition at the time of the procedure. I authorize the above named physician/provider and his/her assistants or designees to perform such unforeseen procedures that are necessary according to their best medical judgment. Transfusions are occasionally necessary during the hospital management of colonoscopy-related bleeding or during management of bleeding due to sever colitis, though the need for transfusion related to FMT alone is rare.

**ASSISTANTS**

I understand that some aspects or important tasks of this procedure may be performed by healthcare providers other than the primary physician/provider (i.e., residents, medical students, physician assistants, advanced practice registered nurses, etc.). I understand that the care provided by these assistants will be within the scope of their practice or privileges granted and will be performed in accordance with the state law and the hospital's policies and , in the case of residents or medical students, based on their skill set and under the supervision of their responsible surgeon.

**PHYSICIAN/PROVIDER DECLARATION**

I have explained the contents of this document to the patient and have answered all the patient's questions, and to the best of my knowledge, I feel the patient has been adequately informed and has consented.

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Signature of Patient or Authorized Agent

Date

Time

\*Must be the Physician/Provider who explained the operation or procedure to the patient or authorized agent.



**PATIENT CONSENT**

I understand that no guarantees have been made to me regarding the results of this operation/procedure and that it may or may not improve my condition. I have had sufficient opportunity to discuss my condition and treatment with my physicians and/or their associates, and all of my questions have been answered to my satisfaction. I believe that I have been given sufficient information and adequate knowledge upon which to make an informed decision about undergoing the proposed operation/procedure. I have read and fully understand this form and I voluntarily authorize and consent to this operation/procedure.

**DO NOT SIGN UNLESS YOU HAVE READ AND THOROUGHLY UNDERSTAND THIS FORM**

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Signature of Patient or Authorized Agent	Date	Time
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Signature *Witness to Consent	Date	Time
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*(optional – required only when provider obtains informed consent from patient or authorized agent by telephone)*  
 \*For telephone consent, this must be the registered nurse (RN) who listens to the provider talk to the patient or authorized agent while obtaining verbal consent. For other consent situations, this should be the provider or RN who observes the patient or authorized agent sign above.

**Interpreter (Check if Applicable  )**

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Signature of Interpreter	Date	Time
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