

UNC Fecal Microbiota Transplant (FMT) Protocol for Clostridium Difficile Infection (CDI)

Sponsor: Division of Gastroenterology and Hepatology

What We Do: We perform stool transplants via colonoscopy for patients with *C. difficile* infection who have not responded to standard therapies.

Criteria of Eligibility for FMT:

1. Confirmed *C. Diff* toxin positive
2. Must have (at least) failed standard therapy with primary agent (metronidazole or vancomycin) and typically 1 vancomycin taper prior to consideration
3. No contraindications to colonoscopy
4. For hospitalized patients with severe CDI, immunoglobulins have been evaluated (IgG, IgM, IgA) with therapy with IVIG prior to consideration of FMT if immunoglobulin deficiency

Additional Criteria of Eligibility for Medicaid Patients:

1. the patient must be 21 years of age and older
2. the patient must have had ≥ 3 episodes of recurrent CDI despite the standard antibiotic therapy
3. the beneficiary is not immunocompromised
4. the donor shall not ingest foods the beneficiary is allergic to

OpenBiome Stool Bank

We collaborate with OpenBiome to provide stool for patients with *C. difficile* infection not responding to antibiotics. OpenBiome uses stool from healthy donors who have no known medical problems and take no medications. They screen potential donors extensively for infectious pathogens, though CMV screening is not performed. Further information is at openbiome.org.

Directions for patients receiving FMT with OpenBiome:

- Antibiotics should be stopped a full 48 hours prior to the FMT
- Patient should take 2 imodiums 2 hours prior to the procedure (not in cases of severe colitis)
- Bathrooms at home should be cleaned with Clorox (see pre-FMT Patient Guide)

Self-Identified Donor:

1. In patients who elect for a self-identified donor, donor will respond to the following eligibility questions:
 - a. No history of high risk sexual behavior or use of illicit drugs
 - b. No tattoos in the last 6 months
 - c. No prior incarceration
 - d. No known communicable disease
 - e. No inflammatory bowel disease or history of gastrointestinal cancer
 - f. No metabolic syndrome (determine by presence of hypertension, obesity and diabetes)
 - g. No chemotherapy or antibiotics in the last 3 months

Donor testing must be current and performed within one month of fecal transplant:

Stool:

1. Stool C difficile toxin
2. Stool O&P
3. Stool bacterial pathogen panel (E.coli, Salmonella, Shigella, Camplobacter, Norovirus, Rotavirus, Cryptosporidium, Giardia)

Serum:

1. RPR
2. Hepatitis A IgM
3. Hepatitis B s Ag
4. Hepatitis B IgG
5. Hepatitis B cAb
6. Hepatitis C Ab
7. HIV-1
8. HIV-2
9. Liver function tests to include: AST, ALT, Alk Phos, Total Bilirubin
10. CMV Viral Load
11. EBV Viral Load

Recipient preparation:

1. Nulytely/Golytely bowel preparation on day prior to scheduled colonoscopy with FMT transplant
2. Recipient will continue vancocymin and stop 2 days prior to FMT

Stool Preparation:

1. Donor provides fresh sample from the morning of the scheduled colonoscopy for the recipient. We advise buying the laxative magnesium citrate, which is available over the counter, to keep on hand and take ~3 hrs prior to the transplant in case donor has not stoood (to encourage stooling). The donor can place stool in a disposable plastic (Tupperware-like) container, and keep this on ice in a disposable cooler for delivery to the endoscopy unit.
2. Stool will be transferred into a 1 liter disposable bottle.
3. 500 ml saline is added to the bottle
4. Vigorous shaking to liquefy the sample, or blender can be used
5. Any remaining solid pieces are removed with a washcloth or porous 4x4s and discarded so that the sample is all liquid, to facilitate dispensation through the colonoscope channel
6. Liquid stool if drawn up into a total of 7 syringes of 50 cc each

Colonoscopy

1. Patient is consented with standard colonoscopy consent. Patient is to understand that the procedure is not for and will not include colon cancer screening.
2. Patient signs additional consent for FMT with risks of: hepatitis, allergic reactions, fever, diarrhea or abdominal pain, or other unreported infections or complications, reported alternative would be prolonged antibiotic therapy for CDI. Reported efficacy rate reported to patient from the literature is 85-95% for FMT.
3. Optional: Patient takes 2 imodium one hour prior to the procedure. Not for patients with suspected severe C. diff colitis
4. Patient undergoes standard colonoscopy with sedation.

5. Endoscopist will enter the terminal ileum if possible, where 100ccs of stool will be instilled. The rest of the prepared stool will be instilled in the cecum. The endoscope is then removed and standard post-procedural care given to the patient.

Legal/IRB

FMT at UNC was reviewed with the legal department. Based on current data available from the FDA, FMT can be performed as long as appropriate informed consent is obtained for the procedure. IRB approval is not indicated as we are not studying outcomes nor publishing results of this intervention (this was confirmed with legal department at UNC).

Table 1: Donor Testing for Fecal Transplant

	UNC	Kelly C, et al.	Bakken J, et al.	Landy J, et al.	van Nood E, et al
Hepatitis A, IgM	✓	✓	✓	✓	✓
Hepatitis B, IgG	✓	✓		✓	✓
Anti-hepatitis BcAg	✓	✓	✓	✓	
Anti-hepatitis BsAg	✓	✓	✓	✓	✓
HCV	✓	✓	✓	✓	✓
HIV 1	✓	✓	✓	✓	✓
HIV 2	✓	✓	✓	✓	
HTLV-1				✓	✓
HTLV-2				✓	✓
Syphilis	✓	✓	✓	✓	✓
CBC				✓	
LFTs	✓			✓	
CMV	✓			✓	✓
EBV	✓			✓	✓
Stool					
<i>C. difficile</i>	✓		✓	✓	✓
Ova & parasites	✓	✓	✓	✓	✓
Bacteria	✓		✓	✓	✓
<i>Giardia</i> antigen	✓	✓	✓		
<i>Cryptosporidium</i> antigen	✓		✓		
<i>Strongyloides</i>					✓
<i>Entamoeba histolytica</i>					✓

References

- Kelly CR, et al. J Clin Gastroenterol 2012;46:145-149.
- Bakken JS, et al. Clin Gastroenterol Hepatol 2011;9:1044-1049.
- Landy J, et al. Aliment Pharmacol 2011;34:409-415.
- van Nood E, et al. New Engl J Med 2013;368:407-15