Standardized Frozen Preparation for Transplantation of Fecal Microbiota for Recurrent *Clostridium difficile* Infection

Matthew J. Hamilton, PhD[1], Alexa R. Weingarden[1], Michael J. Sadowsky, PhD[1,3] and Alexander Khoruts, MD[2,3]

OBJECTIVES: **While fecal microbiota transplantation (FMT) is historically known to be an effective means to treat recurrent *Clostridium difficile* infection (CDI) refractory to standard antibiotic therapies, the procedure is rarely performed. At least some of the reasons for limited availability are those of practicality, including aesthetic concerns and costs of donor screening. The objective of this study was to overcome these barriers in our clinical FMT program.**

METHODS: **We report clinical experience with 43 consecutive patients who were treated with FMT for recurrent CDI since inception of this program at the University of Minnesota. During this time, we simplified donor identification and screening by moving from patient-identified individual donors to standard volunteer donors. Material preparation shifted from the endoscopy suite to a standardized process in the laboratory, and ultimately to banking frozen processed fecal material that is ready to use when needed.**

RESULTS: **Standardization of material preparation significantly simplified the practical aspects of FMT without loss of apparent efficacy in clearing recurrent CDI. Approximately 30% of the patients had underlying inflammatory bowel disease, and FMT was equally effective in this group.**

CONCLUSIONS: **Several key steps in the standardization of donor material preparation significantly simplified the clinical practice of FMT for recurrent CDI in patients failing antibiotic therapy.**

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

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INTRODUCTION

In 1978, *Clostridium difficile* was first recognized as a major cause of diarrhea and pseudomembranous colitis associated with the use of antimicrobial agents. Since this time, infection by *C. difficile* has been steadily growing in incidence, morbidity, and mortality across North America and Europe (1,2). Analysis of the US National Hospital Discharge Survey statistics between 1996 and 2003 revealed a doubling in the prevalence of diagnosis of *C. difficile* infection (CDI), to 0.61/1,000, among inpatients (3). A 2008 survey of 12.5% of all US acute care facilities indicated a CDI prevalence rate of 13.1/1,000, which is at least an order of magnitude higher than that found previously (4). While older patients have disproportionately greater rates of CDI than younger individuals, no age group is spared, and the incidence of CDI-related hospitalizations has been rising even in the pediatric population (5). The increase in incidence has been further compounded by an elevated frequency of severe disease, as evidenced by rising CDI-associated morbidity and case fatality (6,7). This is, in part, related to the emergence of more virulent *C. difficile* strains, such as PCR ribotype 027/North American Pulsed Field type 1 (NAP1), which is characterized by a greater potential for toxin production and antibiotic resistance than other clinically relevant rains (8,9).

Recurrent CDI is one of the most difficult and increasingly common challenges associated with CDI (10). An initial incidence of CDI is followed by a relapse within 30 days in about 20–30% of cases (2,11,12), and the risk of recurrence doubles after two or more occurrences (3). Older age, intercurrent antibiotic use for non-*C. difficile* indications, renal insufficiency, immune deficiency, and antacid medications are some of the known risk factors for recurrence (10,13). The presence of just three clinical criteria: age >65 years, severe disease, and continued use of antibiotics after

[1]Department of Soil, Water, and Climate, BioTechnology Institute, and Microbial and Plant Genomics Institute, University of Minnesota, St Paul, Minnesota, USA; [2]Division of Gastroenterology, Department of Medicine, Center for Immunology, University of Minnesota, Minneapolis, Minnesota, USA; [3]These authors contributed equally to this work. **Correspondence:** Alexander Khoruts, MD, Division of Gastroenterology, Department of Medicine, Center for Immunology, University of Minnesota, 2101 6th Street S.E., Room 3-184, Minneapolis, Minnesota 55414, USA. E-mail: khoru001@umn.edu
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treating the initial CDI episode, are predictive of an almost 90% relapse rate (14). CDI also commonly complicates management of inflammatory bowel disease (IBD), which has recently been recognized as an additional independent risk factor for CDI infection (15,16). CDI in patients with underlying IBD is associated with increased severity of colitis and higher rates of recurrence and colectomy (17).

It is now recognized that the presence of normal, healthy, intestinal microbiota offers protection against CDI. Conversely, severe disruption of normal intestinal microbiota by repeated cycles of antibiotics, including metronidazole and vancomycin that are used to treat CDI, is likely one of the major reason for its recurrence. Chang *et al.* (18) used 16S rDNA sequencing to analyze the fecal microbiota of seven patients with initial and recurrent CDI. They reported that bacterial species diversity was reduced in all patients compared with normal control subjects. The greatest reduction in species diversity, however, was found in the three patients with recurrent CDI and disruption of their gut microbiota was evident at the phylum level with marked reduction in Bacteriodetes, normally one of the two dominant phyla in the colon. Instead, the gut microbiota in these patients were dominated by members of the Proteobacteria and Verrucomicrobia phyla, which normally are only minor constituents of the colon microbiota.

The general aim of antibiotic treatment of recurrent CDI is to preserve the residual colon microbiota and optimize their restoration. Various antibiotic regimens, including long tapered or pulsed dosing with vancomycin (19) and rifaximin "chaser" (20,21) protocols have been used to achieve this objective with partial success. Recently, a new macrocyclic antibiotic fidaxomicin, which is narrow in spectrum and spares *Bacteroides* species, was shown to reduce the initial relapse rate of CDI by 50% compared with vancomycin treatment (11). However, treatment with fidaxomicin did not alter the recurrence rate of CDI caused by the more virulent PCR 027/NAP1 strain. Therefore, despite these advances, it seems likely that the challenges in the treatment of recurrent CDI will remain for the foreseeable future.

Fecal microbiota transplantation (FMT), also commonly known as "fecal bacteriotherapy," represents the one therapeutic protocol that allows the fastest reconstitution of a normal composition of colon microbial communities. In a recent case report, we showed that FMT resulted in prompt and sustained engraftment of donor fecal bacteria in a patient with recurrent CDI (22). The patient did not have a clinical response to vancomycin and achieved only partial control of her symptoms with nitazoxanide. In contrast, FMT, administered by infusion during a colonoscopy, resulted in completely normalized bowel functioning within 2 days of treatment.

For many decades, FMT has been offered by select centers across the world, typically as an option of last resort for patients with recurrent CDI. The mostly commonly earliest cited report for FMT was by Eiseman *et al.* (23) who in 1958 described the use of fecal enemas for patients who likely had severe or fulminant forms of pseudomembranous colitis. Since this time, well over 200 cases have been reported as individual case reports, or small case series, with an ~90% cumulative success rate in clearing recurrent CDI, without any noted adverse events. The history and general methodology used for FMT have been described in several recent reviews (24–26). However, despite the long and successful track record, as well as great clinical need, the availability of the procedure for many patients remains very limited.

The lack of wider practice of FMT is due to multiple nontrivial practical barriers and not due to lack of efficacy. These include lack of reimbursement for donor screening, difficulty in material preparation and administration, as well as aesthetic concerns about doing the procedure in endoscopy or medical office. Moreover, the pharmaceutical industry has shown little interest in technological development of FMT-based therapeutics, in large part due to the wide availability of donor material and its complex composition. Instead, development has been driven mostly by individual clinicians faced with desperate need in their patients.

In 2009, we established the FMT program at the University of Minnesota, and the program has evolved since to overcome or minimize some of the associated challenges. This evolution has resulted in movement from the use of patient-identified individual donors to rigorously screened "universal" volunteer donors, and from the use of fresh donor fecal materials that was crudely prepared in the endoscopy suite to a more standardized laboratory protocol done using frozen fecal extracts. The results of this one center's experience are presented here.

METHODS

Patients

This report includes the first 43 patients who received FMT for recurrent CDI at the University of Minnesota Fairview Medical Center. All patients were identified by direct referral from clinicians at infectious disease and gastroenterology practices in the Minneapolis and St Paul metropolitan area. Inclusion criteria for FMT included a history of symptomatic, toxin-positive, infection by *C. difficile*, and at least two documented subsequent recurrences despite use of standard antibiotic therapy. At least one failed antibiotic regimen had to include a minimum of a 6-week course of tapered or pulsed vancomycin dosage, or at least a 1-month vancomycin course followed by a minimum of 2-week rifaximin "chaser." The only exclusion criteria in the protocol were age <18 years and medical fragility from non-*C. difficile* problems, resulting in life expectancy of <1 year. In the latter situation, we advised patients that the best therapeutic option was an indefinite course of vancomycin. All patients gave informed consent for FMT via colonoscopy, recognizing relatively limited experience with this treatment approach and the intrinsic unknowns associated with its use. The Institutional Review Board at the University of Minnesota approved prospective collection of clinical outcome data (project approval date was 2 October 2009), while recognizing this experience does not constitute a clinical trial, and as such was not designed to test the efficacy of FMT in comparison with any other therapeutic options.

Donor identification and screening

At the start of the program, patients were asked to self-identify potential donors. These included mothers ($n=2$), daughters ($n=1$), sons ($n=3$), wives ($n=1$), husbands ($n=1$), and friends ($n=2$). Before recruitment, the donors were required to submit available medical records and have a separate medical history interview away from the recipient patient. The history included assessment of infectious risk, including identification of known risk factors for HIV and Hepatitis, current communicable diseases, and recent travel to areas of the world with a higher prevalence of diarrheal illnesses. Additional absolute donor exclusion criteria included gastrointestinal co-morbidities and the use of antibiotics within the preceding 3 months. Since gut microbiota are likely involved in various aspects of energy metabolism and the functioning of the immune system, the presence of features of metabolic syndrome, autoimmunity, or allergic diseases were treated as relative exclusion criteria. Donors provided separate informed consent to participate in the protocol, which included risks associated with laboratory screening. The donors underwent serologic testing for HIV and Hepatitis B and C, and stool testing that included screening for routine enteric pathogens, *C. difficile* toxin B, and examination for ova and parasites, and *Giardia* and *Cryptosporidium* antigens.

Given varying logistic difficulties in recruiting individual patient-identified donors, the lack of availability of donor materials when needed, and no evidence to suggest a clear therapeutic advantage of using a related vs. unrelated donor (e.g., son or daughter vs. friend or domestic partner), volunteer donors were recruited into the FMT program. The advantages of this change included removing the burden of donor identification from the patient, improving the efficiency and costs related to donor screening, a more consistent supply of donor fecal microbiota, and the ability to impose extensive and stringent exclusion criteria on donor selection (**Supplementary Appendix 1** online). Two unpaid volunteer donors were recruited during this period, and one of them provided the majority of donated fecal material. Donor medical history was reviewed before every donation and complete laboratory screening, as described above, was done every 6 months.

Donor material preparation

Individual patient-identified donors used in the early phase of the program came into the outpatient endoscopy center 1–2 h before the scheduled procedure. The fecal material was collected in a toilet hat and processed in a dedicated bathroom separate from the procedure room. Approximately 50 g of fecal material was placed into a standard commercial blender (Oster, Subeam, Rye, NY) and homogenized in 250 ml of sterile, non-bacteriostatic normal saline. The slurry was then passed through stainless steel tea strainers to remove larger particles that could interfere with loading the syringes.

The material obtained from volunteer "universal" donors was transported on ice into the laboratory, where it was processed within 2 h of collection. The material was weighed and homogenized in a commercial blender in a dedicated biological cabinet under N_2 gas. The slurry was then passed through 2.0, 1.0, 0.5, and 0.25 mm stainless steel laboratory sieves (WS Tyler, Mentor, OH) to remove undigested food and smaller particulate material. The resulting material passing through the 0.25-mm sieve was centrifuged at 6,000×g for 15 min in a Sorvall SS-34 rotor and resuspended to one-half the original volume in non-bacteriostatic normal saline. The resulting concentrated fecal bacteria suspension was administered to the patient immediately or amended with sterile pharmaceutical grade glycerol (Sigma, St Louis, MO) to a final concentration of 10%, and stored frozen at −80 °C for 1–8 weeks until used. Thawing was done over 2–4 h in an ice bath before the FMT procedure. The frozen preparation was diluted to 250 ml with non-bacteriostatic normal saline before infusion in the donor. This fecal material extract, whether fresh or frozen, was nearly odorless and of reduced viscosity, color, and texture relative to earlier material prepared in the endoscopy center. Filtration of donor material allowed for effortless loading of large tip 60 ml syringes without risk of clogging. All containers, bottles, and sieves used in material preparation were sterilized before use. Fecal material from universal donors was treated in the same manner as that obtained from patient-identified donors.

Transplantation procedure

Patients were maintained on full dose of vancomycin (125 mg, four times daily by mouth) until 2 days before the FMT procedure. The day before the procedure, the patients were prepped using a split dosage polyethylene glycol purge (GoLYTELY or MoviPrep), which is standard in our endoscopy unit, before colonoscopies to wash out residual antibiotic and fecal material. The patients underwent a full colonoscopy under conscious sedation. Mucosal biopsies were taken to rule out lymphocytic colitis in the absence of obvious IBD. The majority of the prepared donor material (220–240 ml) was administered via the colonoscope's biopsy channel into the patient's terminal ileum and cecum. In some cases, however, a small portion (50 ml) was also instilled into colonic areas containing maximal diverticulosis. Recovery procedure was identical to that routinely used for standard colonoscopy patients. All patients were instructed to contact the endoscopist in case of symptom recurrence, and were formally followed in clinic 1–2 months after the procedure. Clearance of CDI was defined by resolution of diarrhea and negative stool testing for *C. difficile* at 2 months following FMT. All patients in this protocol also participated in a study examining fecal bacterial community structure, which involved collection of fecal specimens on days 3, 7, and 14 and 1, 3, 6, and 12 months after the procedure. The research staff collected these specimens from the patient's places of residence, providing additional opportunities for symptom follow-up.

Statistical analysis

Non-categorical data were compared using unpaired Student's *t*-test. Categorical data were compared using Fisher's exact test. GraphPad Prism software (La Jolla, CA) was used to calculate two-tailed and two-sided *P* values that were calculated with each test, respectively.

Table 1. Demographics of patient population compared by type of donor

Donor material	Age (years) (mean±s.d.)	Female gender (%)	Duration (months) of RCDI (mean±s.d.)	Number of relapses (mean±s.d.)	History of hospitalization for CDI (%)	Interim antibiotics (%)	PPI (%)	CRI (%)	IBD (%)	Diverticulosis (%)	Success rate
Individual donor (*n*=10)	61±22	70	12.7±7.3	6.2±3.0	70	60	60	30	30	50	**7/10 (70%)**
Standard donor, fresh material (*n*=12)	55±22	83	13.1±9.8	6.4±3.3	75	42	33	25	50	50	**11/12 (92%)**
Standard donor, frozen material (*n*=21)	59±21	67	10.1±10.0	5.2±3.0	38	43	43	14	24	48	**19/21 (90%)**
Total experience (*n*=43)	59±21	72	12.2±10.3	5.9±3.3	56	48	47	21	33	49	**37/43 (86%)**

CRI, chronic renal insufficiency or failure; IBD, inflammatory bowel disease; PPI, proton pump inhibitor medication; RCDI, recurrent *C. difficile* infection.
The first 10 cases were done using patient-identified individual donors. After that, the protocol shifted to use of a standard donor. Fresh material was used in the earlier cases, and later practice shifted to use of frozen material.

RESULTS

Demographics

The group of patients with recurrent CDI described in this report clearly had refractory disease as evidenced by the average number of sequential relapses and duration of the condition (**Table 1**). Furthermore, many patients had multiple risk factors for high probability of recurrence, such as history of severe CDI as evidenced by hospitalization, frequent use of non-*C. difficile* intercurrent antibiotics, and advanced age (14). All patients failed a long taper or pulsed regimen of vancomycin, and 40% of the patients also failed an additional long course of vancomycin followed by a 2-week rifaximin "chaser" regimen. One of these patients also failed a 4-week course of rifaximin. Several patients (3/43) took 2–4 weeks course of nitazoxanide, which also failed to clear the infection. Patients with IBD were not excluded from the protocol. Thirty-five percent of our patients (14/40) had underlying IBD, including Crohn's disease (6/14), ulcerative colitis (4/14), and lymphocytic colitis (4/14). The patients with IBD were generally younger (**Table 2**), but did not differ in the refractory nature of CDI or severity of presentation than older patients. However, the majority of patients without underlying IBD had moderate-to-severe diverticulosis.

Table 2. Comparison of patients without and with underlying IBD

	Non-IBD (*n*=29)	IBD (*n*=14)	*P* value
Age (years) (mean±s.e.m.)	64.7±3.3	44.6±5.8	0.0021
Female	69%	79%	0.43 (NS)
Duration of RCDI (mean no. of months±s.d.)	13.5±2.1	8.3±3.3	0.09 (NS)
Number of relapses±s.d.	6.2±3.0	4.4±1.3	0.04
Rate of hospitalization	55%	57%	1.00 (NS)
Interim antibiotics	51%	36%	0.35 (NS)
PPI	48%	43%	1.00 (NS)
Renal insufficiency	32%	14%	0.69 (NS)
Diverticulosis	69%	14%	0.0028

IBD, inflammatory bowel disease; PPI, proton pump inhibitor; RCDI, recurrent *C. difficile* infection.
Definition of IBD includes patients with Crohn's disease, ulcerative colitis, and incidentally discovered lymphocytic colitis.

Response to treatment

The overall rate of infection clearance was 86% in response to a single infusion of donor fecal material, as evidenced by symptom resolution and negative PCR testing for *C. difficile* toxin B after 2 months of follow-up (**Table 1**). Negative testing for *C. difficile* toxin B for 2 months was accepted as therapeutic success in patients with underlying IBD, even in the absence of complete symptom resolution. In all, 3/10 patients (30%) who received FMT using material from patient-identified individual donors had a recurrence of CDI. Two standard donors were employed for the remaining 33 cases in this series, but the majority (30/33) were done using material prepared from a single donor. In all, 3/33 patients who received FMT from a standard donor (fresh or frozen) had a recurrence of CDI. The difference in donor source, patient-identified vs. standard, was not significant ($P=0.1270$). There was no significant difference in clearing the infection with fresh (11/12) or frozen (19/21) donor material. All six patients who experienced recurrence of CDI after FMT were offered a repeat procedure. Two of these patients, both >80 years of age, had multiple other active medical problems and preferred to remain on indefinite treatment with vancomycin. Four other patients were treated with a second infusion, and all cleared the infection bringing the overall success rate to 95% (41/43 patients). All second infusions were performed using the standard donor-derived material. One of the recurrences of CDI occurred in a patient who received his first infusion from the second standard donor. The same donor source was used for his second FMT. Three of the four patients who received a second FMT

had underlying IBD, two patients had Crohn's disease, and one had lymphocytic colitis. Finally, the fourth patient had a partial colon resection done for a stricture that developed following her initial CDI episode. She has a colostomy draining her proximal colon and a long segment of residual distal colon. After recurrence of CDI within 3 weeks following her first FMT, we thought it was likely that engraftment in this case was complicated by difficulty in retaining the donor material due to high flow of fecal contents and relatively small size of the infected colon. The second infusion in this case was done with two doses of frozen standard donor material: one via the colostomy into the colon and the other into the jejunum using upper push enteroscopy. *C. difficile* testing of her fecal material was done weekly in the first month and monthly thereafter. No *C. difficile* was found over 3 months of follow-up.

No serious adverse events were noted following FMT in any of the patients, with either fresh or frozen materials. A minority of patients (approximately a third) noted some irregularity of bowel movements and excessive flatulence during the first couple of weeks following the procedure, but these symptoms resolved by the time they were seen in clinic follow-up. Enhanced colitis activity in patients with underlying IBD was not observed and there was improvement in overall colitis activity in all patients with ulcerative colitis, although that is easily attributable to clearing the CDI. Interestingly, all diagnoses of lymphocytic colitis were made for the first time from biopsies taken during the colonoscopies performed at the time of FMT. These patients completely normalized their bowel function and had no diarrhea after FMT without any additional medical therapy for lymphocytic colitis. Follow-up biopsies were not performed in these patients when they became asymptomatic.

DISCUSSION

Recurrent infection is one of the most difficult clinical challenges in the spectrum of *C. difficile*-induced diarrheal disease. The risk of recurrence increases up to 65% after two or more episodes (3), and this risk is nearly certain in older patients who suffered severe CDI and suffered additional disruption of gut microbiota from intercurrent administration of non-*C. difficile* suppressing antibiotics (14). The inclusion criteria for patients in this case series were simple: at least three recurrences and failure of standard antibiotic treatments. Our patients averaged about six recurrences over an average course of 1 year. This population highlights known risk factors for recurrence of CDI other than documented recurrence. The majority had history of at least one hospitalization for severe CDI and almost half took antibiotics after developing CDI for another non-*C. difficile* indication. Patients with IBD dominated the younger age group. Virtually all patients were taking probiotics at presentation and many have also tried toxin-binding resins. We did not systematically collect information on all the various probiotics preparations taken by our patients, and many have tried multiple types through the course of their recurrent infections. The most common preparations contained *Saccharomyces boulardii* and strains of *Lactobacilli*. All patients were recommended to discontinue taking probiotics after FMT. In summary, by all available indicators the patients in this case series had recalcitrant CDI that would not have had a significant response rate to a placebo, and were unlikely to respond to another course of antibiotics or other available therapeutic options.

FMT has been used for decades as a last ditch method to cure recurrent CDI, and there has been growing uncontrolled evidence supporting its efficacy. Here, we report one of the largest single case series. The 95% overall success rate in this series is comparable to the cumulative experience in the literature (24–26), and adds to the impetus for developing this therapeutic approach to make it more widely available. The major issues tackled by our center were those of practicality. In the early phase of the program, we asked the patients to bring in prospective donors, which is the most common approach in practice at this time. Our experience does not contradict the efficacy of this approach. However, donor identification and work-up increased expense of the procedure and introduced a potential delay period. Moreover, some patients who were already exhausted by the illness had difficulty in finding suitable donors. While the ideal state of donor health may not be essential for elderly recipients with limited life expectancy, we felt compromise was not an option for younger patients on any of the donor exclusion criteria. Gut microbiota constitute a human microbial organ with major functions in energy metabolism and function of the immune system (26). Therefore, this transplant procedure has potential implications for systemic physiology of the recipient. While donor health is not a guarantee to optimal composition of gut microbiota, it is currently the only available indicator. For all these reasons, we decided to introduce the standard donor option to our patients. Interestingly, although many patients came into clinic with some potential donor already identified, they all immediately preferred the standard option of an anonymous screened donor upon learning about it.

The next challenge became advanced preparation of the donor material. Little is known about viability of different constituents of fecal microbiota over time, and we did not wish to test this variable. However, since production of fresh material on demand is not always practical, and does create delay and issues of sanitation and aesthetics, we introduced frozen donor material as another treatment option. The clinical efficacy of frozen preparation became quickly evident and it has now become part of the standard protocol in our program.

FMT is typically considered a last choice, desperate therapy option by most clinicians, and to a great extent that is due to multiple aesthetic and practical barriers that stand in the way of its administration. Increased prevalence, morbidity, and mortality of CDI has now reached epidemic proportions and a significant fraction of these patients cannot clear the infection with standard therapies. These patients may benefit from FMT, but it is likely that the procedure is not available to them. Our FMT protocol has now progressed to the point where most obvious aesthetic and practical challenges have been overcome. This also significantly reduces costs associated with screening of potential donors. While effort and organization is required for recruitment and screening of suitable donors, as well as material preparation and banking, execution

of actual FMT has become a simple matter of loading the syringes with thawed, nearly odorless, material and a colonoscopy.

There are a number of limitations to this study. It was not a rigorous clinical trial designed to test efficacy of a particular FMT methodology vs. another, or some other form of therapy. Instead, it was an attempt to standardize FMT, as the procedure protocol evolved in the course of our clinical experience. Additional work is needed to ready this procedure for clinical trials and wider application. Nevertheless, our clinical outcomes provide very convincing evidence for efficacy of the frozen preparations. However, we cannot conclude from this experience alone that the fresh and frozen preparations are equivalent. The complexity of the donor material preparations, technical inability to culture most of the contained microbial constituents by classic laboratory techniques, and our ignorance as to the identity of species that are therapeutically most important precluded simple tests of donor material before FMT that could predict its efficacy. However, we are currently working to characterize the microbial composition of donor material and recipients' fecal samples collected over time by high-throughput 16S rRNA gene sequencing. Results of these experiments should provide some means to compare different donor preparations. In addition, we are working to develop practical laboratory tests that will allow for further standardization of microbial composition of donor preparations.

While application of FMT for recurrent CDI has a long history, case reports suggest that it may also have a place in treatment of IBD and IBS (27–29). Given the potentially important role of gut microbiota in pathogenesis of the metabolic syndrome, FMT is already being explored in a clinical trial for this condition (30). Simplification and standardization of FMT-based therapeutics is critical for its future development. Recent technological advances have also made it possible to gain insight into the composition of gut microbiota and their activity. The study of microbiota in the context of FMT should accelerate development of microbial therapeutics and yield new insights into microbial host interactions.

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CONFLICT OF INTEREST

Guarantor of the article: Alexander Khoruts, MD.

Specific author contributions: Conception and design of the study, performance of the study, data analysis, and manuscript production: Alexander Khoruts; performance of the study and manuscript production: Matthew J. Hamilton; performance of the study: Alexa R. Weingarden; conception and design of the study and manuscript production: Michael J. Sadowsky.

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Potential competing interests: Alexander Khoruts, Matthew J. Hamilton, and Michael J. Sadowsky have filed a patent on FMT-based therapeutics.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Recurrent *Clostridium difficile* infection refractory to antibiotic treatment can be successfully overcome with fecal microbiota transplantation.
- ✓ Practical considerations, including cost of donor screening and aesthetic concerns associated with material preparation and administration currently present significant barriers to fecal microbiota transplantation in practice.

WHAT IS NEW HERE

- ✓ Institution of standard volunteer donor program for fecal microbiota transplantation allows for cost-effective rigorous donor screening.
- ✓ Standard volunteer donor material is easily accepted by patients.
- ✓ Standardized frozen donor fecal bacterial preparations are effective in treating recurrent *C. difficile* infection.

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