

Fecal Microbiota Transplantation



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KEYWORDS

- *Clostridium difficile* • Fecal microbiota transplant • Stool transplant • FMT
- Microbiome

KEY POINTS

- Fecal microbiota transplantation (FMT) is effective for treatment of recurrent *Clostridium difficile* infection (CDI) when standard therapy has failed.
- FMT may have a role in some patients with severe and complicated CDI.
- The following factors are important in selecting patients for FMT:
 - Appropriate indications.
 - Appropriate donor selection.
 - Appropriate method of administering FMT.
 - Appropriate follow-up.

INTRODUCTION

Fecal microbiota transplantation (FMT) is the transfer of stool from a “healthy” donor to a recipient believed to harbor an altered colonic microbiome resulting in disease. The goal is to restore eubiosis, or a “healthy” microbiome. Often referred to as stool transplantation, fecal transplantation, fecal flora reconstitution, or fecal bacteriotherapy, FMT has increasingly become a focus in both the public media and peer-reviewed literature. FMT is an effective treatment strategy for recurrent *Clostridium difficile* infection (rCDI) that has not responded to standard therapy. There is interest in using

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FMT for other gastrointestinal (GI) and non-GI diseases, and multiple studies are under way to determine potential alternative indications.

HISTORY

FMT was first described in the fourth century Dong-jin dynasty. A Chinese doctor administered feces by mouth to patients with food poisoning or severe diarrhea with report of life-saving results.¹ There are also descriptions during the sixteenth century Ming dynasty whereby patients were prescribed fresh or fermented fecal suspensions for a range of GI conditions, including diarrhea, vomiting, constipation, and pain. Some reports also indicate the use of infant feces as therapy.¹ Subsequent accounts refer to Fabricius Aquapendente, an Italian seventeenth century anatomist who used FMT in veterinary medicine.² It was termed “transfaunation.”³

More modern descriptions of use in humans were documented by Eiseman and colleagues⁴ in 1958; 4 patients improved after they were given fecal enemas for treatment of staphylococcal pseudomembranous enterocolitis.

There has been considerable interest in FMT over the past decade. There have been multiple case reports and series describing differing FMT protocols, methods of stool administration, and variable patient responses. The highest success rates have been for rCDI with less robust findings, but active investigation, in other GI and non-GI diseases.⁵

GOAL AND EFFECTS OF FECAL MICROBIOTA TRANSPLANTATION

The main goal of FMT is to restore the “normal” population of bacteria in a dysbiotic colonic environment. Studies have examined the gut microbiome in patients with CDI before and after FMT. There is clearly a shift in the bacterial populations within the post-FMT gut that mirrors the donor stool. Gene-sequencing studies of stool samples have shown increases in the quantity of Firmicutes and Bacteroidetes and decreases in Proteobacteria and Actinobacteria following FMT, suggesting rapid donor engraftment.^{6,7}

SCREENING AND PROCESS OF FECAL MICROBIOTA TRANSPLANTATION

Selection and Screening of Donor

The stool donor may be related or unrelated to the recipient. If related, the donor is typically a spouse or close relative. A systematic review by Gough and colleagues⁸ showed resolution of CDI in 93.3% of studies with related donors (n = 19 studies) and 84% of studies with unrelated donors (n = 4 studies). Kassam and colleagues⁹ similarly assessed the significance of donor type and found no difference in clinical outcome regardless if the donor was anonymous versus patient-selected. The investigators hypothesize that unrelated/anonymous donors likely harbor a completely different microbiome compared with related donors and thus may be more effective in “resetting” the microbiome of the recipients, although this has not been demonstrated in randomized studies. Furthermore, many patients prefer an anonymous donor to eliminate the sometimes awkward conversation requesting a stool sample from a family member.

With mild variation, donor screening protocols have been established to reduce the risks of transmission of an infection from the donor to recipient. Testing includes both stool and serum analysis as well as an extensive clinical and social risk assessment. A listing of donor assessment recommendations is included in **Box 1**. The inclusion of such a screening protocol is important to prevent transmission of infectious organisms

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