Can Fecal Microbial Transplant Effectively Treat Crohn's Disease?

To the Editor:

We read with interest the article by Suskind et al[1] evaluating the safety and potential efficacy of fecal microbial transplant (FMT) in patients with Crohn's disease (CD). The author found that FMT for CD may be a possible therapeutic option for CD. Because their findings are important to current therapy for CD, several questions deserve further attention.

FMT has come to the fore in recent years and is being investigated as a treatment method for a number of gastrointestinal and nongastrointestinal disorders. The use of FMT in CD has attracted increasing attention since the first reports in the 1980s. Unlike its application in recurrent *Clostridium difficile* infection, the success of FMT in CD remains variable. A systematic review in 2012 of FMT for CD found that the majority of patients experienced symptom improvement, disease remission, and cessation of medication after FMT treatment,[2] and a number of randomized controlled trials of FMT for CD are now underway to further characterize treatment efficacy and safety.

These studies raise important questions, why some patients with IBD respond so impressively after a single or several FMT infusions and others fail to do so. It may be that FMT is more effective in cases of short disease duration before colonic dysbiosis becomes deeply established. Alternatively, perhaps FMT is more effective in CD cases in which antibiotic use is potentially associated with disease onset. It may also be that some manifestations of CD-associated dysbiosis are more susceptible than others to rapid reversal after FMT, as occurs with *Clostridium difficile* infection.

Donor characteristics may be equally important in determining interpatient variability in FMT efficacy, in particular the donor's microbial profile. Also, FMT response rates are better with certain donors than with others. This is likely because donor selection is at present a very basic and imprecise process that works on the principle of exclusion rather than inclusion. However, the future lies in identifying and selecting specific donors who have been shown to effect good clinical outcomes based on their particular microbial profile. There is no 1 standard definition for a "good donor," and the definition may vary based on the underlying condition to be treated.

We now await the outcomes of current clinical trials to provide further information. Associated metagenomic studies will prove vital in further understanding and optimizing FMT as a therapeutic strategy in CD and in helping to identify patient and donor factors predictive of response.

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Reply:

I sincerely appreciate the interest of Drs. Dai, Jiang, and Sun in our article and thank them for their comments on fecal microbial transplant (FMT) as a potential therapy for Crohn's disease (CD).

As they note, there are many questions that still require answers before FMT becomes a feasible treatment option in CD. As with any therapeutic agent, efficacy needs to be proven. To do this, optimal dosage, frequency, and route need to be determined. Because no two FMTs are the same, FMT has an additional barrier to overcome, which is to understand and determine how the donor bacterial species of the feces can be optimized for an individual recipient's fecal microbiome. In addition, potential infectious and noninfectious complications need to be further evaluated and risk–benefit of FMT needs to be better understood. As researchers and physicians, we appreciate that no single study can fully assess the efficacy and risk of a therapeutic agent for the treatment of a complex disease, such as CD. Our study, in conjunction with others, will begin the process of chipping away at many unanswered questions that still revolve around the potential therapeutics of FMT in CD.

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