Fecal Microbiota Transplantation: An Interest in IBD?

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Fecal transplant or fecal microbiota transplantation (FMT) has emerged as one of the most exciting and controversial innovations in gastrointestinal disease in the past several years. This treatment, which dates back to 4th Century China [1], has captured the attention of clinicians, scientists, the media and the lay community. FMT is the delivery of the stool from a healthy donor to an individual with disease. This shotgun approach appears to be an effective albeit inelegant way to transplant the intestinal microbiota from one person to another. The goal of FMT is to restore the normal healthy commensal bacterial population and correct an underlying intestinal dysbiosis or imbalance associated with a given disease state. Despite its remarkable success and safety in treating recurrent or relapsing Clostridium difficile infection [2], the therapeutic potential of FMT for other gastrointestinal conditions, including inflammatory bowel disease (IBD) remains unknown. Currently, there are only a handful of reports on FMT, and as such FMT remains an interest in IBD, but an interest that warrants our attention and additional investigation.

In 1989, we find the first published experience with FMT for IBD in The Lancet [3]. Bennet and Brinkman described their success in using FMT enemas on Bennet, a physician who had medically refractory ulcerative colitis. Six months after FMT, Bennet was in clinical remission, off all medications, and had no evidence of active inflammation on flexible sigmoidoscopy. Since that time, there have been several reports of FMT in IBD, many of which suggest a clinical and histological response in IBD [4]. Unfortunately, to date there have been no randomized controlled trials of FMT for IBD, and the data are based on case reports, series and very small pilot studies. In addition, there have been a few reports of FMT in IBD associated with worsening of disease activity [5]. Future trials of FMT will need to establish safety, feasibility, optimal dosing and delivery methods, and which subsets of patients are most likely to benefit based on diagnosis, duration of disease, disease extent, phenotype and disease activity. It is also essential that these studies clarify which ‘healthy’ individuals are
**Clinical issues affecting doctors, healthcare providers, patients and the general public**

- How do we prepare healthcare professionals for FMT and other microbiome-based therapies?
- How do we prepare the public to make informed choices about FMT?
- How do we as a society balance current scientific limitations and social risk with long-term benefits?
- Who will be responsible for maintaining FMT donor banks and the associated costs?

**Uncertainties associated with potential impact of FMT in vulnerable populations**

- Should critically or terminally ill or immunocompromised patients be considered candidates for FMT?
- Should FMT be performed on patients when there are no other treatment options available?
- Should there be age limits for children and the elderly?
- Should pregnant or nursing women be allowed to be FMT donors?
- Should pregnant or nursing women be eligible for treatment with FMT?

**Privacy, protection and confidentiality**

- How do we ensure protection of donor privacy and confidentiality?
- How do we inform donors of a positive screening test result?
- Should minors be allowed to be FMT donors?
- Who owns and controls microbiome information obtained through FMT research?

**Psychological impact and stigmatization**

- How will FMT affect an individual and society's perceptions of that individual?
- How will FMT donation affect donors and society's perceptions of FMT donors?
- How does personal microbiome information affect an individual and society's perceptions of that individual?

**Conceptual and philosophical implications and concepts of health and disease**

- How will a diagnosis of dysbiosis impact an individual and society's perceptions of that individual?
- How will FMT alter perceptions of health and disease?

**Fairness and justice**

- Who will be eligible for FMT?
- Who will cover FMT donor screening costs?
- Who will cover the costs of FMT?
- Should unrelated donors be compensated?
- How will treatment with FMT impact insurability?

**Legal issues and regulation**

- Who should be allowed to perform FMT?
- Who should regulate FMT?
- Who should be responsible for monitoring FMT programs and safety?

**Commercialization of FMT including property rights and accessibility of data and materials**

- Can fecal microbiota profiles be patented?
- Can FMT delivery methods be patented?
- Will patenting of fecal microbiota profiles limit their accessibility and development into useful products?

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**Fig. 1.** Ethical, legal and social issues related to FMT. Reprinted from Kahn et al. [4]. Adapted from The Human Genome Project Information on Ethical, Legal and Social Issues (US Department of Energy Genome Programs, http://genomics.energy.gov).
the optimal donors and which microbiota profiles may have a beneficial impact on patients with IBD.

In addition to the unanswered clinical and microbiological questions surrounding FMT in IBD, there are numerous regulatory, ethical, legal and social issues. As outlined in figure 1, these matters range from societal impact, protection of vulnerable populations to justice and commercialization. Among the most important of these issues is the fact that FMT is highly regulated, and the use of FMT for IBD for treatment or research purposed requires approval of an Investigation New Drug application by the US Food and Drug Administration. This is in addition to local requirements which may include approval of the institutional review board and/or the ethics committee, approval of biosafety, infection control, or microbiology committees, and approval of pharmacy or hospital protocol committees.

There is no doubt that there is great interest in FMT; however, significant research is required to fully understand its therapeutic potential in IBDs. Furthermore, future studies should also explore the significant regulatory, ethical, legal and social issues related to FMT for IBD.

References