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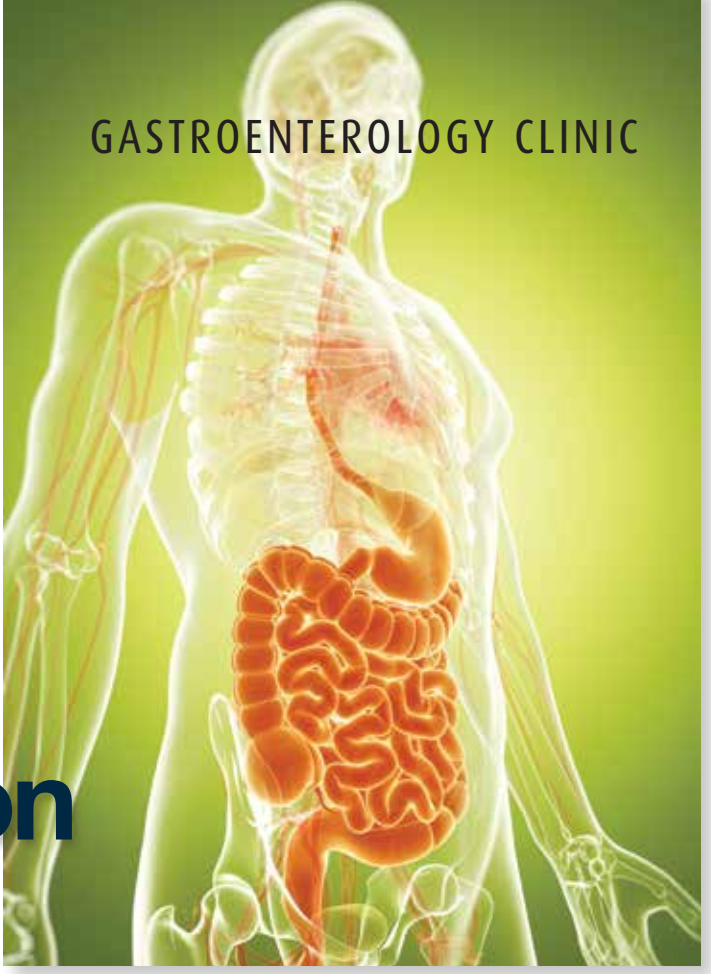

The emerging role of faecal microbiota transplantation

JANE ANDREWS MB BS, FRACP, PhD
SAM COSTELLO MB BS, FRACP

There is an emerging interest in the role of faecal microbiota transplantation for gastrointestinal and other disorders but, as yet, proof of benefit is limited to treating recurrent *Clostridium difficile* colitis. Several ongoing clinical trials are evaluating its potential benefit in inflammatory bowel disease and other gastrointestinal disorders.

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Professor Andrews is a Gastroenterologist and Head of Inflammatory Bowel Disease Services, Department of Gastroenterology and Hepatology, Royal Adelaide Hospital, Adelaide. Dr Costello is a Gastroenterologist, Department of Gastroenterology, The Queen Elizabeth Hospital, Woodville, SA.
Series Editor: Associate Professor Simone Strasser, MD, FRACP, Clinical Associate Professor, Central Clinical School (Medicine), University of Sydney; and Senior Staff Specialist, AW Morrow Gastroenterology and Liver Centre, Royal Prince Alfred Hospital, Sydney, NSW.
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REMEMBER

- *Clostridium difficile* infection (CDI) is a common cause of both community and hospital-acquired diarrhoea, usually occurring after exposure to antibiotics. Reduction in the normal colonic flora with antibiotic exposure can create a potential ecological space within which *C. difficile* can proliferate and produce colitis.[1]
- The currently used antibiotic treatment regimen for CDI of metronidazole or vancomycin alters the normal gut flora that provides colonisation resistance against CDI. For this reason, after successful initial antibiotic therapy of CDI, up to 35% of patients experience a symptomatic recurrence following discontinuation of antibiotics.[2] A subset of patients will have multiple recurrences, and subsequent relapses occur in up to 50 to 65% of patients despite antibiotic therapy.[2] Relapse is seen more frequently in individuals who are immuno-suppressed, older than 65 years of age or require prolonged hospital stays.
- CDI has recently become more frequent, more severe and refractory to standard treatment and more likely to relapse, partly as a result of the emergence of epidemic strains with increased virulence and/or antibiotic resistance since about 2000.[3-5] As a result, several alternative approaches have been used to treat multiple CDI recurrences; faecal microbiota transplantation (FMT) is the most effective of these.
- FMT involves delivering the microbiota from a faecal donor into the bowel of a patient for therapeutic purposes. FMT aims to replenish the host flora that has been

Figures 1a and b. Faecal microbiota transplantation. a (far left). A syringe with the faecal transplant 'loaded'. b (left). Deploying the faecal transplant into the biopsy channel port of a standard colonoscope.

depleted, thus removing a potential microbiological void in which *C. difficile* can proliferate.

- FMT was first performed for the treatment of pseudomembranous colitis in 1958, but it is only recently that it has become a mainstream treatment, largely driven by the increasing problem of recurrent CDI.[6]
- FMT has a cure rate of 80 to 95% in case series and a randomised control trial of CDI refractory to antibiotic treatment, making it by far the most effective therapy in this cohort of patients.[7-10]

ASSESSMENT

- Currently the only evidenced-based indication for FMT is recurrent *C. difficile* colitis. Trials are in progress investigating it as a potential therapy in inflammatory bowel disease, particularly ulcerative colitis, and it has been proposed as a potential treatment of a myriad of other conditions, including irritable bowel syndrome, obesity and autism.[11] However, there is no trial evidence to support the use of FMT for these indications at present.
- FMT would normally be reserved for patients who have had recurrent episodes (more than two) of *C. difficile* colitis despite adequate antibiotic therapy. The decision of when to perform FMT remains at the clinician's discretion, however, and patients in whom a recurrence of *C. difficile* colitis would be potentially catastrophic may be candidates for earlier FMT.
- Screening of the stool donor is strongly recommended to reduce the risk of transmission of disease to the recipient. An infective screen of the donor's blood and stool should be conducted prior to donation (Box). The donor should be fit and healthy and not have any active medical conditions or have received antibiotics in the preceding three months. It is thought safest to ensure that he or she does not have a past history of obesity or metabolic syndrome, autoimmune disease, gastrointestinal disorders such as irritable bowel syndrome, inflammatory bowel disease or malignancy as the potential long-term risks of transmission are unknown. FMT should only be conducted in treatment centres with the ability to conduct the screening, process the faecal material and deliver the FMT under controlled conditions.
- High rates of success have been shown with stools from donors related to the patient and from unrelated donors.[9] However, there are several compelling reasons for favouring unrelated donors, including that unrelated donors can be recruited ahead of time and thoroughly screened and that the stool can be frozen ready for use at short notice. This helps to standardise the procedure and reduces potential problems of confidentiality between donor and recipient.
- No serious side effects have been directly linked to FMT in over 400 published cases. The long-term risks are, however, not known at present.[2]

MANAGEMENT

- In preparing for FMT, 30 to 50 g of donor faeces is mixed with 150 to 200 mL of normal saline to produce a suspension. This can be given immediately to the recipient or frozen with 10% glycerol for later use.
- The donor faeces can be given via three potential routes (Figures 1a and b):[11]
  - colonoscopic insertion (usually into the right colon)
  - nasoenteric tube
  - retention enema.
- FMT via colonoscopy should be considered first line as this technique has a greater therapeutic chance of success. In case series, the results of FMT via colonoscopy are approximately 10% better than via nasoduodenal tube.[2,7-9] In cases where

FAECAL MICROBIOTA TRANSPLANTATION: SUGGESTED DONOR SCREENING TESTS

- Hepatitis A IgM, hepatitis B PCR, hepatitis C PCR, CMV serology, EBV serology, HIV PCR, HTLV-1/2 serology, syphilis, *Strongyloides* serology, *Entamoeba histolytica* serology
- Full blood count, C-reactive protein, electrolyte and liver enzyme levels
- Stool: microscopy and culture, ova, cysts and parasites (including PCR for *Giardia, Dientamoeba fragilis, Cryptosporidium* and *Entamoeba histolytica*), *Clostridium difficile* toxin
- Fasting lipids and blood sugar level

ABBREVIATIONS: CMV = cytomegalovirus; EBV = Epstein-Barr virus; HIV = human immunodeficiency virus; HTLV-1/2 = human T-lymphotrophic virus types 1 and 2; PCR = polymerase chain reaction.

colonoscopy is contraindicated or high risk, nasoenteric tube delivery or enema delivery can be used.

CONCLUSION

Recurrent infection with *C. difficile* is an increasing problem, partly as a result of the emergence of epidemic strains of the bacterium. Faecal microbiota transplant from healthy donors to patients with CDI refractory to antibiotic treatment can prevent further proliferation of *C. difficile* by replenishing depleted host flora. FMT has become a well accepted evidence-based therapy for recurrent *C. difficile* colitis. This condition remains the only evidence-based indication for FMT at present, although trials are in progress in Australia and elsewhere evaluating the potential of FMT in treating other diseases. MT

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