Faecal Microbiota Transplant (FMT) for Recurrent or Refractory Clostridium difficile Infection - Full Clinical Guideline

Reference no.: CG-GASTRO/2023/005

Introduction

Clostridium difficile is a bacterium that lives harmlessly in the gut of around 5% of healthy people. Broad-spectrum antibiotic and immunosuppressant use can alter the balance of flora in the gut, resulting in an overgrowth of *C. difficile*. Symptoms of mild *C. difficile* infection (CDI) include purulent watery diarrhoea, abdominal cramps, nausea and dehydration. In more severe cases the infection can cause bloody diarrhoea and fever. In a few people, CDI can lead to pseudomembranous colitis, sepsis, toxic megacolon, colonic rupture and death. The risk of death increases in those patients with multiple comorbidities.

First line treatment involves rehydration and antibiotic therapy. Clinical response is often favourable, but some people develop recurrent or refractory CDI.

Faecal microbiota transplant (FMT) aims to restore healthy gut flora in people who have recurrent or refractory CDI by introducing enteric bacteria from the faeces of healthy donors.

Recent trial data has shown FMT to be an effective treatment for those with recurrent (≥3 episodes) or refractory CDI. CDI cure rate from a single FMT treatment approaches 80% and exceeds 90% with a second treatment. The use of FMT in these patients is supported by NICE and the costs of obtaining prepared faeces from the University of Birmingham Microbiome Treatment Centre for FMT are covered by NHS England.

Aim and Purpose

This document provides a protocol to ensure patient safety and enable Health Care Professionals to administer a Faecal Microbiota Transplant for the treatment of refractory or recurrent *Clostridium difficile* infection.

Faecal Microbiota Transplantation for Recurrent or Refractory *Clostridium difficile* Infection

Patient Selection

- FMT is indicated for those patients who remain positive for CDI after being treated with standard treatments as per the UHDB *C difficile* guideline (i.e. they have symptoms of CDI and positive toxin and/or GDH antigen) or for those with ≥3 episodes of CDI
- The patient must be suitable for nasogastric tube insertion
- The patient should be able to give informed consent or 'best interests' paperwork must be completed if this is not the case

Patient Consent

Explain the procedure and its risks using the FMT patient information leaflet (Appendix 3). A standard consent for should be signed by the patient. The risks of FMT can include:

- Low risk of perforation from NGT insertion
- Risk of aspiration while NGT in place
- Low risk of transmission of an unknown infectious agent

While FMT can be a lifesaving treatment in immunocompromised patients with CDI, the samples used are from donors who could be CMV positive. If considering treating an immunocompromised patient, please discuss this with one of the medical advisors at the University of Birmingham Microbiome Treatment Centre.

Requesting Sample for FMT

- For patients meeting the criteria for treatment, complete the FMT request form (Appendix 1) and FMT order form (Appendix 2) and submit by email to the University of Birmingham Microbiome Treatment Centre (UoBMTC) at bhs-tr.FMT@nhs.net
- On receipt of the completed request and order forms, the UoBMTC clinical team will assess information on the request form against approved indications for FMT
- If the FMT request is ratified, a delivery date and time will be discussed with the requesting clinician
- In the case of rejection, this will be discussed with the requesting clinician by email

Logistics of FMT Treatment

- FMT is supplied in a 50ml aliquot
- All FMT aliquots are sent with an accompanying validation certificate which should be retained in the patient's clinical notes
- All FMT treatments will be delivered by Blood Bike. In the event that they are unable to deliver, a courier will need to be arranged by the requesting clinician at UHDB
- A named person at a single site address must be identified for delivery
- The sample supplied will be for same day use
- The FMT will be supplied at room temperature, will be ready to use 3 hours following dispatch from UoBMTC and should be used no more than 9 hours from dispatch

FMT Administration

- Ensure the patient has received at least 4 days of antibiotics for treatment of CDI prior to FMT

- Stop the antibiotics for CDI the evening before FMT treatment. Ideally, all antibiotics should be omitted during the FMT administration period, but this is dependent on the patient's clinical presentation
- FMT can be administered by any doctor or staff nurse on any ward by clinicians trained and competent in the placement of NG tubes
- The NGT should be placed in daytime hours according to the UHDB guidance on NGT insertion
- Patient nil by mouth for 6 hours prior to FMT
- Stat dose of oral omeprazole 20mg 2 hours prior to FMT
- Stat dose of oral domperidone 10mg 2 hours prior to FMT
- Ensure that the FMT is fully defrosted at room temperature and that it is being administered prior to the expiry time on the validation certificate
- Transfer the FMT to an enteral syringe
- Connect the syringe to the NGT and administer 50ml FMT into the stomach over 2-3 minutes
- Flush the NGT with 30ml saline
- Remove the NGT 1 hour after the procedure
- The patient can eat 1 hour after the procedure, providing the clinical team are happy with the patient's condition

Disposal in the event that FMT is not used

In the event of an FMT aliquot not being used, the capped syringe or primary container should be disposed of directly into the clinical waste stream.

The FMT validation certificate can be discarded in confidential waste.

Serious Adverse Events (SAE), Serious Adverse Reactions (SAR) or Sudden Unexplained Serious Adverse Reaction (SUSAR)

In the event of an SAE, SAR or SUSAR, immediately contact by phone a member of the UoBMTC clinical team as listed below and follow up with an email to bhs-tr.FMT@nhs.net. Follow usual UHDB protocol for completing an IR1 incident form.

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Documentation Controls

Development of Guideline:	Dr Jess Williams, Consultant Gastroenterologist
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Approved By:	Gastroenterology - 22/11/23 (reviewed no change) Medical Division -
Review Date:	November 2026
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Appendices:

Appendix 1: FMT Request Form

Appendix 2: FMT Order Form

Appendix 3: Patient Information Leaflet

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Appendix 1

Faecal Microbiota Transplant Request Form for CDI

This form is valid for a single dose of FMT for the named patient. We advise a copy of this request is placed in the patients clinical notes. Should a further dose be required additional FMT request and order forms will need to be completed.

IMPORTANT: It is a condition of our MHRA licence that outcome data is supplied at 7 days and 90 days post FMT administration. Failure to adhere to this may result in further FMT requests being refused.

Requester's information

Name, Position and Address:

Contact no: Mobile

Secretary

Email:

Date of Request:

Consultant signature *(please sign)*

Consultant Name *(please print)*

Patient information

Surname:

First Name:

Date of Birth:

Hospital and Ward:

NHS Number:

Sex: **M** **F** Pregnant **Y** **N**

Is FMT contraindicated in this patient?

(delete as appropriate)

Y N If Y provide details:

Is the Patient immunosuppressed/immunocompromised?

Y N If Y provide details:

Hospital Number / PID:

Previous *C.difficile* History (upto past 1 year)

No. of previous episodes of CDI?

Associated *C.difficile* Ribotypes

Information on previous confirmed *C.difficile* episodes

Episode	Start Date	End Date	PCR +	EIA +

Antibiotic treatment given for all previous CDI episodes:

Antibiotic	Start date	End Date

Faecal Microbiota Transplant Request Form for CDI

Current *C.difficile* Episode

Date of onset of current symptoms

Result of CDI test (please select as appropriate):

Stool Toxin positive by Enzyme Immune Assay

Antibiotic treatment given for all current CDI episodes:

Antibiotic	Start date	End Date

Other Antibiotics:

Antibiotic	Start date	End Date

Bristol Stool type:

Stool Frequency (per day)

Stool Toxin Gene positive by PCR

Highest WBC (x10^9/L)

Highest Serum Creatinine (umol/L)

Lowest Albumin (ug/L)

Please tick those that apply:	Y	N
Abdominal Pain: Mild		
Severe		
Peritonism		
Fever >38.5°C		
Hypotension		
Ileus		
Shock		
Toxic Megacolon		
Colitis on radiology		

FMT supply information

FMT ordering is available Monday to Friday 9am–5pm by emailing a completed copy of this form to bhs-tr.FMT@nhs.net

The price of a single FMT aliquot is £650. NHS England is currently covering the cost for FMT used to treat patients with CDI in NHS Trusts in England. Please complete this form in full. Subject to ratification of the FMT request form, information given on the FMT Order form will be used to complete the order.

Specialist advice in relation to FMT is available:

- Monday to Friday from 9 am–5 pm via the Microbiome Treatment Centre Clinical team on 0121 414 4547 and bhs-tr.FMT@nhs.net.

Confirmation of receipt of order will be provided within 24 hours of submission, if not received please contact the FMT team on bhs-tr.FMT@nhs.net or 0121 414 4547

Request ratification *for internal use only*

Name of Dr reviewing request:

Signature of Dr reviewing request:

Position:

Date of Ratification:

Based on the information provided, has the request for Specials use been Ratified? **Yes** **No**

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Appendix 2
FMT Order Form

This form is valid for a single treatment of FMT for the named patient. Should a further treatment be required additional forms will need to be completed. The price of a single FMT aliquot is £650. Please complete the FMT request form and this order form in full. Subject to ratification of the FMT request, information given on this order form will be used to complete the order.

Requester's Information

Requester's Name and Position:

Date of Request:

Email:

Direct contact number:
(Not Bleeps)

Purchasing Information

Purchaser's Name and Billing Address (NHS TRUST):

VAT number:

Purchase Order number:

Patient Information

Patient Name:

Patient's Date of Birth:

Delivery Information:

Date FMT required

Named person responsible for receipt of FMT:

Delivery Method:
(delete as appropriate)

Blood Bike
Requestor's own courier

Name:
Position:
Telephone:

Delivery Address:

Hospital:
Address:

Post Code:
(Essential for blood bike delivery)

Preferred Delivery time

10:00 - 12:00	
12:00 - 14:00	
14:00 - 16:00	

Intended Route

Upper GI Tract	
Lower GI* Tract	

* 3 Aliquots of FMT will be required.

FMT Supply Information

The Product is supplied under the terms of the MHRA Specials licence in response to a bona fide unsolicited order by a person who is a doctor for use by an individual named patient for whose treatment that person is directly responsible, in order to fulfil the special clinical needs of that patient.

* For FMT treatment via lower GI tract, 3 aliquots of FMT will be supplied at a reduced cost of £1300.

All orders for the Product are strictly subject to the University of Birmingham's terms and conditions of sale, which are attached together with this form. **By placing your order you acknowledge and agree to be bound by these terms and conditions.**

FMT Patient Information Leaflet

What is *Clostridium difficile?*

Clostridium difficile (C.diff) are bacteria that live in the bowel. In a healthy person, *C.diff* bacteria can live amongst normal bacteria in the gut and don't cause disease. However, if the normal bacteria are reduced, e.g. by the use of antibiotics to treat other infections, then the numbers of *C.diff* can increase, causing disease.

What are the symptoms of *Clostricium difficile infection?*

C.diff causes diarrhoea, fever, loss of appetite, nausea and abdominal pain. It can also cause life-threatening inflammation of the bowel; however this is a rare complication.

Treatment of *Clostridium difficile* using antibiotics

Treatment with the antibiotics metronidazole, vancomycin and rifaxamin kills the *C.diff* bacteria. However, in some people, diarrhoea returns a few days after stopping the antibiotics. This is called a recurrence. Recurrence can occur when healthy gut bacteria do not return to healthy levels, allowing any remaining *C.diff* bacteria to increase in numbers and cause symptoms again. Patients who have one recurrence are at increased risk of suffering from further recurrences.

Treatment of *Clostricium difficile* disease using a Faecal Microbiota Transplant

A Faecal Microbiota Transplant (FMT) is a filtered suspension of donated faeces prepared in a laboratory. The normal bacteria in the donated faeces replace the bacteria which are missing in the gut of the patient, competing with *C.diff* and preventing is from growing. As *C.diff* is unable to grown, it cannot cause the symptoms of infection and the diarrhoea stops. This is a novel treatment.

The symptoms of *C.diff* infection are stopped in around 91% of patients who receive FMT treatment, compared to only 30-40% of patients who receive antibiotic treatment. Patients usually see improvement in their symptoms within 24-72 hours after the FMT. Flatulence, belching and/or constipation may be experienced in the days following FMT.

What's involved in FMT treatment?

Faeces donors are anonymous, healthy adults between the ages of 18 and 50, who have not taken antibiotics in the past 3 months and have no recent change in bowel habit. They are screened for gut infections and for infections that can be transmitted by bodily fluid (usually blood) including hepatitis A/B/C/E, HIV and syphilis. Only those negative for infections will be allowed to become donors.

The patient will be given vancomycin antibiotic tablets for four days before FMT, which will stop the night before treatment. FMT is given by a tube inserted through the nose, down the throat and into the stomach (called a nasogastric tube).

The patient will receive a tablet of omeprazole in the morning of treatment to reduce the amount of stomach acid, which could kill the bacteria given during the FMT. A tablet of domperidone is also given to promote stomach emptying into the small intestine. The nasogastric tube is placed in the stomach on the morning of the procedure and a syringe containing the FMT is connected to the nasogastric tube. The FMT is administered down the tube. The patient should not smell or taste the FMT. The nasogastric tube is then flushed with saline and removed.

What are the risks of treatment?

There is a theoretical risk of transmission of a pathogen from the donor to the recipient. Donors are screened for common infections spread by blood an faeces and are restricted from donating if any are present. Donors undergo clinical, social and travel risk assessment and are only allowed to donate if no additional risks for infection are found. However, there may be unrecognised pathogens in the FMT which could cause infection in the recipient.

To date, FMT has been used for the treatment of *C.diff* infection in many research studies and clinical trials. Although FMT is sometimes associated with mild, self-limiting gastro-intestinal symptoms, there are no significant safety concerns.

There is a very small risk of perforation from placement of the nasogastric tube. There is also a risk of misplacement of the nasogastric tube into the lungs. Delivery of FMT into the lungs would cause a serious infection. The hospital guidelines on the placement of nasogastric tubes minimise this risk.

What will happen after FMT treatment?

FMT is a new treatment and it is therefore important to understand if the treatment works. In addition to any routine clinical follow up you may have, your doctor will complete an FMT specific questionnaire about your progress 90 days after your treatment. To complete this, your doctor will ask you questions about your health after FMT, any side effects of the treatment and how satisfied you were with the treatment. This data will be collected by your doctor and sent to the University of Birmingham Microbiome Treatment Centre. Your data will be anonymous.