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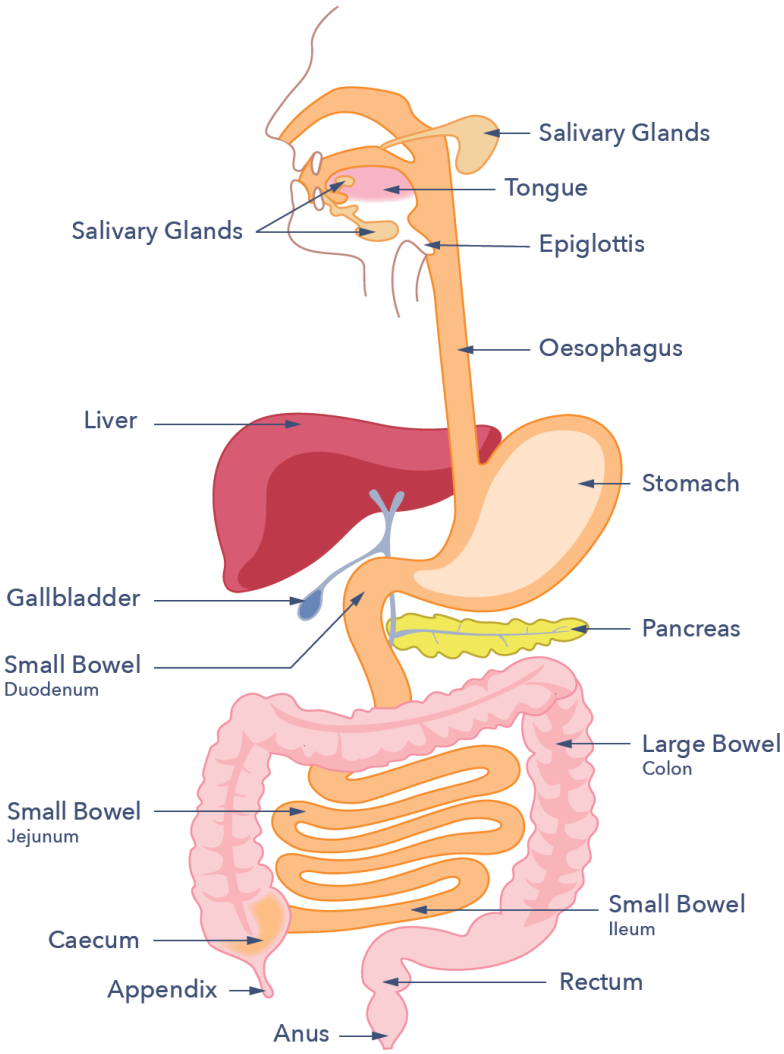
THE DIGESTIVE SYSTEM



THIS FACTSHEET IS ABOUT FAECAL MICROBIOTA TRANSPLANTATION (FMT).

Faecal Microbiota Transplantation (FMT)

Breaking down the name?

- **Faecal microbiota:** Did you know that in addition to undigested food and waste products, faecal material (a.k.a. stool or poo) also contains a vast variety of microbes. These microbes, which include bacteria, viruses and fungi, are collectively referred to as the faecal microbiota.

- **Transplantation**: refers to the transfer of this material from a healthy person into the gut of a person who needs treatment.

FMT is a treatment whereby a stool sample is taken from a healthy, screened 'poo donor'. The sample is processed in a laboratory and then transferred into the gut of a person needing treatment. The purpose of FMT is to introduce beneficial microbes, to help the person's recovery. To make sure the FMT procedure is as safe as possible, the health of the donors is monitored very carefully. Monitoring includes testing the stool sample for harmful microbes or compounds. Once tested and approved, samples are minimally processed and kept frozen until required.

The leaflet explains:

- How FMT is prepared and used
- The use of FMT in NHS clinical practice for the treatment of infection with *Clostridioides difficile* (often referred to as C. diff, the term used below).
- How doctors can get hold of FMT in the NHS
- The use of FMT for research

How is FMT prepared and used?

There are some differences (detailed below) in how FMT is conducted, but the basic procedure is as follows.

- **The donors**
  Donors undergo a screening process (like blood donation) to check they are healthy and suitable. Donors complete a full health questionnaire and have blood and stool samples taken for testing. These tests are done to ensure the donor has a 'healthy' status. Importantly, testing also makes sure the donors

do not carry any infections that could be passed to other people. This screening is repeated at intervals to ensure donors remain eligible. Donors remain anonymous.

- **The faecal samples**
  As well as donors undergoing blood tests (to rule out the presence of infections such as hepatitis), an extensive range of clinical tests is performed on donors' stools. Tests ensure donor stool samples are negative for disease-causing agents such as *Salmonella* and COVID-19. Once a donor sample is given the all-clear, it is processed into FMT, and kept frozen until required. Most FMT in the UK at present is given as a liquid FMT preparation, although some centres are starting to use FMT in a capsule formulation.

- **The person needing treatment (the recipient)**
  If a person is taking antibiotics, the course typically needs to be completed a few days before the FMT procedure. Depending on the sample delivery method, an antacid and/or bowel preparation such as a laxative may also be given. The recipient may also be asked to fast for a few hours before. The procedure is fully explained by a healthcare professional, and the recipient must give their informed consent. The recipient may be offered some additional medicines if appropriate (e.g., sedatives), depending upon the route of administration.

FMT delivery

Currently, FMT is administered *via* two major routes described below:

Upper gastrointestinal tract routes:

- **Nasogastric tube**. A thin flexible tube is inserted through the nose into the stomach (a nasogastric tube). The FMT sample is injected through the tube using a syringe The nasogastric tube is usually inserted before the procedure, and normally can come out a short time (within one hour) after the end of the procedure. Sometimes it is preferred to deliver the FMT beyond the stomach into the small intestine. For this a gastroscopy (see below) is usually required to place the tube.

- **Gastroscopy.** FMT can also be delivered via a thin tube with a camera (an endoscope). This tube is inserted through the mouth into the stomach or small bowel. The FMT sample is injected through the endoscope to reach the area where required and the endoscope is then removed. A longer naso-jejunal tube may be used to deliver the sample into the small bowel. It is usually passed back through the nose at the end of the procedure.

- **Capsules.** In some hospitals, FMT is available in capsule form, to be swallowed by mouth.

Lower gastrointestinal tract route:

The FMT may be administered into the large bowel by means of a rectal enema or colonoscopy. The latter involves the insertion of a thin flexible tube with a camera (a colonoscope) through the anus and into the bowel. The FMT sample usually reaches the end of the small bowel or the start of the large bowel.

FMT can be repeated if it does not work the first time. Usually, recipients can eat or drink shortly (usually one hour) afterwards. Unless the person undergoing treatment is already hospitalised, the procedure does not usually require an overnight stay.

Are there any safety or suitability concerns?

Hospital procedures can have associated risks. Adverse events associated with the delivery of FMT itself are rare. A small number of people might experience fever, or some symptoms related to their gut. Examples include feeling sick (nausea), abdominal (belly) discomfort, bloating, or loose stools for up to a few days post-treatment. These side effects usually resolve within a few days.

The main concern with this relatively novel treatment is the possibility of transferring harmful microbes in the FMT sample. To ensure that FMT is safe and to standardise the procedure, UK experts have established best practice clinical guidelines that cover the following:

- Careful and thorough screening of donors to minimise the risk of transferring harmful microorganisms
- Preparation of the recipients, to optimise the chance of successful treatment
- Screening and preparation of samples.
- Advice on the best ways to deliver FMT samples

The quality and safety of FMT samples must be strictly controlled, and they are regulated like medicines in the UK. The setting up of 'stool banks' is helping to increase the number of hospitals and clinics that can provide FMT. These centres take on the task of screening donors' samples, to ensure their safety. Frozen samples can then be distributed to other sites.

The use of FMT in NHS clinical practice for the treatment of *Clostridioides difficile* (C. diff) infection

Antibiotics are used to treat serious bacterial infections (such as pneumonia or meningitis). While this makes them life-saving medicines, one potential disadvantage is that antibiotics may reduce the number of beneficial microbes in the gut. When this happens, the bacterium C. diff, commonly found in the bowel, can multiply and produce toxins. These toxins cause symptoms like diarrhoea and inflammation, which can range from mild to severe disease. Sometimes this can become recurring and a very serious problem.

FMT was developed as a treatment for people not responding to standard treatment for C. diff and currently remains the only purpose for FMT in routine NHS clinical practice. In August 2022, the National Institute for Health and Care Excellence (NICE) approved the use of FMT for adults who have had two or more episodes of C. diff infection that have not resolved with antibiotics.

Don't do it alone. Interest in FMT has been fuelled by the press and social media. The regulation and restriction of FMT, however, has had unintended consequences. People have been trying to undertake FMT themselves (i.e., 'DIY' FMT), using the internet for instructions, and often for conditions with little clinical evidence. The DIY-er probably knows the stool donor but (of course) cannot test the safety of the faeces donated, potentially putting themselves at serious risk. The means of delivering the sample may also be risky if done outside a clinical setting and can potentially cause serious harm.

How doctors can get hold of FMT in the NHS

There are several approved hospital centres with teams of specialists who are providing FMT to NHS recipients for the treatment of C. diff infection. At the moment, the largest UK centre is the **University of Birmingham Microbiome Treatment Centre (MTC)**. The MTC holds a stool bank license issued by the appropriate UK authority (the Medicines and Healthcare products Regulatory Agency - MHRA) and can provide FMT samples for clinical trials and for the treatment of C. diff infection. MTC is allowed to send FMT samples for treatments across the UK. Currently, it only produces frozen liquid FMT for administration using naso-gastric tubes or endoscopy). It does not produce licensed capsules for export, so FMT cannot be used by GPs in the community. This situation may change in the future. Doctors in the NHS can request FMT for their patients with recurrent C. diff infection by contacting the MTC by phone (0121 414 4547) or by email (bhs-tr.FMT@nhs.net). The terms of the licence do not allow people who need treatment to request FMT for themselves.

Other FMT services in the UK include a licensed FMT stool bank at Guy's and St Thomas' NHS Foundation Trust (www.fmt-trials.org). Their license covers onsite administration of FMT either via colonoscopy or via oral capsules in suitable patients on an outpatient basis. Referrals can be made by medical practitioners to simon.goldenberg@gstt.nhs.uk. The unit also supplies capsule FMT for use in clinical trials at sites across the UK.

Use of FMT for research

Although current clinical guidelines only recommend FMT for severe or recurrent C. diff infection that has not responded to standard therapy, doctors and scientists now recognise that in several other medical conditions (even some that are not directly related to the gut) there are changes to the composition and balance of the gut microbiota. This may contribute to the medical condition. As such, there is increasing interest in whether FMT may be a good therapeutic option for not only

C. diff infection but also for other clinical conditions. Many clinicians, including those in the UK, are investigating the use of FMT for other disorders. At present, FMT research in clinical conditions other than C. diff infection has not reached the level of evidence required for NHS recommendation.

Current research includes the benefit of FMT for:

- Eradication of antimicrobial-resistant microorganisms in the gut
- Inflammatory bowel disease (IBD) – e.g. crohn's disease, ulcerative colitis.
- Irritable bowel syndrome (IBS)
- Liver diseases
- Metabolic disorders and obesity
- Psychiatric disorders
- Response to particular medicines, such as cancer immunotherapy.
- Inflammatory arthritis
- Changing the gut microbes in blood cancer patients

In summary:

- Small clinical trials have shown FMT to be safe for most people. Evidence from future larger, well-designed trials is needed before FMT can be recommended for conditions other than C. diff.
- There is increasing awareness that the gut microbiota may have a role to play in many conditions, and that its manipulation could be a positive therapeutic strategy. IBS is a good example of this. IBS can develop after an infectious episode or antibiotic usage, suggesting disturbance of gut microbiota plays a part in IBS symptoms. To date, only a few clinical trials have investigated the benefit of FMT, so firm conclusions about its potential benefit cannot yet be drawn.
- To date, there have been very few FMT studies in IBD. These were small and varied in design and not all were positive. Despite this, there is some evidence that FMT may induce remission of mild to moderate ulcerative colitis (UC). There have been fewer trials in Crohn's Disease (CD), making it difficult to make any assessment of FMT efficacy.

Extensive research is also focusing on the effects of mixtures of beneficial bacteria prepared as tablets or drinks (called Live Biotherapeutic Products). The mixtures aim to represent the range of bacteria found in faeces from healthy donors. If successful, this could eliminate the need to screen donors and pave the way for individualised treatment for each person; an era of 'personalised microbiota' to complement 'personalised' genomics'. Genomics is where the genetic code is used to guide decisions made about the prevention, diagnosis, and treatment of disease.

Finally…

FMT is a promising novel treatment option. We still have a lot to learn about how it works, and the best way to administer it. More research is needed before it can be recommended in clinical guidelines for anything other than recurrent or refractory

C. diff. Therefore, we don't recommend you have FMT treatment outside the NHS. We have explained the main safety concerns regarding FMT. The NHS follows the established national guidelines, to ensure FMT is as safe and effective as possible.

References available on request.

If you have received a hardcopy of our information but would like further information on conditions or symptoms with links (diarrhoea, IBS, crohn's disease and ulcerative colitis) please do call us on 0207 486 0341 or email us info@gutscharity.org.uk.