



## What is *Clostridioides difficile*?

*Clostridioides difficile* (*C. diff*) are bacteria that live in the bowel (also known as the gut). In a healthy person, *C. diff* bacteria can live amongst normal bacteria in the gut and do not 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 *Clostridioides 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 *Clostridioides difficile* disease using antibiotics

Treatment with the antibiotics such as vancomycin kills the *C. diff* bacteria in most people. However, in some people diarrhoea returns a few days after stopping the antibiotics, this is called a recurrence. Recurrence can occur when the normal 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 recurrence of infection.

## Treatment of *Clostridioides difficile* disease using a Faecal Microbiota Transplant

A Faecal Microbiota Transplant (FMT) is a filtered suspension of donated faeces prepared in the GMP-MU at the University of Birmingham. The normal composition of the gut flora in the donated faeces replaces the flora, which are missing in the gut of the patient. This results in several mechanisms that inhibit the growth of *C. diff* and progression of disease. As *C. diff* is unable to grow it cannot cause the symptoms of infection and the diarrhoea stops. This is a novel treatment for CDI.

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 diarrhoea 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 last 3 months and have had no recent change in bowel habit. They are screened for gut infections and for infections that can be transmitted by bodily fluids (usually blood), including Hepatitis A, B, C, E, HIV and syphilis. Only those negative for these infections will be allowed to be donors. In response to the COVID-19 pandemic all faecal donors are now screened for the SARS-CoV-2 virus, as well as their donated faeces and the FMTs manufactured from their donations.

The patient will be given anti- *C. diff* antibiotics (e.g. vancomycin) for at least four days before FMT, which will stop the night before treatment. FMT can be given to a patient either by a tube inserted through the nose, down the gullet and into the stomach (called a nasogastric tube) or via an endoscope camera which is inserted into the bowel via the rectum (called colonoscopy).

When given by nasogastric tube the patient will receive a tablet of omeprazole on the morning of treatment to reduce the amount of stomach acid which could kill the bacteria being given in the FMT. A tablet of Domperidone will also be given to promote stomach emptying into the small intestine. The nasogastric tube is placed into the stomach 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.

When an FMT is administered by colonoscopy, it is carried out in accordance with the local hospital policy. In general, this will involve the patient receiving a bowel preparation liquid to drink before the colonoscopy, to clear the bowel of faeces. During the procedure the endoscope camera is inserted into the large bowel via the rectum. The FMT treatment is then be sprayed into the bowel via the endoscope.

### 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 and faeces and prevented from donating if any are detected. Donors undergo thorough clinical, social and travel risk assessment and are only allowed to donate if there are no additional risks. 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. FMT is sometimes associated with mild self-limiting gastro-intestinal symptoms. Our screening protocols are highly stringent and address the specific safety alerts around transmission of certain pathogens highlighted by regulatory authorities.

If FMT is delivered by a nasogastric route 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. Steps are taken to ensure correct placement of the tube into the stomach according to your local hospital guidelines, to minimise this risk.

If FMT is delivered by colonoscopy this carries risks associated with the colonoscopic procedure. These would include the risks of sedation and the small risk of bowel perforation. The risks of causing serious harm associated with colonoscopy are very low and will be discussed with you by your local medical team.

### 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, within 7 days of your treatment and at 90 days after your FMT treatment. To complete this questionnaire 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 treatment outcome data will be anonymised in this questionnaire.