The journey towards safely restarting faecal microbiota transplantation services in the UK during the COVID-19 era

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Faecal microbiota transplantation (FMT) is a potentially life-saving treatment for patients with refractory and recurrent *Clostridioides difficile* infection with cure rates of 90%.[1] Substantial implications with regard to the safe provision of FMT were made evident with emerging reports of detectable SARS-CoV-2 virus in stool even before the declaration of the COVID-19 pandemic.[2] Furthermore, data suggesting prolonged and potentially infectious faecal virus shedding in stool samples in asymptomatic carriers who tested negative on nasopharyngeal swabs meant FMT donor screening protocols could no longer rely on symptoms and a nasopharyngeal swab alone.[3,4] The Medicine and Healthcare Regulatory Agency approved University of Birmingham Microbiome Treatment Centre (UoBMTC), was the first to mandate SARS-CoV-2 testing of stool as part of donor screening and called for a halt of FMT production globally until a validated stool assay was available[5] with an evidence-based international consensus on guidance for donor screening being published.[6]

FMT production at UoBMTC was paused in March, 2020 and FMT that was already manufactured from February, 2020, was quarantined. Following consensus agreements with FMT providers globally and a review of updated evidence on safety and efficacy, the shelf life of FMT collected before December, 2019, was extended from 6 months to 12 months. This allowed our centre to treat a further 68 patients with recurrent *C difficile* infection until the stocks were exhausted by August, 2020.

In conjunction with FMT providers globally, we established new donor screening protocols that now include multiple levels of questionnaire-based and molecular screening for SARS-CoV-2 infection or enteric carriage at several timepoints of the donor and FMT production pathway (appendix). However, restarting FMT manufacture principally relied on a validated assay for detection of SARS-CoV-2 in stool, which is not commercially available. Our centre worked towards validating a sensitive and specific assay that uses multiple technologies in parallel for the detection of SARS-CoV-2 in stool.[7] A combination that includes real-time PCR, digital droplet PCR, and nanopore sequencing technology was validated with stool viral spiking experiments and testing of stool samples from more than 100 COVID-19 positive and COVID-19 negative hospitalised patients (on the basis of nasopharyngeal PCR). The assay was approved by the Medicine and Healthcare Regulatory Agency in January, 2021, and has enabled the resumption of donor screening and FMT services in the COVID-19 era. We have now released quarantined FMT aliquots from those manufactured in February, 2020, and have treated several patients successfully.

Although FMT is a safe and a highly effective treatment for recurrent *C difficile* infection, FDA safety alerts in the USA, following serious adverse events as a result of transmission of enteric pathogens, emphasise that there can be no room for complacency.[8] Although our revised protocols are highly robust in screening asymptomatic carriers of SARS-CoV-2, both FMT providers and users need to remain vigilant for new threats during the changing viral pandemic and beyond.

We declare no competing interests.

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See Online for appendix

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