Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Perspectives

Fecal microbiota transplantation and donor screening for *Clostridioides difficile* infection during COVID-19 pandemic

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The emergence and spread of a novel coronavirus (SARS-CoV-2) from Wuhan, China, have become a global pandemic, declared by World Health Organization on March 11, 2020.[1] Coronavirus disease 2019 (COVID-19) caused by the virus is a respiratory illness with clinical presentations ranging from mild non-specific respiratory symptoms to severe organ dysfunction such as acute respiratory distress syndrome. Of note for gastroenterologists, patients of COVID-19 may present with gastrointestinal symptoms such as nausea or diarrhea.[2]

Clostridioides difficile infection (CDI) occurs secondary to loss of intestinal colonization resistance due to depletion of microbiome diversity from antibiotic use, diet or aging. CDI is a challenging disease, with a recurrence rate of 15%–20% and a mortality rate of 5%.[3] When CDI is present as a co-infection with COVID-19, the effect of therapy can be difficult to monitor, if diarrhea persists because of COVID-19. Nine patients at a medical center in US with concomitant SARS-CoV-2 infection and CDI were recently reported; among the 9, 4 patients died and 1 was discharged to hospice.[4] With the pandemic likely continuing in the foreseeable future before a vaccine is available, there is an important yet less-addressed treatment modality, fecal microbiota transplantation (FMT), that needs to be critically discussed in the care of CDI amid the global pandemic.

FMT has been very successful in curing patients with recurrent or refractory *C. difficile* infection (rCDI).[5] The receptor angiotensin-converting enzyme 2 (ACE2) for SARS-CoV-2 is highly expressed in ileal and colonic tissue and

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Table 1 Safety protections relating to COVID-19 for fecal microbiota transplantation donor screening.

Date	Agency/Institution	Recommended measures
March 23, 2020	US FDA	Testing donors and/or donor stool for SARS-COV-2
March 30, 2020	Microbiome Treatment Centre, University of Birmingham	Testing donor stool for SARS-COV-2 by RT-PCR
April 10, 2020	OpenBiome	Testing donors for SARS-COV-2 by nasopharyngeal swab (RT-PCR)
April 22, 2020	FMT Centre of Chinese University of Hong Kong	Multiple donor stool testing at different timepoints by RT-PCR
April 28, 2020	Australian TGA	Testing donors for SARS-COV-2 via stool sample or nasal RT-PCR

ACE2 levels are induced in patients with IBD.[6] While there is currently little evidence for an increased frequency or severity of CDI in COVID-19 patients, death has been reported in patients with co-infection.[4] Whether or not FMT may play a role in such patients, especially those with rCDI, merits further studies.

Safety issues should be of major concern, particularly for experimental application of FMT in non-life threatening, chronic disorders like inflammatory bowel disease or irritable bowel syndrome amid the pandemic. On March 16, an international expert panel urged that in SARS-CoV-2 epidemic countries, the reverse transcriptase PCR (RT-PCR) should be considered in all FMT donors with or without symptoms or a history of travel.[7] Soon on March 23, the US Food and Drug Administration (FDA) responded that the following actions be taken: donor screening with questions directed at identifying donors who may be currently or recently infected with SARS-CoV-2 and testing donors and/or donor stool for SARS-CoV-2, to ensure the safety of FMT.[8] More safety protection measures relating to COVID-19 for FMT products were subsequently proposed (Table 1).[8–12] In addition to the recommended testing procedures, all the screening protocols include questions directed at identifying donors who may be currently or recently infected with SARS-CoV-2.[8–12]

In 2019, the US FDA issued a safety alert with regards to death and life-threatening complications associated with the transmission of antimicrobial-resistant *Escherichia coli* via FMT.[13] We realized that the previous FDA-approved donor screening protocol was insufficient in terms of pathogen screening to avoid donor-related infectious complications. We immediately voiced that *Pseudomonas aeruginosa* should be added to the screening protocol, and such protocol should better be customized according to local epidemiology in different countries.[14] We, therefore, fully agree that during the global pandemic, screening donors for SARS-CoV-2 should be mandatory, especially in countries with high incidence of COVID-19.

Clearer scientific understanding should precede a policy that selectively increases restrictions in donor screening based on positive tests for SARS-CoV-2. We now have learned more with regards to SARS-CoV-2 and COVID-19 that the risk of respiratory transmission is the highest, but the presence of the virus in the digestive tract cannot be ignored. Moreover, a significant proportion of the infection is asymptomatic and young, healthy adults tend to recover sooner than the elderly, with less and shorter virus shedding from the nasopharynx and gut.[15] Recently Ng and colleagues indicated that a single negative test for stool is insufficient to exclude the presence of SARS-CoV-2.[12] Multiple testing at different timepoints may be necessary.[12] To this end, we first suggest that a simple and effective assay to detect the virus in stool should be developed in the near future. We also propose additions to the recommendation. Ideally, throat or nasopharyngeal swab samples should be collected for testing. With this additional measure, the infection or carriage of SARS-CoV-2 can be fully excluded. To ensure safety, swabbing the throat or nasopharynx should be performed in a single room by trained staff with appropriate personal protective equipment, and all the specimens, including the swabs and stool, must be handled in biosafety level 2 laboratories. During the global pandemic of SARS-CoV-2 and before a vaccine is available, it is time to have a consensus on an efficient and stringent protocol to screen FMT donors.

Declaration of Competing Interest

The authors have no conflicts of interest relevant to this article.

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