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Minimising the risk of monkeypox virus transmission during faecal microbiota transplantation: recommendations from a European expert panel

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Faecal microbiota transplantation (FMT) is an established treatment for recurrent *Clostridioides difficile* infection, recommended by several guidelines for this indication.[1,2] FMT is not only more effective than antibiotics for recurrent *C difficile* infection,[3] but also able to prevent *C difficile* infection-related complications.[4] Several actions have been taken to guarantee and expand FMT availability, and to increase its safety. Stool banks are a model that ensures a high level of product quality and reliability of supply.[1,2] The need for stool banks became evident during the COVID-19 pandemic, when, because of concerns about the potential transmission of SARS-CoV-2 virus via faeces, FMT was temporarily withheld in some countries.[5] In response to this issue, the FMT community has provided recommendations with the aim of safely continuing the routine provision of FMT by reorganising workflows, mainly of donor screening.[5] These recommendations have proved to be effective in retaining a similar number of donors and patients as before the pandemic and maintaining safety.

As of Sept 7, 2022, monkeypox virus infection has been reported in over 100 countries or territories since January, 2022, including 97 that have not ever reported an outbreak before.[7] Consequently, on July 23, 2022, WHO declared the monkeypox virus outbreak to be a public health emergency, advocating common actions aimed at preventing it.[8]

Monkeypox virus is a DNA virus belonging to the Poxviridae family, close to the variola virus (known as smallpox). It typically has a 1–2 week incubation period, a prodromal period with fever and lymphadenopathy, and finally a macular rash progressing through papular, vesicular, and pustular stages. Monkeypox virus is usually a self-limiting disease, with symptoms lasting 2–4 weeks.[9]

Monkeypox virus is believed to be transmitted predominantly through direct contact with lesions or infected body fluids, with possible involvement of fomites and large respiratory droplets. However, the current outbreak differs from previous ones because it seems to spread mainly (90–95%) via sexual contact among men who have sex with men, with a high frequency of anogenital lesions and proctitis.[9] Moreover, some affected individuals can be asymptomatic or have few symptoms.[10]

Some reports have identified the monkeypox virus genome in rectal swabs or faecal samples,[10,11] and viable virus has been isolated from rectal swabs in one of these studies,[10] supporting the theoretical risk of transmission of monkeypox virus via FMT.

In August, 2022, the US Food and Drug Administration (FDA) issued a safety alert concerning this risk, advising the need for increased safety protections to be applied to the FMT workflow related to the monkeypox virus, including additional questions to identify donors who might have recent or active infection or be at high risk of infection.[12]

As a European expert panel, we agree that there is a need for expanding the donor questionnaire to decrease the risks of transmission of monkeypox virus. This outbreak appears to spread mainly through sexual contact. Current guidelines for donor screening already recommend excluding individuals with risky sexual behaviour (including sexual contacts with sex workers, with anonymous individuals, or individuals with sexually transmittable diseases), which is also applicable for identifying potential donors with monkeypox virus.[1,2] Moreover, we recommend screening potential donors, at the first evaluation and at each donation, for both the presence of prodromal non-specific symptoms (including fever, lymphadenopathy, or myalgias) or of newly appeared skin lesions (mainly macular rash progressing to vesicula and pustula) within the previous 30 days; or close contact with individuals with proven or suspected infection within the previous 30 days, or both. If either of these items is positive, the potential donor should be prohibited from donating at least for 30 days.

We also agree with the suggestion from the FDA to retrospectively extend this screening to donors whose stool batches have been collected since March, 2022.[12]

Notably, the FDA has not suggested any additional testing. PCR-based tests for detecting viral DNA in biological samples are available for monkeypox virus, but accuracy on stool samples is unknown.

Additionally, the FDA recommends informing patients of the potential risk of monkeypox virus transmission. We agree with the importance of informing patients about the potential risks of transmission of infectious agents but believe that the current incidence of monkeypox virus (which seems to be limited to risks groups who are excluded from donation) does not justify emphasising it as a separate entity.

We agree that, on the basis of current knowledge of the transmission of monkeypox virus and the performance of available tests, the addition of laboratory testing would not increase safety, and is not clinically justified at present.

These recommendations count for both research and clinical practice and should be adapted to local health-care systems and regularly updated on the basis of new insights in the epidemiology of monkeypox virus and potential advantages of specific diagnostics.

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1 Cammarota G, Ianiro G, Kelly CR, et al. International consensus conference on stool banking for faecal microbiota transplantation in clinical practice. *Gut* 2019; **68:** 2111–21.
2 Keller JJ, Ooijevaar RE, Hvas CL, et al. A standardised model for stool banking for faecal microbiota transplantation: a consensus report from a multidisciplinary UEG working group. *United European Gastroenterol J* 2021; **9:** 229–47.
3 Baunwall SMD, Lee MM, Eriksen MK, et al. Faecal microbiota transplantation for recurrent *Clostridioides difficile* infection: an updated systematic review and meta-analysis. e*ClinicalMedicine* 2020; **29-30:** 100642.
4 Cammarota G, Ianiro G, Magalini S, Gasbarrini A, Gui D. Decrease in surgery for *Clostridium difficile* infection after starting a program to transplant fecal microbiota. *Ann Intern Med* 2015; **163:** 487–88.
5 Ianiro G, Mullish BH, Kelly CR, et al. Reorganisation of faecal microbiota transplant services during the COVID-19 pandemic. *Gut* 2020; **69:** 1555–63.
6 Ianiro G, Bibbò S, Masucci L, et al. Maintaining standard volumes, efficacy and safety, of fecal microbiota transplantation for *C. difficile* infection during the COVID-19 pandemic: a prospective cohort study. *Dig Liver Dis* 2020; **52:** 1390–95.
7 US Centers for Disease Control and Prevention. Monkeypox: 2022 global map & case count. www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html (accessed Sept 7, 2022).
8 WHO. WHO Director-General's statement at the press conference following IHR Emergency Committee regarding the multi-country outbreak of monkeypox – 23 July 2022. World Health Organization, 2022. https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-the-press-conference-following-IHR-emergency-committee-regarding-the-multi--country-outbreak-of-monkeypox--23-july-2022 (accessed Aug 28, 2022).
9 Thornhill JP, Barkati S, Walmsley S, et al. Monkeypox virus infection in humans across 16 countries - April–June 2022. *N Engl J Med* 2022; **387:** 679–91.
10 De Baetselier I, Van Dijck C, Kenyon C, et al. Retrospective detection of asymptomatic monkeypox virus infections among male sexual health clinic attendees in Belgium. *Nat Med* 2022; published online Aug 12. https://doi.org/10.1038/s41591-022-02004-w.
11 Peiró-Mestres A, Fuertes I, Camprubí-Ferrer D, et al. Frequent detection of monkeypox virus DNA in saliva, semen, and other clinical samples from 12 patients, Barcelona, Spain, May to June 2022. *Euro Surveill* 2022; **27:** 2200503.
12 US Food and Drug Administration. Safety alert regarding use of fecal microbiota for transplantation and additional safety protections pertaining to monkeypox virus. Aug 22, 2022. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/safety-alert-regarding-use-fecal-microbiota-transplantation-and-additional-safety-protections-0 (accessed Aug 29, 2022).