






Rectally shed SARS-CoV-2 lacks infectivity: time to rethink faecal–oral transmission?

Rune M. Pedersen, Ditte S. Tornby, Line L. Bang, Lone W. Madsen , Marianne N. Skov , Thøger G. Jensen , Isik S. Johansen  and Thomas E. Andersen 

We read with interest the Perspective by Guo et al. (Guo, M. et al. Potential intestinal infection and faecal–oral transmission of SARS-CoV-2. *Nat. Rev. Gastroenterol. Hepatol.* **18**, 269–283 (2021))¹, on the potential faecal–oral transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A comprehensive list of reasons to substantiate that such a transmission route is probable was presented, including the well-documented shedding of viral RNA in faeces, epidemiological reports, and laboratory and animal tests. Viral debris and RNA are often found in large quantities in faeces from patients with COVID-19 as most of the viral material produced in the airways is cleared through swallowing. Furthermore, as argued by Guo et al.¹, studies indicate that intestinal infection by SARS-CoV-2 might contribute to the viral material shed in faeces.

In either case, it is important to emphasize that for the rectally shed virus to transmit to other humans it must retain its infectivity when it leaves the body. Proof in support of this property is obtained by successful isolation of the virus; that is, successful propagation of the sampled virus in laboratory cell culture. Guo et al.¹ refer to four studies in support of infectious virus particles being successfully isolated from patient's faeces^{2–5}. However, three of these studies base their conclusion of successful propagation of SARS-CoV-2 on microscopy observations alone^{2–4}, which is inadequate as it requires additional substantiation by quantitative analysis (such as reverse transcription PCR, RT-PCR) to conclude that virions have increased in number upon culturing^{6,7}. All three papers use electron microscopy to show what appears to be intact SARS-CoV-2 particles in culture supernatants^{2–4}, but identifying SARS-CoV-2 in complex specimens in this way is difficult and error prone^{8,9}, and, even if visually intact virions are identified, it does not provide evidence for infectious capacity. Notably, only Zhou et al. confirmed viral propagation by RT-PCR⁵; a result that was obtained for a single faecal sample⁵ and is, to the best of our knowledge, the only valid evidence reported in






the literature that supports retained infectivity of rectally shed SARS-CoV-2.

One additional study has attempted culturing of rectally shed SARS-CoV-2 with the use of confirmatory RT-PCR. The comprehensive study by Wölfel et al. analysed 13 faecal samples from four patients during their course of COVID-19 and concluded that none of the samples contained culturable virus¹⁰. Results from our hospital are in line with this outcome as we have, to date, not been able to culture rectally shed SARS-CoV-2 from patients with COVID-19 of varying disease course (R.M.P., D.S.T., L.L.B., L.W.M., M.N.S., T.G.J., I.S.J. and T.E.A., unpublished data).

The potential existence of a faecal–oral transmission route has gained widespread attention. We would like to add to this discussion that the evidence in support of the key property that allows such a transmission, that rectally shed SARS-CoV-2 is infectious, remains weak and in our view inconclusive. New data to support this capacity have not emerged since the early reports on this topic, overall questioning whether such transmission is plausible and plays a substantial part in the dissemination of the virus.

There is a reply to this letter by Guo, M. et al. Reply to: Rectally shed SARS-CoV-2 lacks

infectivity: time to rethink faecal–oral transmission? *Nat. Rev. Gastroenterol. Hepatol.* <https://doi.org/10.1038/s41575-021-00503-8> (2021).

Rune M. Pedersen^{1,2}, Ditte S. Tornby^{1,2}, Line L. Bang^{1,2}, Lone W. Madsen ,^{3,4} Marianne N. Skov ,^{1,2} Thøger G. Jensen ,^{1,2} Isik S. Johansen ,^{3,4} and Thomas E. Andersen ^{1,2}✉

¹Department of Clinical Microbiology, Odense University Hospital, Odense, Denmark.

²Research Unit of Clinical Microbiology, University of Southern Denmark, Odense, Denmark.

³Department of Infectious Diseases, Odense University Hospital, Odense, Denmark.

⁴Research Unit of Infectious Diseases, University of Southern Denmark, Odense, Denmark.

✉e-mail: thandersen@health.sdu.dk

<https://doi.org/10.1038/s41575-021-00501-w>

1. Guo, M., Tao, W., Flavell, R. A. & Zhu, S. Potential intestinal infection and faecal–oral transmission of SARS-CoV-2. *Nat. Rev. Gastroenterol. Hepatol.* **18**, 269–283 (2021).
2. Zhang, Y. et al. Isolation of 2019-nCoV from a stool specimen of a laboratory-confirmed case of the coronavirus disease 2019 (COVID-19). *China CDC Wkly* **2**, 123–124 (2020).
3. Xiao, F. et al. Infectious SARS-CoV-2 in feces of patient with severe COVID-19. *Emerg. Infect. Dis.* **26**, 1920–1922 (2020).
4. Wang, W. et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA* **323**, 1843–1844 (2020).
5. Zhou, J. et al. Infection of bat and human intestinal organoids by SARS-CoV-2. *Nat. Med.* **26**, 1077–1083 (2020).
6. Folgueira, M. D. et al. Prolonged SARS-CoV-2 cell culture replication in respiratory samples from patients with severe COVID-19. *Clin. Microbiol. Infect.* **27**, 886–891 (2021).
7. Arons, M. M. et al. Presymptomatic SARS-CoV-2 infections and transmission in a skilled nursing facility. *N. Engl. J. Med.* **382**, 2081–2090 (2020).
8. Goldsmith, C. S. et al. Electron microscopy of SARS-CoV-2: a challenging task. *Lancet* **395**, e99 (2020).
9. Miller, S. E. & Goldsmith, C. S. Caution in identifying coronaviruses by electron microscopy. *J. Am. Soc. Nephrol.* **31**, 2223–2224 (2020).
10. Wölfel, R. et al. Virological assessment of hospitalized patients with COVID-2019. *Nature* **581**, 465–469 (2020).

Competing interests

The authors declare no competing interests.

Reply to: Rectally shed SARS-CoV-2 lacks infectivity: time to rethink faecal–oral transmission?

Meng Guo , Wanyin Tao, Richard A. Flavell  and Shu Zhu 

To determine whether severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can establish a faecal–oral transmission route, it is essential to confirm that infectious virus particles are shed in faeces from patients with COVID-19. We would like to thank Pedersen et al. for their Correspondence on our Perspective (Guo, M. et al. Potential intestinal

infection and faecal–oral transmission of SARS-CoV-2. *Nat. Rev. Gastroenterol. Hepatol.* **18**, 269–283 (2021))¹, which raises some important issues (Pedersen et al. Rectally shed SARS-CoV-2 lacks infectivity: time to rethink faecal–oral transmission? *Nat. Rev. Gastroenterol. Hepatol.* <https://doi.org/10.1038/s41575-021-00501-w> (2021))².