

al. Isolation and molecular characterization of *Toxoplasma gondii* in a colony of captive black-capped squirrel monkeys (*Satmiri boliviensis*). *Parasitol Int* 2015;64:587-90.

Fecal shedding of SARS-CoV-2 in COVID-19 patients: insights from animal coronaviruses

Although the primary clinical signs in human patients with COVID-19 are related to the respiratory tract, shedding of intact virus in the feces can also occur.^{1,2} This raises questions about routes of transmission of SARS-CoV-2 and the mechanisms by which the virus can be found in both respiratory secretions and feces. Importantly, enteric infection with coronaviruses and subsequent fecal shedding are common in a wide range of animal species, including pigs, cattle, dogs, and cats.³⁻⁶ In many cases, both respiratory and enteric infection and shedding can occur.⁷ The range of disease symptoms for COVID-19 patients and the severe nature of clinical signs for a subset of individuals infected with SARS-CoV-2 draw parallels with feline infectious peritonitis in cats. Feline infectious peritonitis is believed to be caused by an internal mutation of an enteric feline coronavirus commonly found in cats. This virus, although conventionally considered an enteric pathogen, does not have a rigid tissue tropism⁸ and likely spreads systemically, including in the respiratory tract. In early studies⁹ of cats with feline coronavirus, the virus could easily be recovered from the oropharynx within just a few days after inoculation, preceding shedding in the feces in some cases. It is not uncommon for cats infected with feline coronavirus to show a range of clinical signs, including diarrhea and upper respiratory tract signs such as sneezing.¹⁰ Likewise, in calves infected with bovine coronavirus, the virus can be detected in respiratory samples before it is detected in fecal samples; however, both respiratory and fecal shedding has been observed for nearly a month in some instances.¹¹ In rhesus macaques infected with SARS-CoV-2, pulmonary disease has

been observed, but viral RNA has also been detected in rectal swabs by means of a quantitative reverse transcription PCR assay.¹²

Gastrointestinal signs have been reported in human patients infected with SARS-CoV-2, alone or in combination with respiratory signs. These gastrointestinal signs vary with respect to time of onset and severity, but can include nausea, loss of appetite, vomiting, diarrhea, and abdominal pain. In one retrospective study,¹³ 16% of patients presented solely with gastrointestinal signs. Importantly, a recent study¹⁴ of SARS-CoV-2 infection in people showed prolonged fecal shedding, with and without shedding from the respiratory system. However, the presence of SARS-CoV-2 RNA in fecal samples was not significantly associated with the presence of gastrointestinal signs, and an extended duration of shedding was not significantly associated with severity of the disease. In that study,¹⁴ fecal samples from 41 of 74 (55%) patients were positive for SARS-CoV-2 RNA, and fecal samples were positive for the virus for a longer time (mean \pm SD, 27.9 \pm 10.7 days) than respiratory samples were (16.7 \pm 6.7 days).

In sum, although COVID-19 is primarily associated with respiratory signs in people, the observation of numerous other clinical signs in some patients requires evaluating the systemic nature of the disease. We suggest that detection of SARS-CoV-2 in the feces of patients does not merely represent the passage of virus from consumed respiratory secretions but may, in fact, reflect shedding resulting from active replication in enteric tissues. We consider it prudent, therefore, to consider the results of studies of animal coronaviruses when trying to understand the human disease. In the public health battle to contain COVID-19, it is important to consider multiple transmission routes and to take into account commonalities between SARS-CoV-2 in people and animal coronaviruses in their natural hosts.

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1. Peng L, Liu J, Xu W, et al. 2019 novel coronavirus can be detected in urine, blood, anal swabs and oropharyngeal swabs samples [published online ahead of print Feb 25, 2020]. *MedRxiv* doi: 10.1101/2020.02.21.20026179.
2. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens [published online ahead of print Mar 11, 2020]. *JAMA* doi: 10.1001/jama.2020.3786.
3. Chasey D, Cartwright SF. Virus-like particles associated with porcine epidemic diarrhoea. *Res Vet Sci* 1978;25:255-256.
4. Clark MA. Bovine coronavirus. *Br Vet J* 1993;149:51-70.
5. Buonavoglia C, Decaro N, Martella V, et al. Canine coronavirus highly pathogenic for dogs. *Emerg Infect Dis* 2006;12:492-494.
6. Pedersen NC. Morphologic and physical characteristics of feline infectious peritonitis virus and its growth in autochthonous peritoneal cell cultures. *Am J Vet Res* 1976;37:567-572.
7. Saif IJ. Animal coronaviruses: what can they teach us about the severe acute respiratory syndrome? *Rev Sci Tech OIE* 2004;23:643-660.
8. Porter E, Tasker S, Day MJ, et al. Amino acid changes in the spike protein of feline coronavirus correlate with systemic spread of virus from the intestine and not with feline infectious peritonitis. *Vet Res* 2014;45:49.
9. Stoddart ME, Gaskell RM, Harbour DA, et al. The sites of early viral replication in feline infectious peritonitis. *Vet Microbiol* 1988;18:259-271.
10. Addie DD, Jarrett O. A study of naturally occurring feline coronavirus infections in kittens. *Vet Rec* 1992;130:133-137.
11. Oma VS, Trávník M, Alenius S, et al. Bovine coronavirus in naturally and experimentally exposed calves; viral shedding and the potential for transmission. *Virology* 2016;13:100.
12. Munster VJ, Feldmann F, Williamson BN, et al. Respiratory disease and virus shedding in rhesus macaques inoculated with SARS-CoV-2 [published online ahead of print Mar 21, 2020]. *Microbiology* doi: 10.1101/2020.03.21.001628.
13. Luo S, Zhang X, Xu H. Don't overlook digestive symptoms in patients with 2019 novel coronavirus disease (COVID-19) [published online ahead of print Mar 20, 2020]. *Clin Gastroenterol Hepatol* doi: 10.1016/j.cgh.2020.03.043.
14. Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples [published online ahead of print Mar 19, 2020]. *Lancet Gastroenterol Hepatol* doi: 10.1016/S2468-1253(20)30083-2.