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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Implications of gastrointestinal manifestations of COVID-19

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In late December, 2019, the first case of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was reported in Wuhan, China.[1] According to WHO situation report 99, there have been more than 2·95 million confirmed cases of COVID-19 globally, with more than 202 000 deaths as of April 28, 2020.[2]

Although respiratory tract manifestations are the most commonly reported symptoms in COVID-19, emerging data suggest that the gastrointestinal tract and liver might also be affected by SARS-CoV-2, on the basis that gastrointestinal epithelial cells and liver cells express angiotensin-converting enzyme 2 (ACE2), the major receptor of SARS-CoV-2.[3] We analysed 204 patients with COVID-19 with full laboratory, imaging, and historical data and found that 103 patients (50%) reported digestive symptoms, such as lack of appetite (81 [79%] of 103), diarrhoea (35 [34%]), vomiting (four [4%]), and abdominal pain (two [2%]). Although most patients presented with fever or respiratory symptoms, for six patients, only digestive symptoms were present during the whole course of disease.[4]

In *The Lancet Gastroenterology & Hepatology*, Ren Mao and colleagues[5] report findings of a systematic review and meta-analysis of data from 35 studies, including 6686 patients with COVID-19. In 29 studies (6064 cases) reporting gastrointestinal symptoms in patients with COVID-19, the pooled prevalence of digestive symptoms was 15% (95% CI 10–21), the most common of which were nausea or vomiting, diarrhoea, and anorexia. Of note, the authors report that around 10% of patients presented with gastrointestinal symptoms without respiratory features when infected with SARS-CoV-2. These patients were more likely to have a delayed diagnosis, leading to potential problems for themselves and individuals with whom they came into contact.

Together with respiratory transmission, there is potential for faecal–oral transmission of SARS-CoV-2. Prolonged presence of SARS-CoV-2 viral RNA has been documented in faecal samples. For example, Wu and

colleagues[6] showed that 41 (55%) of 74 patients had SARS-CoV-2 RNA-positive faecal samples; whereas the respiratory samples of these patients remained positive for SARS-CoV-2 RNA for a mean of 16·7 days, their faecal samples remained positive for a mean of 27·9 days. One patient had RNA-positive faecal samples for 33 days after their respiratory samples became RNA-negative, and another patient tested RNA-positive in their faecal sample for 47 days after symptom onset. The presence of gastrointestinal symptoms was not correlated with faecal sample viral RNA positivity and severity of disease was also not correlated with extended duration of faecal sample viral RNA positivity.

Wang and colleagues[7] examined different types of clinical specimen in patients with SARS-CoV-2 (1070 specimens from 205 patients of mean age 44 years) using RT-PCR, and found that 126 (32%) of 398 pharyngeal swabs (126 of 398) and 44 (29%) of 153 faecal specimens (44 of 153) were positive for SARS-CoV-2 RNA. The authors cultured four SARS-CoV-2 positive faecal specimens with high copy numbers and detected live virus using electron microscopy detection.

These findings imply that in some patients, although SARS-CoV-2 has been cleared in the respiratory tract, the virus continues to replicate in the gastrointestinal tract and could be shed in faeces. However, two major questions remain to be answered. First, how long can SARS-CoV-2 survive in faeces? van Doremalen and colleagues[8] analysed the stability of SARS-CoV-2 in aerosols and on various surfaces, and found that the virus remained viable in aerosols for 3 h. The viability of SARS-CoV-2 on surfaces depended on the type of surface. In the simulated environment in the laboratory, no viable SARS-CoV-2 was detected after 4 h on copper and after 24 h on cardboard. SARS-CoV-2 was more stable on plastic and stainless steel, with viable virus detectable for up to 72 h. However, there are currently no data showing how long SARS-CoV-2 remains viable in faeces.

Second, why can SARS-CoV-2 continue to replicate in the gastrointestinal tract of some patients after it has been cleared from the respiratory tract? Xu and colleagues[9] studied the characteristics of ten paediatric patients with COVID-19 confirmed by RT-PCR and found that eight (80%) of ten patients (eight of ten) persistently tested positive on rectal swabs even after nasopharyngeal tests became negative, which was different from the ratio (41 [55%] of 74) in adults reported by Wu and colleagues.[6] There are some differences in the microenvironment between adult and paediatric gastrointestinal tracts.[10] Is it possible that the complex intestinal flora residing in the gastrointestinal tract might protect SARS-CoV-2 from the human immune system?

The characteristics of gastrointestinal symptoms in COVID-19 are more insidious than the respiratory symptoms, making them easy to overlook. However, some patients might have only gastrointestinal symptoms during the whole course of this disease, and some continue to shed the virus in faeces, despite respiratory samples testing negative. Further investigation is necessary to determine whether these patients represent a potentially overlooked means of transmission of SARS-CoV-2.

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