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knowledge gap of prevalence of viraemic HCV infection in children. As a result, the prevalence of HCV estimated in adolescents and children might be uncertain in some countries.

New large and age-specific national HCV prevalence studies are needed, but their paucity should not be a barrier to beginning efforts to eliminate viral hepatitis as a public health threat, as set out by WHO in 2016. The results of the analysis by Schmelzer and colleagues make it clear that the paediatric population cannot continue to be ignored, as there might be many more than 3 million children infected with HCV globally. Key actions should include targeted, multi-stakeholder plans to improve testing and screening policies aimed at children, as well as fast-track evaluation and approval of third-generation interferon-free pangenotypic treatment regimens, especially for children younger than 12 years.

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Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible?



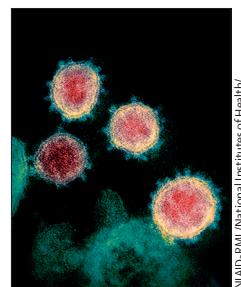
The end of 2019 was marked by the emergence of a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which caused an outbreak of viral pneumonia (COVID-19) in Wuhan, China. At the time of writing, SARS-CoV-2, previously known as 2019-nCoV, has spread to more than 26 countries around the world. According to the WHO COVID-19 situation report-28 released on Feb 17, 2020, more than 71 000 cases have been confirmed and at least 1770 deaths.

Coronaviruses are a family of single-stranded enveloped RNA viruses that are divided into four major genera. The genome sequence of SARS-CoV-2 is 82% similar to severe acute respiratory syndrome coronavirus (SARS-CoV),¹ and both belong to the β -genus of the coronavirus family.² Human coronaviruses such as SARS-CoV and Middle East respiratory syndrome

coronavirus (MERS-CoV), are known to cause respiratory and enteric symptoms.

In the SARS outbreak of 2002–03, 16–73% of patients with SARS had diarrhoea during the course of the disease, usually within the first week of illness.³ SARS-CoV RNA was only detected in stools from the fifth day of illness onwards, and the proportion of stool specimens positive for viral RNA progressively increased and peaked at day 11 of the illness, with viral RNA still present in the faeces of a small proportion of patients even after 30 days of illness.⁴ The mechanism for gastrointestinal tract infection of SARS-CoV is proposed to be the angiotensin-converting enzyme 2 (ACE2) cell receptor.²

In the initial MERS-CoV outbreak in 2012, a quarter of patients with MERS-CoV reported gastrointestinal symptoms such as diarrhoea or abdominal pain at presentation.⁵ Some patients initially presented with both



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fever and gastrointestinal symptoms before subsequent manifestation of more severe respiratory symptoms.⁶ Corman and colleagues⁷ found MERS-CoV RNA in 14.6% of stool samples from patients with MERS-CoV. In-vitro studies have shown that MERS-CoV can infect and replicate in human primary intestinal epithelial cells, potentially via the dipeptidyl peptidase 4 receptor.⁸ In-vivo studies showed inflammation and epithelial degeneration in the small intestines, with subsequent development of pneumonia and brain infection.⁸ These results suggest that MERS-CoV pulmonary infection was secondary to the intestinal infection.

In early reports from Wuhan, 2–10% of patients with COVID-19 had gastrointestinal symptoms such as diarrhoea, abdominal pain, and vomiting.^{9,10} Abdominal pain was reported more frequently in patients admitted to the intensive care unit than in individuals who did not require intensive care unit care, and 10% of patients presented with diarrhoea and nausea 1–2 days before the development of fever and respiratory symptoms.⁹ SARS-CoV-2 RNA has been detected in the stool of a patient in the USA.¹¹ The binding affinity of ACE2 receptors is one of the most important determinants of infectivity, and structural analyses predict that SARS-CoV-2 not only uses ACE2 as its host receptor, but uses human ACE2 more efficiently than the 2003 strain of SARS-CoV (although less efficiently than the 2002 strain).²

Data exist to support the notion that SARS-CoV and MERS-CoV are viable in environmental conditions that could facilitate faecal–oral transmission. SARS-CoV RNA was found in the sewage water of two hospitals in Beijing treating patients with SARS.¹² When SARS-CoV was seeded into sewage water obtained from the hospitals in a separate experiment, the virus was found to remain infectious for 14 days at 4°C, but for only 2 days at 20°C.¹²

SARS-CoV can survive for up to 2 weeks after drying, remaining viable for up to 5 days at temperatures of 22–25°C and 40–50% relative humidity, with a gradual decline in virus infectivity thereafter.¹³ Viability of the SARS-CoV virus decreased after 24 h at 38°C and 80–90% relative humidity.¹³ MERS-CoV is viable in low temperature, low humidity conditions. The virus was viable on different surfaces for 48 h at 20°C and 40% relative humidity, although viability decreased to 8 h at 30°C and 80% relative humidity conditions.¹⁴ At present, no viability data are available for SARS-CoV-2.

The viability of SARS-CoV and MERS-CoV under various conditions and their prolonged presence in the environment suggest the potential for coronaviruses to be transmitted via contact or fomites. SARS-CoV and MERS-CoV are both viable in conditions with low temperatures and humidity.^{12–14} Although direct droplet transmission is an important route of transmission, faecal excretion, environmental contamination, and fomites might contribute to viral transmission. Considering the evidence of faecal excretion for both SARS-CoV and MERS-CoV, and their ability to remain viable in conditions that could facilitate faecal–oral transmission, it is possible that SARS-CoV-2 could also be transmitted via this route.

The possibility of faecal–oral transmission of SARS-CoV-2 has implications, especially in areas with poor sanitation. Coronaviruses are susceptible to antiseptics containing ethanol, and disinfectants containing chlorine or bleach.¹⁵ Strict precautions must be observed when handling the stools of patients infected with coronavirus, and sewage from hospitals should also be properly disinfected. The importance of frequent and proper hand hygiene should be emphasised.

Future research on the possibility of faecal–oral transmission of SARS-CoV-2 should include environmental studies to determine whether the virus remains viable in conditions that would favour such transmission. Study of the enteric involvement and viral excretion of SARS-CoV-2 in faeces is required to investigate whether faecal concentrations of SARS-CoV-2 RNA correlate with the severity of the disease and presence or absence of gastrointestinal symptoms, and whether faecal SARS-CoV-2 RNA can also be detected in the incubation or convalescence phases of COVID-19.

We declare no competing interests.

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