

**EDITORIAL**

## 2019 Novel coronavirus infection and gastrointestinal tract

Since December 2019, several cases of pneumonia of unknown etiology have been reported in Wuhan, Hubei Province, China. On 7 January 2020, a novel coronavirus was identified from a throat swab sample of a patient by the Chinese Center for Disease Control and Prevention, and was subsequently named 2019 novel coronavirus (COVID-19) by the World Health Organization. As of 21 February 2020, nearly 75 114 cases of human COVID-19 infections have been confirmed in China, with at least 2239 reported deaths. Additional cases have spread to other countries in Asia, Europe, America, Oceania, and Africa.

Six coronaviruses species are known to cause human diseases, among them severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are both zoonotic in origin, which can cause severe respiratory illness and high mortality. And COVID-19 is the seventh. Phylogenetic analysis of the complete viral genome (29 903 nucleotides) has shown that the COVID-19 is most closely related (89.1% nucleotide similarity) to a group of SARS-like coronaviruses.<sup>1</sup> This fact could partly explain the behavior of this novel coronavirus in human infection.

Retrospective studies from Wuhan, China have indicated that the main clinical manifestations of COVID-19 are fever, cough and dyspnea. Less common symptoms include the production of sputum, headache, hemoptysis and some gastrointestinal symptoms. It seems that gastrointestinal symptoms, such as diarrhea (2%-10.1%), and nausea and vomiting (1%-3.6%), are not very common at present.<sup>2,3</sup> However, a significant proportion of patients presented initially with those atypical gastrointestinal symptoms.

There is evidence not only of animal-to-human transmission but of human-to-human transmission of COVID-19 among close contacts or through virus-laden aerosols. Although more evidence is needed, Zhang et al<sup>4</sup> from the People's Hospital of Wuhan University have reported the presence of viral nucleic acids in the fecal samples and anal swabs of patients with COVID-19. Therefore, there is a possibility of fecal-oral transmission in COVID-19 infection. More attention should be paid to the hand hygiene and disinfection of patients' vomitus, feces, and other bodily fluids.

Previous studies have uncovered several receptors to which different coronaviruses bind, such as angiotensin-converting enzyme 2 (ACE2) for SARS-CoV. One study showed by molecular modeling that there is a structural similarity between the receptor-binding domains of SARS-CoV and COVID-19, which means that COVID-19 may use ACE2 as the receptor despite the presence of amino acid mutations in the COVID-19 receptor-binding domain.<sup>5</sup> This finding was subsequently verified by another study which suggested that liver abnormalities might also occur in patients with COVID-19 because the cholangiocytes are targeted by

these viruses through ACE2.<sup>6</sup> ACE2 is known to be abundant in the epithelia of the lungs and intestine in humans, which might enhance the evidence of this possible route for COVID-19. Yet other authors have indicated that the expression of ACE2 is primarily located on the luminal surface of differentiated small intestinal epithelial cells, whereas lower expression has been observed in the crypt cells and the colon.<sup>7</sup> They have also linked the amino acid transport function of ACE2 to the microbial ecology in the gastrointestinal tract in which ACE2 mutants exhibit decreased expression of antimicrobial peptides and show altered gut microbial composition. Therefore, we speculate that COVID-19 may, to some extent, be related to the gut microbiota.

However, the connection between the lung and the gastrointestinal tract is not completely understood. It is well known that the respiratory tract houses its own microbiota, but patients with respiratory infections generally have gut dysfunction or secondary gut dysfunction complications, which are related to a more severe clinical course of the disease, thus indicating gut-lung crosstalk. This phenomenon can also be observed in the patients with COVID-19. Numerous studies have shown that modulating gut microbiota can reduce enteritis and ventilator-associated pneumonia, and it can reverse certain side effects of antibiotics to avoid early influenza virus replication in lung epithelia.<sup>8</sup> Currently, there is no direct clinical evidence that the modulation of gut microbiota plays the therapeutic role in the treatment of COVID-19, but we speculate that targeting gut microbiota may be a new therapeutic option or at least an adjuvant therapeutic choice. In early February, the guidance (version 5) established by the China's National Health Commission and National Administration of Traditional Chinese Medicine<sup>9</sup> recommended that in the treatment of patients with severe COVID-19 infection, probiotics may be used to maintain the balance of intestinal microecology and prevent secondary bacterial infection, which shows that the Chinese government and first-line medical staffs accept the importance of the role of gut microbiota in COVID-19 infection.

Huge efforts from the Chinese government and accelerated related research have been done over this period. Although no specific antiviral treatment has been recommended to date, we speculate that probiotics may modulate the gut microbiota to alter the gastrointestinal symptoms favorably and may also protect the respiratory system. Further studies may focus on this point. It would be interesting to investigate whether the benefits of ACE2 on pulmonary disease may be mediated via modulation of gut and/or lung microbiota. Finally, we call upon all first-line medical staffs to be cautious and pay more attention to atypical


patients with an initial presentation of gastrointestinal symptoms, especially those from the epidemic area. We hope that, with the joint efforts and great support, COVID-19 will soon be overcome.

#### CONFLICT OF INTEREST

None.

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