

# Covid-19 and the Human Gut: A New Runner on the Tract

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**Abstract** The severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) dwells in the respiratory airways, however, its digestive tract presence, infectivity, mucosal attachment and penetrating mechanisms, enteric proliferation, stool shading, flashed bio-aerosol spreading and fecal-oral transmission is far from being understood. The present review opens some skylights to lighten the long, tortuous, dark and challenging tunnel of the gastrointestinal tract and his uninvited covid-19 viral new inhabitant.

**Keywords:** covid-19, SARS-CoV-2, corona virus, gut, intestine, gastrointestinal tract, endoscopy, stool, infectivity, transmission

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## 1. Introduction

At the end of 2019, the Chinese Wuhan's health authorities were investigating cases of an acute respiratory syndrome. The epidemiologic investigation linked the respiratory distress to a local Seafood Market. Quite quickly genomic analysis linked the etiology to a new virus, a member of the coronavirus family, initially named 2019 novel coronavirus (2019-nCoV). Today the virus is called coronavirus disease 2019 (COVID-19) or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The name SARS directs the target organ of the virus to the upper respiratory ways and lungs, but it appears that the gastrointestinal tract is also affected. The present review intends to summarize and update the readers on the enteric aspects of the covid-19.

### 1.1. Covid-19 Update

In his latest brief, the world health organization-director-general declared that in the currently evolving Pandemic, more than 2 million cases of COVID-19 have now been reported to his organization, sadly enough, more than 135,000 people have lost their lives worldwide [2]. It is the third outbreak of a Coronavirus in the present century, following the SARS and the MARS epidemics, few years ago. Understand and prevent pathogens crossing from animals to humans is crucial since an estimated 70% of all new viruses come from animals. The two past epidemic animal sources, the Himalayan palm civet for SARS-CoV and the dromedary camel for MERS-CoV were detected, not yet for the origin of the new SARS-CoV-2 [3,4]. To date, the COVID-19 outbreak spread to 6 continents, affected most of the countries and

represents a global health concern with an estimated case-fatality rate of 2-3%. Coronaviruses are RNA viruses like influenza, however, the present SARS-CoV-2 is more contagious, more aggressive and fatal than the winter outbreaks of the influenza viruses. There are already two variants for SARS-CoV-2, the L type and the S type that were identified and most probably, according to virologists, it will continue to mutate. The viruses are on our planet for more than 4 billion years, compared to the homo sapiens who resides here for only 1-2 million years [5]. The novel phenomenon of the covid-19 entry into a new species, namely, human being, represent a new evolutionary event that our immune barriers has to detect and react accordingly. Over reaction like the cytokine storm, might be detrimental [6]. It adapts to a more efficient and more capable replication in that new host species and more efficient transmission between the infected species. It can be generalized that till herd immunity will develop, any person without pre-existing immunity is susceptible to the covid-19 infection [7]. Finally, being a new human viral infection, the covid-19 present much more questions than answers. Its origin, biology, epidemiology, infectivity, short and long-term pathology and complications, specific immune protective mechanisms and effective mode of therapies are far from being elucidated [1,4,8,9].

### 1.2. The Gastrointestinal Virome and Phageome

An ocean of information and expanding scientific knowledge is available on the enteric microbiotic composition and diversity in human development and homeostasis while the dysbiotic morbidity in specific human chronic disease is still evolving. In fact, the gut microbes are extensively explored, but, the enteric virus's

incidence, characterization, biology, functions and relations with their prokaryotic neighbors are still in the initial steps of exploration. In fact, more and more knowledge is accumulating regarding intestinal luminal viruses and bacteriophages. It appears that they outnumber bacteria in a ratio of 10:1 [10]. Being an absolute parasite, they penetrate microbes, integrate their genetic material into the host genome, thus, dominating their destiny [11]. The outcome is microbial deadly lysis or a transient symbiotic relation when integration of the viral genetic sequences into the host genome is occurring. The later possibility is called lysogeny [12]. The enteric phageome (collection of bacteriophages) is crucial in orchestrating the homeostatic maintenance of the luminal microbiome composition, diversity and functionality. Comparably to the dysbiome, the list of phageomic aberrations in specific human pathologies is expanding. Crohn's disease, ulcerative colitis, type 2 diabetes and celiac disease are some examples [13]. When a pathological virome invades the gastrointestinal (GI) luman it can induce acute or chronic gastroenteritis and once in a while a devastating outbreak or epidemics. Enteroviruses, rotavirus, Hepatitis A, poliovirus are such an example. The present review will introduce a new virus that strikes the globe right now with a severe Pandemic, namely, the covid-19, a member of the coronavirus family that invades our GI tract.

## 2. Gastrointestinal Aspects

Most of the epidemiological, clinical and pathological publications on covid-19 virus concentrate on the upper and lower respiratory tracts [14]. Despite this, other organs like kidney, liver, heart, vessels and intestine are also affected. Follow bellow is the place of the GI tract in the SARS-CoV-2 puzzle.

### 2.1. Symptoms

Covid-19 cohabit the enteric tract and some presenting symptoms and enteric complains were described in Wuhan, Chine and outside of Wuhan. Out of 651 patients, 11.4% presented with at least one GI symptom like nausea, vomiting or diarrhea. Interestingly, patients with GI symptoms had more severe or critical picture and family clustering, compared to those without GI symptomatology [15]. In another Chinese province, in Zhejiang, 8% of the hospitalized patients had diarrhea [16] and in a study from Wuhan, diarrhea occurred in 49.5% of the patients [17]. Some patients with diarrhea don't have respiratory symptoms while the debate about digestive symptoms in the more severe compared to the non-severe patients is unresolved. Diarrhea as presenting symptom was described in elderly, adults and children [18]. It appears that along the Chinese epidemics, in the later stage, the proportion of patients with diarrhea increased when compared with the pre - epidemic stage. At least, 12 infected patients had GI bleeding and the rate of diarrhea in children was similar (9.6% - 15%) as adults but they had a higher rate of vomiting [18].

According to a very recent report from Wuhan, 31% of patients with covid-19 induced pneumonia had diarrhea. A higher proportion of patients with diarrhea had viral RNA

in stool than patients without diarrhea. Intriguingly, elimination of SARS-CoV-2 from stool took longer than elimination from the nose and throat [19]. Even asymptomatic or hypo-symptomatic SARS-Cov-2 positive infant can excrete the virus in their stool without any diarrhea [20]. Finally, abdominal pains accompany patients with GI symptomatology [21] but, anorexia was reported as the most common GI symptom [18].

### 2.2. Pathophysiology and Pathology

The Spike protein is a homotrimers that protrude from the covid-19 surface, thus, facilitating the attachment of the viral envelope to host cells by binding to its receptor, the angiotensin-converting enzyme 2 (ACE2) [22]. At the beginning of the covid-19 epidemic it was thought that this receptor is expressed in lower respiratory tract cells, explaining the respiratory symptoms and lung pathology. Later on, it was reported that ACE2 is highly expressed in esophageal epithelium, in the lining enterocytes from ileum and in the colonocytes of the colon [23]. The virus presence in the GI lumen in close proximity to its corresponding receptor strongly suggests the covid-19 can actively infect, replicate and induce enteric pathology with possible fecal transmission [3,14,17,18,19,20,21,23].

The GI topographic pathology induced by the SARS-CoV-2 involves all the gut segments, from the esophagus to the distal colon. The esophagus squamous epithelium might present lymphocytic infiltration and the stomach plasma cells and lymphocyte infiltrations and edema. The entire GI mucosa can present various degree of necrosis, degeneration and shedding of the epithelium [18,24]. The virus tropism of covid-19 to the GI mucosa was reported in several earlier studies. Nucleocapsid proteins and the virus itself was detected in cytoplasm of gastric, duodenal and colonic glandular epithelial cells, as well as in the stools [18,25,26]. Those pathological findings attest for the virus capacities to penetrate, attack and damage the GI tract and activate the host immune system to react against the invader.

### 2.3. Shading in Stools

Substantial evidences exist for the covid-19 virus cohabitation of the GI tract and for its stool excretion. Its stool presence can be detected even in asymptomatic patients, in all age ranges, including infants [17,18,19,20,21,25,26]. Interestingly enough, at least in asymptomatic patients, fecal excretion of this new coronavirus can last for 42 days, even when nasopharyngeal samples are negative [27]. The differential positivity of the swabs might change along the disease duration. The throat samples tend to be positive in the first days, while the rectal swabs, in the latter period of the infection [28]. The stool shading of the virus might explain the extensive infectivity and the pandemic extension of the covid-19.

### 2.4. Fecal Transmission Possibilities

In contrast to the well-established aerosol droplet's transmission, the topic of fecal transmission of the disease and the degree of infectivity of the stools is still unknown.

Whenever discussing the subject, all the publications use the words: possible, potential or add a question mark [18,21,23,29,30,31]. Additionally, toilet stool flushing can produce bio-aerosols, thus enhancing contamination [31]. Historically, an index case of the Hong Kong SARS outbreak started with diarrhea suggesting a flashed bio-aerosol spreading [32]. Life pathogens are carried by bio-aerosols generated by water toilet flushing [33], small enough to be air-born infective messengers [34]. Most recently, the longer shedding of the SARS-CoV-2 was substantiated in children stools, compared to their respiratory tract. The authors concluded that other transmission routes, in addition to the droplet one, are also plausible [35]. Shedding seems to be present in feces for a longer time than in the respiratory tract of adults and children. Those are important implications for public health, transmission, infection control and future pandemic therapeutic strategies. The fecal transmission rout possibility, should be thoroughly investigated and not underestimated.

## 2.5. Covid-19 and Endoscopies

Despite the unresolved puzzle of fecal-oral transmission, the GI endoscopist team are worry about their professional safety and rightfully so. The GI presence and fecal shading of the virus might put them at risk and the gastroscopes/colonoscopes might represent a contaminated instrument that might spread the virus. Those are the reasons why various endoscopy and GI associations, originated from highly infected countries, put forward new guidelines to decrease the risks [36-41]. The guidelines cover pre, intra and post procedure recommendations. Adult's precautions are somewhat different from the pediatric ones, all present holistic approach to protect all the persons involved in the endoscopic procedures. Professional are encouraged to read the various recommendations and adopt them as necessary.

## 3. Conclusions

The SARS-CoV-2 is a new viral Pandemic that is spreading worldwide with more hidden knowledge than clinical and scientific facts. More and more information is accumulating on the GI symptoms, enteric dissemination and pathology, mechanism of mucosal attachment, fecal shading and potential fecal-oral transmission of the viral particle. Raising awareness, adapting suitable protective precautions and more attention to the undiscovered mode of dissemination is highly encouraged. It might change our contemporary struggle and improve public and the medical team safety and health.

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