A quick look at the latest developments in the COVID-19 pandemic

Ling Xue¹, Jiao Li¹,², Lin Wei¹ and Cuiqing Ma¹

Abstract
In December 2019, a new respiratory disease manifesting as viral pneumonia emerged in Wuhan, China. Isolation and identification of the virus showed that the pathogen causing this disease was a novel coronavirus. On January 12, 2020, the World Health Organization named the novel coronavirus causing the outbreak 2019 novel coronavirus (2019-nCoV). The disease caused by the virus was named coronavirus disease 2019 (COVID-19). Later, the Coronavirus Study Group of the International Committee on Taxonomy of Viruses formally named this virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus shows strong infectivity and high lethality, arousing widespread concern. As an emerging virus, a comprehensive understanding of SARS-CoV-2 is missing. To provide a reference and a theoretical basis for further study of SARS-CoV-2, recent advances in our understanding of the virus are summarized in this review.

Keywords
SARS-CoV-2, COVID-19, 2019-nCoV, novel coronavirus, pandemic, etiology, pathogenesis

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Introduction
Coronaviruses are widespread in nature, only infect vertebrates and can cause respiratory, enteric, hepatic and neurologic system diseases in humans and animals.¹ Coronaviruses can be divided into four genera: alpha, beta, gamma, and delta coronaviruses.² Alpha and beta coronaviruses mainly infect mammals, while gamma and delta coronaviruses infect birds and bats, respectively. The novel coronavirus (SARS-CoV-2) belongs to the family Coronaviridae, genus Betacoronavirus, and is closely related to other coronaviruses, such as the SARS coronavirus and the middle East respiratory syndrome coronavirus. The spike protein on the virus surface is responsible for viral entry into host cells, and the main protease (Mpro) is an essential enzyme for virus replication. The virus is transmitted from person to person through respiratory droplets, direct contact, and environmental surfaces. The incubation period of COVID-19 is generally 3-7 days, and the median incubation period is 5 days. The virus can be transmitted in the initial stage of the disease, and infected patients may be asymptomatic carriers. The basic reproductive number (R0) of COVID-19 is estimated to be approximately 3.5, indicating the high transmissibility of the virus. The virus can cause severe outcomes in patients with underlying chronic diseases, such as cardiovascular disease, diabetes, chronic kidney disease, and chronic respiratory disease. The virus can also cause severe pulmonary injury, leading to acute respiratory distress syndrome and even death. The current treatment strategies include supportive care, antiviral treatment, and immunotherapy. The development of effective vaccines and antiviral drugs is crucial for controlling the COVID-19 pandemic.

¹Department of Immunology, Key Laboratory of Immune Mechanism and Intervention on Serious Disease in Hebei Province, Hebei Medical University, Hebei Medical University, Shijiazhuang, China
²The Second Hospital of Hebei Medical University, Shijiazhuang, China

Corresponding author:
Cuiqing Ma, Department of Immunology, Key Laboratory of Immune Mechanism and Intervention on Serious Disease in Hebei Province, Hebei Medical University, No. 361 Zhongshan East Road, Shijiazhuang 050017, China. Email: macuiqing@hebmu.edu.cn

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delta coronaviruses mainly infect birds.\textsuperscript{3} Seven coronaviruses can infect humans including the alpha coronaviruses, HCoV-229E and HCoV-NL63, and the beta coronaviruses, HCoV-OC43, HCoV-HKU1, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and SARS-CoV-2.\textsuperscript{4–7} HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 infections are relatively common in human populations. These viruses generally cause only mild respiratory symptoms similar to the common cold.\textsuperscript{8} However, SARS-CoV, MERS-CoV,\textsuperscript{9} and SARS-CoV-2 have higher infection and death rates.

**Etiological characteristics**

**Structural characteristics**

SARS-CoV-2 is an enveloped coronavirus. The virion is round or elliptic, often pleomorphic, and has a diameter between 60 nm and 140 nm.\textsuperscript{10,11} The virion can look like a crown when observed under electron microscopy. The viral spike protein present on the envelope is the most important surface protein of the virus and mediates infection. The spike protein contains two subunits: S1 and S2. S1 comprises the receptor binding domain (RBD) that recognizes cellular receptors, and S2 plays an important role in the process of membrane fusion.\textsuperscript{12} The spike protein determines the specificity and host range of the virus, and its sequence can be altered through gene recombination or mutation of the RBD.\textsuperscript{13} In addition, the spike protein is an important target of host neutralizing antibodies and plays a vital role in vaccine design.

**Genetic characteristics**

SARS-CoV-2 is a positive-sense, single-stranded RNA virus, and is prone to mutation. The viral genome is about 30 kb in length,\textsuperscript{14} encoding several open reading frames including ORF1ab and the S, E, M, and N genes.\textsuperscript{10} The genome encodes non-structural proteins, structural proteins and helper proteins. The S, E, M, and N genes encode the spike protein, envelope protein, membrane protein and nucleoprotein, respectively. The SARS-CoV-2 genome shares high homology with the genomes of bat coronaviruses,\textsuperscript{10,15,16} suggesting a likely origin of the virus in bats.

**Physical and chemical properties**

SARS-CoV-2 has difficulty surviving at high temperatures and in low humidity environments.\textsuperscript{17} The virus can be effectively inactivated at 56°C for 30 minutes.\textsuperscript{18} At least one study demonstrated a significant positive correlation between ambient average relative humidity levels (23.33%–82.67%) and confirmed cases of COVID-19.\textsuperscript{17} Coronaviruses are enveloped lipophilic viruses that are easily dissolved and destroyed by lipid solvents. Most approved disinfectants including ether, 75% ethanol, chlorinated disinfectants, peroxyacetic acid, and chloroform can effectively kill coronaviruses. In addition, the virus is also sensitive to ultraviolet light.\textsuperscript{18}

**Pathogenic mechanism**

SARS-CoV-2 is an emerging coronavirus whose effects on the human body are not yet fully understood. Preliminary studies have suggested that the pathogenic mechanism of SARS-CoV-2 is similar to that of SARS-CoV. Both viruses bind to the cell surface receptor angiotensin converting enzyme 2 (ACE2) in human airway epithelial cells via the S protein on the envelope and enter the host cell.\textsuperscript{16,19–22} ACE2 is highly expressed in alveolar cells type 2 as well as in the esophagus, ileum, colon, heart, kidney, bladder and testis.\textsuperscript{23–28} These findings suggest that ACE2, which
is highly expressed in esophageal epithelial cells, intestinal epithelial cells, cardiomyocytes, and bladder epithelial cells, may allow SARS-CoV-2 to invade several human organs and lead to multiple organ damage and failure.

**Clinical features**

Human populations are generally susceptible to SARS-CoV-2. As of June 15, 2020, there were 84,823 confirmed cases and 4,645 deaths in China, with 7,823,334 confirmed cases and 431,541 deaths globally. Currently, the mortality rate is about 5.5% in China and globally, lower than that of SARS (10%) and MERS (36%). Based on current epidemiological data, the incubation period of SARS-CoV-2 appears to be long, ranging from 1 to 14 days but lasting for 3 to 7 days in most cases. The clinical manifestations of SARS-CoV-2 are similar to those of SARS-CoV. Both viruses primarily cause lower respiratory symptoms, but the clinical features associated with SARS-CoV-2 are milder than those associated with SARS-CoV. The symptoms of most patients are nonspecific: fever, cough, and fatigue are the main manifestations. A few patients have symptoms such as nasal congestion, runny nose, and diarrhea. Severe cases can develop into acute respiratory distress syndrome. SARS-CoV-2 can be detected in sputum, nose and throat swabs, alveolar lavage fluid and other samples by real-time reverse transcription polymerase chain reaction. Specific IgM and IgG antibodies can be detected in the sera of COVID-19 patients. Laboratory examinations showed that lymphocytes were decreased while levels of C-reactive protein, aspartate aminotransferase, and alanine aminotransferase were increased in most patients. On imaging examination, bilateral pneumonia can be seen with patchy shadows or ground-glass opacity. Cases with milder symptoms may not show pneumonia.

Most patients have a good prognosis, while a few progress to critical condition. The elderly, especially those with a history of chronic diseases and surgeries, are more susceptible to infection and have higher mortality rates and worse prognosis.

**Transmission and prevention**

SARS-CoV-2 can infect many animals as well as humans, and entry into human populations most likely represents a zoonotic transmission event. Some groups suggested that the natural host of the virus is the bat, although the intermediate hosts remain unclear. Other wild animals may also be involved in transmission such as minks and pangolins.

SARS-CoV-2 is highly infectious and pathogenic. The affinity of the SARS-CoV-2 S protein for ACE2 is approximately 10- to 20-fold higher than that of SARS-CoV, which may explain why SARS-CoV-2 is highly infectious. In the face of this outbreak, we need to raise our awareness of personal protection and do all we can to reduce the spread of the virus. Since the middle of December 2019, there has been persistent human-to-human transmission. Sources of infection are primarily patients with COVID-19 and asymptomatic cases. The modes of transmission include droplet, contact, and aerosol spread as well as potential transmission via the fecal-oral route. No evidence of vertical transmission was observed in women who acquired SARS-CoV-2 infection in late pregnancy. Thus, we should avoid eating wild animals, improve our knowledge of SARS-CoV-2, and enhance awareness of personal protection strategies.

SARS-CoV-2 is a novel coronavirus, and an effective vaccine has yet to be developed.
Inactivated vaccines, mRNA vaccines, DNA vaccines, viral vector vaccines, and other vaccine candidates are under development. Some have already entered clinical trials. A recombinant adenovirus type 5 vector vaccine, developed by Chen Wei’s team, showed good safety and immunogenicity in a phase I clinical trial, rapidly inducing both humoral and T-cell responses against SARS-CoV-2 in most participants. Currently, this vaccine is in phase 2 clinical trials, where its safety, tolerability and immunogenicity will be further evaluated.

**Diagnosis and treatment**

Detection of SARS-CoV-2 nucleic acid is the gold standard for diagnosis of SARS-CoV-2 infection. Methods for antigen detection, antibody detection and simpler nucleic acid detection are also being developed. IgM/IgG antibody rapid detection assays have appeared on the market and have been applied for clinical case detection. Compared with nucleic acid detection, antibody detection is often faster and more convenient. Antibody detection also has good sensitivity and specificity, and can be used as a supplement to nucleic acid detection. In general, diagnosis of COVID-19 is based on comprehensive analysis of epidemiological risk factors, clinical manifestations, laboratory examinations, imaging examinations and pathogen detection results.

There are no specific antiviral drugs against SARS-CoV-2, and recovery from COVID-19 basically depends on immunity and complementary clinical therapy. Because of the urgency of the SARS-CoV-2 pandemic, current treatments for SARS-CoV-2 are largely based on clinical experience with SARS and MERS. The inhibitory effects of antiviral agents approved or under development on SARS-CoV-2 are being tested, including agents developed to treat human immunodeficiency virus or influenza virus infections. Potential COVID-19 therapies include antiviral drugs (interferon-α, lopinavir/ritonavir, ribavirin, and hydroxychloroquine) as well as antimicrobial agents. Respiratory support is provided in severe cases including oxygen therapy, non-invasive mechanical ventilation, invasive mechanical ventilation, and extracorporeal membrane oxygenation.

Antibodies obtained from the plasma of convalescent patients have been used in clinical therapy. Passive antibody transfer was previously used to treat SARS and influenza infection and achieved good results. However, this therapy has some limitations, including limited availability of specific antibodies and the existence of certain safety risks. Thus, safe and effective specific therapeutic antibodies must be developed for clinical treatment. Clinical case studies showed that the antiviral drug remdesivir, which has broad spectrum antiviral effects, is effective in inhibiting SARS-CoV-2. However, data from a clinical trial by a Chinese research team showed that remdesivir does not provide significant clinical or antiviral effects in severe cases of COVID-19. Some clinical trials of remdesivir are still ongoing to determine whether the drug is effective for treatment of patients with COVID-19. In addition, baricitinib, chloroquine, and some Chinese patent drugs with antiviral activity were also found to have therapeutic effects on COVID-19.

**Conclusion**

Our understanding of the etiology, transmission route and pathogenic mechanism of SARS-CoV-2 is still preliminary and not comprehensive. Some countries, including China, have controlled the COVID-19 epidemic well, but the virus is still spreading in other parts of the world at an alarming rate. COVID-19 may become a seasonal disease coexisting with humans for a long
time. There are currently no safe and specific antiviral drugs for treatment of patients with COVID-19, and vaccine development will take time. Therefore, the basic biological characteristics, transmission mode, and strategies for prevention and treatment of SARS-CoV-2 need to be further studied. In addition, broad-spectrum anti-coronavirus drugs and specific monoclonal antibodies against SARS-CoV-2 need to be developed. In this review, we aimed to provide a reference and theoretical basis for further studies of the prevention and treatment of COVID-19.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

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ORCID iD
Ling Xue https://orcid.org/0000-0001-6910-4228

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