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COVID Issue Paper

Coronavirus Disease 19, the Large-Scale Coronavirus Pandemic

Samad Farashi Bonab[1], Abdolfattah Sarrafnejad[2] & Nemat Khansari[1*]

[1]*Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

[2]*Department of Immunology, School of Health, Tehran University of Medical Sciences, Tehran, Iran*

[*]**Correspondence to:** Dr. Nemat Khansari, Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

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Coronaviruses are enveloped viruses possessing a positive-sense single stranded RNA genome and a capsid with helical symmetry. These viruses have the largest genome (26 to 32 kilobases) among RNA viruses. These viruses were termed Coronavirus due to their crown-like morphology under electron microscope. Coronaviruses infect humans, other mammals, and birds and can cause respiratory, enteric, hepatic, and neurologic diseases as well as kidney and cardiac problems. So far, seven species of Coronaviruses are known to cause human disease. Most human Coronavirus diseases had a zoonotic origin. The four human Coronavirus (HCoV)-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1 are endemic and prevalent [1]. Other human Coronaviruses include severe acute respiratory syndrome Coronavirus (SARS-CoV), Middle East respiratory syndrome Coronavirus (MERS-CoV), and the newly identified severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) that are highly transmissible and pathogenic in humans. HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoV-HKU1 usually cause mild symptoms, like common cold and/or diarrhea, while SARS-CoV, MERS-CoV and SARS-CoV-2 cause severe lower respiratory tract infection with a higher chance to develop acute respiratory distress as well as extra-pulmonary symptoms. SARS firstly appeared in 2002 and MERS in 2012. SARS-CoV is an animal virus from an animal reservoir, especially bats, that spread to civet cats and firstly infected humans in the Guangdong province of southern China in 2002. SARS patients experience fever, dry cough, dyspnea (labored breathing), headache, and hypoxemia. Progressive respiratory failure due to alveolar damage can result in death in some patient [2,3]. The first case of MERS, also known as camel flu, was reported from Saudi Arabia in June 2012 in a patient

with severe respiratory illness and acute kidney injury. Then more cases of MERS-CoV infection reported in Saudi Arabia and the spread of MERS was reported in several other countries. Typical symptoms of MERS include fever, cough, diarrhea, and shortness of breath. Some patients with MERS exhibit serious respiratory disease which may result in death [4,5]. Molecular investigation indicated that bats in Saudi Arabia are infected with several Coronaviruses and virus from one bat showed 100% nucleotide identity to virus from the human index case-patient indicating that bats might play a role in human infection [6]. MERS-CoV is a zoonotic virus and bats are a likely original reservoir, and dromedary camels are a reservoir host. Epidemiologic evidences suggest that MERS transmission occurs through direct contact with live camels or humans with symptomatic MERS, as well as individuals with asymptomatic MERS [7].

At now, the large-scale Coronavirus disease 19 (COVID19) is the largest Coronavirus pandemic that started on 12 December 2019 from a local seafood market in Wuhan, China. Both SARS-CoV-2 (COVID19 virus) and SARS-related Coronaviruses use the same cell receptor (angiotensin converting enzyme-II) for entering host cells. The virus genome sequences obtained from five patients at an early stage of the COVID19 outbreak share 79.6% sequence identity to SARS-CoV. In addition, whole genome of SARS-CoV-2 has 96% identity to a bat coronavirus. No obvious genetic recombination was found in the genome of SARS-CoV-2 [8]. SARS-related Coronaviruses are thought to be transmitted from bats to humans in origin. Furthermore, some bat SARS-related Coronaviruses have been previously shown to have the potential to infect humans [9-11]. SARS-CoV-2 is transmitted to human directly through respiratory droplets of infected people or indirectly through contact with virus-contaminated surfaces and substances [12]. Main clinical symptoms of COVID19 include fever, dry cough, dyspnea, headache and pneumonia. Progressive respiratory failure due to alveolar damage leads to death in some patients. Decreased numbers of lymphocytes and sometime other leukocytes occurs in patients [8]. All available evidence suggests that SARS-CoV-2 has a zoonotic origin.

Since September 2012, 27 countries have reported cases of MERS-CoV. At the end of November 2019, a total of 2494 laboratory-confirmed cases of MERS, including 858 associated deaths (case-fatality rate: 34.4%) were reported [13]. In addition, 8422 SARS cases and 916 SARS-related deaths were reported worldwide. At 23 April 2020, laboratory-confirmed COVID-19 cases and deaths were 2,544,792 and 175,694, respectively [14]. These findings emphasis the risk of SARS-CoV-2 to humans worldwide.

Immune responses can control Coronavirus infection. SARS-CoV-2 isolated from the bronchoalveolar lavage fluid of a patient was neutralized by convalescent sera from several surviving patients (Zhou *et al.*, 2020). However, some features of immune responses are involved in the alveolar damage in COVID19 patients.

Innate immune cells such as macrophages and natural killer (NK) cells promote clearance of viruses by various mechanisms such as removing or destruction of virus infected cells. Innate immune cells also trigger prolong adaptive immune responses against viruses and also induce tissue repair. Adaptive immune cells (T cells and B cells) stimulated by SARS-CoV-2 antigens presented on antigen presenting cells, such as dendritic cells and macrophages, can potently inhibit virus replication via covering virus peplomers, which are crucial for entering virus to host cells, by antibodies and through destroying of virus-infected cells by CD8+ T cells. In contrast, pulmonary and systemic inflammatory responses triggered by the innate immune responses

as well as antigen-specific CD4+ T cells during SARS-CoV-2 infection result in profound accumulation of immune cells as well as lung tissue destruction (alveolar damage) and subsequently severe respiratory disorders and even death in some COVID19 patients. Profound inflammatory cytokines production and inflammatory responses are responsible for the accumulation of various immune cells in lung tissue and subsequent respiratory disorder. Furthermore, increased complement activation which is triggered by viral antigen-antibody complexes is involved in lung tissue destruction during that SARS-CoV-2 infection.

Identification of SARS-CoV-2-infected people can be performed using antibody-based techniques such as solid phase immunochromatographic assay or ELISA (enzyme-linked immunosorbent assay). These techniques are beneficial for confirming COVID19 patients that show disease symptoms but their PCR test are negative. However, their specificity is lower than real-time RT-PCR. It is also important to know that antibody-based techniques fail to detect SARS-CoV-2 infection up to 8-14 days after beginning the infection due to the fact that production of SARS-CoV-2-specific antibody in the patient requires at least 8-14 days.

It should be noted that antibody-based diagnostic procedures are mostly beneficial for testing quarantined people or in a lockdown area for people who need permission to go back to work if they do have IgG antibody in their serum but do not show any COVID related symptom. Presence high levels of SARS-CoV-2-specific antibodies in the peripheral blood of people by no means provide immunity that protect people from SARS-CoV-2 infection.

At present, there is no efficient Coronavirus-specific therapy and vaccine for COVID19; thus , the best control route for COVID19 spread is avoiding virus entrance into body and social distancing is the best way for stay COVID19 free and help stop pandemic of the infection.

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