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COMMENTARY

Hot Topic Commentary on COVID-19

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Abstract

The recent pandemic outbreak of COVID-19 (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) worldwide caught the health care systems in every country around the world by storm and without a proper defense mechanism to cope and control such a pandemic. In this special Theme issue, we would like to discuss the latest treatment modalities available around the world in tackling this dreadful disease.

Keywords Coronavirus · COVID-19 · SARS-CoV-2 · Drugs for COVID-19

The recent pandemic outbreak of COVID-19 (severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) worldwide caught the health care systems in every country around the world by storm and without a proper defense mechanism to cope and control such a pandemic. In this special Theme issue, we would like to discuss the latest treatment modalities available around the world in tackling this dreadful disease.

COVID-19 is caused by a novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has been identified and characterized [1]. SARS-CoV-2 is the seventh coronavirus known to infect humans with some coronavirus SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2-caused severe diseases, whereas other coronavirus HKU1, NL63, OC43, and 229E were associated with mild clinical symptoms [2].

SARS-CoV-2 is a single-stranded RNA virus with 29,891 bases, shares 79.6% sequence identity to SARS-CoV, and is 96% identical at the whole-genome level to a bat coronavirus [1]. SARS-CoV-2 appears to encode 29 proteins and the receptor-binding spike protein encoded by the S gene containing the receptor-binding domain (RBD), which binds directly to the human of angiotensin-converting enzyme 2 (ACE2), promotes membrane fusion, and uptakes of the virus into human cells including the lung [1, 3, 4]. Upon entering the human cells, SARS-CoV-2 like other coronaviruses will hijack the cellular protein synthesis machinery to synthesize and assemble the viral proteins with subsequent viral replication [5]. In the human body, viruses in general will trigger a series of good versus bad host responses including autophagy, apoptosis, stress response, and innate immunity [6]. More than 80% of SARS-CoV-2 infected individuals would be asymptomatic to mild symptom (this percentage could be higher, since many infected asymptomatic people were not tested), most likely with the activation a good response. The good responders would activate the body's innate immune system including the induction of interferon (IFN) and activation of anti-viral defense mechanisms such as natural killer cells, and anti-viral T cells [6–9]. However, in about 20% of SARS-CoV-2 infected individuals, especially the immunocompromised, elderly, patients with underlying health conditions with cardiovascular and pulmonary problems such as diabetics, obesity, hypertension, chronic obstructive pulmonary disease (or COPD, such as emphysema), asthma, pulmonary fibrosis, and interstitial lung disease [10, 11] would encounter more severe disease characterized by significant respiratory symptoms leading to acute respiratory distress syndrome (ARDS) and even death. Studies of SARS-CoV and MERS-CoV found that these 2 viruses appear to have evolved mechanisms to attenuate or delay IFN production, resulting in enhanced inflammatory host responses and severe lung injury [5, 6, 12–14]. This

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aberrant host immune response with the production of powerful inflammatory cytokines, known as cytokine storm found in SARS-CoV and MERS-CoV infected patients, would correlate with disease severity and poor prognosis [6, 9, 12–15]. Severe COVID-19 patients infected with SARS-CoV-2 would show a major inflammatory response [16, 17]. Xiong et al. through transcriptomic analyses of COVID-19 patients identified several immune pathways and pro-inflammatory cytokines CCL2, CXCL2, CCL8, CXCL1, IL33, and CCL3L1 in BALF and CXCL10, TNFSF10, TIMP1, C5, IL18, AREG, NRG1, and IL10 in peripheral blood mononuclear cells (PBMC) induced by SARS-CoV-2 infection, suggesting a sustained inflammation and cytokine storm [18]. The authors concluded that SARS-CoV-2 infection–induced excessive cytokine release correlates with lung tissue injury and COVID-19 pathogenesis [18]. This estimated 20% of patients developing more severe disease with SARS-CoV-2, most likely due to genetics, epigenetics, and or other factors, have dampened innate immune response to fight the virus with enhanced viral load leading to cytokine storm, severe inflammatory/oxidative stress response, and severe lung injury secondary to ARDS. While there is a clear understanding that the respiratory system is dramatically impacted in COVID-19, there is evidence that other organ systems are also affected. Emerging data suggest that SARS-CoV-2 may lead to damage to other organs including the heart and brain. Nearly 20% of hospitalized patients with COVID-19 have evidence of cardiac damage [17]. Furthermore, neurologic symptoms have been reported in patients and infection of SARS-CoV-2 reported in the brainstem of both humans and experimental animals [18, 19].

Currently, there is no vaccine and or specific therapeutic drug targeting the SARS-CoV-2. Hence, it remains a major challenge to decide what potential therapeutic regimen to prevent and treat the severely sick COVID-19 patients. Effective vaccines are essential to combat against the extremely contagious SARS-CoV-2. At present, several vaccines are already being trialed either in animal models or humans, in record-breaking speeds, as scientists in China, Europe, and the USA raced to create the first COVID-19 vaccine. Currently, some of the potential therapeutic drugs been used are as follows: remdesivir, hydroxychloroquine/chloroquine, lopinavir-ritonavir, IL-6 monoclonal antibodies (toculizumab, sarilumab; Kevzara, Actemra), interferon, arbidol, favipiravir, angiotensin-converting enzyme 2 (ACE2) receptor blocker, colchicine, traditional Chinese herbal medicinal products (phytochemicals most likely possessing anti-inflammatory/anti-oxidative stress effects, anti-viral effects and or other effects), and acupuncture, among others [19, 20]. This special Theme issue on "COVID-19" will highlight and update some of the latest advances in the prevention and treatment of COVID-19.

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Compliance with Ethical Standards

Conflict of Interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Papers of particular interest, published recently, have been highlighted as: • Of importance •• Of major importance

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