International Reviews of Immunology

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/iiri20

*COV*ert *ID*entities of current worldwide pandemic

Kumar Akhilesh, Das Nilanjana & Kumar Himanshu

To cite this article: Kumar Akhilesh, Das Nilanjana & Kumar Himanshu (2021) *COV*ert *ID*entities of current worldwide pandemic, International Reviews of Immunology, 40:1-2, 1-4, DOI: 10.1080/08830185.2021.1884375

To link to this article: https://doi.org/10.1080/08830185.2021.1884375

INTERNATIONAL REVIEWS OF IMMUNOLOGY
2021, VOL. 40, NOS. 1-2, 1–4
https://doi.org/10.1080/08830185.2021.1884375

Taylor & Francis
Taylor & Francis Group

EDITORIAL

*COV*ert *ID*entities of current worldwide pandemic

Akhilesh Kumar[a], Nilanjana Das[a] and Himanshu Kumar[a,b]

[a] Laboratory of Immunology and Infectious Disease Biology, Indian Institute of Science Education and Research (IISER), Bhopal, India; [b] Editor-in-Chief, International Reviews of Immunology

Recent decades have witnessed the emergence of several new devastating diseases caused by RNA viruses, including Ebola, Zika, Nipah, and Coronaviruses. Before 2002, coronaviruses were known to cause mild flu-like symptoms without causing any fatality. However, in 2002, sporadic emergence of infectious severe acute respiratory syndrome (SARS) killed around 750 people in several parts of world [1]. Later, it was reported that SARS was caused by SARS-Coronavirus (CoV), a type of coronavirus. In December 2019, a cluster of fatal, mysterious respiratory illnesses were caused by another strain of coronavirus (SARS-CoV-2) in Wuhan, China and it rapidly spreaded through an extensive air, ground, and sea transportation network. This epidemic spread all over the world and turned into a pandemic. As of the publication date, 88,387,352 people have been infected; 1,919,204 people have lost their lives globally, and there have been massive economic losses all over the world [2]. The disease is known as coronavirus (COVID-19) and the virus belongs to *Betacoronavirus* of family *Coronaviridae*. Members of *Coronaviridae* infect a broad range of avian and mammalian hosts, causing mild symptoms, but, sometimes, mutations can cause the virus to jump from an animal host to humans. Several members from this family of viruses have gained the capability of human-to-human transmission, and can cause widespread disease, such as SARS (2002), Middle East Respiratory Syndrome (MERS-2012), and the ongoing COVID-19.

An analysis of the nucleotide sequences suggests that SARS-CoV-2 shares 79% similarity to SARS-CoV, 50% to MERS-CoV, and 96% to Bat CoV RaTG13, indicating that SARS-CoV-2 might have evolved from bat coronaviruses. Interestingly, despite the high similarity among these viruses, they are considerably different in the severity of clinical manifestations. All these viruses are transmitted while coughing or sneezing through droplet infection via respiratory route. The infection clinically presents with mild to severe flu-like symptoms. However, SARS-CoV-2 has a fatality rate of 2.3%, much lower than SARS-CoV (9.5%) and MERS-CoV (34.4%). SARS-CoV infection leads to high fever in most (97%) of the cases while only 43.1% SARS-CoV-2 patients showed fever higher than 37.5 °C [3]. This suggests that the low severity and often asymptomatic infections may facilitate disease spread and could be the reason behind the high rate of community transmission of this virus.

SARS-CoV-2 is an enveloped, single-stranded, positive sense RNA virus. The genome is 29.9 kb packed inside a helical capsid made of nucleocapsid (N) protein, which is further encapsulated in an envelope formed by the envelope (E) protein and lipid bilayer derived from the host cell. Apart from nucleocapsid, envelope, and various non-structural proteins, genomic RNA also encodes for membrane (M) and spike (S) proteins (Figure 1). The M and small envelope proteins (E) are involved in virus assembly, whereas the S protein facilitates virus entry into the cell by binding to angiotensin-converting enzyme (ACE) 2 receptors present on the host cell surface. As the spike protein plays a crucial role in the cell membrane fusion process, it also determines host tissue tropism and host range. Mutations in this region are giving rise to new and infectious/pathogenic strains. Three distinct variants of the virus have been identified: Ancestral type-A and mutated type-C variants are prevalent in Europe and the United States; type-B has spread in East Asian countries [4]. A new strain of SARS-CoV-2 has recently been identified during random genetic sequencing of positive COVID-19 samples in the United Kingdom. This strain has several mutations, but among them, N501Y mutation alters one of the six key residues in the receptor-binding domain (RBD) in the spike protein, making it up to 70% more transmissible among humans (Figure 2). Such mutations were predicted to happen, and several mutant strains might already be transmitting unnoticed. These mutations might lead to reinfections or could limit the efficacy of newly developed vaccines.

Host immune response against SARS-CoV-2 starts upon virus entry into the epithelial cells of the respiratory

CONTACT Himanshu Kumar, Ph.D. Himanshu.Kumar@taylorandfrancis.com Editor-in-Chief, International Reviews of Immunology, Laboratory of Immunology and Infectious Disease Biology, Indian Institute of Science Education and Research (IISER), Bhopal By-pass road, Bhopal 462 066, India.

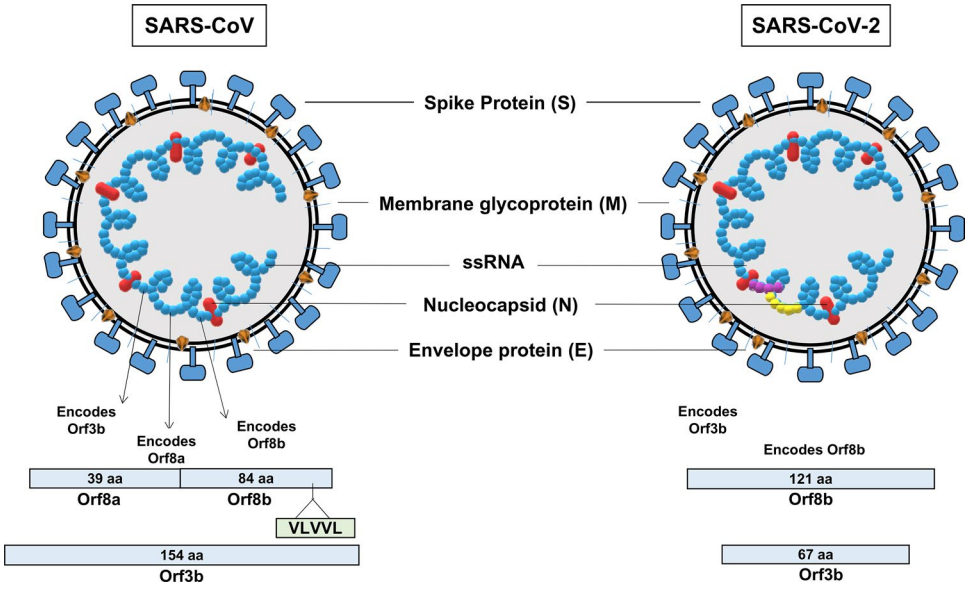

Figure 1. Similarity and differences between SARS-CoV and SARS-CoV-2.

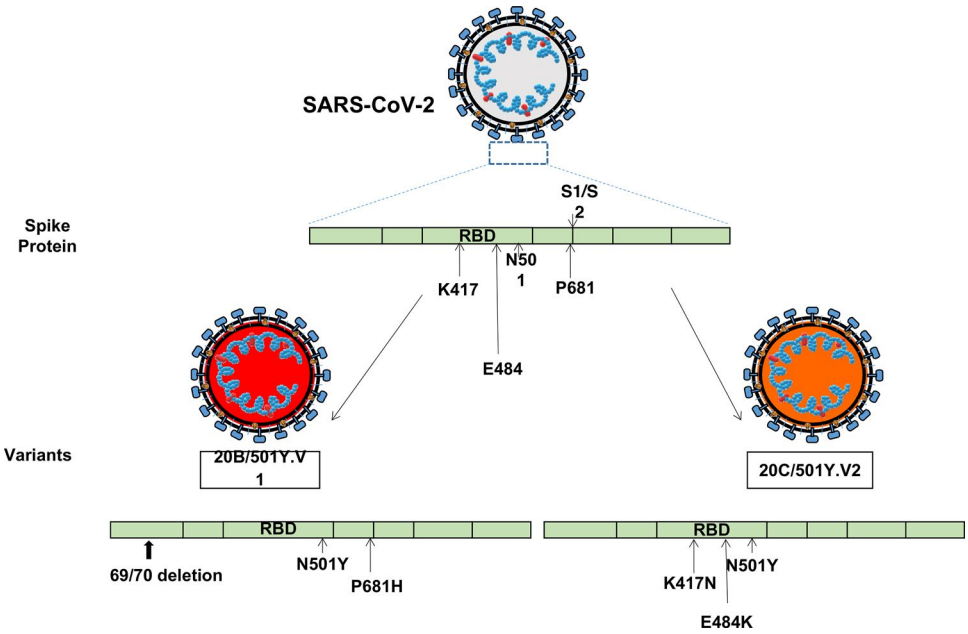

Figure 2. Mutants of SARS-CoV-2.

system. Viral RNA is sensed by intracellular RNA sensors, leading to the production of antiviral factors such as type-I interferons and pro-inflammatory cytokines, and activation of inflammasomes to induce release of IL-1β and IL-18. Damage-associated molecular patterns (DAMPs) from damaged epithelial cells along with pro-inflammatory cytokines attract tissue-resident macrophages, which release higher levels of pro-inflammatory cytokines along with subepithelial dendritic cells and, recruit lymphocytes to fight against the virus. In severe cases of COVID-19, viruses are not effectively cleared by the host immunity resulting in the heightened pro-inflammatory response, which leads to a cytokine storm. Cytokine storm can disrupt the physiological homeostasis and induce a state of vascular shock leading to multiorgan failure, which is the primary cause for high mortality (67%) among severe cases of COVID-19 (Figure 3). Interestingly, fever, one of the most basic innate immune responses during virus infection, has been highly effective against virus infection. According to a recent report, patients who survived had significantly high (37.3 °C) body temperature than those who could not survive (36.8 °C) [5]. This special issue of

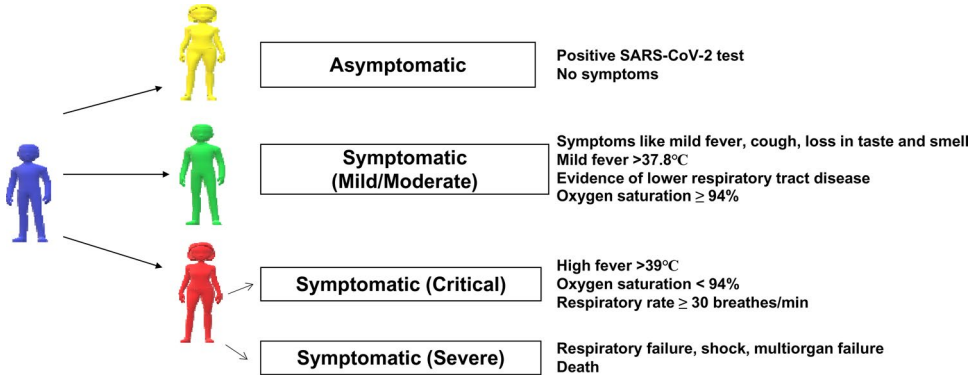

Figure 3. Spectrum of SARS-CoV-2 infected patients.

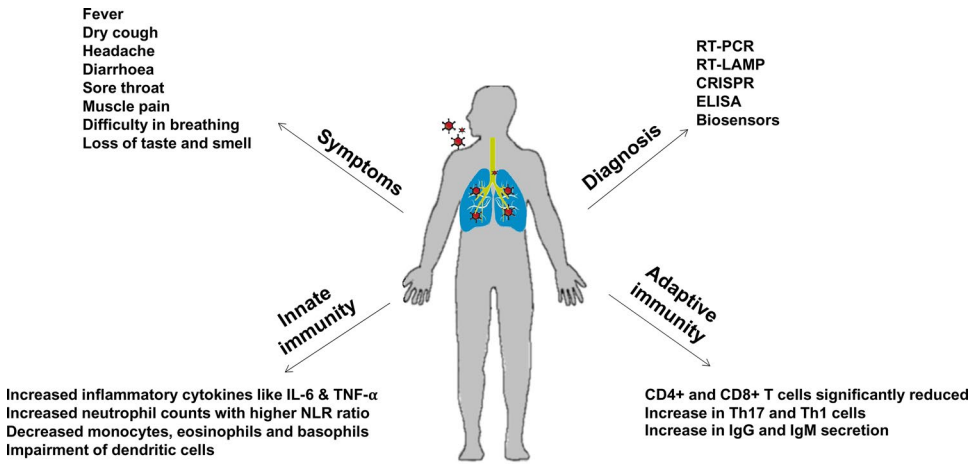

Figure 4. Immune responses and symptoms during SARS-CoV-2 infection and diagnostic tools for virus detection.

International Reviews of Immunology focuses on the fundamental biology of corona family viruses, host–virus interaction, the clinical outcomes or effects of virus infection on host physiology, and the newly developed tools for diagnosis of virus infection.

Coronaviruses have caused widespread diseases in the past; however, the current COVID-19 pandemic is far more severe than SARS and MERS epidemic, which had pandemic potential. It has spread to almost every part of the world and the virus has started to mutate so that it can evade the host's immune system. Different strains of SARS-CoV-2 have been found in different parts of the world; therefore, novel therapeutic and vaccine strategies need to be developed as soon as possible. The first review article in this issue discusses the similarities and differences in viral structure, symptoms, and outcomes of SARS-CoV, MERS-CoV, and SARS-CoV-2 viruses [6]. This comparison could improve the understanding of structural aspects of coronaviruses' and may help the clinicians, virologists, and immunologists to develop therapeutics against this family of viruses. Understanding the interaction between host and viruses is very important for the development of therapeutics. Different companies worldwide have had approval for vaccine. The second review article in this issue discusses the host–virus interactions and the probable pathogenic mechanisms by which it infects the host [7]. Thus, this review will help immunologists, virologists, and scientists involved in the development of vaccines (Figure 4).

SARS-CoV-2 infection induces fever, headache, dry cough, sore throat, tiredness, muscle pain, diarrhea, loss of taste, and smell. However, in severe cases, patients develop pneumonia, severe acute respiratory syndrome, and multiorgan failure, leading to death [8]. Although people with comorbidities like hypertension, diabetes, obesity, and cardiovascular disorders are naturally more prone to COVID-19, studies suggest that the state of the host's immune system at the time of infection also plays a crucial role. Both innate and adaptive immunity plays an essential role in clearing off pathogens from the host. Additionally, the cellular metabolism in immune cells is the key deciding factor for the differentiation of different subsets of immune cells, which play pivotal role in immune defense/immune pathogenesis. The third review

article in this issue discusses about the metabolic changes in macrophages, T cells, B cells, dendritic cells, NK cells, and vascular epithelial cells during SARS-CoV-2 infection and the outcome of disease [9]. This article could help in understanding the link between symptoms, age, and SARS-CoV-2 infection and can help in the cell-specific therapeutics against COVID-19. The fourth review article in this issue discusses about the function of the DCs, their role in COVID-19 pathogenesis and their link to SARS-CoV-2 induced morbidities [10]. Dendritic cells are antigen-presenting cells that present the antigens and stimulate the naive T cells. They act as a link between innate and adaptive immune systems and play an essential role in fighting infections. However, during SARS-CoV-2 infection it has been reported that functions of DCs were impaired and the ratio of conventional DCs to plasmacytoid DCs are also increased in severe COVID-19 patients [11]. These reviews will help immunologists and virologists to understand the programming of DCs during SARS-CoV-2 and other related virus infections (Figure 4).

It is well established that the best tool to fight the COVID-19 pandemic is the early detection and quarantine of infected individuals. Current diagnostic techniques like Real-time Polymerase chain reaction (RT-PCR), quantitative(q)RT-PCR, and clustered regularly interspaced short palindromic repeats (CRISPR) are expensive, time-consuming, and are not accurate to a great extent as contamination or low viral load in the samples can give false-negative results. Serological tests can also give false positive or negative results due to low antibody titers in the serum. Therefore, rapid and accurate point of care diagnostics is urgently needed to distinguish between symptomatic and asymptomatic individuals. Electrochemical immune sensors could prove to be a viable solution; they are rapid and inexpensive and do not need trained personnel. The last two articles in this issue focus on diagnostic methods for SARS-CoV-2. Datta et al. discuss the different methods used for diagnosing SARS-CoV-2 infection, and Ranjan et al. highlight the disadvantages of the molecular diagnostic platforms and the advantages of the electrochemical sensors for diagnosing SARS-CoV-2 infection [12]. Community spread of SARS-CoV-2 is the main reason behind the rapid emergence of COVID-19 clusters around the world, and therefore, efficient air and wastewater sampling methods and testing for SARS-CoV-2 could prove highly useful in the ongoing fight against this pandemic [13]. These reviews help the readers to understand the different methods available for the diagnosis of SARS-CoV-2 infection and detection of the virus in diverse environmental samples (Figure 4).

References

1. WHO. 2003. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003.
2. World Health Organization. 2021. COVID-19 Weekly Epidemiological Update 22.
3. Zhou Z, Yang Z, Ou J, et al. Temperature dependence of the SARS-CoV-2 affinity to human ACE2 determines COVID-19 progression and clinical outcome. *Comput Struct Biotechnol J*. 2021;19:161–167. doi:10.1016/j.csbj.2020.12.005.
4. Forster P, Forster L, Renfrew C, Forster M. Phylogenetic network analysis of SARS-CoV-2 genomes. *Proc Natl Acad Sci USA*. 2020;117(17):9241–9243. doi:10.1073/pnas.2004999117.
5. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. *JAMA Intern Med*. 2020;180(7):934–943. 1doi:10.1001/jamainternmed.2020.0994.
6. Emerging human coronavirus infections (SARS, MERS, and COVID-19): Where they are leading us. *Int Rev Immunol* 2021;40(1-2):5–53. doi:10.1080/08830185.2021.1800688.
7. Pathogenesis guided therapeutic management of COVID-19: an immunological perspective. *Int Rev Immunol* 2021;40(1-2):54–71. doi:10.1080/08830185.2021.1840566.
8. Singhal T. A review of Coronavirus Disease-2019 (COVID-19). *Indian J Pediatr*. 2020;87(4):281–286. doi:10.1007/s12098-020-03263-6.
9. How could we forget immunometabolism in SARS-CoV2 infection or COVID-19? *Int Rev Immunol* 2021;40(1-2):72–107. doi:10.1080/08830185.2021.1840567.
10. Dendritic cells in COVID-19 immunopathogenesis: insights for a possible rolein determining disease outcome. *Int Rev Immunol* 2021;40(1-2):108–125. doi:10.1080/08830185.2021.1844195.
11. Zhou R, To KK, Wong YC, et al. Acute SARS-CoV-2 infection impairs dendritic cell and T Cell responses. *Immunity*. 2020;53(4):864–877.e5. doi:10.1016/j.immuni.2020.07.026.
12. Rapid diagnosis of SARS-CoV-2 using potential point-of-care electrochemical immunosensor: Towards the future prospects. *Int Rev Immunol* 2021;40(1-2):126–142. doi:10.1080/08830185.2021.1872566.
13. Molecular Diagnostic Tools for the Detection of SARS-CoV-2. *Int Rev Immunol* 2021;40(1-2):143–156. doi:10.1080/08830185.2021.1871477.