ETHIOPIAN INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 03, March-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

Axmedova D.K.

Department of Phthisiatry and Pulmonology, Microbiology, Virology, and Immunology

Assistant Andijan State Medical Institute.

THE ROLE OF THE BODY DURING VIRAL INFECTION

Abstract: Since the emergence of SARS-CoV-2 in December 2019, there has been an unparalleled global effort to characterise the virus and the clinical course of disease. Coronavirus disease 2019 (covid-19), caused by SARS-CoV-2, follows a biphasic pattern of illness that likely results from the combination of an early viral response phase and an inflammatory second phase. Most clinical presentations are mild, and the typical pattern of covid-19 more resembles an influenza-like illness—which includes fever, cough, malaise, myalgia, headache, and taste and smell disturbance—rather than severe pneumonia (although emerging evidence about long term consequences is yet to be understood in detail).[1] In this review, we provide a broad update on the emerging understanding of SARS-CoV-2 pathophysiology, including virology, transmission dynamics, and the immune response to the virus.

Key words: Infection, immune response, virus, protein, genome.

Any of the mechanisms and assumptions discussed in the article and in our understanding of covid-19 may be revised as further evidence emerges. SARS-CoV-2 is an enveloped β-coronavirus, with a genetic sequence very similar to SARS-CoV-1 (80%) and bat coronavirus RaTG13 (96.2%).2 The viral envelope is coated by spike (S) glycoprotein, envelope (E), and membrane (M) proteins. Host cell binding and entry are mediated by the S protein. The first step in infection is virus binding to a host cell through its target receptor. The S1 sub-unit of the S protein contains the receptor binding domain that binds to the peptidase domain of angiotensin-converting enzyme 2 (ACE 2). In SARS-CoV-2 the S2 sub-unit is highly preserved and is considered a potential antiviral target. Coronaviruses have the capacity for proofreading during replication, and therefore mutation rates are lower than in other RNA viruses.

As SARS-CoV-2 has spread globally it has, like other viruses, accumulated some mutations in the viral genome, which contains geographic signatures. Researchers have examined these mutations to study virus characterisation and understand epidemiology and transmission patterns. In general, the mutations have not been attributed to phenotypic changes affecting viral transmissibility or pathogenicity. The G614 variant in the S protein has been postulated to increase infectivity and transmissibility of the virus.3 Higher viral loads were reported in clinical samples with virus containing G614 than previously circulating variant D614, although no association was made with severity of illness as measured by hospitalization outcomes.3 These findings have yet to be confirmed with regards to natural infection. Quantitative reverse transcription polymerase chain reaction (qRT-PCR) technology can detect viral SARS-CoV-2 RNA in the upper respiratory tract for a mean of 17 days (maximum 83 days) after symptom onset.[7] However, detection of viral RNA by qRT-PCR does not necessarily equate to infectiousness, and viral culture from PCR positive upper respiratory tract samples has been rarely positive beyond nine days of illness.[5] This corresponds to what is known about transmission based on contact tracing studies, which is that transmission capacity is maximal in the first week of illness, and that transmission after this period has not been ocumented.[8]Severely ill or immune-compromised patients may have relatively prolonged virus shedding, and some patients may have intermittent RNA shedding; however, low level results close to the detection limit may not constitute infectious viral particles. While asymptomatic individuals (those with no symptoms

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 03, March-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

throughout the infection) can transmit the infection, their relative degree of infectiousness seems to be limited. People with mild symptoms (paucisymptomatic) and those whose symptom have not yet appeared still carry large amounts of virus in the upper respiratory tract, which might contribute to the easy and rapid spread of SARS-CoV-2.7 Symptomatic and pre-symptomatic transmission (one to two days before symptom onset) is likely to play a greater role in the spread of SARS-CoV-2.[2] A combination of preventive measures, such as physical distancing and testing, tracing, and self-isolation, continue to be needed. The role of faecal shedding in SARS-CoV-2 transmission and the extent of fomite (through inanimate surfaces) transmission also remain to be fully understood. Both SARS-CoV-2 and SARS-CoV-19 remain viable for many days on smooth surfaces (stainless steel, plastic, glass) and at lower temperature and humidity (eg, air conditioned environments). Thus, transferring infection from contaminated surfaces to the mucosa of eyes, nose, and mouth via unwashed hands is a possible route of transmission. This route of transmission may contribute especially in facilities with communal areas, with increased likelihood of environmental contamination. However, both SARS-CoV-19 and SARS-CoV-20 are readily inactivated by commonly used disinfectants, emphasising the potential value of surface cleaning and handwashing.[5] SARS-CoV-2 RNA has been found in stool samples and RNA shedding often persists for longer than in respiratory samples7; however, virus isolation has rarely been successful from the stool. No published reports describe faecal-oral transmission. In SARS-CoV-19, faecal-oral transmission was not considered to occur in most circumstances; but, one explosive outbreak was attributed to aerosolisation and spread of the virus across an apartment block via a faulty sewage system. It remains to be seen if similar transmission may occur with SARS-CoV-20. After viral entry, the initial inflammatory response attracts virus-specific T cells to the site of infection, where the infected cells are eliminated before the virus spreads, leading to recovery in most people. In patients who develop severe disease, SARS-CoV-2 elicits an aberrant host immune response. For example, postmortem histology of lung tissues of patients who died of covid-19 have confirmed the inflammatory nature of the injury, with features of bilateral diffuse alveolar damage, hyaline-membrane formation, interstitial mononuclear inflammatory infiltrates, and desquamation consistent with acute respiratory distress syndrome (ARDS), and is similar to the lung pathology seen in severe Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS).[4] A distinctive feature of covid-19 is the presence of mucus plugs with fibrinous exudate in the respiratory tract, which may explain the severity of covid-19 even in young adults. This is potentially caused by the overproduction of pro-inflammatory cytokines that accumulate in the lungs, eventually damaging the lung parenchyma.

Some patients also experience septic shock and multi-organ dysfunction. For example, the cardiovascular system is often involved early in covid-19 disease and is reflected in the release of highly sensitive troponin and natriuretic peptides. Consistent with the clinical context of coagulopathy, focal intra-alveolar haemorrhage and presence of platelet-fibrin thrombi in small arterial vessels is also seen.[7] Cytokines normally mediate and regulate immunity, inflammation, and haematopoiesis; however, further exacerbation of immune reaction and accumulation of cytokines in other organs in some patients may cause extensive tissue damage, or a cytokine release syndrome (cytokine storm), resulting in capillary leak, thrombus formation, and organ dysfunction.

Covid-19 leads to an antibody response to a range of viral proteins,but the spike (S) protein and nucleocapsid are those most often used in serological diagnosis. Few antibodies are detectable in the first four days of illness, but patients progressively develop them, with most achieving a detectable response after four weeks.[6] A wide range of virus-neutralising antibodies have been reported, and emerging evidence suggests that these may correlate with severity but wane over time.[7] The duration

eISSN: 2349-5715 pISSN: 2349-5707

Volume: 12, Issue 03, March-2025 SJIF 2019: 4.702 2020: 4.737 2021: 5.071 2022: 4.919 2023: 6.980 2024: 7,662

and protectivity of antibody and T cell responses remain to be defined through studies with longer follow-up. CD-4 T cell responses to endemic human coronaviruses appear to manifest cross-reactivity with SARS-CoV-2, but their role in protection remains unclear.[8]

References:

1. Cevik M, Bamford CGG, Ho A. COVID-19 pandemic-a focused review for clinicians.
2. Clin Microbiol Infect 2020;26:842-7. doi: 10.1016/j.cmi.2020.04.023 pmid: 32344166
3. Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science 2020;367:1444-8 doi: 10.1126/science.abb2762 pmid: 32132184
4. Korber B, Fischer WM, Gnanakaran S, etalSheffield COVID-19 Genomics Group. Tracking changes in SARS-CoV-2 spike: evidence that D614G increases infectivity of the covid-19 virus.
5. Cell 2020;182:812-827.e19. doi: 10.1016/j.cell.2020.06.043 pmid: 32697968
6. Wrapp D, Wang N, Corbett KS, etal. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science 2020;367:1260-3. doi: 10.1126/science.abb2507 pmid: 32075877
7. Wölfel R, Corman VM, Guggemos W, etal. Virological assessment of hospitalized patients with COVID-2019. Nature 2020;581:465-9. doi: 10.1038/s41586-020-2196-x pmid: 32235945
8. Hui KPY, Cheung MC, Perera RAPM, etal. Tropism, replication competence, and innate immune responses of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and in-vitro cultures. Lancet Respir Med 2020;8:687-95. doi: 10.1016/S2213-2600(20)30193-4 pmid: 32386571
9. Cevik M, Tate M, Lloyd O, etal. SARS-CoV-2, SARS-CoV-1 and MERS-CoV viral load dynamics, duration of viral shedding and infectiousness: a living systematic review and meta-analysis.Lancet Microbe 2020; (forthcoming) doi: 10.1016/S2666-5247(20)30172-5.
10. Cheng H-Y, Jian S-W, Liu D-P, Ng TC, Huang WT, Lin HHTaiwan COVID-19 Outbreak Investigation Team. Contact tracing assessment of covid-19 transmission dynamics in Taiwan and risk at different exposure periods before and after symptom onset.
11. JAMA Intern Med 2020;180:1156-63. doi: 10.1001/jamainternmed.2020.2020 pmid: 32356867