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Review Article

Emergence, virology, immune response after SARS-CoV-2 infection, and role of immunopathology behind vaccination

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Abstract

In mid-January 2020, the WHO received information from the International Commission of Health about an outbreak of disease in the capital of Hubei province, Wuhan, in Central China. There was no evidence of human transmission or infection among health-care workers at that stage. Initially, the cases identified visiting the Wuhan live and seafood market prompted a suspicion that might be the source of the pandemic. Stumbling of more than 200 vaccines started with preclinical progress, but only approximately 40 vaccines entered clinical trials where some were not approved for human trials. This review addresses the genome sequence, immunopathology induced by virus, and vaccine.

Keywords: Immune response, immunopathology, SARS-CoV-2, virology

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INTRODUCTION

In mid-January 2020, the WHO received information from the International Commission of Health about an outbreak of disease in the capital of Hubei province, Wuhan, in Central China. There was no evidence of human transmission or infection among health-care workers at that point. Initially, the cases identified visiting the Wuhan live and seafood market prompted a suspicion that might be the source of the pandemic.[1] Thorough investigation, surveillance, and follow-up were done among 41 cases with 7 severely ill cases and 1 death with cardinal health condition. Symptoms were fever and difficulty in breathing with radiograph of chest revealing pneumonic infiltrates with ground-glass opacity of both the lungs.[2] The virus was termed as novel coronavirus or SARS-CoV-2 (severe acute respiratory syndrome 2). Illness caused by it in humans was termed as coronavirus disease 2019 (COVID-19). SARS-CoV-2 is a beta virus with a short-stranded RNA material ranging from 26 to 32 kbs length.[3] It caused death of huge populations worldwide, and the genetic sequence of the SARS-CoV-2 was released publicly by March 2020. COVID-19 was declared as pandemic with the global spread. By June 2020, more than 6 million people got infected with 3 lakh deaths.[4] By 2021, more than 100 million people across 220 countries were infected globally with more than two million deaths by COVID-19. The virus is composed of spike protein (S protein) which binds to the host receptors – transmembrane protease and peptidase receptors (Transmembrane protease and peptidase receptors (TMPRSS2) and angiotensin-converting enzyme 2 [ACE2]) ensuing infection and internalization. The genomic sequence was similar to SARS bat-derived virus

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and SARS-CoV (ZCX21 and ZC45).[5] Stumbling of more than 200 vaccines started with preclinical progress, but only approximately 40 vaccines entered clinical trials where some were not approved for human trials. This review addresses the genome sequence, immunopathology induced by virus, and vaccine.

GENERAL VIROLOGY BEHIND CORONAVIRUS

Therapeutic discovery of coronavirus depends on its lifecycle, structure, and pathogenesis. Comparative characters of betacoronavirus SARSCoV were identified in November 2002 in about 29 global countries with 9.6% death rate. Host for this virus was reported as a species of *Rhinolophus sinicus* (bat); the transmission to humans is through the meat consumption and manipulation of the larvae.[6-8] MERS-CoV cases in 27 world countries[9] reported in june 2012 where human transmission occurs with camels as intermediate host[10] with a mortality rate of 34.4%.[11] SARSCoV2 2019 was believed to be from China where it constitutes the hotspot for intense bat viral transmission. In all of the above infections, dissemination of viral transmission among global countries is from the infected to the noninfected human transmission. The target receptors were identified as ACE2 (SARSCoV and SARSCoV2) and dipeptidyl peptidase 4 (MERSCoV). Compared to the other group, rapid and high speed of spread is esteemed in SARSCoV2 [Figure 1].[12] Coronavirus is an enveloped beta RNA virus with a singlestrand genome length maintained by proofreading replication. Coronavirus RNA genome is enveloped by outer matrix (M) protein, nucleocapsid, surface spike (S) protein, and envelope (E) protein. The viral genome has 11 open reading frames located at 3' and 5' terminals of genomic mRNA synthesized by transcription [Table 1].[13]

NATURAL DISEASE PATHOLOGY

The primary effects of the disease involve the respiratory tract with asymptomatic infection[14] or mild fever, fatigue, persistent cough, rash,[15] diarrhea,[16] loss of appetite, and anosmia.[17] SARS-CoV2 invades the axons of the nervous system through the neuroepithelium of the olfactory region and bulb, were the virus binds to the host receptors (ACE2) of the respiratory system[18] leading to loss of taste and smell in more than 60% of cases of leading to severe respiratory dstress and mortality.[19] Pneumonic infiltrate in computed tomography chest scans divulges with ground-glass opacity including asymptomatic occasions. The severe systemic conditions such as hemostasis, cardiac arrest, diabetes, and renal damage along with age (more than 70 years) play a vital risk factor for increased mortality.[20] Other factors are obesity, intensive care unit admission, and gender (male fatality 2.4 times more than female). The factors considered for increased male mortality are ACE receptor expression, smoking, and alcohol consumption habits. Furthermore, it is noted that responsible behaviors in pandemic among women are more than men. In addition to it, male sex chromosome enhances immunological difference.[21] Infection fatality rate of COVID-19 positive cases was 0.1%-0.4%.[22]

DISCUSSION

SARS-CoV favors respiratory epithelial cells and pneumocytes. There is a release of inflammatory infiltrates (polymorph neutrophils, monocytes, and macrophages, increase in interferonalpha, interleukin1, interleukin6, tumor necrosis factor, chemokines 2,9,10).[23,24] This results in edema, desquamation, fibrosis of epithelium, and pneumocyte cells with systemic damage.[25,26] In addition to the observed maladaptive cytokine release, elevations in additional traditional biochemical markers of acute infection, including C-reactive protein and ferritin (both positive acute-phase reactants), occur. Continual decrease in lymphocytes and significant elevations in neutrophils are evident.[27,28] As such, the neutrophil-to-lymphocyte ratio appears to be a useful indicator of disease prognostication and management.[29] The mechanisms behind progressive lymphopenia in severe COVID-19 remain unclear, although T-cell redistribution, Tumour necrosis factor alpha mediated apoptosis and direct cytopathic injury are suggested.[30,31] It is also important to notice that immune cell infiltration can cause the excessive secretion of proteases and reactive oxygen species, fostering further damage, and hyperinflammation. In addition, direct virus infection of immune cells such as monocytes and macrophages is proposed to contribute to dysregulated immune reaction, as has been observed in SARS. Nevertheless, the precise contribution of direct viral immune cell infection is unknown and highly debated.[1] Finally, recent data also suggest that SARS-CoV-2-specific antibody titers are elevated in patients with severe disease. It is unclear whether increased antibody prevalence in severe COVID-19 patients suggests potential antibody-dependent enhancement or is just a result of higher viral antigen exposure. Further studies are needed to gauge the contribution of antibodies to both physiological and pathogenic host responses. Since a hyperinflammatory profile according to cytokine storm has been robustly related to COVID19 severity and is responsible for patient mortality. Most initial literature has focused on the dysregulation of immune reaction in COVID-19 patients and therefore the potential value of immune-modulating

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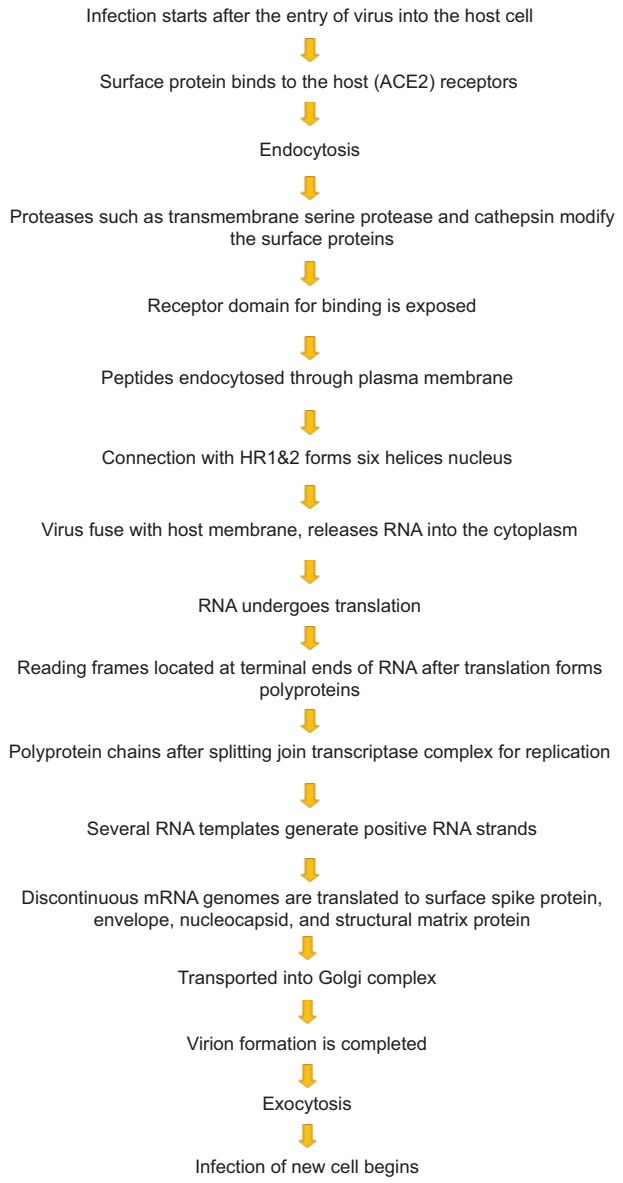

Figure 1: Virology and immunopathological pathway of SARSCoV2 vaccination

Table 1: Open reading frame and its functions related to SARS-CoV-2

ORF	Functions
1a and 1b	Encrypt polyproteins to nonstructural multiple proteins
2	Encodes surface protein, binds to host determinant ACE2
4	Encrypts the envelope viroporin
5	Encodes membrane protein in assembling and release of virus
9	Encrypts the nucleocapsid protein

ACE2: Angiotensin-converting enzyme 2, ORF: Open reading frame

treatments. However, evidence of alarming coagulation abnormalities and high incidence of thrombotic events in COVID-19 patients is prevalent.

CONCLUSION

The governing authorities in all countries have enforced guidelines approved by higher authorities and taken all needful actions to quarantine people infected with the virus and are trying to break the community spread. Antibodies, drugs, and vaccines developed for emerged coronaviruses previously are being potentially used to curtail SARS-CoV-2 infection. We are still battling the disease with a hope to successfully eradicate the disease from the world.

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Conflicts of interest

There are no conflicts of interest.

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