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REVIEW ARTICLE

OVERVIEW OF SARS-COV-2 INFECTION IN HUMAN BODY

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ABSTRACT

Novel coronavirus was first reported on December 2019 in Wuhan, Hubei Province, China and so far more than 33,00,000 infections and over 2,34,000 deaths have been reported. The detail mechanism of action of this virus to host cell or body is remaining unknown. This virus could transfer during human-to-human close contacts, with a basic reproductive number about 2.5. To identify the target for vaccine therapy or other antiviral drug design, it is important to understand the virus attachment mechanism to the host, replication, transmission, etc. This study is an overview of these mechanisms reported so far from different research groups. This review will help us to understand COVID-19 and its mechanism of action in human body.

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INTRODUCTION

Among the four genera (α, β, γ, δ CoV), SARS-CoV-2 is enveloped non-segmented positive-sense RNA virus is included in the β coronavirus with two other familiar SARS-CoV and MERS-CoV viruses. They have a genomic sequence similar up to 96.2% with bat CoV RaTG13 and up to 79.5% similar to SARS-CoV indicate that the origin might be the bat and several analytical methods concluded that turtle, pangolin, and snakes might be the intermediate hosts (Guo *et al*., 2019). The incubation period ranges from 2-14 days. The length of quarantine should be at least 14 days (Linton *et al*., 2019). The main route of transmission of the virus is the respiratory droplet transmission. Besides, aerial droplets, contact, fecal-oral and aerosol transmission can also occur. Asymptomatic cases play a critical role in the transmission process. WHO has published its estimation of reproduction rate (R_0) to be 2.0-2.5 using early information (Wu *et al*., 2020).

Genomics of SARS-CoV-2: The genome-wide phylogenetic tree based on genomic analyses suggested that SARS-CoV-2 was closest to RaTG13 but their difference at neutral sites was much higher than previously realized. With population genetic analyses of 103 genomes of SARS-CoV-2, the two types (L and S types) had been well defined by just two single-nucleotide polymorphisms (SNPs) and showed nearly complete linkage across SARS-CoV-2 strains. The L type is more aggressive than the S type (Tang *et al*., 2020). In the nucleocapsid region, 2019-nCoV and bat-like coronavirus shared the same amino acid sequences near 309 and 380 positions in which the SARS virus showed different sequences. In positive selection process, on the spike glycoprotein 536 and 644 amino acid positions have different sequences of all 3 corona viruses. Mutation in these regions increases infection and pathogenicity than bat SARS-like coronavirus (Benvenuto *et al*., 2020). In another study, on the ORF1ab region, the different amino acid residue was observed in specific positions in all three coronaviruses. The position 501 similar to the non-structural protein 2 (nsp2) 321 position had different amino acid and speculated the higher stability of the protein. The stabilizing mutation of nsp2 gives information about the nosogenic feature. Position 723 and 1110 similar to nonstructural protein 3 (nsp3) 543 and 192 positions respectively and the destabilizing mutation of nsp3 in these positions gave a concept of the basic mechanism of COVID 2019 distinct from SARS (Angeletti *et al*., 2020). Two mutations were also observed in amino acidic position 3691 and 9659 in NSP6 protein and the concomitant ORF 10 regions. In both amino acidic positions, different amino acid residues were identified in different regions of the world and in all cases, the stability of the protein structure was reduced due to mutation. One mutation on the NSP6 had affected the antiviral response by binding the outer membrane of NSP6 which had abundant phenylalanine residue to the ER.

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This binding induced the viral infection against autophagy which was required to trap viral cargo had brought from autophagosome to lysosome for degradation (Benvenuto, 2020). The median number of intra-host variants found 4 (range 0-51 in different samples) suggested a high mutation rate in a study on bronchoalveolar lavage fluid (BALF) of 8 SARS-CoV-2 patients, 25 community-acquired pneumonia (CAP) patients, 20 healthy controls. Polymorphisms were observed in population data suggesting purifying selection against mutations (Shen *et al*., 2020).

Structure of spike glycoprotein and binding mechanism with ACE2: Membrane spike (S) glycoproteins of coronaviruses that form homotrimers protrude from the viral surface mediate entry into host cells (Walls *et al*., 2020). The S glycoprotein has two functional subunits, S1 and S2. S1 is responsible for binding the host cell receptor and S2 is for the fusion of the viral and cellular membrane with the help of two tandem domains named heptad repeats (HR1) and HR2 (Guo et al., 2019). Coronavirus entry into host cells requires a complex process of receptor binding and proteolytic processing of the S protein. SARS related coronaviruses interaction with angiotensin-converting enzyme 2 (ACE2) via S^B. In comparison with SARS-CoV S^B, SARS-CoV-2 S^B engages human ACE2 (hACE2) with higher affinity. The capping loops in the binding domain produce an increased electrostatic interaction between the spike protein and the cellular receptor in SARS-CoV-2 in comparison to that of SARS-CoV. The higher number of protein-protein interaction and the longer capping loops could explain the rise in binding affinities in SARS-CoV-2 (-15.7 Kcal/Mol) as compared with SARS-CoV (-14.1 Kcal/Mol). So these higher affinity values might be related to the dynamic of infection and the rapid spread observed in this virus. In the S protein of SARS-CoV-2, a furin cleavage site at the S1/S2 boundary is cleaved during biosynthesis, which is a unique feature of SARS-CoV-2. SARS-CoV-2 utilizes some human proteases including human airway trypsin-like protease (HAT), cathepsins and transmembrane protease serine 2 (TMPRSS2) (Walls *et al*., 2020**;** Shereen, 2020; Ortega, 2020). Another study determined the structural basis for receptor recognition by SARS-CoV-2 and compared the hACE2-binding affinity among SARS-CoV-2, SARS-CoV, and RaTG13.

To understand the structural basis for hACE2 recognition by SARS-CoV-2, the scientists aimed to crystallize the SARS-CoV-2 RBD/hACE2 complex. The study observed that compared with SARS-CoV RBM, SARS-CoV-2 RBM forms a larger binding interface and more contacts with hACE2. Introduced mutations reduced the hACE2-binding affinity of the SARS-CoV-2 spike. The scientists also confirmed that the structural features of SARS-CoV-2 RBM, including the ACE2-binding ridge and the hotspots-stabilizing residues, all contribute critically to the high hACE2-binding affinity of SARS-CoV-2 (Shang *et al*., 2020). SARS-CoV-2 S protein entry on 293/hACE2 cells was determined which mainly mediated through endocytosis and that PIKfyve, TPC2, and cathepsin L were critical for virus entry. The scientists further elucidated that a SARS-CoV-2 S protein could trigger syncytia in 293/hACE2 cells independent of exogenous protease (Ou *et al*., 2020).

ACE2 receptor and CD147 molecule as a viral receptor: ACE2 is expressed in the oral cavity. ACE2 expression in the tongue is higher than other parts of the oral cavity. ACE2 is expressed in oral epithelial tissues and in lymphocytes found in oral mucosa supported the fact that the oral cavity can be a route of virus transmission (Xu *et al*., 2020). ACE2 protects lungs from a lung injury, also it is a receptor for SARS-CoV-2. So SARS-CoV-2 is deadly as it interrupts the lung-protective pathway. Alveolar epithelial type 2 cells express ACE2, so it functions as a viral reservoir. Heart, kidney, endothelium, and intestine also express ACE2, which explains multi-organ damage in corona virus infection (Zhang, 2020; Zhang, 2020; Zhou et al., 2020). CD147 is a transmembrane glycoprotein that is highly expressed in tumor and pathogen-infected cells play a vital role in the entry of the SARS-CoV-2 virus into the host cell. The localization of CD147 and spike protein (SP) is in the inclusion bodies of Vero E6 cells (Wang *et al*., 2020).

Replication of the virus in human cells: SARS-CoV-2 attach with the receptor ACE2 by its S glycoprotein in a similar way as of SARS-CoV but with efficiency higher than 10 to 20 fold than SARS-CoV. A direct membrane fusion between virus and plasma membrane was identified due to a proteolytic cleavage at position S2 prime of SARS-CoVs protein and also clathrin dependent and independent endocytosis could help in the entry of the virus. However, MERS-CoV membrane fusion required two- step furin activation. MERS-CoV could bind with a different receptor named DPP4 or CD26. After entering into the host cell, the viral RNA is released into the cytoplasm and translated into 2 viral replicase poly proteins, pp1a and pp1ab and encode 16 non-structural proteins (NSPs) with the help of first ORF (ORF 1a/b) which comprises about 2/3 of viral RNA. The structural proteins are created by proteinases with the help of remaining ORFs. Subsequent 1/3 of viral RNA accounted for four main structural proteins: spike (S), envelope (E), nucleocapsid (N) and membrane (M) protein with some secondary proteins. The RNA dependent RNA polymerase enzyme produces sub-genomic mRNA via discontinuous transcription following the translation of accessory viral proteins. The new viral particles form virion that could become manifest into the ER-Golgi intermediate compartment. The vesicles containing the virion, then fuse with the plasma membrane and release the virus out of the cell (Guo *et al*., 2019; Shereen *et al*., 2020; Li, 2020).

Multiple organ failure with SARS-CoV-2 infection: SARS-CoV-2 interacts with ACE2, reduces the amount of ACE2 and leads to lung edema, which is one of the common clinical abnormalities in severe COVID-19 patients. Hypoxemia is induced by alveolar damage, overproduction in inflammatory factors and increased vascular permeability (Li *et al*., 2020). The similar function pattern with MERS-CoV and SARS-CoV suggests that SARS-CoV-2 can cause myocardial damage and increase difficulty in the recovery of patients. In a study, it was observed that very severe COVID-19 patients with increased cardiac troponin I levels might have a high possibility of myocardial injury which is identified as a myocardial injury biomarker. Myocardial injury can be occurred by SARS-CoV-2 infection via the ACE2 receptor. The similar pathogenicity with SARS-CoV also suggests that there is an increase in free fatty acid can cause cardiovascular damage in SARS-CoV-2 infection. Moreover, many antiviral drugs can induce cardiovascular damage (Zheng, 2020; Zhou *et al*., 2019). The association of mortality with cardiovascular disease was assayed and showed that the mortality rate was higher in patients with a cardiac injury who were older and possessing more frequent comorbidities in comparison with patients without cardiac injury. Researchers gave a hypothesis that

intense inflammatory response to the preexisting cardiovascular disease might worsen the situation of patients with COVID-19 infection (Shi *et al*., 2020). 193 COVID-19 infected patients had proteinuria, hematuria, elevated level of blood urea nitrogen (BUN), the elevated level of uric acid, the elevated level of D-dimer. Kidney dysfunction also reported in COVID-19 patients amenable for acute kidney injury (AKI) in some of the patients. The mortality rate of infected patients with acute kidney injury is higher than patients without AKI. Kidney dysfunction in COVID-19 patients might be explained by kidney-lung crosstalk theory. As the ACE2 receptor is also expressed in the kidney with a much higher level, SARS-CoV-2 could also damage renal epithelial cells. These damaged cells could accelerate the release of a large number of inflammatory substances which could damage lung and other organs (Li *et al*., 2020). The virus could easily infect and replicate in the gastrointestinal tract through ACE2 mediated transfer into the host cell. Gastrointestinal symptoms developed before respiratory tract illness or fever in some cases of COVID-19 in both adults and pediatrics patients. Infectious SARS-CoV-2 was isolated from the stool of infected patients which indicates that SARS-CoV-2 could be transmitted via fecal route.

The PCR based study suggested that the virus survived longer in the gastric tract than the respiratory system. Liver injury was shown in COVID-19 patients might be caused by a direct viral infection of hepatocytes, immune-related injury or drug hepatotoxicity or even more binding through the expressed ACE2 receptor to the cholangiocytes. It is assumed that liver injury might be caused by bile duct rather than liver cells because of the higher amount of ACE2 receptor in bile duct cells. It was suggested using liver biopsy that, liver injury was occurred by SARS-CoV due to apoptosis in liver cells. Apoptosis can be induced by SARS-CoV specific protein 7a. Histological changes like micro-vesicular steatosis and mild lobular activity due to the SARS-CoV-2 virus infection or drug instigating injury were seen on liver biopsy of a death COVID-19 patient. There might be a connection between liver damage and inflammatory responses because of cytokine storm in response to the CoVs (Tian *et al*., 2020; Wong *et al*., 2020; Xu *et al*., 2020).

The ACE2 is also expressed in the brain. The neurotropic property of other corona viruses and neurological signs such as headache, nausea, vomiting and severe patients showed acute cerebrovascular diseases and impaired consciousness in some COVID-19 patients give a hint that SARS-CoV-2 might have the neuro invasive potential and cause acute respiratory failure in infected patients. The penetration route of CoVs into the central nervous system (CNS) by a synapse-connected route after invading the peripheral nerve terminal was evidenced. Moreover, CoVs annihilated the respiratory center and infect the neural cell lines were also responsible for acute encephalitis was documented. There was a possibility of SARS-CoV-2 penetrating astrocytes of the astroglial cell by endocytosis as which was observed in ZIKA and TBEV viruses. The neuro inflammation in response to SARS-CoV-2 caused by breakage of BBB due to huge cytokine storm along with chemokine or other inflammation signals consequences in loss of the normal brain function which was exhibited by reactive astrogliosis followed by microglia activation. Neuro-inflammation initiated by prolonged hypoxia could cause hippocampus damage as well as cortical areas gave rise to delirium and cognitive deterioration and involved in mild to severe neuropsychiatric disorders (Li *et al*., 2020; Steardo *et al*., 2020). Ageusia and anosmia associated with fever (37.5°C) were observed in a significant number of patients in Italy. The underlying cause of ageusia and anosmia probably due to the direct damage of the virus on the olfactory and gustatory receptors (Vaira *et al*., 2020). As there is evidence that SARS-CoV can be transported via mucous membrane including conjunctiva it is assumed that tear and conjunctival transmission is likely to be developed by SARS-CoV-2. RT-PCR analysis of tear and conjunctival secretion of 30 patients found that the SARS-CoV-2 virus is present in one patient only with conjunctivitis (Xia *et al*., 2020)

COVID-19 in case of children and infants: Children are appeared to be less affected by the virus. Asymptomatic and mild symptoms were common in young children. Some presumption was constructed due to develop the mild form of COVID-19 disease in children. In both adults and children, the response to the virus showed an individual pattern. Besides, young children were prone to develop various viruses in the mucosa of the lungs and airways that resisted the SARS-CoV-2 progress. Adults tended to build up a huge amount of ACE2 receptor due to the effect of taking drugs for hypertension that was ACE2 inhibitor or blocker which was not seen in the children. This assumes that the causes of lower infectivity of the children compared to the adults. There was evidence that adults were developed severe acute respiratory distress syndrome (ARDS) more likely than children in respiratory illness due to hyper-inflammation which was a progressive lethal phase of severe COVID-19 disease. It provides a lower risk of developing a severe form of the disease in the children. Although children with disease conditions were more prone to infection, there are very less number of pieces of evidence (Mehta *et al*., 2020; Brodin, 2020). No maternal-infant vertical transmission has been documented. Moreover, a negative result was found in seek of the presence of in amniotic fluid, cord blood, neonatal throat swab, and breast milk (Lu, 2020).

Impact of other diseases in case of COVID-19: Patients with beta-thalassemia (SCD) diagnosed with COVID-19 infection indicated that viral infection can cause acute chest syndrome (ACS) in sickle cell patients. SCD patients have weakened immune response, so they are more prone to viral diseases. The vulnerability of both young and adult SCD patients to the COVID-19 was found. COVID-19 is also likely to affect these patients more intensely. Patients have a higher percentage of acute chest syndrome (ACS) and respiratory complications. SCD patients face more mortality rates due to COVID-19 than normal patients (Beerkens et al., 2020). The uncontrolled cytokine storm can be developed in patients with Epstein Bar (EB) virus and the combined mechanism with SARS-CoV-2 consequences in death for the COVID-19 patients (Wang *et al*., 2020). The overall discussion will help us to understand the pathogenesis of novel corona virus and will assist to design antiviral drugs or vaccines.

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REFERENCES

Angeletti, S., Benvenuto, D., Bianchi, M., Giovanetti, M., Pascarella, S., Ciccozzi, M. 2020. COVID-2019:The role of the nsp2 and nsp3 in its pathogenesis. J Med Virol. doi:10.1002/jmv.25719.

Beerkens, F., John, M., Puliafito, B., Corbett, V., Edwards, C. 2020. COVID-19 Pneumonia as a Cause of Acute Chest Syndrome in an Adult Sickle Cell Patient. American Journal of Hematology. doi:10.1002/ajh.25809.

Benvenuto, D., Angeletti, S., Giovanetti, M., Bianchi, M., Pascarella, S., Roberto Cauda, R., Ciccozzi, M., Cassone, A. 2020. Evolutionary analysis of SARS-2-CoV: how mutation of Non-Structural Protein 6 (NSP6) could affect viral autophagy. The Lancet Infectious Diseases. Manuscript Number: THELANCETID-D-20-01185.

Benvenuto, D., Giovanetti, M., Ciccozzi, A., Spoto, S., Angeletti, S., Ciccozzi, M. 2020. The 2019-new coronavirus epidemic: Evidence for virus evolution. J Med Virol., 92:455–459.

Brodin, P. 2020. Why is COVID-19 so mild in children? Acta Paediatrica.doi:10.1111/apa.15271.

Guo, Y-R., Cao, Q-D., Hong, Z-S., Tan, Y-Y., Chen, S-D., Jin, H-J., Tan, K-S., Wang, D-Y., Yan, Y. 2020. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. Military Medical Research, 7: 11.

Li, L., Huang, Q., Wang, DC., Ingbar, DH., Wang, XD. 2020. Acute lung injury in patients with COVID-19 infection. Clin Transl Med. doi:10.1002/ctm2.16.

Li, X., Geng, M., Peng, Y., Meng, L., Lu, S. 2020. Molecular immune pathogenesis and diagnosis of COVID-19. Journal of Pharmaceutical Analysis. doi:10.1016/j.j pha.20 20.03.001.

Li, Y-C., Bai, W-Z., Hashikawa, T. 2020. The neuroinvasive potential of SARS-CoV-2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol. doi: 10.1002/jmv.25728.

Li, Z., Ming Wu, M., Yao, J., Guo, J., Liao, X., Song, S., Li, J., Duan, G., Zhou, Y., Wu, X., Zhou, Z., Wang, T., Hu, M., Chen, X., Fu, Y., Lei, C., Dong, H., Xu, C., Hu, Y., Han, M., Zhou, Y., Jia, H., Chen, X., Yan, J. 2020. Caution on Kidney Dysfunctions of COVID-19 Patients. medRxiv preprint. doi:10.1101/2020.02.08.20021212.

Linton, NM., Kobayashi, T., Yang, Y., Hayashi, K., Akhmetzhanov, AR., Jung, S-M., Yuan, B., Kinoshita, R., Nishiura, H. 2020. Incubation Period and Other Epidemiological Characteristics of 2019 Novel Coronavirus Infections with Right Truncation: A Statistical Analysis of Publicly Available Case Data. Journal of Clinical Medicine., 9: 538. doi:10.3390/jcm9020538.

Lu, Q., Shi, Y. 2020. Coronavirus disease (COVID-19) and neonate: What neonatologist need to know. J Med Virol. doi:10.1002/jmv.25740

Mehta, NS., Mytton, O., Mullins, E., Fowler, TA., Falconer, C., Murphy, O., Langenberg, C., Jayatunga, W., Eddy, D., Nguyen-Van-Tam, JS. 2020. SARS-CoV-2 (COVID-19): What do we know about children? A systematic review. The Lancet Infectious Diseases. Manuscript Number: THELANCETID-D-20-01196.

Ortega, JT., Serrano, ML., Pujol, FH., Rangel, HR. 2020. Role of changes in SARS-COV-2 spike protein in the interaction with the human ACE2 receptor: an in silico analysis. EXCLI Journal, 19: 410-417.

Ou, X., Liu, Y., Lei, X., Li, P., Mi, D., Ren, L., Guo, L., Guo, R., Chen, T., Hu, J., Xiang, Z., Mu, Z., Chen, X., Chen, J., Hu, K., Jin, Q., Wang, J., Qian, Z. 2020. Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Nature Communications, 11: 1620.

Shang, J., Ye, G., Shi, K., Wan, Y., Luo, C., Aihara, H., Geng, Q., Auerbach, A., Li, F. 2020. Structural basis of receptor recognition by SARS-CoV-2. Nature. doi:10.1038/s41586-020-2179-y.

Shen, Z., Xiao, Y., Kang, L., Ma, W., Shi, L., Zhang, L., Zhou, Z., Yang, J., Zhong, J., Yang, D., Guo, L., Zhang, G., Li, H., Xu, Y., Chen, M., Gao, Z., Wang, J., Ren, L., Li, M. 2020. Genomic diversity of SARS-CoV-2 in Coronavirus Disease 2019 patients. Clin Infect Dis. [Epub ahead of print]

Shereen, MA., Khan, S., Kazmi, A., Bashir, N., Siddique, R. 2020. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. Journal of Advanced Research, 24: 91–98

Shi, S., Qin, M., Shen, B., Cai, Y., Liu, T., Yang, F., Gong, W., Liu, X., Liang, J., Zhao, Q., Huang, H., Yang, B., Huang, C. 2020. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID – 19 in Wuhan, China. JAMA Cardiol. doi:10.1001/jamacardio.2020.0950.

Steardo, L., Steardo Jr, L., Zorec, R., Verkhratsky, A. 2020. Neuroinfection may potentially contribute to pathophysiology and clinical manifestations of COVID-19. Acta Physiol (Oxf).doi: 10.1111/apha.13473.

Tang, X., Wu, C., Li, X., Song, Y., Yao, X., Wu, X., Duan, Y., Zhang, H., Wang, Y., Qian, Z., Cui, J., Lu, J. 2020. On the origin and continuing evolution of SARS-CoV-*2*. National Science Review. doi:10.1093/nsr/nwaa036/5775463

Tian, Y., Rong, L., Nian, W., He, Y. 2020. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. Aliment Pharmacol Ther. doi: 10.1111/apt.15731.

Vaira, LA., Salzano, G., Deiana, G., Riu, GD. 2020. Anosmia and ageusia: common findings in COVID-19 patients. Laryngoscope. doi: 10.1002/lary.28692.

Walls, AC., Park, Y-J., Tortorici, MA., Wall, A., McGuire, AT., Veesler, D. 2020. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Cell, 180: 1–12

Wang, K., Chen, W., Zhou, Y-S., Lian, J-Q., Zhang, Z., Du, P., Gong, L., Zhang, Y., Cui, H-Y., Geng, J-J., Wang, B., Sun, X-X., Wang, C-F., Yang, X., Lin, P., Deng, Y-Q., Wei, D., Yang, X-M., Zhu, Y-M., Zhang, K., Zheng, Z-H., Miao, J-L., Guo, T., Shi, Y., Zhang, J., Fu, L., Wang, Q-Y., Bian, H., Zhu, P., Chen, Z-N. 2020. SARS-CoV-2 invades host cells via a novel route: CD147-spike protein. bioRxiv preprint. https://doi.org/10.1101/2020.03.14.988345.

Wang, L., Zou, A., Wang, J., Su, Q., Sun, X., Luo, C., Lin, L., Hu, J., Huang, B., Zhou, F., Li, W., Gong, X., Liu, H., Zou, Z., Ni, J., Liu, J., Wang, R., Liu, Z., Zhou, C. 2020. Matrix Analysis of Clinical Characteristics and Dynamic Observation of Immunological Features in 90 Cases of COVID-19. The Lancet Respiratory Medicine. Manuscript Number: thelancetrm-D-20-00427.

Wong, SH., Lui, RNS., Sung, JJY. 2020. Covid-19 and the Digestive System. J Gastroenterol Hepatol. doi: 10.1111/jgh.15047.

Wu, D., Wu, T., Liu, Q., Yang, Z. 2020. The SARS-CoV-2 Outbreak: What We Know. International Journal of Infectious Diseases. doi:10.1016/j.ijid.2020.03.004

Xia, J., Tong, J., Liu, M., Shen, Y., Guo, D. 2020. Evaluation of coronavirus in tears and conjunctival secretions of patients with SARS-CoV-2 infection. J Med Virol. doi:10.1002/jmv.25725.

Xu, H., Zhong, L., Deng, J., Peng, J., Dan, H., Zeng, X., Li, T., Chen, Q. 2020. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. International Journal of Oral Science, 12:8.

Xu, L., Liu, J., Lu, M., Yang, D., Zheng, X. 2020. Liver injury during highly pathogenic human coronavirus infections. Liver Int. doi: 10.1111/liv.14435.

Zhang, B., Liu, G., Liu, X., Chen, S., Huang, B., Yang, Z., Xu, C., Chen, J., Jiang, H. 2020. Multi-organ damage of critically ill patients with hyoxemia affected by SARS-CoV-2 infection. The Lancet Global Health. Manuscript Number: LANGLH-D-20-00751.

Zhang, H., Penninger, JM., Li, Y., Zhong, N., Slutsky, AS. 2020. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med. 46:586–590.

Zheng, Y-Y., Ma, Y-T., Zhang, J-Y., Xie, X. 2020. COVID-19 and the cardiovascular system. Nature Reviews Cardiology. doi:10.1038/s41569-020-0360-5

Zhou, B., She, J., Wang, Y., Ma, X. 2020. The Clinical Characteristics of Myocardial injury in Severe and Very Severe Patients with 2019 Novel Coronavirus Disease. Manuscript Number: THELANCET-D-20-01688.

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