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Rising Concern on Damaged Testis of COVID-19 Patients



To the Editor:

Nowadays, COVID-19, an appalling pandemic disease characterized by respiratory failure, has affected a lot of people around the world and the number is still climbing high. According the data from the World Health Organization, up to April 9, 2020 this pandemic has infected 1,395,136 and totally killed 81,580 infected.¹ Knowing from the work of Guan et al, 637 from 1096 infectors, 58.1%, is male.² More importantly, a great number of these suffers are in the childbearing age. Thus, it is a significant question on the table that whether SARS-CoV-2, the virus causing COVID-19, could attack the testis.

As has been widely reported, the spikes of SARS-CoV-2 virus interact with Angiotensin-converting enzyme 2 (ACE2) on the cell membrane to infect the cell.³ Except expression in the lung, ACE2 extensively expresses in alimentary canal, kidney, and heart and the Spermatogonia, Sertoli, Leydig cell in testis also rich in ACE2 expression.^{4,5} It is not hard for people to conjecture that testis may be infected by this virus, which further leads to some reproductive problems. As revealed in a single-center study, the serum sex-related hormones ratio of testosterone to luteinizing hormone and the ratio of follicle stimulating hormone to luteinizing hormone, to some extent represent reproductive ability, has a significant discrepancy between infectors and healthy control.⁶ The cases of secondary infection also stand a warning sign that testis is the potential hotbed for SARS-COV-2. However, a latest semen and testis biopsy showed a nonpositive result of virus determined by reverse transcription polymerase chain reaction test, though the case was limited and without histopathology and reverse transcription polymerase chain reaction may meet a false negative when applied to detected the virus sequence.⁷ These confusing results guide us into the “SARS-CoV-2 and testis damage” maze.

SARS virus, the “cousin” of SARS-COV-2 sharing 78% genetic homology and in the same family and genus, also utilized ACE2 to invade cells in a similar way. Remarkably, a series of studies of autopsy have indicated that SARS causes orchitis characterized by widespread germ cell destruction, few or no spermatozoon in the seminiferous tubule, thickened basement membrane, and leukocyte infiltration. However, SARS virus sequence was not detected in testis by in situ hybridization. The precipitation of IgG

in the seminiferous epithelium of SARS testis reflected dramatically immune response.^{8,9} The pathology of SARS-CoV-2 testis should be further identified which promises for more specific guideline during clinical practice.

As the dynamic changes of SARS-CoV-2 in infected soma are complex and the broad expression of ACE2 in testis, considering observed damaged testis in SARS patients, the possibility of COVID-19 induced testis damaged and functional dysfunction could not be erased and ignored. Therefore, we highly suggest that the male survivors of COVID-19, especially those with reproductive needs, should be examined for testicular function and reproductive function after recovery.

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References

1. The World Health Organization, Coronavirus disease (COVID-19) outbreak situation, (n.d.). Available at: <https://who.sprinklr.com>; Accessed at 18:08, 9 April 2020.
2. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708–1720.
3. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181:271–280.
4. Wang Z, Xu X. scRNA-seq profiling of human testes reveals the presence of the ACE2 receptor, a target for SARS-CoV-2 infection in spermatogonia, Leydig and Sertoli cells. *Cells*. 2020;9:920.
5. Fan C, Li K, Ding Y, Lu WL, Wang J. ACE2 expression in kidney and testis may cause kidney and testis damage after 2019-nCoV infection. *medRxiv*. 2020. 2020.2002.2012.20022418.
6. Ma L, Xie W, Li D, et al. Effect of SARS-CoV-2 infection upon male gonadal function: a single center-based study. *medRxiv*. 2020. 2020.2003.2021.20037267.
7. Song C, Wang Y, Li W, et al. Detection of 2019 novel coronavirus in semen and testicular biopsy specimen of COVID-19 patients. *medRxiv*. 2020. 2020.2003.2031.20042333.
8. Xu J, Qi L, Chi X, et al. Orchitis: a complication of severe acute respiratory syndrome (SARS). *Biol Reprod*. 2006;74:410–416.
9. Ding Y, He L, Zhang Q, et al. Organ distribution of severe acute respiratory syndrome (SARS) associated coronavirus (SARS-CoV) in SARS patients: implications for pathogenesis and virus transmission pathways. *J Pathol*. 2004;203:622–630.