



## Letter

# COVID-19 and impairment of spermatogenesis: Implications drawn from pathological alterations in testicles and seminal parameters

Mohammad Ishraq Zafar<sup>a</sup>, Honggang Li<sup>a,b,\*</sup>

<sup>a</sup> Institute of Reproductive Health/Center of Reproductive Medicine, Tongji Medical College, Huazhong University of Science and Technology, Hangkong Road 13, Wuhan 430030, China

<sup>b</sup> Wuhan Tongji Reproductive Medicine Hospital, Sanyang Road 128, Wuhan 430013, China

## ARTICLE INFO

## Article History:

Received 13 November 2020

Accepted 17 November 2020

Available online xxx

We thank Drs. Marion Bendayan and Florence Boitrelle for bringing up the possible cause of impaired spermatogenesis in COVID-19 patients in the view of our research paper, which was published recently in the EClinicalMedicine journal. Multiple factors, including high fever, antiviral drug treatment, immunoglobulins, or glucocorticoids, might cause or participate in the manifestation of impaired spermatogenesis in the patients infected with SARS-CoV-2, based on previous related researches on other virus infections.<sup>1</sup> As for the direct SARS-CoV-2 infection to the testicular cells, there is no direct evidence to date. However, the analysis of ACE2 AND TMPRSS2 co-expression in testicular cells implies that the chance of direct infection to testicular cells is meager.<sup>2</sup> Although positive findings of SARS-CoV-2 by RT-qPCR in the autopsied testicular specimens were reported in a small proportion of deceased COVID-19 male patients,<sup>3</sup> it cannot exclude the virus within the blood vessels of the testis.<sup>4</sup> The detection of SARS-CoV-2 in the autopsied testicular specimens of COVID-19 via in-situ hybridization, immunohistochemistry, or electron microscope is still needed.

High fever may participate in impairing spermatogenesis in COVID-19 patients, given that scrotal heat stress (>39 °C) can lead to the decrease of sperm concentration and motility. However, noticeable pathological alterations in the autopsied testicular specimens of COVID-19 patients, including interstitial edema and congestion (both in testes and epididymides), red cell exudation, and obvious T-lymphocyte and macrophage infiltration around small blood vessels (both in testes and epididymides), is indicative of the other factors

participate in the manifestation. IgG precipitation in seminiferous tubules is in the line of the findings observed in SARS,<sup>5</sup> referring to orchitis of autoimmune origin. The presence of CD3+ and CD68+ cells is physiological in the epididymis, but our study reported an increased level of CD+3 and CD68+ in COVID-19 patients compared to the control. A similar finding has been reported by Xu et al. (2003) in SARS patients.<sup>5</sup>

We agree with Drs. Marion Bendayan and Florence Boitrelle that it should be cautious while drawing conclusions from the semen results to that of the testis. The contribution of bilateral testes and epididymides to the semen volume is small (less than 10%). Thus, the increased levels of proinflammatory cytokines and chemokines, including IL-6, TNF- $\alpha$ , and MCP-1, may be a manifestation of increased levels of these immune factors in the male reproductive tract as the systemic immune response upon developing the SARS-CoV-2 infection.

### Declaration of Competing Interest

None to declare.

### References

- Li R, Yin T, Fang F, et al. Potential risks of SARS-CoV-2 infection on reproductive health. *Reprod Biomed Online* 2020 Jul;41(1):89–95 Epub 2020 Apr 30. doi: [10.1016/j.rbmo.2020.04.018](https://doi.org/10.1016/j.rbmo.2020.04.018).
- Pan F, Xiao X, Guo J, et al. No evidence of severe acute respiratory syndrome-coronavirus 2 in semen of males recovering from coronavirus disease 2019. *Fertil Steril* 2020 Jun;113(6):1135–9 Epub 2020 Apr 17. doi: [10.1016/j.fertnstert.2020.04.024](https://doi.org/10.1016/j.fertnstert.2020.04.024).
- Yang M, Chen S, Huang B, et al. Pathological Findings in the Testes of COVID-19 Patients: clinical Implications. *Eur Urol Focus* 2020 Sep 15;6(5):1124–9.
- Bradley BT, Maioli H, Johnston R, et al. Histopathology and ultrastructural findings of fatal COVID-19 infections in Washington State: a case series. *Lancet* 2020;396(10247):320–32.
- Xu J, Qi L, Chi X, et al. Orchitis: a complication of severe acute respiratory syndrome (SARS). *Biol Reprod* 2006;74:410–6. doi: [10.1095/biolreprod.105.044776](https://doi.org/10.1095/biolreprod.105.044776).

DOI of original article: <http://dx.doi.org/10.1016/j.eclinm.2020.100604>, <http://dx.doi.org/10.1016/j.eclinm.2020.100670>.

\* Corresponding author at: Institute of Reproductive Health/Center of Reproductive Medicine, Tongji Medical College, Huazhong University of Science and Technology, Hangkong Road 13, Wuhan 430030, China.

E-mail address: [lhgyx@hotmail.com](mailto:lhgyx@hotmail.com) (H. Li).

<https://doi.org/10.1016/j.eclinm.2020.100671>

2589-5370/© 2020 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)