



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



ELSEVIER



OPINION

Is Sexual Route a Matter of Concern for the SARS-CoV-2/COVID-19?

Shailesh Kumar Patel,^a Mamta Pathak,^a Ranjit Sah,^b Akshay Kumar,^c Yashpal Singh Malik,^d
Alfonso J. Rodríguez-Morales,^{e,f} and Kuldeep Dhama^a^aDivision of Pathology, ICAR-Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh, India^bDepartment of Microbiology, Tribhuvan University Teaching Hospital, Institute of Medicine, Kathmandu, Bagmati, Nepal^cDepartment of Cardiothoracic Surgery, Medanta Hospital, Gurgaon, Gurugram, Haryana, India^dDivision of Biological Standardization, ICAR-Indian Veterinary Research Institute, Izatnagar, Uttar Pradesh, India^ePublic Health and Infection Research Group, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia^fGrupo de Investigación Biomedicina, Faculty of Medicine Fundación Universitaria Autónoma de las Américas, Pereira, Risaralda, Colombia

Received for publication June 6, 2020; accepted June 9, 2020 (ARCMED_2020_901).

The ongoing Coronavirus Disease 2019 (COVID-19) pandemic due to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have infected 8.19 million people globally (June 17, 2020). This virus is detected in respiratory aerosols, stool, urine, and saliva, but whether non-respiratory body fluids like vomit, breast milk, urine, or semen contain viable infectious viruses is yet to be unraveled (1). Moreover, no evidence of sexual transmission is yet available. Detailed investigations in this regard are warranted. However, all forms of sexual contact are reported to carry a potential risk of viral transmission as it is readily transmitted by fomites and aerosols. Then, infected individuals may spread the respiratory secretions onto their personal objects and skin, leading to further transmission to a sexual partner (2). The SARS-CoV-2 shares 80% sequence homology with the SARS-CoV and utilizes the angiotensin-converting enzyme 2 (ACE2) receptors with higher binding affinity than SARS-CoV (3,4). The expression of ACE2 is reported in a wide range of human reproductive tissues like seminiferous ducts cells, spermatogonia, Sertoli and Leydig cells, suggesting the potential risk of SARS-CoV-2 infection in the male reproductive system (5). Besides, the presence of furin cleavage sites in SARS-CoV-2 increases the ability of the virus to internalize into cells, and enhanced expression of furin domains in the epididymis further increases the risk of infection to genitalia (3,6). As orchitis attributed to germ cell destruction along with testicular damage was reported in SARS-CoV infection, the possibility of testicular damage and

fertility-related concerns in COVID-19 patients could not be ignored (7) (Figure 1).

The possibility of the SARS-CoV-2 presence in semen is under investigation, and only a few case reports are available. The absence of viral RNA was reported in the semen of an individual with the history of SARS-CoV-2 infection, and this was further confirmed in a small cohort study conducted in China (8,9). In contrast, semen samples from 6 (15.8%) COVID-19 patients were reported positive for SARS-CoV-2 in a study, including 38 individuals, among which two recovered from the disease (10). Henceforth the concentration, survivability, and shedding time of SARS-CoV-2 in semen should be investigated. Many methodological concerns were raised, and further studies are required (11). Additionally, considering the possibility of SARS-CoV-2 sexual transmission, COVID-19 patients were advised to avoid parenthood and not participate in fertility programs (gamete donation, gestational carriers, and assisted reproductive technology).

Although as many as 27 viremia associated viruses were reported in human semen, but this number may represent only the tip of the iceberg and need investigation. Moreover, non-sexually transmitted viruses may be present in genital secretions (12,13). Hence, a detailed investigation on viral detection followed by its persistence in testes may prove crucial for deadly viruses like SARS-CoV-2 in clinical practice till confirmation of the sexual transmission status. The data derived from the SARS-CoV infection suggests that andrological consultation and evaluation of gonadal function, including detailed semen examination, must be carried out in COVID-19 recovered patients, especially in reproductive age. Apart from avoiding contact with saliva and blood of COVID-19 patient, examination for detection of SARS-CoV-2 in the semen of the infected

Address reprint requests to: Alfonso J Rodríguez-Morales, Public Health and Infection Research Group, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira, Colombia; Phone: +573008847448; FAX: +5763213206; E-mail: arodriguezm@utp.edu.co

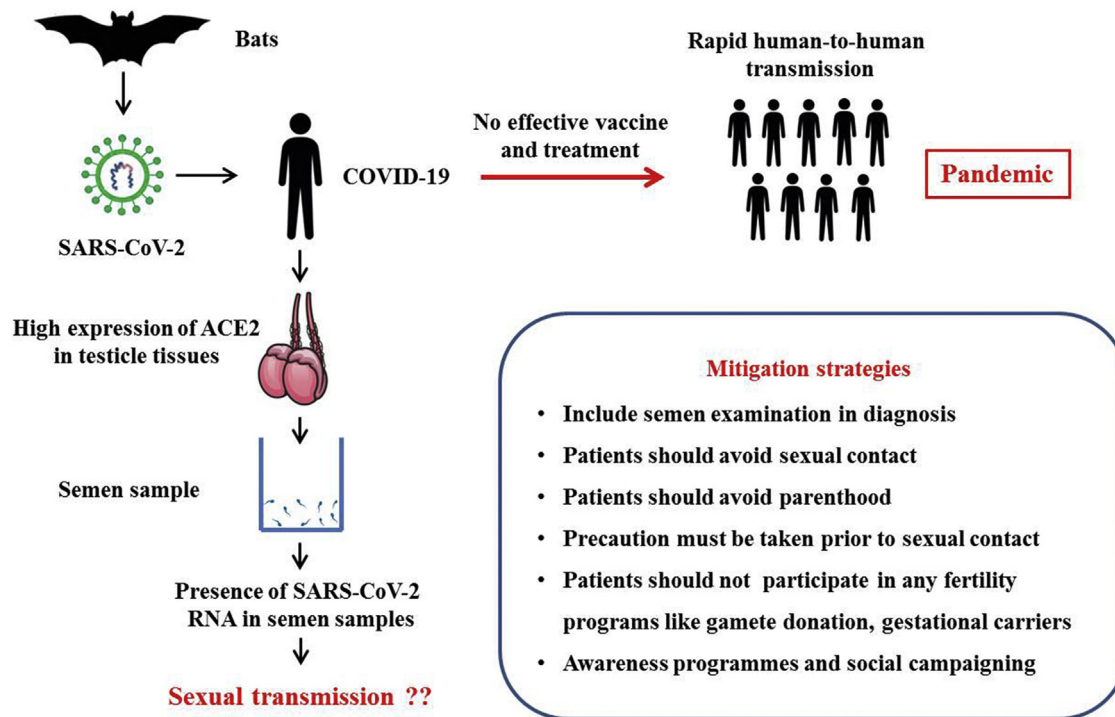


Figure 1. An overview of the possibility of the sexual route of transmission for the SARS-CoV-2/COVID-19.

and the recovering patients and monitoring fetal development are required to prevent and control COVID-19 (10).

References

- Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020;382:1708–1720.
- Turban JL, Keuroghlian AS, Mayer KH. Sexual Health in the SARS-CoV-2 Era. *Ann Intern Med*, 2020; <https://doi.org/10.7326/M20-2004>.
- Shang J, Ye G, Shi K, et al. Structural basis of receptor recognition by SARS-CoV-2. *Nature* 2020;581:221–224.
- Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med* 2020;382:727–733.
- 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.
- Thimon V, Belghazi M, Dacheux JL, et al. Analysis of furin ectodomain shedding in epididymal fluid of mammals: demonstration that shedding of furin occurs in vivo. *Reproduction* 2006;132:899–908.
- Cardona-Maya WD, Du Plessis SS, Velilla PA. SARS-CoV-2 and the testis: similarity with other viruses and routes of infection. *Reprod Biomed Online* 2020;40:763–764.
- 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;113:1135–1139.
- Paoli D, Pallotti F, Colangelo S, et al. Study of SARS-CoV-2 in semen and urine samples of a volunteer with positive naso-pharyngeal swab. *J Endocrinol Invest*, 2020:1–4.
- Li D, Jin M, Bao P, et al. Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019. *JAMA Netw Open* 2020;3:e208292.
- Paoli D, Pallotti F, Turriziani O, et al. SARS-CoV-2 Presence in seminal fluid: myth or reality. *Andrology*, 2020; <https://doi.org/10.1111/andr.12825>.
- Feldmann H. Virus in Semen and the Risk of Sexual Transmission. *N Engl J Med* 2018;378:1440–1441.
- Mead PS, Duggal NK, Hook SA, et al. Zika Virus Shedding in Semen of Symptomatic Infected Men. *N Engl J Med* 2018;378:1377–1385.