

The COVID-19 pandemics: shall we expect andrological consequences? A call for contributions to ANDROLOGY

Manuela Simoni¹ and Marie-Claude Hofmann²

¹ Unit of Endocrinology, Center of Excellence in Andrology and Sexual Medicine, Dept. of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy

² Department of Endocrine Neoplasia and Hormonal Disorders, University of Texas MD Anderson Cancer Center, Houston, TX, USA

The coronavirus 2 (SARS-CoV-2) pandemic represents and will represent the greatest health, economic and social crisis of the new millennium. According to the World Health Organization (WHO) report published on April 14, 2020, the pandemic SARS-CoV-2 affects 213 countries worldwide, with 1,848,439 infected patients and 117,217 confirmed deaths (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>) to this date. Men are much more prone to become seriously ill than women. Fortunately, the majority of men, especially in younger age, survive the infection.

From a medical point of view, there is no doubt that most problems related to the reproductive system can be postponed in the face of the urgent and acute medical care required by the current situation. But what do we know about the andrological consequences of SARS-Cov-2 infection and what should we expect?

The severe acute respiratory syndrome related to SARS-CoV-2 it is the final and, probably, most serious step of the virus infectious process. The viral entry into target cells depends on the SARS-CoV-2 spike (S) protein and requires S protein priming by cellular proteases, allowing fusion of viral and cellular membranes¹. SARS-CoV-2 engages angiotensin-converting enzyme 2 (ACE2) as the entry receptor^{2,3}, and employs the transmembrane protease, serine 2 (TMPRSS2) for S protein priming^{4,5}. The virus/ACE2 interaction has been previously demonstrated at the atomic resolution level for the SARS-CoV transmissibility^{6,7} and, since SARS-CoV and SARS-CoV-2 share 80% sequence identity⁸, SARS-CoV-2 could use a similar entry mechanism, possibly with even higher ACE2 affinity compared to SARS-CoV⁹. Therefore, every tissue in the human body expressing the ACE2 receptor could be targeted and damaged by the infection, including testis¹⁰, Leydig cells¹¹ and seminal fluid¹². The ACE2 receptor seems involved in spermatogenesis, mainly influencing sperm maturation and spermiation¹². Finally, several cases of orchitis have been described in the presence of SARS-CoV, although the virus itself was not isolated in the testicular tissue¹³.

Given this background, there are a number of andrological questions related to the COVID-19 epidemics that require a scientific answer: Why are men more susceptible than women? Does the virus pass the blood-testis barrier and is it found in the seminal fluid? Is there any effect on androgen production? Does SARS-Cov-2 infect the testis and, if yes, with what consequences? What are the effects of the virus and virus-related issues (asymptomatic infection, isolation, quarantine) on sexual function, sexual behaviour and reproduction at large?

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ANDR.12804

This article is protected by copyright. All rights reserved

Another question related to this new medical emergency is that medical interventions considered non-essential health care procedures, such as certain andrology treatments, are now suspended. However, there are interventions that cannot be postponed and patients may need interventions also in times of COVID-19, e.g. semen cryopreservation before cancer therapy. All these aspects require consideration, thoughts and research.

Many andrologists worldwide are concerned about the consequences of SARS-CoV-2 infection for their patients, and are asking the journal to be the platform for scientific discussion. We think that ANDROLOGY is the right forum for any type of sound scientific contributions about all andrological aspects of the COVID-19 epidemics. Therefore, we would like to invite submissions of Clinical and Basic Research Articles, as well as Opinion Articles on this very actual and relevant topic. Every contribution will be subjected to peer review as any article submitted to the journal and, if accepted, will be immediately available online as Accepted Article.

References

1. 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.
2. Gheblawi M, Wang K, Viveiros A, et al. Angiotensin Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System. *Circulation research*. 2020.
3. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. *Nat Microbiol*. 2020;5(4):562-569.
4. Matsuyama S, Nagata N, Shirato K, Kawase M, Takeda M, Taguchi F. Efficient activation of the severe acute respiratory syndrome coronavirus spike protein by the transmembrane protease TMPRSS2. *J Virol*. 2010;84(24):12658-12664.
5. Glowacka I, Bertram S, Muller MA, et al. Evidence that TMPRSS2 activates the severe acute respiratory syndrome coronavirus spike protein for membrane fusion and reduces viral control by the humoral immune response. *J Virol*. 2011;85(9):4122-4134.
6. Li F, Li W, Farzan M, Harrison SC. Structure of SARS coronavirus spike receptor-binding domain complexed with receptor. *Science (New York, NY)*. 2005;309(5742):1864-1868.
7. Li W, Zhang C, Sui J, et al. Receptor and viral determinants of SARS-coronavirus adaptation to human ACE2. *The EMBO journal*. 2005;24(8):1634-1643.
8. Chen Y, Guo Y, Pan Y, Zhao ZJ. Structure analysis of the receptor binding of 2019-nCoV. *Biochemical and biophysical research communications*. 2020.
9. Wrapp D, Wang N, Corbett KS, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. *Science (New York, NY)*. 2020;367(6483):1260-1263.
10. Fagerberg L, Hallstrom BM, Oksvold P, et al. Analysis of the human tissue-specific expression by genome-wide integration of transcriptomics and antibody-based proteomics. *Mol Cell Proteomics*. 2014;13(2):397-406.
11. Douglas GC, O'Bryan MK, Hedger MP, et al. The novel angiotensin-converting enzyme (ACE) homolog, ACE2, is selectively expressed by adult Leydig cells of the testis. *Endocrinology*. 2004;145(10):4703-4711.
12. Kohn FM, Miska W, Schill WB. Release of angiotensin-converting enzyme (ACE) from human spermatozoa during capacitation and acrosome reaction. *Journal of andrology*. 1995;16(3):259-265.
13. Xu J, Qi L, Chi X, et al. Orchitis: A Complication of Severe Acute Respiratory Syndrome (SARS)1. *Biology of reproduction*. 2006;74(2):410-416.