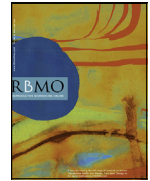




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COMMENTARY

SARS-CoV-2 and the testis: similarity with other viruses and routes of infection

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ABSTRACT

Since the start of the latest coronavirus (SARS-CoV-2) outbreak, the number of infected individuals and cases of coronavirus disease (COVID-19) has been increasing exponentially worldwide. Of interest is existing evidence that orchitis can develop due coronavirus infection. It is therefore not unreasonable to believe that SARS-CoV-2 could be transmitted by semen. Consequently, it is of paramount importance that individuals who could potentially be infected take all possible care to mitigate the likely risk of passing on the infection through sexual intercourse.

Since the novel coronavirus (SARS-CoV-2) outbreak in December 2019, the number of cases of infected individuals has been increasing exponentially, leading to the coronavirus disease (COVID-19) being declared a global pandemic on the 11 March 2020.

Rothe and collaborators (Rothe *et al.* 2020) were the first to report that a male acquired the infection through transmission that appears to have occurred during the incubation period of the index patient, who did not present with any symptoms at that stage. This case raises questions about possible new routes of transmission.

There is evidence about the relationship between members of the coronavirus family and orchitis in both humans (SARS-CoV) (Xu *et al.* 2006) and cats (feline coronavirus) (Sigurðardóttir *et al.* 2001). However, whether the virus is present in the testicular epithelium remains a matter of debate due to

conflicting results (Zhao *et al.* 2003; Ding *et al.* 2004; Gu *et al.* 2005; Xu *et al.* 2006). As testicular damage and germ cell destruction was clearly observed in these cases (Xu *et al.* 2006), it is not unreasonable to believe that SARS-CoV-2 could be transmitted by semen, potentially providing a possible route of transmission of the pathogen. This could occur in asymptomatic patients, in patients with mild symptoms or even during the incubation period. This potential route of transmission has been proposed for other viral infections that were previously considered unlikely to be transferred sexually, including Ebola (Cardona-Maya *et al.* 2019) and Zika viruses (Cardona Maya *et al.* 2016, Feldmann 2018). It was also recently reported that angiotensin-converting enzyme 2 (ACE2) has been shown to be one of the major receptors that mediate the entry of SARS-CoV-2 into human cells. Using online datasets, Fan and colleagues (Fan *et al.* 2020) clearly demonstrated that ACE2 is highly expressed in Leydig cells and cells of

the seminiferous tubules in the human testis. Thus, the binding of the virus to these ACE2-positive cells could not only cause severe alteration of testicular tissue but also provide a sites for viral infection. It should therefore be of some concern that this recent coronavirus outbreak may have a serious impact on fertility worldwide. Although the actual situation has yet to be substantiated in patients infected with SARS-CoV-2, the American Society for Reproductive Medicine (ASRM) and the Society for Assisted reproductive Technology (SART) have already issued warnings to this extent (SART, 2020). The advice given is that prospective parents, ART patients, gamete donors and gestational carriers who meet the diagnostic criteria for SARS-CoV-2 should avoid becoming pregnant or participate in any fertility programs (Society for Assisted Reproductive Technology, 2020). The Center for Diseases Control and Prevention (CDC) has also stated that it is not yet known whether non-respiratory body fluids from an infected person

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KEYWORDS

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including vomit, urine, breast milk or semen can contain viable, infectious viruses (CDC, 2020). In Italy, one of the early COVID-19 epicenters, authorities are mandating that all gamete donors should be interviewed concerning the presence of respiratory symptoms and/or recent travel to high-risk areas, even in the absence of evidence of transmission of the virus within reproductive cells. A 2-week suspension from the end of symptoms is implemented in the case of donors showing respiratory symptoms, while a similar 2-week suspension is required from donors who have returned from an area at risk (La Marca et al., 2020).

Furthermore, based on current knowledge, it is of paramount importance that individuals who could potentially be infected take all possible care to mitigate the likely risk of passing on infection through sexual intercourse. Precautionary measurements should be practiced by candidates who have not yet been tested positive for SARS-CoV-2, and also by those previously infected, even after the signs and symptoms have resolved. It is recommended to avoid possible transfection by refraining from sexual relations without protection, as the virus could persist for a longer period of time in the male reproductive system compared with other body fluids, rendering the testis a potential viral reservoir.

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