


# It is currently unknown whether SARS-CoV-2 is viable in semen or whether COVID-19 damages spermatozoa

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## Abstract

Research is needed to understand the presence of the SARS-CoV-2 virus in semen, sexual transmissibility, and impact on sperm quality. Several studies have examined men recovering from COVID-19, but large-scale community-based testing is needed to ascertain the effects on the male reproductive tract, and the potential for prolonged transmission.

## KEYWORDS

COVID-19, SARS-CoV-2, coronavirus, semen, spermatozoa, sexual transmission, assisted reproductive technology

With the rapid emergence of the global COVID-19 pandemic, it is imperative to understand all routes of transmission of the causative agent, SARS-CoV-2 via bodily fluids. For most emerging pathogens, the role of semen as a transmission source has been highly understudied, if at all. There may be skepticism about studying SARS-CoV-2 in semen when the leading route of transmission via droplet spread can also happen during sexual activity, but transmission via semen or spermatozoa may be also relevant to a large number of infertility patients undergoing assisted reproductive technologies (ART).

Knowledge of other viruses present in semen provides precedence for looking at semen and sexual transmission. Over 25 viruses have been found in human semen, and sexual transmission has been confirmed in several viruses traditionally considered to be non-sexually transmitted.<sup>1</sup> The broad range of virus families found in human semen lends evidence that SARS-CoV-2 could be detected either in the testis or in seminal fluid. SARS-CoV-2 is found in blood and plasma although the degree of viremia is still unknown and it could be confined to the most severe infections. Viruses capable of causing viremia can pass the blood-testis barrier in the presence

of systemic or local inflammation, or in men with otherwise compromised blood-testis barriers (eg, anti-sperm antibodies).<sup>2</sup> Once present, viruses can persist in the male reproductive tract because testicular immune response is restricted to enable sperm survival, making the testes an immunologically privileged site.<sup>2</sup> The sexual transmissibility of these persistent viruses is understudied, but research shows the potential of sexual transmission to cause delayed outbreaks after the first wave of cases.<sup>1</sup> The viral loads that lead to viremia need to be understood, along with the degree of viremia that could cause SARS-CoV-2 to reach the testis at levels that could be transmissible via seminal fluid.

SARS-CoV-2 transmissibility across another reproductive barrier, the placenta, is also not understood and evidence to date is limited and conflicting. In a recent study, no evidence was found for transplacental transmission in women who developed COVID-19 pneumonia,<sup>3</sup> whereas an examination of a cohort of 33 neonates born to mothers in Wuhan China with COVID-19 found that three infants presented with SARS-CoV-2 infection. Evidence of vertical transmission was limited because one infant could have had bacterial sepsis

and the other two changed from positive to negative by postnatal day 6, without further follow-up reported.<sup>4</sup>

The presence of the virus in semen and spermatozoa, sexual transmissibility via semen, and impact on sperm quality needs to be studied. Among the few prior studies of men infected with Zika, there was evidence of increased sperm abnormalities<sup>5</sup> and the presence of inflammatory cells in semen, suggesting damage to the male reproductive tract.<sup>6</sup> In a recent non-peer reviewed source, Ma et al (2020) reported that SARS-CoV-2 can affect the testes and the production of follicle-stimulating hormone, testosterone, and luteinizing hormone.<sup>7</sup> Angiotensin-converting enzyme 2 (ACE2), the key binding receptor that allows SARS CoV and SARS-CoV-2 entry into host cells is highly expressed in the testes.<sup>8</sup>

The few studies on SARS-CoV-2 and semen thus far have shown conflicting results. Two studies were unable to detect the presence of SARS-CoV-2 in semen from men who had recovered from COVID-19.<sup>9,10</sup> These studies report differing conditions and varying disease severity of study participants. Pan et al (2020) analyzed samples collected from men one month after diagnosis exhibiting milder symptoms, while Song et al (2020) included symptomatic and asymptomatic men, and testis tissue specimens from a deceased patient. An additional study analyzed the semen of a patient with mild symptoms and did not detect the virus eight days after receiving a positive test.<sup>11</sup> However, a study of 38 male patients with COVID-19 found that 4 of 15 patients (26.7%) in the acute stage of infection and 2 of 23 patients (8.7%) in recovery had detectable SARS-CoV-2 present in semen samples.<sup>12</sup> In addition to the semen studies, one study of 48 males and 20 females compared the viral clearance time of SARS-CoV-2 between sexes and observed that females achieved a negative PCR result two days earlier than males.<sup>13</sup>

These studies used small sample sizes and examined confirmed cases of COVID-19 during recovery; given the high numbers of asymptomatic and untested people who may have high viral loads, there is a possibility of SARS-CoV-2 presence in the semen of men who unknowingly have the virus. Community-based testing and semen analysis in symptomatic and asymptomatic men are necessary to determine the virus' presence in semen for those of varying degrees of illness.

Among the myriad health consequences of the COVID-19 pandemic is the potential risk to male fertility. Human viral infections, including mumps, sexually transmitted infections, and tuberculosis, are known to cause lasting damage to the testes. Xu et al (2016) found orchitis in deceased patients believed to be caused by the SARS virus.<sup>14</sup> One recent study of men with confirmed COVID-19 reported 19% of participants experienced scrotal discomfort comparable to that in orchitis.<sup>9</sup> Unfortunately, no current studies of recovered patients have examined semen quality. Given the variable nature of semen quality and the low fertility predictive power of semen analysis, future studies will need to be well designed and statistically powered to be of use, including the analysis of confounding factors such as medications used to treat the infection. As seen with orchitis and epididymitis, infections requiring immune responses

from sertoli, leydig, and epididymal epithelial cells present important threats to testicular integrity, spermatogenesis and male fertility.<sup>15,16</sup>

Virus transmission may be facilitated by ART, especially intracytoplasmic sperm injection (ICSI). Although most ART involves washing and repeated dilution of the semen sample, virus particles could theoretically be transmitted directly via ICSI. Therefore, possible effects on early embryogenesis and development must also be considered. Semen and sperm studies are needed going forward for proper care and guidance of men and women at risk of COVID-19 infections and to those recovering from illness.

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MJP, SA, and LMN conceived of the idea and conducted the literature review and writing. DC and CNM added individual contributions and revisions. All authors approved the final version and report no conflict of interest.

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