

COVID-19: semen impairment may not be related to the virus

Sir,

In just a few months, several million humans have been infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This brutal pandemic, called coronavirus-19 disease (COVID-19), disproportionately affects men and may have lasting impacts relating to aspects such as fertility. Some of these impacts are described in the literature, and others may be published in the coming months. The impacts of COVID-19 and SARS-CoV-2 on sperm and male reproductive function have been debated since the beginning of the pandemic. To answer the question, Gacci *et al.* (2021) assessed sperm parameters and seminal markers of inflammation in patients cured of COVID-19. They showed a high proportion of patients with oligo-azoospermia and patients with seminal inflammatory markers unrelated to the presence of virus in semen. The authors suggested that these signs were specifically due to COVID-19. However, there are symptoms of COVID-19 (e.g. fever) with known andrological impacts that should be highlighted.

Beyond the presence or absence of virus in semen, it is clear that COVID-19 can be accompanied by deregulation of spermatogenesis. Fever is a symptom observed in over 80% of patients infected with COVID-19. This fever alone can have a negative impact on the physiological mechanisms of scrotal heat regulation, which are overwhelmed when body temperature rises by even one degree Celsius. Therefore, even a fever of limited duration can decrease sperm count and/or motility and/or vitality, can induce autophagy and may alter sperm DNA integrity as previously described (Carlsen *et al.*, 2003; Sergerie *et al.*, 2007; Durairajanayagam *et al.*, 2015). The return to the basal state of the sperm parameters can take a long time, at least 3 months (Carlsen *et al.*, 2003; Lazarus and Zorngiotti, 1975). Fever induced by COVID-19 can, therefore, alter sperm parameters even in the absence of virus in the semen and even in the absence of immune response. In infertile men with altered sperm parameters in the basal state, this fever could have a more deleterious impact. For this reason, it has already been recommended to monitor sperm parameters and to delay ART management for three months in men who have been diagnosed with COVID-19 and developed a fever (Hamdi *et al.*, 2020).

In addition, leukocytospermia (also called pyospermia) is defined by the WHO as the presence of $>1.10^6$ granulocytes (not lymphocytes)/ml. This leukocytospermia is traditionally accompanied by an increase in IL-6 and IL-8 (Shimoya *et al.*, 1995; Saxena *et al.*, 2019). Leukocytospermia can be a sign of a bacterial or viral infection, systemic inflammation or simply an infrequent ejaculation. A very recent study even showed that leukospermia could be found in about 25% of young men, without the cause always being identified

(La Vignera *et al.*, 2020). A high proportion of men with leukospermia was found by Gacci *et al.* However, since there is a lack of information on the time of sexual abstinence or the treatments taken by these men, it is difficult to conclude that there is a significantly strong association between COVID-19 and leukocytospermia.

Finally, the majority of patients included in the study were hospitalized. Semen collection took place up to 35 days (in average) after the second negative nasopharyngeal-swab. The medications or drugs received during the hospitalization may also have had an impact on the sperm parameters. In any case, the evolution of sperm parameters, whether after fever or after hospitalization should have been monitored at least 7–90 days after the end of symptoms. This would in fact have made it possible to evaluate the reversibility of sperm damage at the end of a period of time corresponding to a spermatogenesis cycle with epididymal maturation.

In conclusion, fever, medication, long sexual abstinence may explain the alteration of semen parameters. These effects could be reversible and are not specific to the COVID-19. It is for this reason that it was recommended, from the beginning of the pandemic, to delay ART activities to 3 months post-infection with SARS-CoV-2, especially in case of fever. In the absence of fever, the effects of the new coronavirus on semen remain unknown.

Conflict of interest

None.

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