

Absence of 2019 novel coronavirus in semen and testes of COVID-19 patients

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Dear Editor,

The COVID-19 pandemic has affected >200 countries with over one million confirmed cases as of April 1, 2020. Similar to severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome (MERS) in 2012, the 2019-nCoV infection causes mainly pneumonia, suggesting that the virus primarily targets the respiratory system and transmits via air droplets and contact. In addition to oropharyngeal swabs, the 2019-nCoV has also been detected in blood, urine, and facial/anal swabs, suggesting other potential means of transmission [1-3]. Among COVID-19 patients, there are more men than women [1]. Yet, although recent reports found no evidence of either sexual or vertical transmission by women infected with the 2019-nCoV [4, 5], very little is known about the potential impact of 2019-nCoV infection on the male reproductive system. Of interest, bioinformatic analyses have revealed that angiotensin-converting enzyme 2, a receptor utilized by the 2019-nCoV, is abundantly expressed in the testis and male reproductive tract [6, 7], raising an urgent question of potential sexual transmission through semen by men. To address this question, we conducted a study with the approval of the Institutional Review Board (IRB) of Nanjing Medical University by examining the 2019-nCoV RNA in semen samples collected from 12 patients in their recovery phase, as well as in testicular samples from one patient who died of COVID-19 during the acute phase.

The 12 men (aged between 22-38 years) who were diagnosed with COVID-19 between January 31 and March 14, 2020 in Wuhan were recruited with written informed consent. Eleven were categorized into the mild or common subgroup while one was placed in the asymptomatic subgroup. In addition, one 67 year-old patient who died of COVID-19 on March 10, 2020 in Wuhan was included, after written informed consent was obtained from the family. The clinical characteristics, laboratory findings, chest

CT scans, treatment and clinical outcome data of the 13 men are summarized in Table S1. Diagnosis of COVID-19 was based on the detection of either 2019-nCoV RNA on pharyngeal swabs using quantitative RT-PCR (qRT-PCR) or anti-2019-nCoV antibodies (both IgM and IgG) in serum by colloidal gold-based immunoassays, following the New Coronavirus Pneumonia Prevention and Control Program (7th edition) published by the National Health Commission of China [8]. Pharyngeal swabs were collected on the admission day and every few days thereafter and processed for 2019-nCoV RNA detection using the kit (Huirui Biotechnology, Shanghai, China) recommended by the Chinese Center for Disease Control and Prevention (CDC) following the WHO guidelines [8]. The recovery phase was defined as the period after viral clearance (two consecutive negative qRT-PCR tests), or a substantial resolution on chest CT scans with much lessened symptoms. The semen samples were collected through masturbation according to the WHO guideline [9]. To avoid virus contamination from non-semen sources, the process included passing urine, thorough washing of hands and penis with soap, drying of hands and penis, and then ejaculating the semen into a sterile and wide-mouthed container [9]. The testes were collected from the deceased patient.

Among the 12 patients in the recovery phase, nine were positive for anti-2019-nCoV IgG, but negative for anti-2019-nCoV IgM. Among the 9 IgG-positive patients, 8 showed negative pharyngeal swab 2019-nCoV RNA test results while one (Patient 1) remained positive, suggesting that once IgG appears, the virus has largely been cleared. Notably, patients 9-12 displayed negative 2019-nCoV RNA test results, but their IgG remained positive during hospitalization, confirming prior infection. The deceased patient (Patient 13) tested positive for both 2019-nCoV RNA in pharyngeal swabs and IgM and IgG in serum, consistent with the acute phase of infection. At the time of semen sampling from patients 2-8, their pharyngeal swab RT-PCR test results had turned from positive to negative for at least one week

(Figure 1). All semen samples from patients 2-8 were negative in 2019-nCoV RNA tests. Semen samples from patients 9-12, who had been negative in pharyngeal swab 2019-nCoV RNA tests but positive for anti-2019-nCoV IgG in their sera, were also negative in 2019-nCoV RNA tests. Of importance, patient 1 was persistently positive in pharyngeal swab 2019-nCoV RNA tests even after serum IgG became positive during the recovery stage, yet his semen showed no detectable 2019-nCoV RNA, implying that the 2019-nCoV does not directly infect the testis and the male reproductive tract. The deceased patient (patient 13), who died during the acute phase, tested negative for 2019-nCoV RNA in the testis samples, suggesting that the 2019-nCoV does not directly infect the testis or male genital tract even in the acute phase.

Our data suggest that the 2019-nCoV is absent from the semen and testes in men infected by COVID-19 at both acute and recovery phases. Thus, it is highly unlikely that the 2019-nCoV can be sexually transmitted by men. This is the first report showing that the 2019-nCoV is absent from both the semen and testis specimens of COVID-19 patients. Given the relatively small sample size, more patients are needed to confirm our findings. Multiple rounds of 2019-nCoV RNA testing on semen samples would be ideal during the course of disease. However, it is impractical to collect multiple semen samples while the patients are sick. Our data also imply that the 2019-nCoV does not directly infect the testis and male genital tract. A definitive answer regarding potential viral attacks on the testis will require more detailed physiological and pathological examinations of the male reproductive system of male COVID-19 male patients after their recovery.

Yours sincerely,

Conflict of interest statement: The authors declare that there are no conflicts of interest.

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