**Autopsy Study of Testicles in COVID-19: Upregulation of Immune-Related Genes and Downregulation of Testis-Specific Genes**

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*The Journal of Clinical Endocrinology & Metabolism*, Volume 108, Issue 4, 1 April 2023, Pages 950–961, <https://doi.org/10.1210/clinem/dgac608>

**Context**

Infection by SARS-CoV-2 may be associated with testicular dysfunction that could affect male fertility.

**Objective**

Testicles of fatal COVID-19 cases were investigated to detect virus in tissue and to evaluate histopathological and transcriptomic changes.

**Methods**

Three groups were compared: (a) uninfected controls (subjects dying of trauma or sudden cardiac death; n = 10); (b) subjects dying of COVID-19 (virus-negative in testes; n = 15); (c) subjects dying of COVID-19 (virus-positive in testes; n = 9). SARS-CoV-2 genome and nucleocapsid antigen were probed using RT-PCR, in situ hybridization, and immunohistochemistry (IHC). Infiltrating leukocytes were typed by IHC. mRNA transcripts of immune-related and testis-specific genes were quantified using the nCounter method.

**Results**

SARS-CoV-2 was detected in testis tissue of 9/24 (37%) COVID-19 cases accompanied by scattered T-cell and macrophage infiltrates. Size of testicles and counts of spermatogenic cells were not significantly different among groups. Analysis of mRNA transcripts showed that in virus-positive testes immune processes were activated (interferon-alpha and -gamma pathways). By contrast, transcription of 12 testis-specific genes was downregulated, independently of virus positivity in tissue. By IHC, expression of the luteinizing hormone/choriogonadotropin receptor was enhanced in virus-positive compared to virus-negative testicles, while expression of receptors for androgens and the follicle-stimulating hormone were not significantly different among groups.

**Conclusion**

In lethal COVID-19 cases, infection of testicular cells is not uncommon. Viral infection associates with activation of interferon pathways and downregulation of testis-specific genes involved in spermatogenesis. Due to the exceedingly high numbers of infected people in the pandemic, the impact of virus on fertility should be further investigated.

COVID-19, autopsy, testis, SARS-CoV-2, innate immunity, testis-specific genes