

## Comment

# Linking COVID-19 vaccine and male infertility – not on fertile ground

Justin La<sup>1,2</sup>  and Darren J. Katz<sup>1,2,3</sup> 

<sup>1</sup>Men's Health Melbourne, <sup>2</sup>Department of Urology, Western Health, and <sup>3</sup>Department of Surgery, Western Precinct, University of Melbourne, Melbourne, Vic., Australia

Uncertainty brings fear and, without a doubt, the emergence of the SARS-CoV-2 virus and the ongoing COVID-19 pandemic have left the public divided and healthcare systems strained [1]. Although this contagious virus is a novel strain to humans, the diligent international collaboration of the scientific community has led to significant strides in understanding it. With the concerted scientific effort to prevent this disease and control the pandemic, several vaccines such as the mRNA (BNT162b2 and mRNA-1273) and adenovirus vector (ChAdOx1 nCoV-19 and Ad26.COV.S) vaccines came to fruition expeditiously and, after significant rigorous analysis, have been given emergency use or full approval by the UK Medicines and Healthcare products Regulatory Agency (MHRA), the US Food and Drug Administration (FDA), the European Medicines Agency (EMA) and the Australian Therapeutic Goods Administration (TGA).

Despite the proven short- to medium-term safety profiles and efficacy of these vaccines in preventing COVID-19 infection, hospitalization and death, vaccine hesitancy remains rampant across the world. A significant driver of vaccine hesitancy is the pervasive misinformation and anti-vaccine campaigns on social media platforms promoting unsubstantiated vaccine falsehoods, one of which is the risk of infertility [2].

To further explore the veracity of anti-vaccine campaigns and gain public trust in vaccinations, some recent studies have looked at the effects of the COVID-19 vaccines on male fertility. In a small prospective cohort study of healthy adult men, Gonzalez et al. [3] did not see a decrease in semen parameters up to 70 days after COVID-19 mRNA vaccination, which is within the spermatogenesis timeframe. In this study, the semen parameters of vaccinated men, interestingly, improved significantly in volume, sperm concentration and motility but these findings may be due to a statistical limitation (regression to the mean in a small sample size). Whilst we are not suggesting that this paper proves that the COVID vaccine may actually *improve* seminal parameters, the underlying signal is that there was no deterioration of any sort in semen parameters. Although semen parameters are generalized markers for male fertility potential, the study is reassuring, especially considering the well-documented

impairment of semen characteristics seen in men infected with the SARS-CoV-2 virus [4].

In addition to the effect on semen parameters, COVID-19 has also been linked to other male reproductive complications. Erectile dysfunction and the development of orchitis are two such examples [5,6]. Erectile dysfunction is thought to be affected by COVID-19 through vascular, neurological and endocrine dysfunction as a result of direct viral insult or hyperinflammation. Orchitis has also been hypothesized to occur due to systemic inflammation and hypercoagulable states, and there is also the possibility of SARS-CoV-2 virus entry into cells via ACE2 and TMPRSS2 receptors in the testes. Histological examination of the testes of individuals who died from COVID-19 have demonstrated significant interstitial oedema, leukocyte infiltration, Sertoli cell vacuolization and sloughing of spermatocytes, signifying significant testicular parenchyma damage [7]. This probably explains the acute impairment of semen characteristics seen clinically in men with symptomatic COVID-19. On the flip side, COVID-19 vaccination has been shown to be associated with a decreased incidence of epididymo-orchitis. In a US database study of 663 775 men, Carto et al. revealed that men vaccinated against COVID-19 had 43.2% decreased odds of being diagnosed with epididymo-orchitis [8].

Necessity is the mother of invention, and the COVID-19 pandemic has accelerated developments in medicine and its practice. These include the adoption of telehealth, information technology, and, of course, medication and vaccine development [9]. Vaccines approved for the prevention of the SARS-CoV-2 virus and resultant COVID-19 disease are considered safe and efficacious. They are the forefront of the strategy in fighting the current COVID-19 pandemic but require the trust and adoption of the public. Based on limited studies, short-term data confirm that COVID-19 infection has the potential to cause testicular damage and diminish male fertility potential. However, COVID-19 vaccines have not been shown to affect spermatogenesis, an extension of male fertility potential. Currently, there is no reliable evidence to support the relationship of COVID-19 vaccination and male infertility, and the fear of causing male infertility should not be a reason to avoid the COVID-19 vaccine.

Therefore, there are three key ‘take-home’ points to be used by health practitioners when counselling male patients who are concerned about unfounded male fertility impacts of the COVID-19 vaccine:

- 1 Severe COVID-19 disease can harm testes and impair sperm characteristics.
- 2 The vaccine can help prevent infection and, thereby, maintain fertility potential in the short term.
- 3 There are no reliable data linking COVID-19 vaccination to impairment of sperm characteristics.

## Disclosure of Interests

The authors declare that they have no conflict of interests.

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Correspondence: Darren Katz, Level M, 233 Collins Street, Melbourne, Vic. 3000, Australia.

e-mail: dkatz@menshealthmelbourne.com.au