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human reproduction LETTERS TO THE EDITOR

Risk of contamination with SARS-CoV-2 in ART

Sir,

We read with interest the article by Kteily and colleagues regarding the non-detectability of SARS-CoV-2 mRNA in semen, follicular fluid, vaginal secretions and residual medulla in asymptomatic patients who undergo ART (Kteily *et al.*, 2022). Their study focused only on the presence of viruses in patients' residual material samples. However, based on their findings, they curiously concluded that '*no additional measures to prevent staff or cross-patient contamination need to be implemented in the IVF and andrology laboratories*'.

This statement is far too general, not justified by the specific finding of authors, and may create a false and dangerous feeling of security both for patients and the staff. Cross-contamination issues in assisted reproduction are not restricted to physical contact with infected samples but involve other standard processes and activities. The SARS-CoV-2 pandemic aggravated these dangers considerably, including but not restricted to standard procedures of cryopreservation applied in the majority of IVF cycles.

As already discussed in this journal (Parmegiani and Vajta, 2021), contamination of liquid nitrogen and nitrogen vapour (LN_2/NV) may occur at any step from manufacturing to final use, including transport, storage, distribution, preparation for cryopreservation and all stages of the procedure. Airborne contaminants such as SARS-CoV-2 can come into contact with LN_2/NV and remain cryopreserved (Parmegiani *et al.*, 2020). Irrespective of a possible impact directly on gametes and embryos, the risk of cross-contamination from LN_2/NV exists and may cause general symptoms, serious disease, death and further spreading (Scarica *et al.*, 2021). This fact has been acknowledged recently by many authors; they suggested implementing 'good manufacturing' practices in ART, including the use of single-personalized-disposable vitrification containers (Maggiulli *et al.*, 2020); the sterilization of liquid nitrogen before use (Arav, 2020; Alteri *et al.*, 2021); and the washing of cryopreserved specimens with sterile LN_2 before thawing/warming (Hickman *et al.*, 2020; Shapiro *et al.*, 2020). Even the Sixth Edition (June 2021) of the "*WHO Laboratory Manual for the Examination and Processing of Human Semen*" suggests (i) the sterilization of LN_2, (ii) the decontamination of cryopreserved specimens before warming and (iii) the periodic refilling of dewars/tanks with sterile LN_2 (World Health Organization, 2021). Last but not least, some scientists cited by Kteily *et al.* for articles published a decade ago have since changed their minds regarding the negligibility of contamination risk. They now suggest taking precautions for the safe use of liquid nitrogen (Pomeroy and Schiewe, 2020).

Accordingly, while we congratulate the authors for the interesting research article, we suggest reconsidering their general conclusion and focusing their statement on the area that has been investigated in their present work.

Conflict of interest

L.P. reports fees from Origio-Coopersurgical and is a shareholder of Nterilizer Srl. G.V. is a shareholder and CSO at VitaVitro Biotech Co., Ltd., Shenzhen, China.

References

Alteri A, Pisaturo V, Somigliana E, Viganò P. Reply: COVID-19 in liquid nitrogen: a potential danger still disregarded. *Hum Reprod* 2021;**36**:260–226.

Arav A. A recommendation for IVF lab practice in light of the current COVID-19 pandemic. *J Assist Reprod Genet* 2020;**37**:1543.

Hickman C, Rogers S, Huang G, MacArthur S, Meseguer M, Nogueira D, Portela R, Rienzi L, Sharp T, Ye H. Managing the IVF laboratory during a pandemic: international perspectives from laboratory managers. *Reprod Biomed Online* 2020;**41**:141–150.

Kteily K, Pening D, Diaz Vidal P, Devos M, Dechene J, Op de Beeck A, Botteaux A, Janssens S, Van den Abbeel E, Goldrat O *et al.* Risk of contamination of semen, vaginal secretions, follicular fluid and ovarian medulla with SARS-CoV-2 in patients undergoing ART. *Hum Reprod* 2022;**37**:235–241.

Maggiulli R, Giancani A, Fabozzi G, Dovere L, Tacconi L, Amendola MG, Cimadomo D, Ubaldi FM, Rienzi L. Assessment and management of the risk of SARS-CoV-2 infection in an IVF laboratory. *Reprod Biomed Online* 2020;**41**:385–394.

Parmegiani L, Vajta G. COVID-19 in liquid nitrogen: a potential danger still disregarded. *Hum Reprod* 2021;**36**:260.

Parmegiani L, Vajta G, Alikani M. Covid-19: airborne transmission is being underestimated, and Covid-19 in liquid nitrogen is a potential threat. *BMJ* 2020;**370**:m2720.

Pomeroy KO, Schiewe MC. Cryopreservation and IVF in the time of Covid-19: what is the best good tissue practice (GTP)? *J Assist Reprod Genet* 2020;**37**:2393–2398.

Scarica C, Parmegiani L, Rienzi L, Anastasi A, Cimadomo D, Klinger FG, Licata E, Sosa Fernandez L, De Santis L. SARS-CoV-2 persistence at subzero temperatures. *J Assist Reprod Genet* 2021;**38**:779–781.

Shapiro H, Zaman L, Kennedy VL, Dean N, Yudin MH, Loutfy M. Managing and preventing blood-borne viral infection transmission in assisted reproduction: a Canadian Fertility and Andrology Society clinical practice guideline. *Reprod Biomed Online* 2020;**41**:203–216.

World Health Organization. Chapter 6.3.3: risk of cross-contamination. In: *WHO Laboratory Manual for the Examination and*

Processing of Human Semen, 6th edn. 2021, 175. https://www.who.int/publications/i/item/9789240030787

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Reply: Risk of contamination with SARS-CoV-2 in ART

Sir,

We thank Vajta *et al.* (2022) for raising an important point regarding the conclusion of our manuscript (Kteily *et al.*, 2022). Out of the context of the paper, we agree that the sentence '*no additional measures to prevent staff or cross-patient contamination need to be implemented in the IVF and andrology laboratories*' could be considered as too reassuring in the general context of the pandemic. In our discussion, we discussed the need for the implementation of *additional* procedures for asymptomatic patients, assuming that all IVF centers already apply the 'good manufacturing practice' principles, independently of the COVID-19 pandemic (www.eshre.eu/guidelines).

The risk of cross-contamination during ART procedures, including the risk of accidental or external contamination of liquid nitrogen (LN_2), is present for many viruses and is extensively discussed in the literature. However, we would note that the use of sterile LN_2 and straw decontamination before semen warming mentioned by Vajta *et al.* are considered as 'other precautions that can be taken to avoid or limit contamination' if standard precautions such as the use of high secure straws or vapor N_2 cannot be secured (World Health Organization, 2021). Similarly, Pomeroy and Schiewe (2020) suggested the use of UV disinfected LN_2 in case of open devices systems. Finally, the opinion paper published by international laboratory managers actually questioned the use of sterile LN_2 for sample washing at warming (Hickman *et al.*, 2020).

Nevertheless, we agree that the risk of contamination of LN_2 through SARS-CoV-2 survival on surfaces and aerosol remains uncertain and requires further investigation. To reduce this risk, prevention measures have been implemented in all health institutions, including IVF centers, to reduce the risk of patients–staff and staff–staff contamination. Several scientific societies including ESHRE provide guidance regarding sanitary measures in IVF clinics. ESHRE published recommendations on triage questionnaire and testing strategies with updates according to the pandemic evolution as well as general sanitary measures such as the room disinfection procedures, distancing and the wearing of masks and gloves (https://www.eshre.eu/Europe/Position-statements/COVID19). Regarding IVF laboratory activities, the main principle is to strictly follow good laboratory practice (www.eshre.eu/guidelines) such as the use of high security straws and/or vapor phase storage tanks and pay particular attention to reduce exposure to native follicular fluid and sperm as much as possible by dilution and by using of individual closed containers (https://www.eshre.eu/Europe/Position-statements/COVID19). Our study confirmed that no additional measures should be taken to insure the safely handling of human material from asymptomatic patients in the IVF laboratory.

Conflict of interest

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References

Hickman C, Rogers S, Huang G, MacArthur S, Meseguer M, Nogueira D, Portela R, Rienzi L, Sharp T, Ye H. Managing the IVF laboratory during a pandemic: international perspectives from laboratory managers. *Reprod Biomed Online* 2020;**41**:141–150.

Kteily K, Pening D, Diaz Vidal P, Devos M, Dechene J, Op de Beeck A, Botteaux A, Janssens S, Van den Abbeel E, Goldrat O *et al.* Risk of contamination of semen, vaginal secretions, follicular fluid and ovarian medulla with SARS-CoV-2 in patients undergoing ART. *Hum Reprod* 2022;**37**:235–241.

Pomeroy KO, Schiewe MC. Cryopreservation and IVF in the time of Covid-19: what is the best good tissue practice (GTP)? *J Assist Reprod Genet* 2020;**37**:2393–2398.

Vajta G, Scarica C, Parmegiani L. Risk of contamination with SARS-CoV-2 in ART. *Hum Reprod* 2022;**37**:1095–1096.

World Health Organization. *WHO Laboratory Manual for the Examination and Processing of Human Semen*, 6th edn. Geneva: World Health Organization, 2021.

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