Letter: COVID-19 in liquid nitrogen: a potential danger still disregarded.

Sir,

We read with interest the article by Alteri and colleagues and their attempt to provide a pragmatic tool to rethink the appropriateness and safety of cryopreservation procedures critically in ART centres in the context of the current COVID-19 pandemic. Their SWOT (Strengths, Weaknesses, Opportunities and Threats) analysis on cryopreservation procedures of reproductive samples during the pandemic, including the attractive and informative figure, was extremely interesting (Alteri et al., 2020). To carry out their risk-analysis, they considered in detail the series of events that would need to occur for cross-contamination of a pathogen in the liquid nitrogen in an ART laboratory:

- i) damage to a storage container containing infected oocytes/embryos/sperm;
- ii) virus entry in another storage container;
- iii) virus interaction with the still non-infected oocytes/embryos/sperm.

Nevertheless, their risk analysis focused only on potential risks carried by infected gametes or patients. For a complete risk-analysis, we believe that we should focus on the real problem: the contamination of liquid nitrogen and nitrogen vapour (LN₂/NV), which can occur at any step (from manufacturing to final use including transport, storage, distribution and preparation for cryopreservation), rather than on the hypothetical presence of COVID-19 in our gametes and embryos. Airborne contaminants such as COVID-19 can come into contact with LN₂/NV and remain cryopreserved (Parmegiani et al., 2020). Aerosol and surface stability of COVID-19 has been investigated (van Doremalen et al., 2020), but the risk of this virus being accidentally cryopreserved in LN₂/NV has not yet been studied. The use of contaminated LN2/NV risks virus awakening and the contamination of warmed samples, environment, and operators.

In conclusion, the risks in this pandemic are not just related to contaminated patients, operators, cells and tissues, but to the liquid nitrogen itself. We would like to issue a warning about this risk, which is still largely disregarded; our plea to ART practitioners is not to underestimate the potential risk of LN2/NV-mediated COVID-19 infection and to put in place strategies to prevent this eventuality.

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Conflict of Interest Disclosures:

Dr Parmegiani reports fees from Origio-Coopersurgical, Merck, and Irvine-Fujifilm and is shareholder of Nterilizer Srl . Prof Vajta reported receiving personal fees and being a founder, shareholder and consultant to VitaVitro Shenzhen Pty Ltd.

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