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LETTER

Sperm washing – yes or no? An open issue still to be debated

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We are pleased that our recent publication (Fenizia *et al.*, 2020) has opened a constructive discussion (Garolla *et al.*, 2020). We agree with Garolla and colleagues that there are detrimental effects of human papilloma virus (HPV) on fertility and pregnancy outcomes, which is why we feel it is important to investigate some potential countermeasures. As stated in our paper, further studies should be performed. However, we would like to reply to the authors' specific concerns as follows: (i) PCR is the preferred designated method for virus detection, including clinical diagnosis of HPV (Depuydt *et al.*, 2019), HIV (Fearon, 2005) and SARS-CoV-2

in the current COVID-19 pandemic (Sethuraman *et al.*, 2020). Highly specific and highly sensitive, PCR allows HPV-detection of only a few copies in the whole ejaculate, including cell-free HPV in seminal plasma. Moreover, we believe that consideration of the findings of Song *et al.* (2017) scarcely apply to HPV detection, given that the aim there was to investigate intra-clonal heterogeneity in cancer, making bulk analyses inappropriate in that case; (ii) notoriously, HPV is still detected upon 'standard' sperm-washing procedures (Foresta *et al.*, 2011), as confirmed in Figure 1 in Garolla *et al.* (2020). However, we apply the 'combined' sperm-washing procedure, which differs from the

'standard' one (Fenizia *et al.*, 2020; Savasi *et al.*, 2007); (iii) thus far, there is no universal HPV-screening in assisted reproductive technology procedures and we aim to raise awareness of the potential importance of this step. We also recommend caution and we encourage other suitable beneficial approaches to be adopted, including an anti-HPV vaccine (Garolla *et al.*, 2018). Indeed, we believe that a joint, double-blinded study could be helpful in defining more appropriate guidelines, as proposed at the 2019 meeting of the Italian Society for the Study of Fertility and Sterility and Reproductive Medicine (SIFES-MR).

REFERENCES

- Depuydt, C.E., Donders, G.G.G., Verstraete, L., Vanden Broeck, D., Beert, J.F.A., Salembier, G., Bosmans, E., Ombelet, W. **Infectious human papillomavirus virions in semen reduce clinical pregnancy rates in women undergoing intrauterine insemination.** *Fertility and Sterility* 2019; 111: 1135–1144. doi:10.1016/j.fertnstert.2019.02.002
- Fearon, M. **The laboratory diagnosis of HIV infections.** *Can. J. Infect. Dis. Med. Microbiol.* 2005; 16: 26–30
- Fenizia, C., Vittori, C., Oneta, M., Parrilla, B., Granata, A., Ibba, S., Biasin, M., Clerici, M., Trabattoni, D., Savasi, V. **Human papillomavirus in spermatozoa is efficiently removed by washing: a suitable approach for assisted reproduction.** *Reprod. Biomed. Online* 2020; 40: 693–699. doi:10.1016/j.rbmo.2020.01.030
- Foresta, C., Pizzol, D., Bertoldo, A., Menegazzo, M., Barzon, L., Garolla, A. **Semen washing procedures do not eliminate human papilloma virus sperm infection in infertile patients.** *Fertility and Sterility* 2011; 96: 1077–1082. doi:10.1016/j.fertnstert.2011.04.009
- Garolla, A., De Toni, L., Bottacin, A., Valente, U., De Rocco Ponce, M., Di Nisio, A., Foresta, C. **Human Papillomavirus Prophylactic Vaccination improves reproductive outcome in infertile patients with HPV semen infection: a retrospective study.** *Sci. Rep.* 2018; 8. doi:10.1038/s41598-018-19369-z
- Garolla, A., De Toni, L., Menegazzo, M., Foresta, C. **Caution in the use of standard sperm-washing procedures for assisted reproduction in HPV-infected patients.** *Reprod. Biomed. Online* 2020
- Savasi, V., Ferrazzi, E., Lanzani, C., Oneta, M., Parrilla, B., Persico, T. **Safety of sperm washing and ART outcome in 741 HIV-1-serodiscordant couples.** *Hum. Reprod.* 2007; 22: 772–777. doi:10.1093/humrep/del422
- Sethuraman, N., Jeremiah, S.S., Ryo, A. **Interpreting Diagnostic Tests for SARS-CoV-2.** *JAMA* 2020. doi:10.1001/jama.2020.8259
- Song, Y., Tian, T., Shi, Y., Liu, W., Zou, Y., Khajvand, T., Wang, S., Zhu, Z., Yang, C. **Enrichment and single-cell analysis of circulating tumor cells.** *Chem. Sci.* 2017; 8: 1736–1751. doi:10.1039/C6SC04671A

Received 23 June 2020; received in revised form 6 July 2020; accepted 13 August 2020.

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