## Statement - COVID-19 Vaccination - Male and Female fertility, treatments to get pregnant, pregnancy

**REDLARA -** Red Latinoamericana de Reproducción Asistida (Latin American Network of Assisted Reproduction)

**SBRA -** Associação Brasileira de Reprodução Ássistida (Brazilian Association of Assisted Reproduction)

**Pronúcleo -** Associação Brasileira de Embriologistas em Medicina Reprodutiva (Brazilian Association of Embryologists in Reproductive Medicine)

**ASPAMER -** Asociación Panameña de Medicina Reproductiva (Panamanian Association of Reproductive Medicine)

**SAMER -** Sociedad Argentina de Medicina Reproductiva (Argentinian Association of Reproductive Medicine)

**AVEMERE** - Asociación Venezolana de Medicina Reproductiva y Embriología (Venezuelan Association of Reproductive Medicine and Embryology)

**SURH -** Sociedad Uruguaya de Reproducción Humana (Uruguayan Society of Human Reproduction)

**SBRH -** Sociedade Brasileira de Reprodução Humana (Brazilian Society of Human Reproduction)

**AMMR -** Asociación Mexicana de Medicina Reproductiva (Mexican Association of Reproductive Medicine)

**FPGO** - Federación Paraguaya de Ginecología y Obstetricia (Paraguayan Federation of Gynaecology and Obstetrics)

**AGFERH -** Asociación Guatemalteca de Fertilidad y Reproducción Humana (Guatemalan Association of Fertility and Human Reproduction)

More than two years into the SARS-CoV-2 pandemic, the effects of the virus on the male and female reproductive system remain controversial. On the one hand, men with active infection harbor the virus for a short period, from 2 to 11 days (Guo et al., 2021; Holtmann et al., 2020), symptoms eventually referred to reproduction organs can be simply attributed to hyperthermia and/or or hypoxia. Infections in remission showed the virus in the semen in 1.4% versus 6% of the cases evaluated in the active phase, not seeming to worsen the spermogram parameters. A single case described as a positive semen test at 21 days of recovery showed that the stable partner, under unprotected sex, tested negative with oropharyngeal, rectal and vaginal smears (Gacci et al., 2021), indicating viral RNA and not a live virus active in the semen. In women, one can theoretically expect compromise of the ovary, uterus and vagina, as well as the endometrium and breasts, with menstrual disorders and secondary infertility (Jing et al., 2020), effects that have also not been clear to date (Li et al., 2021).

A variety of vaccines for SARS-CoV-2 have been developed, at record speed, thanks to the efforts of the world scientific community, associated with some government and industry efforts (Garg et al., 2021). However, the World

Health Organization (WHO) has defined a situation of "vaccine hesitancy" (WHO, 2014), i.e., a delay or complete refusal to receive the vaccine, regardless of availability, with vaccines authorized through strict approval standards, with attenuated virus or m-RNA particles. Publications of false information that the incompletely inactivated virus or its particles have the potential ability to change the genetic information of an individual, could be introduced into the body, has negatively impacted patients who wish to become pregnant or even undergoing treatment to become pregnant, as well as pregnant women, lactating women and babies (Cha, 2021).

In this way, considering that:

- More than 4 billion doses of vaccines have been given (Chen et al., 2021) to date, the CDC- Vaccine Adverse Event Reporting System, among more than 72 million Americans vaccinated, has recorded a small number of mild menstrual disorders (NIH, 2021).
- Two recent studies demonstrate that vaccination had no influence on seminal parameters such as sperm concentration, seminal volume or sperm motility (Gonzalez et al., 2021; Safrai et al., 2022). Likewise, follicular steroidogenesis and oocyte quality did not differ between vaccinated and non-vaccinated individuals (Bentov et al., 2021).
- Also, Orvieto et al. (2021) recording parameters
  of IVF cycles, also reported no difference between
  total and mature eggs retrieved, fertilization rates,
  and high-quality embryos. Aharon et al. (2022)
  complemented the information that nothing different was evidenced in relation to the rate of pregnancies and ongoing pregnancies, comparing vaccinated and non-vaccinated patients.
- 4. Preconception vaccination or vaccination before the 20<sup>th</sup> week of pregnancy did not define a higher rate of spontaneous abortion in 2,456 pregnant women (Zauche *et al.*, 2021).
- There were no descriptions of placental compromise, perinatal or postnatal changes related to mRNA vaccines (Shanes et al., 2021), for women or their babies.
- IgA levels were detected in nursing mothers at 2 weeks after vaccination, with IgG index increased at 4 weeks (one week after the second dose of mRNA vaccines), suggesting protection for the baby (Romero Ramírez et al., 2021).
- The severity of COVID-19 illness, risk of death and adverse obstetric outcomes, and growing data on vaccine safety and effectiveness during pregnancy should outweigh any potential for individual adverse effects to the woman or her child.

The medical societies hereby represented recommend vaccination against the SARS-CoV-2 virus with the vaccine available, which should be encouraged with patients who are undergoing treatment to become pregnant, who are already pregnant, or even have recently given birth. To date, there is no evidence that the fertility potential of either men or women is affected by the use of vaccines.

## **REFERENCES**

Aharon D, Lederman M, Ghofranian A, Hernandez-Nieto C, Canon C, Hanley W, Gounko D, Lee JA, Stein D, Buyuk E, Copperman AB. In Vitro Fertilization and Early Pregnancy Outcomes After Coronavirus Disease 2019 (COVID-19) Vaccination. Obstet Gynecol. 2022. Epub ahead of print. PMID: 35080199 DOI: 10.1097/AOG.00000000000004713

Bentov Y, Beharier O, Moav-Zafrir A, Kabessa M, Godin M, Greenfield CS, Ketzinel-Gilad M, Ash Broder E, Holzer HEG, Wolf D, Oiknine-Djian E, Barghouti I, Goldman-Wohl D, Yagel S, Walfisch A, Hersko Klement A. Ovarian follicular function is not altered by SARS-CoV-2 infection or BNT162b2 mRNA COVID-19 vaccination. Hum Reprod. 2021;36:2506-13. PMID: 34364311 DOI: 10.1093/humrep/deab182

Cha AE. False claims tying coronavirus vaccines to infertility drive doubts among women of childbearing age. The Washington Post. 2021 Feb 21.

Chen F, Zhu S, Dai Z, Hao L, Luan C, Guo Q, Meng C, Zhang Y. Effects of COVID-19 and mRNA vaccines on human fertility. Hum Reprod. 2021;37:5-13. PMID: 34734259 DOI: 10.1093/humrep/deab238

Gacci M, Coppi M, Baldi E, Sebastianelli A, Zaccaro C, Morselli S, Pecoraro A, Manera A, Nicoletti R, Liaci A, Bisegna C, Gemma L, Giancane S, Pollini S, Antonelli A, Lagi F, Marchiani S, Dabizzi S, Degl'Innocenti S, Annunziato F, et al. Semen impairment and occurrence of SARS-CoV-2 virus in semen after recovery from COVID-19. Hum Reprod. 2021;36:1520-9. PMID: 33522572 DOI: 10.1093/humrep/deab026

Garg I, Shekhar R, Sheikh AB, Pal S. COVID-19 Vaccine in Pregnant and Lactating Women: A Review of Existing Evidence and Practice Guidelines. Infect Dis Rep. 2021;13:685-99. PMID: 34449637 DOI: 10.3390/idr13030064

Gonzalez DC, Nassau DE, Khodamoradi K, Ibrahim E, Blachman-Braun R, Ory J, Ramasamy R. Sperm Parameters Before and After COVID-19 mRNA Vaccination. JAMA. 2021;326:273-4. PMID: 34137808 DOI: 10.1001/jama.2021.9976

Guo L, Zhao S, Li W, Wang Y, Li L, Jiang S, Ren W, Yuan Q, Zhang F, Kong F, Lei J, Yuan M. Absence of SARS-CoV-2 in semen of a COVID-19 patient cohort. Andrology. 2021;9:42-7. PMID: 32598557 DOI: 10.1111/andr.12848

Holtmann N, Edimiris P, Andree M, Doehmen C, Baston-Buest D, Adams O, Kruessel JS, Bielfeld AP. Assessment of SARS-CoV-2 in human semen-a cohort study. Fertil Steril. 2020;114:233-8. PMID: 32650948 DOI: 10.1016/j.fertnstert.2020.05.028

Jing Y, Run-Qian L, Hao-Ran W, Hao-Ran C, Ya-Bin L, Yang G, Fei C. Potential influence of COVID-19/ACE2 on the female reproductive system. Mol Hum Reprod. 2020;26:367-73. PMID: 32365180 DOI: 10.1093/molehr/qaaa030

Li K, Chen G, Hou H, Liao Q, Chen J, Bai H, Lee S, Wang C, Li H, Cheng L, Ai J. Analysis of sex hormones and menstruation in COVID-19 women of child-bearing age. Reprod Biomed Online. 2021;42:260-7. PMID: 33288478 DOI: 10.1016/j.rbmo.2020.09.020

NIH-National Institutes of Health. Office of Extramural Research. Notice of special interest (NOSI) to encourage administrative supplement applications to investigate COVID-19 vaccination and menstruation (Admin Supp – Clinical Trial Optional). Bethesda: NIH; 2021 [Accessed 2021 Oct 19]. Available at: https://grants.nih.gov/grants/guide/notice-files/NOT-HD-21-035.html

Orvieto R, Noach-Hirsh M, Segev-Zahav A, Haas J, Nahum R, Aizer A. Does mRNA SARS-CoV-2 vaccine influence patients' performance during IVF-ET cycle? Reprod Biol Endocrinol. 2021;19:69. PMID: 33985514 DOI: 10.1186/s12958-021-00757-6

Romero Ramírez DS, Lara Pérez MM, Carretero Pérez M, Suárez Hernández MI, Martín Pulido S, Pera Villacampa L, Fernández Vilar AM, Rivero Falero M, González Carretero P, Reyes Millán B, Roper S, García Bello MÁ. SARS-CoV-2 Antibodies in Breast Milk After Vaccination. Pediatrics. 2021;148:e2021052286. PMID: 34408089 DOI: 10.1542/peds.2021-052286

Safrai M, Herzberg S, Imbar T, Reubinoff B, Dior U, Ben-Meir A. The BNT162b2 mRNA Covid-19 vaccine does not impair sperm parameters. Reprod Biomed Online. 2022. Epub ahead of print. PMID: 35279377 DOI: 10.1016/j. rbmo.2022.01.008 DOI: https://doi.org/10.1016/j. rbmo.2022.01.008

Shanes ED, Otero S, Mithal LB, Mupanomunda CA, Miller ES, Goldstein JA. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Pregnancy: Measures of Immunity and Placental Histopathology. Obstet Gynecol. 2021;138:281-3. PMID: 33975329 DOI: 10.1097/AOG.00000000000004457

WHO - World Health Organization. Report of the SAGE working group on vaccine hesitancy. Geneva: WHO; 2014. Available at: https://www.who.int/immunization/sage/meetings/2014/october/1\_Report\_WORKING\_GROUP\_vaccine\_hesitancy\_final.pdf

Zauche LH, Wallace B, Smoots AN, Olson CK, Oduyebo T, Kim SY, Petersen EE, Ju J, Beauregard J, Wilcox AJ, Rose CE, Meaney-Delman DM, Ellington SR; CDC v-safe Covid-19 Pregnancy Registry Team. Receipt of mRNA Covid-19 Vaccines and Risk of Spontaneous Abortion. N Engl J Med. 2021;385:1533-5. PMID: 34496196 DOI: 10.1056/NEJMc2113891