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The COVID-19 pandemic and reproductive health

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This introduction tees off an outstanding collection of Views and Reviews articles on the effects of the SARS-CoV-2 and COVID-19 on human reproductive health. These articles written by the experts in the field review the current literature on COVID-19 and male reproductive health, female reproductive health, and the assisted reproductive technology laboratory. Despite the prolonged nature of the pandemic and the number of people infected worldwide, there still are limited data on the effects of the virus and infection on human reproductive health and human fertility. The investigators distill a vast and often conflicting series of reports into a digestible summary to guide patient counseling and institute the safest practices into the assisted reproductive technology laboratory. (Fertil Steril® 2021;115:811–2. ©2021 by American Society for Reproductive Medicine.)

Key Words: COVID, embryos, gametes, human fertility, pregnancy, SARS-CoV-2

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The COVID-19 pandemic has had profound and shifting effects on the practice of reproductive medicine. Initially during the first wave in March 2020, it was guided by fear and a paucity of data, leading to cancellation of elective treatment cycles and near shutdown of in vitro fertilization (IVF) labs out of an "abundance of caution." Now, in January 2021, during the third and most severe phase of the pandemic to date, we soldier on with an intense fatigue given the duration and fluctuating demands of the pandemic, a wary optimism with vaccination of health care workers and first responders largely achieved and the at-risk patient population now the focus, better survival rates, and the abundance of data available on SARS-Cov-2 and COVID-19 (although there is still a paucity of conclusions). This Views and Reviews was constructed such that a cadre of investigators and experts in the field of reproductive medicine sifted through the voluminous and often conflicting data that has appeared to date. They have provided us with the current evidence of best practices in reproductive medicine in examining the role of the virus and COVID-19 on human reproduction and how best to counsel patients. It is divided into 3 parts with contributions from acknowledged thought leaders in each of the fields: an article on male reproductive health, one on female reproductive health, and one on the andrology and assisted reproductive technology (ART) laboratory.

Patel et al. (1) have assembled an all-star cast of experts in male reproductive health with representatives from the University of Utah as well as Cornell and Columbia Universities. Their article addresses some of the basic mechanisms of infection of SARS-Cov-2 as well as the human immune response and possible gender-related differences in that response. They also provide a thorough introduction of viral effects on the male reproductive tract by summarizing the effects of mumps, HIV-1, and Zika viruses before moving on to SARS-CoV-2. There are limited and conflicting data about the presence of the SARS-CoV-2 in semen, including limited reverse transcription-polymerase chain reaction data of viral presence. Recent data from a small case series have suggested infection of the testes in postmortem studies on the basis of immunohistochemical detection of the SARS-CoV spike protein, and electron microscopy has shown coronavirus-like particles suggestive of viral infection in the testes (2). However, the conclusions show that the data are limited and semen and male reproductive health effects of COVID-19 infection still are being established will be echoed throughout this series.

Joseph et al. (3) at Emory University in Atlanta, Georgia and at the University of Florida have reported the effects of COVID-19 on pregnancy and implications for female reproductive health. There still is uncertainty about whether there is any association between COVID-19 and early pregnancy loss and whether there is little association with any pattern of birth defects. There are stronger epidemiologic data that pregnant women with COVID-19 experience a more severe course with greater likelihood for hospital and intensive care unit

Received February 3, 2021; accepted February 3, 2021; published online February 6, 2021.
The author has nothing to disclose.
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Fertility and Sterility® Vol. 115, No. 4, April 2021 0015-0282/$36.00
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https://doi.org/10.1016/j.fertnstert.2021.02.003

admission and likely greater mortality risk. They are more likely to undergo cesarean section, but the indications are likely varied and not entirely because of maternal illness. Preterm birth also may be more common among infected women. Radical changes in the health care system have occurred, including the use of telehealth appointments for obstetric care that offer hope for the future in increasing access to care for underserved populations. The investigators make an impassioned plea for the inclusion of pregnant women in COVID-19 vaccine trials, identifying the substantial history of efforts to include such women in vaccine trials and the dismal results to date, although industry-sponsored COVID-19 vaccine trials in pregnant women and children are now underway. The most recent data regarding the effects of the vaccine on pregnancy are that a total of 18 women in the Moderna and Pfizer vaccine trials randomized to receive the active vaccine have conceived without any known vaccine-attributed morbidity. However, this is the same limited case series level of knowledge that precludes any definitive conclusions and leads to a lack of evidence-based guidance. Thus, the World Health Organization can switch its recommendations for maternal vaccination overnight from "against" to "for" (echoing the original positions of the Centers for Disease Control and American College of Obstetricians and Gynecologists).

Sparks and Kresowik (5) at the University of Iowa performed a thorough and systematic review of SARS-CoV-2 infection risks and practice guidelines for infection control in ART. They took a structured approach in their article as they assessed the risk for transmitting as well as best practices to prevent infection in an ART practice and laboratory. They identified 4 areas of potential risk for bidirectional infection in the ART clinic: patient to staff, staff to staff, staff to cell, and cell to cell. The review succinctly summarized the theoretical versus actual risk of these events, and there remains scant scientific evidence for most of the transmissions, especially staff to cell and cell to cell. The widespread introduction and acceptance of social distancing and universal use of personal protective equipment reportedly contribute to the low risk within the ART practice and laboratory.

This is likely not the last Views and Reviews that we will see on the effects of COVID-19 on human reproductive health and ART practice. As ongoing studies with long term follow-up are completed and as large registries disseminate data on post-infection and post-vaccination reproductive health issues, we will see a clearer picture of COVID-19 infection and human fertility.

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