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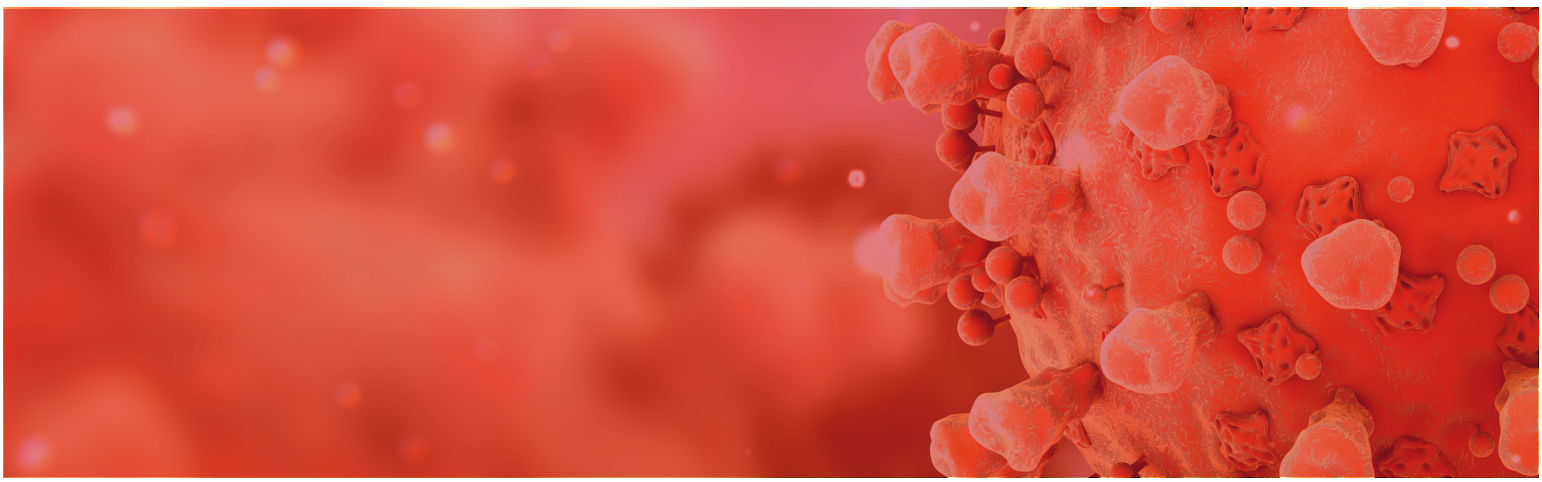
American Society for Reproductive Medicine

Impacting Reproductive Care Worldwide

Patient Management and Clinical Recommendations During the Coronavirus (COVID-19) Pandemic

As of March 17, 2020



PATIENT MANAGEMENT AND CLINICAL RECOMMENDATIONS DURING THE CORONAVIRUS (COVID-19) PANDEMIC

(as of March 17, 2020)

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KEY RECOMMENDATIONS

This ASRM guidance is in response to the coronavirus (COVID-19) global pandemic. Our goal is to provide practices with recommendations that guard the health and safety of our patients and staff, and recognize our social responsibility, as an organization and as a community of providers and experts, to comply with national public health recommendations. This guidance recommends the following:

1. Suspend initiation of new treatment cycles, including ovulation induction, intrauterine inseminations (IUIs), *in vitro* fertilization (IVF) including retrievals and frozen embryo transfers, as well as non-urgent gamete cryopreservation.
2. Strongly consider cancellation of all embryo transfers whether fresh or frozen.
3. Continue to care for patients who are currently "in-cycle" or who require urgent stimulation and cryopreservation.
4. Suspend elective surgeries and non-urgent diagnostic procedures.
5. Minimize in-person interactions and increase utilization of telehealth.

Note: This guidance will be revisited periodically as the pandemic evolves, but no later than March 30, 2020, with the aim of resuming usual patient care as soon and as safely as possible.

INTRODUCTION

Along with others in the global community, reproductive medicine professionals and their patients are battling an unprecedented viral pandemic. The priority of the ASRM is to maximize the wellbeing of patients, staff, and society at large. As such, ASRM aims to provide guidance and support based on existing scientific knowledge, to its members and the patients they care

for during the coronavirus (COVID-19) pandemic. This guidance addresses a gap in current guidelines addressing COVID-19, which only indirectly mention infertility and its treatment.

The recommendations laid out in this document are guided by COVID-19's steep daily rise in incidence, the impact of the virus on patient health and fertility care providers, and the known and unknown impact of coronavirus on fertility, pregnancy and transmission patterns. These recommendations are aimed at guarding the health and safety of patients and providers, while also recognizing that it is our social responsibility, as an organization and as a community of providers and experts, to comply with national public health recommendations and apply them to all reproductive settings during this unprecedented time.

The role of ASRM during this pandemic is to proactively do our share in blunting the impact of this pandemic, while recognizing the need to safeguard limited health infrastructure resources. However, we also understand our patients' time-sensitive aspirations to achieve pregnancy, and so we will regularly reassess these recommendations with a hope to resume initiation of comprehensive fertility care as soon as possible.

BACKGROUND

The world is facing a new viral pandemic, COVID-19 (Coronavirus Disease 2019), that has spread quickly owing to its rapid community transmission, high virulence and sustained surface viability. Many infected and contagious individuals may only have mild symptoms, including fever, or, more rarely, be asymptomatic. COVID-19 is a respiratory illness caused by the novel coronavirus Severe Acute Respiratory Syndrome (SARS)-CoV-2, a single-stranded RNA virus. For the purposes of clarity, we will use the term "COVID-19" to represent the viral respiratory disease and "coronavirus" to represent the SARS-CoV-2 virus.

The current spread of this new coronavirus has been rapid, and the infection rate has been exponential. Current infection rates and mechanisms of transmission can be found on the CDC Coronavirus website. Primary transmission is believed to occur through respiratory droplets from coughing and sneezing and contagion requires close proximity (less than 6 feet distance) between individuals (Cascella et al, 2020). The role of asymptomatic or pre-symptomatic viral shedding in transmission is not fully understood (Chan et al, 2019; Hoehl et al, 2020). The incubation period for COVID-19 is 3 to 7 days but can be as long as 2 weeks from infection to symptoms (Li et al, 2020).

COVID-19 is associated with fever and with mild symptoms (non-pneumonia and mild pneumonia) in approximately 80% of patients, severe disease (dyspnea, tachypnea, decreased blood oxygen saturation, or lung infiltrates) in approximately 14% of cases. Critical disease (respiratory failure, septic shock, and/or multiple organ dysfunction or failure) occurs in 5% of cases (Cascella et al, 2020; Wu et al, 2020). Many patients may be infectious 1-2 days prior to the onset of symptoms (Xu March 2020). Mortality rates range from 0.9% to 2.3% (Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020) with most deaths occurring in older individuals (>70 years old), those with critical disease, and/or those with coexisting medical morbidity (e.g., cardiovascular disease, diabetes, chronic respiratory disease, cancer, etc.) (Li et al, 2020).

While the flu causes a large number of deaths globally every year (estimated to be between 290,000 and 646,000 annually (Iuliano et al, 2018)), it should be noted that COVID-19 differs from the flu in a number of important ways:

- The pathophysiology, epidemiology and transmission dynamics of COVID-19 are not fully understood.
- There are currently no specific medications for the treatment of COVID-19. For example, there are no antiviral drugs licensed by the U.S. Food and Drug Administration (FDA) to treat patients with COVID-19. Some patients have received an investigational new drug, Remdesivir, through compassionate use outside of a clinical trial setting. At this time, it is unclear whether the drug can be used safely in pregnant or breastfeeding women.
- COVID-19 is a "novel" infection (new to humans) and host immunity is assumed to be minimal.
- COVID-19 is more contagious than the flu.
- COVID-19 has a 10 to 15-fold greater mortality rate than the flu.
- COVID-19 impacts the lungs differently than does the flu.

Bacterial pneumonia appears to be described more often in influenza infection than in coronavirus infection. Superimposed bacterial infection, if unsuccessfully treated with antibiotics, may potentially lead to sepsis, cardiovascular collapse and death. Not all COVID-19 patients will require hospitalization, and treatment is largely supportive (which might include invasive or non-invasive respiratory support).

Clinical deterioration with the development of acute respiratory distress syndrome (ARDS), characterized by rapid-onset and widespread pulmonary inflammation, bilateral non-cardiogenic pulmonary edema, severe hypoxemia and low alveolar ventilation/perfusion ratio, appears to occur in the second week of illness. Most deaths are associated with the development of ARDS.

Unlike regular bacterial pneumonia, there are no pharmaceutical treatments for ARDS, and the only treatment is mechanical ventilation. Twenty to thirty percent of hospitalized patients with COVID-19 and pneumonia have required intensive care for respiratory support. At this time, high-dose corticosteroids are not recommended due to concerns about prolonged viral shedding, as seen in cases of Middle East Respiratory Syndrome coronavirus (MERS-CoV) infection.

Together with other countries, the U.S. is facing an epidemic that is estimated to infect 96 million U.S. citizens in the coming weeks and months. The magnitude of the epidemic will strain the healthcare system and has the real potential to exceed its capacity. Unfortunately, testing and screening for coronavirus will be insufficient to contain the virus because it has already infiltrated communities across the U.S. in preceding weeks. Consequently, as the epidemic spreads across the U.S., the severity of the disease, the number of infected individuals, and the shortage of supplies, together make it necessary to suspend all non-urgent care, including fertility treatment.

Owing to the nature of spread and risk for increased mortality, societal demands must be considered in all our activities and recommendations. Primary approaches to address the public health impact of COVID-19 include containment, risk mitigation, including enhanced personal hygiene and social distancing, and resource optimization and preservation. Please refer to the CDC website for current guidance. Consequently, the following recommendations are based on the public health concepts of containment, mitigation, and resource optimization, and apply to all reproductive medicine practices regardless of setting, and take into consideration the health of patients, providers, physicians, clinical staff, and the population as a whole. These recommendations should be expected to change as the pandemic evolves. Therefore, to ensure the latest and most up-to-date guidance, ASRM will review this guidance no later than March 30th, and periodically thereafter as indicated.

RECOMMENDATIONS

These guidelines aim to mitigate risk for patients, physicians, nurses, providers, laboratory and clinical staff, and the community, and enhance critically needed resource conservation.

1) RISK MITIGATION AND SOCIAL DISTANCING

Optimizing the response to COVID-19 requires consideration of more than the medical implications of the virus itself on individuals, gametes, embryos, and fetuses. Lessons learned from past pandemics, and from countries in which coronavirus infection has already become widespread, suggest that public health strategies such as social distancing, crowd avoidance, and other techniques are crucial to "flatten the curve" of coronavirus dissemination.

ASRM recommends adherence to the following:

- Adhere to CDC infection prevention recommendations, which include appropriate hand washing, avoidance of close contact, and remaining home when febrile.
- Consider assessing patient health status, including body temperature, before gaining access into clinical spaces.
- Follow CDC healthcare facility recommendations regarding separating individuals with fever and respiratory symptoms.
- Follow CDC and your local health department guidelines regarding appropriate testing and quarantine, if warranted.
- Minimize the number of physicians, providers, and patients in clinic.
- Encourage nursing and staff conversations by phone.
- Limit the number of visitors to a single support person, or encourage alternative methods of participation, such as by phone or video.
- Implement procedures for staff to work virtually or from home, understanding that such arrangements need to be individualized.
- When urgent procedures must be performed, minimize the time the patient is waiting in the reception area or waiting room.
- Encourage cross-training of staff in the event of staff absences.
- Institute a system for telehealth for new and returning patients.
- To comply with public health authority recommendations for social distancing, reproductive medicine practices are encouraged to shift office-based practice to a telehealth model. Telehealth refers to the use of telephone or secure computer-based, audio-video in lieu of face-to-face, office-based consultations between a provider and patient.
- It is appropriate and encouraged to use telehealth to perform new patient consultations, follow-up consultations for existing patients, patient education in preparation for planned treatment, mental health consultations by mental health professionals, nurse counseling, and nurse counseling, as well as patient care coordination and administrative discussions.
- Some state governments have mandated that insurers cover a telehealth visit as if it was its in-office counterpart. Beyond government mandated changes, some insurers have responded to the COVID-19 pandemic and changed their policies to cover a telehealth visit as if it was its in-office counterpart.
- Conduct inventory of available personal protective equipment (PPE) and develop strategies to optimize use and supply.

2) PATIENT TRAVEL

Non-essential travel, especially to highly impacted areas, should be avoided when possible. Having large numbers of people congregating in travel centers (airports, train stations, etc.), and sitting closely in airplanes, trains, buses, etc. directly contradicts the principles of social distancing and could promote disease spread.

ASRM recommends adherence to the following:

- Implement a travel policy consistent with CDC travel guidance that limits business travel and discourages personal travel.
- Advise patients they should avoid travel to a reproductive care center outside of their country, state, or, in some cases, city, for the sole purpose of non-urgent IVF, egg donation, or gestational surrogacy.
- Implement alternative plans for care of the infant following delivery for those intended parents who have contracted with a gestational carrier in a region affected by travel restrictions.
- Utilize telehealth in circumstances when patients are geographically distant from their physician.

3) PRACTICE MANAGEMENT

Modifying or suspending the active in-person management of patients is consistent with the principles of risk mitigation and resource conservation.

ASRM recommends adherence to the following:

- Suspend initiation of new treatment cycles, including ovulation induction, intrauterine insemination (IUIs), in vitro fertilization (IVF), and non-urgent gamete cryopreservation.
- Continue care in cases that are urgent. For the purposes of this document, "urgent" refers to all treatment that is time-sensitive, such as impending gonadotoxic therapy or extirpative reproductive surgery.
- While age and diminished ovarian reserve are time-sensitive, at present these should not be included in the definition of urgent care.
- It is recommended that practices that are unable to provide urgent care refer patients to local community or regional partners, who have the relevant capabilities.
- Strongly consider cessation of embryo transfers, whether fresh or frozen, given the paucity of data surrounding the impact and potential risk of COVID-19 on pregnancy, the fetus and child well-being.
- Continuation of care should be considered and individualized for patients who have already initiated oral medications, such as clomiphene citrate or letrozole, or injectable gonadotropin therapy either for IUI, oocyte cryopreservation, or in-vitro fertilization.
- Treatment should be limited to a single cycle and further treatment postponed after cycle completion.
    - Patients who were planning to proceed with oocyte retrieval should be counseled to proceed with cryopreservation of embryos with plans for deferred transfer.
- Directed oocyte donation cycles, where the donor has begun ovarian stimulation, may be continued and embryos should be cryopreserved for future use.
- Suspend all elective surgeries, consistent with the recommendations of the American College of Surgeons.

- Suspend performing all non-urgent interventional diagnostic procedures, such as hysterosalpingograms.
- Counsel patients on the fact that risks of infection for the pregnant woman who develops COVID-19 are still relatively unknown (CDC) (SMFM) (Rasmussen et al, 2020).

Currently, there are no data on the risk of pregnancy complications when COVID-19 is acquired during the first or early second trimester of pregnancy. Other known coronavirus infections during pregnancy, such as SARS, have been associated with spontaneous miscarriage, preterm delivery, and intrauterine growth restriction (Wong et al, 2004).

Evaluate practice staffing models to ensure that the necessary physician, nursing, anesthesia, and embryology team members are available to provide any critically needed and urgent care.

4) MANAGEMENT OF THE EMBRYOLOGY AND ANDROLOGY LABORATORIES

A critical component of modern infertility therapy are the embryologists, andrologists, and their laboratories.

ASRM recommends adherence with the following:

Staffing and Equipment

- Laboratories should be staffed with the minimum number of personnel required to perform all quality control activities to ensure gamete and embryo safety and performance of urgent cases.
- Consideration should be given to rotating and cross-training lab members in the event of staff illness, exposure, or the need for quarantine.
- If all/majority of members of a laboratory team are quarantined, programs should either refer patients to a facility able to provide care or hire temporary embryology staff to maintain continuity of care.
- The CDC guidelines on safe laboratory practices should be followed.
- In-person interactions of laboratory staff with patients should be minimized.

Handling Specimens from COVID-19 Infected Individuals

- Patients with active COVID-19 should not undergo fertility treatment, unless they require urgent fertility preservation.
- Given the lack of evidence to suggest blood-borne, sexual, or transplacental transmission, special precautions, such as with HIV and hepatitis, are not currently required. As always, the use of universal precautions is imperative.
- Any laboratory spaces, biosafety cabinets, or incubators previously used for handling specimens from individuals infected with coronavirus should be thoroughly decontaminated with a disinfectant product that meets the U.S. Environmental Protection Agency (EPA)'s criteria for use against coronavirus; the manufacturer recommendations should be followed, including dilution, contact time, and safe handling. Such cleaning should be done immediately after use and before the equipment is put back into general service.

Tissue Storage

- Each clinic should develop and/or review their written emergency plans for tank storage and maintenance and ensure that tank maintenance continues without interruption.
- It is unknown whether cross-contamination may occur between stored tissues from coronavirus infected to non-infected samples. However, until proven otherwise, it is recommended that samples from coronavirus infected patients be handled in the same manner as tissues from patients who are seropositive for other infectious diseases.

5) PSYCHOLOGICAL HEALTH AND WELL-BEING OF PATIENTS AND STAFF

In order for all reproductive medicine teams to ensure that they are prepared and proactive in providing emotional and psychological support for patients and staff, it is essential that they understand the impact of the threat, how it manifests in patients, healthcare providers, and staff, and how mental health professionals are vitally important in addressing these needs in patients and staff alike. Patient and staff concerns include:

- The COVID-19 pandemic presents an unprecedented threat of unimaginable proportions to the psychological and emotional wellbeing of patients and staff.
- The invisibility and uncertainty of the pandemic may result in feelings of panic, terror, helplessness, hopelessness, and loss of control.
- Patient concerns include cancellation of treatment cycles and/or the inability to initiate a treatment cycle, fear of running out of time and never achieving pregnancy, the potential impact of the coronavirus and COVID-19 on pregnancy and the fetus, and the risk of exposure and infection in the medical office.
- Medical staff concerns include managing patient anxiety and questions, exposure or exposing others to COVID-19, childcare concerns with school cancellations, increased workload due to limited staffing, and financial uncertainty.

ASRM recommends adherence to the following:

- Practices should recognize the increased need for emotional and psychological support in both patients and staff. Mental health professionals should be utilized to help support patients and staff at risk for serious psychological or emotional issues.
- Practices should be prepared to facilitate the appropriate referrals when indicated.
- Telemental health should be used to increase accessibility to mental health professionals and to be consistent with social distancing practices.
- Mental health professionals also can be utilized to train staff on managing the increased demands of patients in crisis, to provide community resources for coping, and to provide psychoeducation on how to reduce the risk of traumatization.

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