The COVID-19 pandemic continues to impact the vast majority of the world. The experience of the past few weeks has highlighted a few features of the pandemic, including: a) increasing regional, socioeconomic, and ethnic variability in SARS-CoV-2 transmission and COVID-19 incidence; b) a resurgence in cases and deaths in the United States as efforts to reopen local economies and resuming work have been undertaken; c) the extended presence of the threat; d) the continued absence of an effective and safe vaccine and/or targeted therapies; e) the expanding availability and use of testing; and f) the need to ensure that essential medical care, including reproductive care, is provided in this environment, while maximizing the safety of patients, their families, and healthcare personnel.

Considering these observations, the present update by the ASRM Coronavirus/COVID-19 Task Force (the “Task Force”)

1 affirms the recommendations presented initially in Update No. 3 (American Society for Reproductive Medicine Patient Management and Clinical Recommendations during the Coronavirus (COVID-19) Pandemic - Update No. 3, April 24, 2020), when the Task Force issued recommendations for gradually and judiciously resuming the delivery of reproductive care, and which were elaborated upon further in Updates No. 4 and No. 5.

1 This guidance document was developed under the direction of the Coronavirus/COVID-19 Task Force of the American Society for Reproductive Medicine. These recommendations are being provided as a service to its members, other practicing clinicians, and to the patients they care for, during the coronavirus pandemic. While this document reflects the views of members of the Task Force, it is not intended to be the only approved standard of practice or to dictate an exclusive course of treatment. Clinicians should always use their best clinical judgment in determining a course of action and be guided by the needs of the individual patient, available resources, and institutional or clinical practice limitations. The Executive Committee of the American Society for Reproductive Medicine has approved this guidance document.

The ASRM Coronavirus/COVID-19 Task Force members for this update included Ricardo Azziz MD, MPH, MBA, Natan Bar-Chama MD, Marcelle Cedars MD, Christos Coutifaris MD, PhD, Mark Cozzi MBA, Jodie Dionne-Odom MD, Kevin Doody MD, Eve Feinberg MD, Elizabeth Hern MBA, Jennifer Kawwass MD, Sigal Klipstein MD, Paul Lin MD, Anne Malave PhD, Alan Penzias MD, Samantha Pfeifer MD, Catherine Racowsky PhD, Laura Riley MD, Enrique Schisterman PhD, James Segars MD, Peter Schlegel MD, Hugh Taylor MD, and Shane Zozula BS, in consultation with other experts.
Since the last update, the Task Force has observed the following:

- As of July 8, 2020, COVID-19 cases have exceeded 3 million in the US with over 133,000 deaths.
- In the past four weeks viral spread across much of the U.S. has increased 90% from the levels of disease present in late May, and rates of infection in the U.S. have risen to 60,000 new cases per day, the highest rates of infection to date.
- In 32 U.S. states infections increased sharply after reopening measures were instituted.
- As much of the U.S. is experiencing a rapid increase in cases, hospital resources have again become strained, as was observed in the North Eastern states earlier in the epidemic.
- The prevalence of disease continues to disproportionately affect Latino and African American individuals, infections are increasing in younger people overall, and availability of an effective vaccine still appears to be a long way off.
- Currently, many states and locales are re-instituting or instituting measures to reduce spread of disease.
- There is mounting concern that more restrictive recommendations similar to those presented initially by the Task Force on March 17, 2020 may need to be enacted in specific regions because of significant flares in the incidence of COVID-19, which are now affecting increasing numbers of individuals of reproductive age.
- The recent resurgence of viral transmission reaffirms that we will need to continue to practice in a COVID-19 environment for the foreseeable future.

As stated in Update No. 4 (American Society for Reproductive Medicine (ASRM) Patient Management and Clinical Recommendations During the Coronavirus [COVID-19] Pandemic – Update No. 4, May 11, 2020), and reiterated in Update No. 5 (published June 8, 2020), the Task Force continues to support the measured resumption of care with appropriate and prudent measures for disease prevention and implementation of travel restrictions and quarantines when appropriate.

In the current update, further information is provided regarding travel for third-party reproduction, COVID-19 and pregnancy, the importance of mitigation strategies, and concerns regarding COVID-19 and psychosocial dynamics. The next update from the Task Force will be in four weeks (on or about August 10, 2020), unless conditions warrant greater frequency.

THIRD PARTY REPRODUCTION
The Task Force reaffirms the “Third Party Reproduction Recommendations” provided in Update 4, and further elaborates, as follows:

- Given the continued restrictions on international travel, we recommend careful consideration of country of origin for intended parents, regional conditions in the gestational carrier’s state of residence and in the clinic where treatment is being sought. Careful consideration of local disease prevalence and adherence to travel restrictions should be factored into decision making for oocyte donation cycles where the intended parent and oocyte donor reside in different states.
- When possible, utilization of oocyte vitrification or shipment of frozen sperm for embryo creation should be considered as an alternative to travel when oocyte donor and intended parents reside in different states.
• **FDA guidance on donor/recipient eligibility for SARS-CoV-2** does not recommend additional donor screening for COVID-19 at this time. The ASRM Task Force recommends documenting whether the donor has had close contact with an individual who has tested positive for COVID-19, has had a positive test for COVID-19 in the absence of symptoms, or has presence of symptoms associated with COVID-19 infection such as fever, cough, shortness of breath, sore throat, anosmia and lack of taste. Temperature should be documented in the physical exam.

• If a testing strategy is employed either at baseline prior to cycle start or prior to retrieval or transfer, any donors or gestational carriers who test positive should have their cycle cancelled. Intended parents should be carefully counseled prior to stimulation start regarding this possibility.

• Even in circumstances in which the oocyte donor and recipient couple both reside within driving distance to the IVF clinic, consideration should be given to segmentation of the treatment process (planned cryopreservation of all embryos) if the local prevalence of COVID-19 is high. This will avoid initiation and then cancellation of the recipient treatment should the oocyte donor’s treatment need to be discontinued due to positive COVID-19 screening or testing.

PREGNANCY AND COVID-19

The Task Force reaffirms the “Pregnancy and COVID-19” information provided in Update 4, and further elaborates on this below, where new is italicized.

1. **What we know about the impact of COVID-19 on pregnancy:**
   • Full term newborns delivered from mothers with active COVID-19 infections have done well overall (Shalish et al, 2020).
   • Severe illness, including COVID-19, may precipitate premature labor or lead to early delivery with resultant neonatal complications of prematurity (Liu et al, 2020; Zhu et al, 2020).
   • A case series of nine women affected with COVID-19 that delivered via cesarean section showed no viral RNA in the amniotic fluid, cord blood, or breastmilk (Chen et al, 2020).
   • Preeclampsia was reported in six of eight women with severe COVID-19 pneumonia admitted to the intensive care unit while there were no symptoms of preeclampsia in 34 women with mild forms of COVID-19 (Rolnik 2020).
   • A study published in MMWR suggests that pregnancy is associated with increased risk for intensive care unit (ICU) admission and receipt of mechanical ventilation but is not associated with increased risk for mortality (Ellington et al, 2020). The authors highlighted several limitations to their study, including missing data on underlying conditions for a large proportion of cases. It is also worth noting that as of June 30, 2020, there were 10,537 cases of COVID-19 and 30 total deaths in pregnant women with COVID-19. Thus, pregnant women represent a small fraction of the 3 million cases and 130,000 deaths that have occurred overall in the U.S. Nonetheless, the report highlights the importance of taking measures to prevent infection in pregnant women.
   • Most women admitted to hospitals in the United Kingdom with SARS-CoV-2 infection tend to be in the late second or third trimester with 10% needing respiratory support, 1% dying, and 5% of neonates testing positive for SARS-CoV-2 RNA. Over half the admitted patients were from Black or other ethnic minority groups (Knight et al, 2020).
• In the U.S., one-third of pregnant women with laboratory-confirmed COVID-19 are hospitalized, compared to 5.8% of non-pregnant women. After adjusting for age, underlying co-morbidities, race and ethnicity, pregnant women are more likely to be admitted to an ICU, and receive mechanical ventilation. Despite this, the risk of death is similar to that of non-pregnant women (Ellington et al, 2020).

• A meta-analysis of 24 studies involving 136 COVID-19 infected patients revealed a preterm delivery rate of 38% and cesarean delivery rate of 76%, much higher than international averages (Matar et al, 2020).

• A prospective cohort study of 241 pregnant women from five New York city hospitals, all with laboratory-confirmed SARS-CoV-2 infection, demonstrated that the majority were asymptomatic; however, almost one-third of these women became symptomatic during their delivery admission. The worse the respiratory symptoms, the higher the rate of cesarean section, which reached a high of 92%, and the higher the rate of preterm delivery. Admission to the ICU was required for 7% of women and mechanical ventilation needed for 4%. Obesity was associated with COVID-19 severity (Khoury et al, 2020).

• Another prospective study analyzing data from 462 SARS-CoV-2 infected pregnant women in 11 New York city hospitals demonstrated an ICU admission rate of 19%, of which 15% died. Hispanic women constituted the largest ethnic group in the study (Blitz et al, 2020).

• The American Academy of Pediatrics recommends breast milk as the best choice for feeding newborns delivered even to women with COVID-19 as it an unlikely source of transmission of SARS-CoV-2 (American Academy of Pediatrics, 2020).

2. What we don’t know about the impact of COVID-19 on pregnancy:

• No data yet exist regarding the impact of SARS-CoV-2 infection on the fetus during the first or second trimesters of pregnancy. It should be noted that other maternal viral infections have been shown to impact the fetus even in the absence of direct fetal infection.

• Adverse perinatal outcomes have been reported (Mehan et al, 2020), but it is unclear whether these outcomes are directly related to COVID-19.

• Evidence of vertical transmission of COVID-19/SARS-CoV-2 is still unclear but possible, although data should be interpreted with caution:
  o Neonatal COVID-19 is uncommon and respiratory outcomes are favorable (Shalish et al, 2020). The outcomes of 217 neonates born to mothers with positive SARS-CoV-2 testing demonstrated no strong evidence for vertical transmission when delivery was via cesarean section (Shalish et al, 2020). Alternatively, a recent case report in JAMA (Dong et al, 2020) described the presence of IgM antibodies in the neonate at birth and suggested that vertical transmission may be possible.
  o Three other case reports suggested the potential for intrauterine infection. One described a 19-week pregnancy loss in a patient with active COVID-19 infection (Baud et al, 2020). The second reported the case of a woman at 22 weeks of gestation who elected to terminate; examination of the placenta and umbilical cord, but not the fetus, demonstrated the presence of SARS-CoV-2 (RNA) infection with macrophage infiltration (Hosier et al, 2020). The third report is of a patient with COVID-19 at 28 weeks gestation and rapid deterioration. The placenta was visualized using electron microscopy and coronavirus virions were seen invading into syncytiotrophoblasts in placental villi (Algarroba et al, 2020).
- Another case report documented birth of an asymptomatic neonate born to a woman with COVID-19 who tested negative at birth and at three days of life, but tested positive after 14 days of life, suggesting that infection may have been acquired postnatally (Buonsenso et al, 2020).
- There are also case reports that indicate no evidence of vertical transmission. One report described the case of a 38 weeks pregnant woman with hypertension and systemic lupus erythematosus with COVID-19. During labor and delivery, oropharyngeal, vaginal, urinary, placental, and neonatal samples were collected for PCR analysis for SARS-CoV-2. All PCRs, except for the oropharyngeal, were negative and vertical transmission was not observed (Grimminck et al 2020). A report of two cases of women infected with SARS-CoV-2 in the third trimester have been documented by maternal nasopharyngeal swabs collected after admission. Specimens of maternal serum, cord blood, placenta tissue, amniotic fluid, vaginal swab, breast milk, and newborn’s nasopharyngeal swab were collected at or after delivery. Serial qRT-PCR assays failed to detect SARS-CoV-2 in any of the specimens collected after delivery. Both babies developed low grade fever and lymphopenia that responded to antibiotics (Fan et al, 2020).
- Data are emerging on a form of coagulopathy associated with COVID-19 (DiRienzo et al, 2020). Whether this is directly related to the viral infection or is associated with hypertensive disorders of pregnancy, or with fetal growth restriction, is yet to be determined.

**MITIGATION STRATEGIES**

The originally localized foci of infection in the U.S. have evolved to a broader distribution with a progressive increase in the number of COVID-19 cases. While effective treatments are emerging and mortality rates might be decreasing, a vaccine is not yet available. As such, mitigation continues to hold a central and critical role in the prevention of disease spread. Evidence-based scientific observations have allowed recognition that the provision of medical care in this era will need to be undertaken in the context of disease mitigation for the foreseeable future. Mitigation strategies include early PCR testing for disease detection with isolation of affected individuals, ubiquitous mask usage and social distancing.

In the early days of the pandemic, the Task Force recommended halting all but the most urgent and time sensitive of fertility services. Once it was apparent that hospital resources would not be overwhelmed and that sufficient personal protective equipment (PPE) would be available, these restrictions were gradually loosened. The recent resurgence of COVID-19 cases in previously affected and new locales threatens the continued ability to safely provide reproductive care. More than ever, personal and societal responsibility must be focused on preventing disease and decreasing its burden on the healthcare system. Only with continued efforts to limit further transmission of infection can our ability to provide reproductive care be protected.

Scientific investigations have unequivocally demonstrated that universal mask wearing decreases disease transmission. Masks should be worn by patients and staff when within a medical facility without exception, even when alone or not in close proximity to others. This includes in areas such as bathrooms, changing areas and semen collection rooms.
Baseline PCR testing for COVID-19 should be encouraged prior to starting any type of fertility treatment and prior to surgical interventions. Additionally, given the lack of current data, a prudent strategy may be to encourage patients who test negative for COVID-19 to self-quarantine throughout the course of their treatment and ideally into early pregnancy.

During this pandemic, all individuals have a responsibility both to protect themselves and to act in the best interest of society. Universal mask wearing, strict adherence to social distancing, and viral testing for early detection and quarantine of affected individuals will not only protect patients and staff, but will help minimize community spread, limiting further infection in the current pandemic and maintaining a robust medical infrastructure for reproductive health.

COVID-19 AND PSYCHOSOCIAL DYNAMICS
As the ubiquitous and invisible COVID-19 pandemic continues, as local communities and the U.S. and world economy are attempting to re-open, and as therapeutics and a vaccine have yet to be developed, many in the healthcare community, including both providers and patients, are experiencing ongoing anxiety, emotional fatigue, and a sense of hopelessness. As a direct response to the unprecedented politicization of scientific data and unrelenting exposure to conflicting messaging we are witnessing a growing movement within society of non-compliance and even defiance of effective mitigation procedures (masks, social distancing, etc.). The reasons for these behaviors in the U.S. are complex, having to do with the intersection of individual, psychosocial, sociocultural, and sociopolitical factors in an individualistic society where personal freedom is highly valued.

As a result of this loosening and abandonment of safety procedures that are designed to protect public health, certain regions of the United States are experiencing an alarming increase in COVID-19 cases. Reproductive care providers need to be aware of local and personal attitudes affecting noncompliance with mitigation habits, and adjust clinic safety procedures accordingly. Medical personnel can have a powerful positive impact on individual and public health and on the acceptance of mitigation strategies by providing patients with accurate information about mitigation and protection procedures, by reinforcing prosocial behaviors around protection, by being positive role models, and by linking mitigation strategies and precautions to successful personal, as well as public, outcomes and protection from COVID-19.

REFERENCES
