AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE (ASRM) PATIENT
MANAGEMENT AND CLINICAL RECOMMENDATIONS DURING THE
CORONAVIRUS (COVID-19) PANDEMIC

UPDATE No. 12 - *January 18, 2021*
Testing and Vaccine Truths

It has been one year since the first case of COVID-19 was identified in the United States (U.S.). Despite the downturn in transmission rates in the U.S. during the summer months, the pandemic continues to have a firm grip on the nation, with most states experiencing a continued upswing in case numbers. At this time, there is widespread community transmission of COVID-19 and high numbers of hospitalized patients in most U.S. states. Given the morbidity and mortality of COVID-19, prevention remains a top priority.

In the current update, the ASRM Coronavirus/COVID-19 Task Force (the "Task Force")[1] continues to support strict adherence to its earlier recommended mitigation strategies for disease prevention, including use of Personal Protective Equipment (PPE), implementation of travel restrictions and quarantines when appropriate (see Update #3).

Additionally, the Task Force is issuing this update to assist reproductive care specialists in counseling their patients and their communities regarding the long-term effects of having suffered COVID-19, the new variants of SARS-Cov-2 being reported, truths about use of testing and vaccines for SARS-CoV-2, when to consider performing surgery after a COVID-19 diagnosis, and information regarding vaccine hesitancy and pandemic-related stress.

Since the last update published on December 16, 2020, the Task Force has observed the following:

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[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, John Petrozza MD, Samantha Pfeifer MD, Catherine Racowsky PhD, Enrique Schisterman PhD, James Segars MD, Peter Schlegel MD, Hugh Taylor MD, and Shane Zozula BS, in consultation with other experts.

- As of January 16th, the U.S. continues to lead the world in COVID-19 deaths and cases. COVID-19 cases now exceed 24.1 million in the U.S. with more than 399,000 deaths.

- At the time this update was published, daily cases in the U.S. exceeded 240,000, as compared with 252,000 on December 16, 2020 when the Task Force published Update No. 11. Statewide positivity and transmission rates differ markedly by region. Ten states have average daily case rates above 85/100,000, with Arizona (126.5/100,00) and California (107.9/100,000) leading, while nine states have average daily case rates below 40, with Hawaii having less than 20/100,000.

- As of January 17, 2020, the U.S. Food and Drug Administration (FDA) issued Emergency Use Authorizations (EUAs) for two SARS-CoV-2 vaccines in the U.S., one for the Pfizer-BioNTech COVID-19 vaccine (approved on December 11, 2020), and one for the Moderna vaccine (approved on December 18, 2020).

- There is variation in acceptance of vaccination among demographic subgroups with likelihood of getting vaccinated lower among women, individuals under 50 years of age, Black people, and those without a college degree (1).

COVID-19 long-term effects

While the majority of those infected will survive, the overall death rate from COVID-19 remains over 1% (https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days). It is increasingly recognized that some people suffer from long term consequences after COVID-19 infection. These lingering symptoms can include muscle weakness, sleep difficulties, anxiety, depression, hair loss, anosmia, joint pain, palpitations and decreased pulmonary function. In a recent study, 76% of patients hospitalized with COVID-19 reported at least one lingering symptom six months after infection, and this proportion was higher in women (2). Given the continued morbidity and mortality of COVID-19, prevention remains a top priority.

New SARS-CoV-2 Variant

SARS-Covid-2 is an RNA virus which can easily accumulate mutations and change over time. New viral variants of SARS-CoV-2 (N501Y) were first identified in the United Kingdom and South Africa in December 2020 and are rapidly replacing the current circulating strains of the virus in those regions. Over the past month, similar variants have been identified in 31 countries, including the U.S. These new variants have mutations in the receptor-binding site domain and appear to be more easily transmitted than the current strain. Studies are underway to compare viral shedding, transmissibility, and infection outcomes associated with new variants and the current strain.

COVID-19 Testing Truths

- Testing is useful to confirm a diagnosis of COVID-19 infection in a person with symptoms and to screen for asymptomatic infection (3). Two ways to test for active COVID-19 infection are: a) Polymerase Chain Reaction (PCR) nucleic acid amplification testing (NAAT), and b) antigen (Ag) testing.

- PCR testing for COVID-19 is highly sensitive and can detect a wide range of SARS-CoV-2 viral levels in a sample. This type of testing generally requires a dedicated laboratory with highly trained personnel. The turnaround time for PCR results can be rapid (within an hour) or not rapid (within

days), depending on the type of test that is used, local laboratory capacity, and testing demand.

- Rapid PCR assays can be performed as a point-of-care (POC) test by less trained staff. These tests tend to have lower sensitivity (81%) compared to standard PCR NAAT tests.
- Samples for PCR NAAT testing can be collected in a variety of ways. Recommended test collection methods include nasopharyngeal swab, mid-turbinate swab, anterior nasal swab, saliva, or a combined anterior nasal/oropharyngeal swab. Oropharyngeal swabs are less useful.
- [Newer Ag testing also detects active COVID-19 infection](). Ag testing is available as a rapid, inexpensive test that can be performed as a POC test and does not require specialized equipment. Samples are collected via nasopharyngeal or nasal swabs.
- [Ag testing is less sensitive than PCR NAAT testing](). A negative test may be falsely negative due to testing issues or the timing of sample collection, especially in a person with characteristic clinical symptoms or a high-risk exposure.
- Alternatively, both PCR and Ag testing have excellent specificity. A positive COVID-19 test by PCR or Ag should be assumed to be a true positive test.
- COVID-19 vaccination will not result in a positive PCR NAAT or Ag test.
- Most COVID-19 tests will detect new viral variants as well as the current strain. Specialized laboratory testing is required to distinguish between the new and older viral variants.
- Antibodies to COVID-19 are detectable in most people within 2 weeks of infection. Antibody (serologic) testing is not recommended when evaluating a person with COVID-19 symptoms. Although antibody testing may be positive after COVID-19 vaccination, most commercially available antibody tests detect nucleocapsid proteins. This is different from the spike protein antibodies induced by most COVID-19 vaccines.
- Strategies to reduce quarantine for those exposed or infected using symptom monitoring and diagnostic testing have been [updated by the U.S. Centers for Disease Prevention and Control (CDC)](). A 14-day quarantine is still recommended for those exposed to the disease, but the following options are available:
  - o Quarantine may end after day 10 without testing and if no symptoms have been reported (risk estimate approximately 1% with upper limit of 10%).
  - o Quarantine may end after day 7 if diagnostic testing within 48 hours of planned quarantine discontinuation, but not earlier than day 7 (risk estimate approximately 5% with upper limit of 12%).
  - o All exposed persons should monitor for symptoms for 14 days after exposure.

COVID-19 Vaccination Truths

Widespread vaccination is critical to slowing the spread of SARS-CoV-2 virus, reducing COVID-19 and bringing an end to the pandemic. While vaccination will be a critical strategy in our response to the pandemic, reaching population-level immunity on a global scale will take time. It is not yet known whether the vaccine will prevent those with asymptomatic or mild infections from spreading the virus. Until sufficient herd immunity is attained (whether via acquired or natural immunity and/or or vaccine-induced immunity), effective mitigation strategies including face masks, social distancing, hand washing, and staying home when sick will remain critical elements in reducing transmission, including for those who have already been vaccinated.

General COVID-19 vaccine truths include:
- Currently available mRNA-based COVID-19 vaccines from Pfizer-BioNTech and Moderna have

documented safety and efficacy in large randomized clinical trials, preventing up to 95% of severe disease.

- The known and potential benefits of these vaccines outweigh the known and potential harms of COVID-19 infection.
- Common side effects of vaccination include pain and swelling at the injection site, fever, chills, tiredness, and headache. These symptoms may persist for a few days. Side effects may be more significant following the second injection.
- Although COVID-19 variants demonstrate alterations in the spike proteins, early data suggest that mRNA vaccines may be effective against identified variants of COVID-19.
- There is a lag between vaccine administration and protection, a window during which infection can still occur, so mitigation strategies must be followed during this time. Those who have been vaccinated should continue to strictly adhere to mitigation strategies until data are available on the impact of vaccination on preventing asymptomatic and mild infection.

COVID-19 vaccine truths for patients desiring conception or who are pregnant include:
- Available data indicate that COVID-19 vaccines do not cause infertility in women or men.
- In the randomized blinded Pfizer-BioNTech trial, a similar number of women conceived after receiving the vaccine as those who received the placebo.
- The coronavirus's spike protein and syncytin-1 (protein that mediates placental cell fusion) share small stretches of the same genetic code but are otherwise completely different in structure. The vaccine does not induce an immune reaction against the syncytin-1 placental protein.
- mRNA vaccines are taken up rapidly by muscle cells at the injection site and the mRNA is degraded in the cell once the protein is made so it does not cross the placenta.
- COVID-19 vaccination is recommended for women who are contemplating pregnancy or who are pregnant in order to minimize risks to themselves and their pregnancy.

Elective Surgery After COVID-19 Diagnosis

The timing of elective surgery after a COVID-19 diagnosis should consider the risk for potential post-operative complications. Residual symptoms such as fatigue, dyspnea, muscle aches, and chest pain are common after COVID-19 infection and can last for more than 90 days. Additionally, there is concern that COVID-19 infection may have a profound negative impact on cardiac function. The American Society of Anesthesiologists and the Anesthesia Patient Safety Foundation have issued a Joint Statement on Elective Surgery and Anesthesia for Patients after COVID-19 Infection. The statement suggests wait times for elective surgery from the date of COVID-19 diagnosis. While data are limited, mostly based on cancer surgery and prior studies during the 2009 AH1N1 pandemic, this knowledge base has been used to create the guidelines depicted in **Table 1**.

Table 1. Guidelines to delaying elective surgery after COVID-19 diagnosis

COVID-19 Symptoms	Level of Care	Comorbidities	Approximate delay in elective surgery from diagnosis
Asymptomatic or non-respiratory symptoms (e.g., anosmia, GI symptoms)			4 weeks
Respiratory Symptoms	Not hospitalized	No DM or immunocompromised	6 weeks
	Not hospitalized	DM or immunocompromised	8 weeks
	Hospitalized		8 weeks
	ICU (requiring mechanical ventilation, NIPPV, HFNC)		12 weeks

Abbreviations: DM: type 2 is diabetes mellitus; GI: gastrointestinal; HFNC: high flow nasal cannula; NIPPV: non-invasive positive pressure ventilation.

These timelines should consider the patient's current residual symptoms, patient co-morbidities, and the risk of delaying the surgery. These guidelines do not discriminate between the use of general anesthesia, the need for intubation, sedation, monitored anesthesia care, or regional anesthesia, suggesting that surgical intensity (e.g., egg retrieval versus myomectomy) should be considered. Of note, these guidelines are not meant to be definitive, and will evolve as more information becomes available. A discussion with the anesthesiologist is advised. Finally, repeat testing for COVID-19 is not recommended by the CDC for *asymptomatic* patients within 90 days of symptom onset.

Vaccine Acceptance, Mental Health, and COVID-19

As COVID-19 cases rise and vaccines are becoming available, the lack of adherence to safe mitigation and vaccination practices presents a threat to the safe delivery of fertility services. Fertility clinics will benefit from learning about relevant obstacles and remediation strategies in order to reinforce adherence to safe mitigation and vaccination behaviors.

The novelty and enormity of the threat of COVID-19, combined with the specific safe mitigation recommendations and the emergent vaccines present unique challenges for behavioral change. Mitigation actions (masks, social distancing, isolation, and shutdowns) have been strange and unfamiliar. The speed with which the COVID-19 vaccines have been developed has been met with skepticism and mistrust. Lessons from the 1918 Spanish Flu (4) pandemic include: a) individuals do not appreciate the risks they undertake, b) people are resistant to social isolation, and c) people's dangerous behaviors may be unconscious. Developments in technology, social media, misinformation, the infodemic, politics, and many other factors have increased complexity of messaging and education.

Some key findings from a December 2020 Kaiser Family Foundation (KFF) poll describe trends in vaccination hesitancy:

- Positively, the share of the public saying they would *definitely* or *probably* get a vaccine has

increased, from 63% in September 2020 to 71%, and this increase is observed both across racial and ethnic groups, and among those identifying as either Democrat or Republican.

- About a quarter (27%) of public remains 'vaccine hesitant'.
- Vaccine hesitancy is highest among:
  o Republicans (42%).
  o People aged 30-49 years (36%).
  o Rural residents (35%).
  o Black adults (35%).
  o Essential workers (33%).
  o Those who work in a health care delivery setting (29%).
- The main reasons for vaccine hesitancy are:
  o Worries about possible side effects (59%).
  o Lack of trust in the government to ensure the vaccines' safety and effectiveness (55%).
  o Concerns that the vaccine is too new (53%).
  o Concerns over the role of politics in the development of the vaccines (51%).
  o Among Black adults, 47% do not trust vaccines in general and 50% are worried they may get COVID-19 from the vaccine.
- The most trusted source/s for information on COVID-19 vaccines are:
  o An individual's personal health care provider (85%).
  o Some local, state, and national messengers – including the CDC, the FDA, the head of the National Institute of Allergy & Infectious Diseases (Dr. Anthony Fauci), and state and local health officials.
  o Trust in government-affiliated sources divides along partisan lines, with Democrats tending to express higher levels of trust than Republicans.

Bavel and colleagues' recent appraisal from research in social and behavioral science (5) makes the following recommendations using social and behavioral science to support COVID-19 pandemic response:

- Communication must strike a balance between breaking through optimism bias, without inducing excessive feelings of anxiety and dread (appealing to fear only affects behaviors if people feel capable of dealing with the threat).
- Efforts should be made to promote shared values and cooperation.
- Utilize and create social norms.
- Stress leadership as role models.
- Consider that very different strategies might be called for in varying cultural contexts.
- Leverage online interactions to combat isolation and loneliness.
- Inducing more adaptive mind-sets about stress may increase positive emotion, reduce negative health symptoms and boost physiological functioning under acute stress.

Additionally, a study by Pennycook et al. (6) demonstrated that asking people to reflect on the veracity of vaccine information decreases misinformation from social media and increases accuracy. The American Psychological Association's Equity Flattens the Curve Initiative also suggests considering the following to increase vaccine acceptance and ameliorate pandemic-related stress:

- Community leaders, grassroots activists, as well as all types of healthcare providers, need to be able to recognize barriers to vaccination acceptance, while at the same time maintaining respect for individual differences.
- Different groups have been variously affected by the virus, with marginalized and economically disadvantaged groups bearing more cases and higher mortality rates.
- Vaccine acceptance is stymied by historical root causes, including unethical practices by public health systems directed at Black, Indigenous, and People of Color (BIPOC), religious traditions that prohibit vaccinations, anti-vaxxers, and the politicization of vaccine development.
- Trust in leadership and social norms can play a large part in building confidence in vaccine acceptance.
- Meeting people where they are, and tailoring interventions, is important.

The following are suggestions for Healthcare Providers:
- Be a trusted leader and a powerful role model.
- Ask patients, providers and clinic staff questions and help them reflect on their understanding of disease mitigation and vaccination information.
- Tailor these discussions appropriately with all parties.
- Reinforce accurate information and suggest reliable sources of information about safe mitigation and vaccination.
- Reinforce the importance of mitigation practices (masks, social distancing, etc.) and vaccination for the safety of self and others and encourage the development of social norms for these behaviors.
- Encourage the use of telemental health and support groups, and provide access to mental health resources (e.g., the ASRM Mental Health Professional Group) for all parties to promote resilience and help change mindsets through growth (7).

Note: The American Medical Association (AMA) has published an update to the Current Procedural Terminology (CPT®) code set that includes new vaccine-specific codes to report immunizations for the new coronavirus, SARS-CoV-2. Click here to view information about these codes.

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