The novel coronavirus disease 2019 (COVID-19) is a growing pandemic that is impacting daily life across the globe. Though disease is often mild, in high-risk populations, severe disease often leads to intubation, intensive care admission (ICU) admission, and in many cases death. The implications for pregnancy remain largely unknown. Early data suggest that COVID-19 may not pose increased risk in the pregnant population. Vertical transmission has not been confirmed. Because no treatment, no vaccine and no herd immunity exist, social distancing is the best mechanism available to protect patients and health care workers from infection.

This review will discuss what is known about the virus as it relates to pregnancy and then consider management considerations based on these data.

The severe acute respiratory syndrome–novel coronavirus-2 (SARS-CoV-2), also known as COVID-19, has emerged as a deadly global pandemic. Since its identification in Wuhan, China, in December 2019, over 1,000,000 individuals have tested positive, with likely hundreds of thousands more infected without a confirmatory diagnostic test in just 4 months worldwide.

The viral illness ranges in severity from a mild cold to pneumonia and death. At this time, the virus has been documented on every continent except Antarctica, with especially severe outbreaks in China, Italy, and New York City. Available data suggest the incubation period is approximately 5 days but can range from 2 to 14 days.1 The estimated reproduction number (Ro) for COVID-19 is between 2.2 and 2.35.2,3 Ro is a mathematical term that describes how infectious a disease or pathogen is. Said another way, this value is the average number of people who catch a disease from one contagious person. Infections are more severe and mortality markedly higher in individuals who are older than 50 years, or have underlying chronic illness such as heart disease and diabetes.4 Early data suggest that in the general population, 80% of cases are mild (nonpneumonia or mild pneumonia), 14% develop more severe disease, and 6% develop critical illness.5 Clearly, those with chronic respiratory conditions, such as asthma, chronic obstructive pulmonary disease, and cystic fibrosis, are also at heightened risk.

The virus is spread through respiratory droplets. Symptoms of the infection include fever, cough, dyspnea, myalgias, headaches, and gastrointestinal symptoms. A recent study suggested that approximately 42% of infected individuals will have both gastrointestinal and respiratory symptoms, and that those who presented with gastrointestinal symptoms had longer time from onset to admission and worse prognoses.6 Laboratory abnormalities include leukopenia, lymphopenia,
and in some cases thrombocytopenia. About 20% of infected individuals will develop severe disease, including a pneumonia with acute respiratory distress syndrome (ARDS)-like process.\textsuperscript{7,8} Those individuals develop pathognomonic findings on computed tomographic (CT) scan including ground glass abnormalities early in the disease course.\textsuperscript{5} Emerging data also suggest that the virus can affect the heart, causing a viral myocarditis and associated cardiac injury in patients with or without underlying cardiac pathology.\textsuperscript{10} At this time, COVID-19 does not appear to cause microangiopathy in the heart or in other vascular beds. The median time from symptom onset to intensive care unit (ICU) admission is 10 days.\textsuperscript{11}

Mortality rates are varied, though appear to be between 0.6 and 4% depending on population, though as not all infected patients are tested, the true denominator is unknown.\textsuperscript{11,12} Older patients, those with underlying medical conditions, and those with bacterial superinfection in the lungs, are at higher risk adverse outcomes (►Fig. 1).\textsuperscript{4,13} Mortality among these populations is also much higher. Specifically, as high as 6% for those with hypertension, 7.3% for those with diabetes, and 6.3% for those with chronic respiratory pathologies.\textsuperscript{10,14} Among hospitalized patients, mortality is as high as 13%.\textsuperscript{7} The median time from symptom onset to death is 13 days.\textsuperscript{1}

At this time, no treatment for the virus exists. Treatment in mild cases includes oral hydration and symptomatic relief. For severe cases, supportive care is the standard of care. The use of systemic corticosteroids for severe pneumonia has been associated with worse outcomes in influenza, SARS, and Middle East respiratory syndrome (MERS), and thus is not recommended at this time.\textsuperscript{15} Though one small nonrandomized trial of hydroxychloroquine and azithromycin suggested a decrease in viral burden, this study only included those with mild disease.\textsuperscript{16} A recent systematic review on this topic found that chloroquine may be effective at treating COVID-19, but its use should only occur in clinical trials or as part of the monitored emergency use of unregistered interventions framework.\textsuperscript{17} Though aggressive research efforts are underway, no vaccine is available at this time.

In this review, we will discuss the available evidence related to COVID-19 surrounding pregnancy, then discuss management considerations for infected pregnant women (and those who are persons under investigation), as well as noninfected pregnant women, during this time. In cases where no available data exist for COVID-19, we will draw on data from other recent coronavirus outbreaks, including SARS and MERS.

**COVID-19 in Pregnancy**

At this time, there are no reported cases of COVID-19 in the first trimester. Thus, the implications for miscarriage and teratogenicity are unknown. One case of first trimester MERS has been reported, and this pregnancy was uncomplicated.\textsuperscript{18} Among cases of SARS, where first trimester infection was noted in the setting of a documented intrauterine gestation with cardiac activity (\(n = 3\)), no anomalies or miscarriage was noted.\textsuperscript{19} In a recent epidemiologic study by Rasmussen et al, no association between exposure to circulating influenza and rates of spontaneous abortion was seen.\textsuperscript{20}

Data exist regarding infection in pregnancy is rapidly accumulating.\textsuperscript{21–24} At this time, in general, pregnant women do not appear to be at increased risk of developing COVID-19 compared with the general population. Additionally, unlike other respiratory infections, early data do not demonstrate
increased risk of severe infection among pregnant women. The report from China by the World Health Organization included 147 pregnant women, 8% of whom developed severe disease (defined as respiratory rate > 30 or oxygen saturation < 93%), and 1% developed critical infection (defined as need for mechanical ventilation or other system failure and ICU admission). Cases of severe maternal infection have been described, including need for extracorporeal membrane oxygenation (ECMO) and multisystem organ failure, though no cases of maternal death have been reported at time of this writing. Multiple smaller studies are emerging with a common theme, women who are receiving care for obstetrical reasons and are asymptomatic, but develop symptoms 2 to 3 days into their stay, often postpartum. The majority of the infections in these cases are mild. However, the exposure of health care workers during the asymptomatic phase of illness has led to significant impacts on the workforce in some centers.

The infection does not appear to increase the risk of preeclampsia. Nor did women with preeclampsia appear to have worse outcomes, compared with women with COVID-19 without preeclampsia. In accounts where delivery specific details are available, preterm prelabor rupture of membranes does not appear to occur at higher rates than the general population (n = 1, at 36 2/7 weeks). Preterm labor is not specifically described in any of these reports. Risk of preterm delivery is difficult to ascertain from the existing literature. Though some of the reported deliveries occurred preterm, the rationale for early delivery is not well documented and most were at greater than 36 weeks of gestation. However, other respiratory viruses have been associated with increased risk of preterm birth, including H1N1, SARS, and MERS. One case of intrauterine fetal demise has been documented with COVID-19, this occurred in the setting of multisystem organ failure and ECMO. Maternal critical illness is known to be associated with increased rates of fetal demise, especially in the setting of ECMO. In a recent review of ECMO for a variety of indications in pregnancy, fetal survival was approximately 65%. This review also analyzed influenza-related cases separately, where fetal survival was 71%.

Currently, in the published data relating to COVID-19, all pregnancies were delivered within 2 weeks of disease. Thus, the impact of COVID-19 infection on fetal growth in the setting of ongoing pregnancy is unclear. However, data from the H1N1 epidemic does suggest increased risk of small for gestational age infants. Similarly, though less data exist, women who were infected with SARS and remained pregnant also appeared to be at increased risk for intrauterine growth restriction.

At this time, vertical transmission of COVID-19 has not been confirmed. SARS and MERS also have no reported cases of vertical transmission. Early data from Chinese series show no virus in the amniotic fluid, vaginal mucus, cord blood, or neonatal throat swab at the time of delivery. Other series have also been reassuring for lack of vertical transmission. However, some smaller neonatal series have found very early infections in infants born to COVID-19-positive mothers. In one series, infants who had been immediately separated from a COVID-19-positive mother, have tested positive 2 to 3 days after delivery. In another report, an infant was born with elevated immunoglobulin (Ig)-M in the setting of strict infection control measures, suggesting possible infection during delivery, though authors state that vertical transmission cannot be ruled out. At this time, more rigorous studies are needed. In series from China, the vast majority of women were delivered via cesarean. However, that likely relates more to local delivery practices rather than obstetrical necessity. There are no reports of breast milk samples containing virus.

### Management Considerations during the COVID-19 Pandemic

#### Outpatient Care

In the current climate, because there is no treatment and no vaccine, the best option is prevention. The Centers for Disease Control (CDC) and the American College of Obstetricians and Gynecologists (ACOG) both recommend that all people avoid travel, gatherings of any sort, social visits, and going out to restaurants or bars. Clear data suggest that practices of social distancing are effective means to halt the spread of the pandemic. Additionally, it is recommended to frequently clean commonly touched surfaces, including computers, cell phones, counter tops, doors knobs, etc. When in public places, recommendations are to maintain a distance of at least 6 feet from other people as much as possible.

In health care settings, social distancing can be challenging. Providers should consider spacing out work stations or only using every other computer. Other measures to be considered include, ensuring computers and all work room surfaces are cleaned frequently, and alcohol-based hand sanitizer is added to work rooms. Many clinics are making safety huddles virtual. Health care systems are actively implementing aggressive screening guidelines for patients. Some clinics are having patients check in virtually or by phone from their cars, and then are “calling” them in and taking vitals in the clinic room. This practice avoids patients sitting in waiting rooms, as well as being exposed to each other in intake rooms.

With regard to prenatal care, many practices are spacing out visits for the appropriate low-risk patients. Though no formal guidance exists on this, Table 1 shows the format that our health care system has utilized, with Table 2 outlining who is defined as low-risk. For patients with diabetes who need blood glucose monitoring, consider telephone, or video visits. Home blood pressure cuffs with phone visits can also be used for patients with chronic hypertension or postpartum blood pressure checks. For patients who are receiving 17-P weekly in the clinic, consider having the patients’ transition to home administration. Makena (Walther, MA) has an order form and patients can sign the order sheet online to facilitate telehealth visits. The online order form is available at https://www.eprescribemakenaai.com/.

ACOG has designed a triage system which can be used over the phone for patients who are concerned they are infected.
or persons under investigation, as far as guidance about the appropriate clinical setting for evaluation (ACOG algorithm). Many women with mild infection and no comorbidities can be directed to stay home with symptomatic treatment, hydration, and rest. Testing of this population should occur based on local recommendations but clinical evaluation is not necessary.

To avoid unnecessary contact between infected patients and other patients or health care personnel, patients with active infection, as well as those under quarantine, without urgent issues, can often defer prenatal visits until outside of the infectious window. For those with urgent obstetric concerns or who need prenatal visits and are under quarantine, some areas have created COVID-19-specific obstetric clinics, such that all patients within a single health system could be seen in the same place, a practice known as “cohorting.” The goal would be to avoid exposure to noninfected patients. Clinical practices that cover multiple offices or inpatient settings may also consider “cohorting” providers. Another option to minimize contact is to tele-read ultrasound and then “video visit” into a room to review the findings of the exam with the patient. Some ultrasound units are utilizing more cine clips, from these clips, the sonographer or reading provider can obtain single-image capture after the fact to minimize time in the room. Many health care systems are initiating mask wearing for all clinical providers and patients, even in the outpatient setting.

For patients who recover from the virus and have not delivered, assessment of fetal growth may be considered given the elevated risks of growth restriction associated with other severe respiratory viruses. In the setting of normal fetal growth, antenatal testing is not indicated. Though some experts have suggested that the use of nonsteroidal anti-inflammatory medications could worsen symptoms, no studies have borne this out and thus ACOG continues to recommend the use of aspirin for prevention of preeclampsia in women at risk.

For women in the third trimester without a medical indication for delivery who become infected, providers may consider waiting until the patient is no longer within the 14-day quarantine period or the patient tests negative prior to induction or scheduled repeat cesarean depending upon gestational age. Many offices are offering virtual postpartum visits for the appropriately selected patients, such as those who are low risk, had mild or no perineal

### Table 1 Low-risk prenatal care visit schedule

<table>
<thead>
<tr>
<th>Gestational age (wk)</th>
<th>Proposed visit</th>
<th>Tests</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>8–12</td>
<td>Viability ultrasound New to nurse visit New OB provider visit</td>
<td>Aneuploidy screening (without ultrasound) Genetic counseling</td>
<td></td>
</tr>
<tr>
<td>12+</td>
<td>Return OB provider visit</td>
<td>Anatomy ultrasound</td>
<td></td>
</tr>
<tr>
<td>18–20</td>
<td>Telehealth visit–return OB visit</td>
<td>Schedule 6 wk from prior visit 3rd trimester laboratories TDAP vaccine</td>
<td></td>
</tr>
<tr>
<td>24–26</td>
<td>Telehealth visit–return OB visit</td>
<td>Schedule 4 wk from prior visit</td>
<td></td>
</tr>
<tr>
<td>28–30</td>
<td>Return OB provider visit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>32–34</td>
<td>Return OB provider visit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥37 until delivery</td>
<td>7–10 day return OB provider visits</td>
<td>GBS screen</td>
<td></td>
</tr>
<tr>
<td>Postpartum</td>
<td>Telehealth–1 week mood check</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: GBS, Group B Strep; OB, obstetric; TDAP, Tetanus, Diphtheria and Pertussis.

*Consider having aneuploidy screening with new OB laboratories depending on gestational age.

*Consider doing as video visit/telehealth.

As desired/indicated.

*Consider alternate nursing blood pressure check and fetal heart rate checks with return OB visit from 37–41 weeks if limited providers.

### Table 2 Risk stratification for altered prenatal care scheduling

<table>
<thead>
<tr>
<th>Low risk pregnancy</th>
<th>Low risk with extra ultrasounds</th>
<th>Additional telehealth visits may be needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothyroidism</td>
<td>Dichorionic-diagnomic twins</td>
<td>Moderate to severe anxiety/depression</td>
</tr>
<tr>
<td>Tobacco, cannabis use</td>
<td>Monochorionic–diagnomic twins</td>
<td>Posttraumatic stress disorder</td>
</tr>
<tr>
<td>No medical complications</td>
<td>Marginal cord insertion</td>
<td>Chronic hypertension</td>
</tr>
<tr>
<td>Prior cesarean section</td>
<td>Velamentous cord insertion</td>
<td>Diabetes (types 1,2 gestational)</td>
</tr>
<tr>
<td>Advanced maternal age (&lt;40)</td>
<td>Class-3 obesity</td>
<td></td>
</tr>
<tr>
<td>Pregnancy via in vitro fertilization</td>
<td>Placenta previa</td>
<td></td>
</tr>
<tr>
<td>Class 1 or 2 obesity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild anxiety/depression</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
lacerations, and whose contraception can be sent directly to their pharmacy. For patients who undergo cesarean delivery, skin closure with subcuticular suture is preferred to staples as it would prevent an in-person visit for staple removal.

**Inpatient Care**

Given the risk of asymptomatic viral shedding, some centers have begun universal screening of patients on labor and delivery. Many hospital systems have also implemented face masks for all health care personnel while in the hospital. When patients who are infected or person under investigation (PUI) need admission for an obstetric reason, all personnel who take care of the patient should wear appropriate personal protective equipment (PPE).

Visitor policies should be evaluated to limit potential exposures. Visitors should be screened for symptoms prior to admission to the unit, and then screened regularly if the patient remains in the hospital for more than a day. Some centers are not allowing any support persons on labor and delivery units, while others only completely restrict visitation for PUI or confirmed COVID-19 patients. Minimizing moving patients with COVID-19 from room to room is also important, thus consideration should be given to keeping the patient in the delivery room during the postpartum course if possible. Care providers who enter the room should also be minimized as much as possible. If room transfer is needed, the patient should wear a mask during transport between rooms.

Infection, even severe infection, is not necessarily an indication for delivery. Similarly, infection at term is not an indication for cesarean delivery, outside usual obstetrical indications. In rare cases, among severely ill pregnant woman in the third trimester, delivery may be necessary to improve respiratory status. There is no existing evidence that a passive second stage in the setting of mild to moderate infection is beneficial and usual indications for operative vaginal delivery may be employed. For the intubated and sedated patient who is in labor, a passive second stage may be considered. Standard antibiotics for group B streptococcal colonization or cesarean surgical site prophylaxis are still recommended.

For women hospitalized with COVID-19, corticosteroids for fetal benefit should be withheld after 34 weeks, even if delivery appears to be imminent, as there is evidence that systemic steroids are associated with poorer outcomes for people with COVID-19. Prior to 34 weeks, decision to give corticosteroids should be made on a case-by-case basis. Pregnant women with COVID-19 pneumonia should be managed with supportive care. Both chest X-ray and CT of the chest are considered safe in pregnancy with fetal shielding if deemed clinically necessary, and should not be withheld for fetal concerns. Vital sign norm parameters vary in pregnancy compared with the non-pregnant state. Thus when caring for pregnant patients with COVID-19, the threshold for care escalation may be different than that for nonpregnant patients. Oxygen saturation lower than 95% on room air, respiratory rate above 30, and pulse greater than 120 are appropriate triggers for evaluation and consideration of care escalation. Additionally, it is critical to note that acid/base parameter is different for the pregnant patient. As the obstetric provider caring for an intubated pregnant patient, it is important to ensure that the critical care team is aware of these different parameters, which vary from the nonpregnant state as early as the first trimester. Leftward tilt should also be considered when possible for intubated pregnant women to minimize veno caval compression by the gravid uterus. Fetal monitoring in critically ill patients should only occur as a noninvasive measure of maternal status or if delivery would not compromise maternal status. It should be noted that fetal heart rate changes in this setting may be related to changes in maternal hemodynamics, respiratory status, and/or acid base status, and correction of these often results in improvement in fetal status without the need for delivery. For pregnant women who are critically ill and/or immobile, prophylactic anticoagulation can also be considered. In the setting of maternal critical illness, need for ECMO, or decomposition, decisions about delivery are complex and require discussion with a multidisciplinary team.

After delivery, consideration of mother/infant separation, to minimize risk of transmission to the neonate is recommended by the CDC. The neonate can be cared for by a family member, wearing appropriate PPE. In cases where separation is declined or there are capacity constraints, a physical barrier should be placed in the room, and the bassinet should be more than 6 feet from the mother. The mother should also don a face mask and wash her hands prior to breastfeeding. In cases where separation is selected, pumping and receipt of bottled maternal breast milk is the recommended feeding method in these cases. Pump parts should all be washed with soap and water, and the pump itself disinfected according to manufacturer instructions. When possible, patients with COVID-19 or PUI should have their own designated breast pump during admission.

Inpatient care teams, including nursing, obstetric providers and anesthesia may consider running “COVID-19 simulation” to practice donning and doffing, as well as provider movements, in urgent scenarios, as these may vary from the usual workflow to ensure appropriate PPE use.

**Conclusion**

COVID-19 represents the largest pandemic of the century. The highly contagious nature and more severe infection phenotypes than other similar respiratory infections, along with rapid rate of spread have left many health systems overwhelmed with

| Table 3 Arterial blood gas measurement alterations in pregnancy |
|-----------------|-----------------|-----------------|-----------------|
| Arterial blood gas measurement | 1st trimester | 3rd trimester | Nonpregnant |
| pH                  | 7.42–7.46       | 7.43           | 7.4            |
| PaO2 (mm Hg)        | 105–106         | 101–106        | 93             |
| PaCO2 (mm Hg)       | 28–29           | 26–30          | 37             |
| Serum HCO3 (mEq/L)  | 18              | 17             | 23             |

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critically ill patients and understaffed due to quarantined and infected health care workers. Though, based on limited data, COVID-19 does not appear to be associated with worse outcomes in pregnant women than in the general population, many challenges still exist for the obstetric care provider. With social distancing as the best protective mechanism, prenatal care spacing and increased telehealth prenatal visits, are recommended to keep patients and providers safe. Infected, but otherwise low-risk pregnant women with mild disease do not need clinical assessment, and may be tested based on local practices. This population can likely have a telehealth visit or defer prenatal care for at least 2 weeks until no longer infected. COVID-19 infection, even when severe, is not necessarily an indication for delivery. If delivery is indicated for other reasons, operative delivery should be reserved for usual obstetric indications. Though there is no clear evidence of vertical transmission, for neonates born to infected women or PUI, mother/baby separation should be considered to avoid transmission through respiratory droplets. Pumped or expressed breastmilk can be given to the neonate via bottle. Though this mother/baby separation should be considered to avoid transmission, operative delivery should be reserved for usual obstetric indications. If delivery is indicated for other reasons, operative delivery should be reserved for usual obstetric indications. Though there is no clear evidence of vertical transmission, for neonates born to infected women or PUI, mother/baby separation should be considered to avoid transmission through respiratory droplets. Pumped or expressed breastmilk can be given to the neonate via bottle. Though this is pandemic is changing the way we provide prenatal care, following practices of social distancing and proper PPE use, should allow provision of safe care for women and their fetuses.

Conflict of Interest
None declared.

References
33. Chen S, Huang B, Luo DJ, et al. [Pregnant women with new coronavirus infection: a clinical characteristics and placental pathological analysis of three cases]. Zhonghua Bing Li Xue Za Zhi 2020;49(00):E005