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## Care of the COVID-19 exposed complex newborn infant

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## ARTICLE INFO

## ABSTRACT

As we confront COVID-19, the global public health emergency of our times, new knowledge is emerging that, combined with information from prior epidemics, can provide insights on how to manage this threat in specific patient populations. Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), both caused by coronaviruses, caused serious respiratory illness in pregnant women that resulted in adverse perinatal outcomes. Thus far, COVID-19 appears to follow a mild course in the vast majority of pregnant women. A significant proportion of pregnant women appear to be asymptomatic carriers of SARS-CoV-2. However, there is limited information on how COVID-19 impacts the fetus and whether vertical transmission occurs. While these knowledge gaps are addressed, it is important to recognize the highly efficient transmission characteristics of SARS-CoV-2 and its potential for causing serious disease in vulnerable individuals, including health care workers. This review provides perspectives from a single center in New York City, the epicenter of the pandemic within the United States. It offers an overview of the preparations required for deliveries of newborns of mothers with COVID-19 and the management of neonates with particular emphasis on those born with complex issues.

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### Background

At the time of this writing, the COVID-19 pandemic is racing across the globe with more than 4 million confirmed infections and 285,000 reported deaths.<sup>1</sup> The United States of America leads the world in the number of recorded infections (1.4 million) and deaths (88,730) thus far.<sup>2</sup> The pandemic surged in New York City, the epicenter of the pandemic within the United States in late March and early April 2020,

with more than 10,000 new cases/day at its peak.<sup>2</sup> Within 3 weeks of the first identified COVID-19 case in New York City on March 1, thousands of infected individuals were seeking medical care, including pregnant women. Even as the pandemic reached the United States, our understanding of how COVID-19 affects pregnant women and perinatal outcomes was limited. Knowledge of the impact of prior viral respiratory pandemics on pregnant women provided useful lessons as we monitored and prepared for the current public health crisis.

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## Coronavirus infections and perinatal outcomes

The four coronaviruses that generally circulate in humans—HCoV-NL63, HCoV-229E, HCoV-OC43 and HKU1—cause minor illnesses like the common cold.<sup>3</sup> Two new coronaviruses with greater pathogenic potential have emerged over the past two decades—Severe acute respiratory syndrome associated coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV).<sup>3</sup> A third novel coronavirus, SARS-CoV-2, is the causative pathogen of the current COVID-19 outbreak that is now rapidly spreading across the globe.<sup>4</sup> Through serial genetic evolution, recombination, and adaptation in their natural and intermediate animal host reservoirs, these three novel coronaviruses have acquired more virulent traits and have caused severe disease in human hosts.<sup>3</sup>

The first case of SARS was reported in the Guangdong province in China in November 2002 and spread to 26 countries, infected 8098 individuals and caused 774 deaths before the global threat was contained in July 2003.<sup>5</sup> SARS infection followed a more severe course in pregnant women than in non-pregnant women.<sup>6</sup> Sixty percent of pregnant women with SARS required intensive care unit admission, 40% received invasive mechanical ventilation and 30% died.<sup>6</sup> A pooled estimate of reports of pregnant women with SARS shows a 21% early pregnancy loss and a 38% preterm delivery rate.<sup>7,8</sup> There was one report of fetal demise and no neonatal deaths were reported. Two infants born several weeks after maternal infection were small for gestational age. It is unclear if the growth restriction was related to maternal illness or high dose steroid treatment. There are no reports of vertical transmission.<sup>7,8</sup>

Middle East respiratory syndrome was first reported in Saudi Arabia in 2012.<sup>9</sup> Since the original report, there have been 2494 laboratory confirmed cases of MERS with 858 deaths yielding a higher case fatality rate of 34% compared to SARS (10%).<sup>9</sup> There are limited reports of MERS infections in pregnant women. Of 11 women who were diagnosed with MERS during pregnancy, there were 3 reported deaths, 2 pregnancy losses and 3 premature births, including one neonatal death.<sup>10</sup> Again, there were no reports of vertical transmission.<sup>10</sup>

Our understanding of the impact of COVID-19 on pregnant women and perinatal outcomes continues to develop. Based upon limited and preliminary reports, predominantly from China, the disease course of COVID-19 in pregnant women appears to be unlike SARS or MERS.<sup>11,12</sup> As in the general population, the vast majority of pregnant women (86%) with COVID-19 experience only mild or moderate symptoms.<sup>11-12</sup> Moreover, universal screening for COVID-19 at presentation to the labor and delivery ward in our institution has uncovered asymptomatic infection in as many as 33% of expectant women.<sup>12</sup>

At the time of this writing and based upon published reports, we are aware of pregnancy and perinatal outcomes in 460 women with COVID-19 during pregnancy.<sup>11-27</sup> It is very likely that more women were infected during pregnancy than has been reported. There were 13 reported maternal deaths.<sup>13,14,27</sup> Fifteen pregnancy losses have been reported to date.<sup>11-27</sup> Of 448 neonates, 112 (25%) infants were delivered

prematurely, prior to 37 weeks. There were 5 neonatal deaths including one set of twins born at 24 weeks.<sup>11-27</sup> Birth weight was available in 69 infants, of these 13 neonates were born low birth weight (<2500 gs).<sup>11-27</sup> Compared to SARS and MERS infections during pregnancy, cumulative and preliminary analysis of published reports suggests that COVID-19 infections in pregnant women result in a lower maternal mortality, fewer pregnancy losses, lower rate of premature births and fewer neonatal deaths (Table 1).

Questions regarding vertical transmission of SARS-CoV-2 remain unresolved. Pooled estimate from published data to date report 28 positive results from 418 nasopharyngeal swab tests for SARS-CoV-2 in neonates.<sup>11-27</sup> While there are no reports of SARS-CoV-2 identified in amniotic fluid, umbilical cord blood or breast milk, there are 3 reports at the time of writing, of placental invasion of the virus.<sup>28-30</sup> Studies have detected IgM in newborns suggesting intrauterine infection but the sensitivity and specificity of these tests are unknown.<sup>16</sup> Moreover, intrapartum transmission through aspiration of the virus during cesarean or vaginal delivery cannot be excluded.<sup>25</sup> These conflicting findings support the need for additional studies to assess the risk of vertical transmission of SARS-CoV-2. For the time being, as this is an unresolved question, health care providers should continue to exercise appropriate precautions while caring for neonates born to mothers with COVID-19 until infection in the neonate has been excluded.

The sections that follow provide recommendations and considerations for the care of neonates born to COVID-19 positive mothers.

## Resuscitation

During the SARS epidemic in 2003, significant risk of transmission of infection to healthcare workers was recognized especially during aerosolizing procedures such as endotracheal intubation.<sup>31</sup> Modifications to usual resuscitation practices were developed through a simulation process of critical events in Toronto during that epidemic.<sup>32</sup> The practices developed in that process have informed practices during the current COVID-19 pandemic with modifications for different populations and environments.

At the time of birth, healthcare workers are exposed to two patients, the mother and the newborn infant. Even in the absence of vertical transmission, healthcare workers caring for the newborn infant could be exposed to maternal secretions carrying viral particles that remain present on the

**Table 1 – Pooled estimates from published reports (See text for references) of maternal mortality and perinatal outcomes**

| Outcome                     | SARS n (%)  | MERS n (%)  | COVID-19 n (%) |
|-----------------------------|-------------|-------------|----------------|
| Maternal mortality          | 3/19 (15.8) | 3/11 (27.3) | 13/422(3.1)    |
| Pregnancy losses            | 4/19 (21)   | 2/11 (18.2) | 15/463 (3.2)   |
| Neonates delivered          | 13          | 9           | 448            |
| Premature birth (<37 weeks) | 5/13 (38.5) | 3/9 (33.3)  | 112/448 (25)   |
| Neonatal death              | 0/13 (0)    | 1/9 (11.1)  | 5/448 (1.1)    |

infant or to droplet or airborne particles transmitted from the mother. Healthcare workers must take precautions to prevent viral transmission while also ensuring appropriate high-quality care to both the mother and newborn.

One of the principles of performing resuscitation during a highly transmissible infectious disease outbreak is to minimize healthcare worker exposure by utilizing the smallest team that will safely accomplish an effective resuscitation. Neonatal resuscitation at the time of birth varies in intensity depending on the condition of the newborn infant and is predictable based on risk factors. Many hospitals have team structures that allow for different sized resuscitation teams depending on the expected complexity of the resuscitation. When risk factors for neonatal resuscitation are present, the minimal recommended team composition includes 2 providers and increases to 4 or more providers for more complex resuscitations.<sup>33</sup>

During the COVID-19 pandemic, we have modified the neonatal resuscitation team composition based on both the complexity of expected resuscitation and the mother’s SARS-CoV-2 test status (Fig. 1). In order to minimize team members in the room, we utilize a “reserve” system for some team members to be outside of the room. It is important that the reserve team members are already wearing personal protective equipment (PPE) since the time it takes to don PPE can be 1.5–4.5 min.<sup>32,34,35</sup> In order to conserve PPE, some items such as the gown may be reused if the team members did not enter the patient’s room.

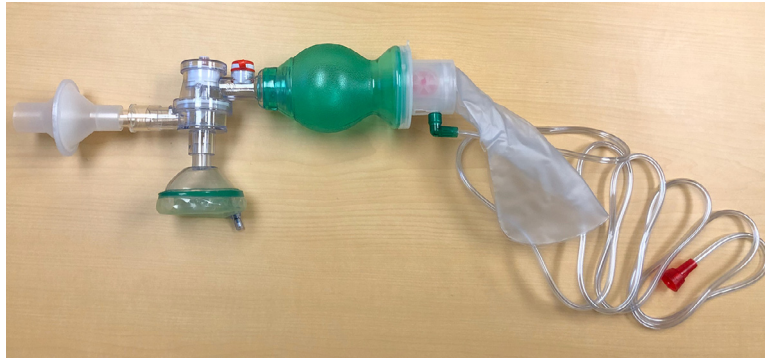
Maintaining a safe environment during a pandemic also includes keeping equipment and materials needed for resuscitation clean and unexposed to infectious particles. At the onset of the COVID-19 pandemic in our institution, we organized dedicated resuscitation carts that include all of the

supplies needed for resuscitation of potentially exposed infants, including PPE for the team members. The carts are kept outside the room; a separate team member is designated to pass materials inside the room if needed. We have found that communication between the team inside the room and outside the room is critical to the success of this process. We use mobile phones covered in plastic and place a call using speaker mode prior to the start of resuscitation so that the team members can easily communicate during the resuscitation. The team member who manages the cart is also assigned the task of “Event Recorder” which can only be accomplished with an open line of communication. In addition to the supplies cart, we also keep a dedicated transport incubator near the delivery room so that we can quickly move the infant from the delivery room to the NICU if the infant requires NICU admission.

Many of the interventions of resuscitation can lead to aerosolization of viral particles and therefore could increase the potential for transmission. Mask ventilation and endotracheal intubation are procedures commonly needed during neonatal resuscitation that have been identified as aerosolizing procedures.<sup>35</sup> Modifications to some of these procedures have been suggested to minimize the risk of transmission. A two-person technique for mask ventilation can minimize face mask leak and thus reduce risk of aerosolization. Placing a viral filter on the expiratory side of the ventilating device (Fig. 2) may also minimize the risk of transmission. The most experienced team member performs endotracheal intubation under videolaryngoscopy guidance (if available) to minimize the number of attempts, increase the distance between the clinician and the airway, and thus decrease the risk of transmission during the procedure.

| Guidance for Neonatal Resuscitation Team Attendance at Deliveries                           |   |  |  |
|---|---|--|--|
| “Low Suspicion” COVID19 Pending and Mother Asymptomatic                                     | “Confirmed or High Suspicion” COVID19+/PUI (symptomatic) Mothers  |  |  |
|   | No OB Risk Factors for Peds at Delivery   | Low OB Risk Factors for Peds at Delivery   | High OB Risk Factors for Peds at Delivery  |
| Peds Team will be called to attend deliveries for <b>OB Risk Factors only.</b>              | <u>In-Room Team</u>   | <ul style="list-style-type: none"> <li>• RN1</li> <li>• APP1</li> </ul>                                      | <ul style="list-style-type: none"> <li>• RN1</li> <li>• APP1</li> <li>• Fellow/Att1*</li> </ul>  |
| <ul style="list-style-type: none"> <li>• Team structure based on OB Risk Factors</li> </ul> | <u>Outside Room Team</u>  | <ul style="list-style-type: none"> <li>• APP1</li> <li>• RN1</li> <li>• RN2</li> <li>• Fellow/Att</li> </ul> | <ul style="list-style-type: none"> <li>• Fellow/Att/APP2</li> <li>• RN2</li> <li>• RT</li> </ul> |
|   |   | APP1 & RN1 in PPE  | Fellow/Att in PPE  |
|   | If resuscitation needed APP1 & RN1 enter room and Fellow/Att dons PPE   | If PPV needed Fellow/Att* enters room and brings ventilation equipment into room                             | If chest compressions needed Fellow/Att/APP2 enters room   |
|   |   |  | If baby needs meds – outside RN2 prepares and passes meds  |
|   |   |  | RT has vent ready for transport to NICU  |
|   | <div style="border: 1px solid black; padding: 5px; display: inline-block;"> <b>*The most experienced intubator performs intubation</b> </div> |  |  |

**Fig. 1 – Guidance for Neonatal Resuscitation Team Attendance at Deliveries.** Team members are designated as per our academic center organization. These specific roles could be modified based on an individual hospital’s resources. Fellow/Att signifies either a fellow or attending physician. RN 1 and 2 are NICU nurses. APP1 and 2 are Advanced Practice Providers.



**Fig. 2**–Self-Inflating bag set-up with viral filter on expiratory side (Arrow). We have chosen to place the viral filter in this location to avoid added dead-space on the inspiratory side.

The International Liaison Committee on Resuscitation has reviewed the available evidence for viral transmission of SARS-CoV-2 infection during resuscitation and offered guidance for providers.<sup>36</sup> While these recommendations are not intended for neonatal patients, they do include caution that cardio-pulmonary resuscitation could be an aerosolizing procedure and that appropriate PPE should be worn. They also suggest a two-person technique for mask ventilation, use of a viral filter on resuscitation equipment, and use of a videolaryngoscope for endotracheal intubation. It is likely that recommendations will evolve as more evidence for viral transmission becomes available during this pandemic.

### Care of the preterm infant of COVID-19 positive mother

Reported data from infants born to mothers with SARS-CoV-2 infection have generally indicated favorable outcomes.<sup>11-27</sup> To our knowledge, twenty eight neonates thus far had a positive test result from nasopharyngeal swabs.<sup>11-27</sup> Of these, we are aware of three neonates who were born prematurely, delivered between 31 and 33 weeks<sup>13,14,23</sup> and followed a clinical course consistent with their gestational age. It is currently unknown if newborns with COVID-19 are at increased risk for severe disease. For these reasons care of preterm infants should continue in accordance with the current standards. However, to protect the NICU health care workers from confirmed or suspected cases of SARS-CoV-2 infection, it is critical to consistently implement care practices that include proper isolation and cohorting, use of appropriate PPE and safe airway/respiratory care. In addition, it is imperative to maintain best feeding and bonding practices to improve overall neonatal outcomes. Thus, NICUs must establish necessary safety and best practices using guidelines from the Centers for Disease Control and Prevention and the American Academy of Pediatrics for the care of infants of COVID-19 positive mothers.<sup>37,38</sup>

#### Isolation and cohorting

All preterm infants born to mothers with confirmed or suspected COVID-19 (while awaiting test results) require isolation in a single room (if available) with contact/droplet

precautions. This isolation should preferably be in a negative pressure room (or single room with door closed) if aerosol-generating procedures (AGP) are performed, e.g., endotracheal intubation, nasal continuous positive airway pressure (NCPAP), non-invasive intermittent positive pressure ventilation (NIPPV), mechanical ventilation, or delivery of aerosolized medication. Infants should be kept in an incubator for at least 14 days and until tests are negative for SARS-CoV-2. When single rooms are not available, it is feasible to cohort infants of COVID-19 positive mothers who do not require AGP ensuring at least six feet distance between infants.

#### PPE for health care workers

Health care workers must wear a gown, gloves, eye protection (face shield or goggles), and surgical face mask when caring for a preterm infant with confirmed or suspected COVID-19. Although N95 respirators can be used when providing direct patient care to these infants, they are required for AGP.

#### Airway/Respiratory management

The main issue with providing any type of respiratory support to preterm infants with suspected or confirmed viral infection is the generation of aerosol-containing particles that can spread the disease.<sup>39</sup> This could happen due to the proximity to the infant's upper airway or through leakage from the interface or respiratory circuits. While there is a lack of scientific evidence on the use of various protective measures during AGP in preterm infants, physiology driven methodologies can be utilized for preterm infants with suspected or confirmed SARS-CoV-2 infection.

#### Manual ventilation

Studies in adults suggest that manual ventilation is not associated with increased risk of viral transmission and there is three times higher risk of acquiring a viral infection during endotracheal intubation compared to manual ventilation.<sup>40,41</sup> In a simulated adult lung injury model, Hui and colleagues have shown that lower tidal volumes produce less air dispersion.<sup>42</sup> Inexperienced health care workers may increase exhaled air dispersion by 40% during bag-mask ventilation.<sup>43</sup> These data suggest that in preterm infants, avoidance of manual ventilation merely for the purpose of preventing air dispersion may not be necessary.



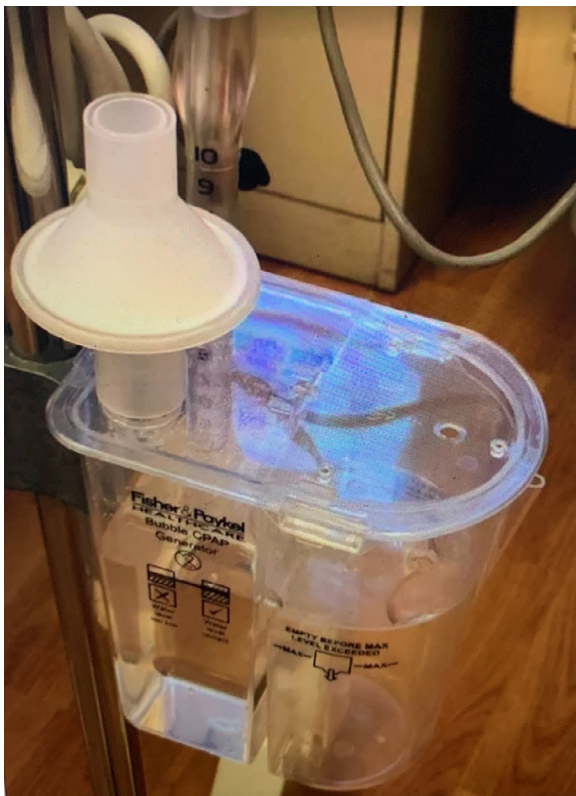
The use of viral/bacterial filters during manual ventilation is effective in reducing viral dispersion.<sup>43,44</sup> However, the addition of a filter adds weight, increases mask leaks and adds dead space that could interfere with effective ventilation. Thus, in extremely low birth weight infants it may be reasonable to avoid filters during bag and mask ventilation to avoid hypercapnia and its deleterious effects.

#### Airway care

Oral and nasopharyngeal suctioning are essential parts of airway care in preterm infants. Available information from systematic review of AGP suggest that airway suctioning is not associated with increased risks of SARS transmission.<sup>40</sup> However, studies in adults suggest that continuous suctioning is more effective in reducing aerosol dispersion as opposed to intermittent suctioning.<sup>43</sup>

#### Noninvasive respiratory support

NCPAP and NIPPV are used as first line of therapy for many preterm infants requiring respiratory support.<sup>45</sup> Nonetheless, there are concerns that using NCPAP or NIPPV during viral illnesses may result in droplet secretion dispersion as infected aerosols and nosocomial transmission. NIPPV can generate droplets  $>10 \mu\text{m}$  in size that may deposit onto the local surfaces that may serve as additional sources of infection.<sup>46</sup> Therefore, during the use of NCPAP or NIPPV essential risk mitigation strategies include: isolation in a well-ventilated negative pressure room with optimal air exchange, use of proper PPE, leakage avoidances around the interface, and addition of viral/bacterial filters on the exhalation port of the bubble NCPAP water reservoir (Fig. 3). The use of high-flow



**Fig. 3 – Bubble CPAP with viral filter on expiratory side.**

nasal cannula is not recommended as the high flow may be associated with a significant dispersion of viral particles.<sup>47</sup>

#### Endotracheal intubation

Tracheal intubation in adults has been shown to be consistently associated with SARS transmission to health care workers.<sup>40</sup> In neonates, no such data is currently available during endotracheal intubation for ventilation or surfactant administration. However, viral transmission is still biologically plausible due to close proximity to an infant's airway during the procedure. Thus, the most skilled available provider should perform this procedure using a cuffed endotracheal tube after donning proper PPE.

#### Mechanical ventilation

Preterm infants requiring mechanical ventilation should be isolated preferably in a negative pressure room with droplet precautions. Use of cuffed endotracheal tubes is recommended to minimize leaks and aerosol dispersion. Placement of viral/bacterial filter on the expiratory limb of the ventilator circuit may aid in capturing viral particles from the exhaled gasses. When performing endotracheal suction, a closed suction circuit with a viral/bacterial filter is recommended.

#### Testing infant for SARS-CoV-2

All infants born to COVID-19-positive mothers should have a nasopharyngeal swab specimen for SARS-CoV-2 obtained at 24 hrs of age. If the 24-hour test result are negative repeat testing should be performed according to symptoms and local testing resources, e.g., day of life 5 and 14. At our institution, our Infection Prevention and Control team recommends re-testing the newborn at 14 days and earlier if symptoms develop in the newborn (described in detail in other chapters of this edition of the Seminars). Exposed asymptomatic infants can be cleared of the COVID-19 status at 14 days, the incubation period of SARS-CoV-2. Discontinue transmission precautions 14 days after exposure if the infant's SARS-CoV-2 tests are negative.

#### Breast milk issues and kangaroo care

Though breastfeeding is ultimately a personal decision, the Centers for Disease Control and Prevention, World Health Organization and the Academy of Breastfeeding Medicine all support giving mother's breast milk to their infants even if they are infected with COVID-19. CDC has no specific guidance for breastfeeding during infection with similar viruses like SARS-CoV or MERS-CoV. Studies to date have not detected SARS-CoV-2 in breast milk<sup>15</sup>. Nothing is known about the passage of remdesivir, that is currently being used as a potential treatment, into breast milk. Limited data from other antivirals used in the treatment of influenza indicate that their active metabolite are poorly excreted into breast milk.<sup>48,49</sup> Risks and benefits of breast-feeding should be discussed with COVID-19-positive mothers of preterm infants who are considering breast feeding and appropriate breast, pump and hand hygiene should be observed between pumping sessions. Properly labelled bottles of expressed breast milk should be transported to the NICU by asymptomatic

caregivers not known to have had COVID-19. Kangaroo care can be initiated when mothers who were COVID-19-positive are cleared to visit the NICU.

### **Visitation in the NICU**

Visitation in the NICU should be limited to one asymptomatic designated visitor(s) as per the hospital visitor policies. Only the designated visitor(s) should be allowed for all infants of multiple gestation. Parents/guardian should be provided visitor letters explaining COVID-19 policies. All visitors must be screened prior to entry into the hospital and prior to entry into the NICU for symptoms consistent with COVID-19 including subjective or measured fever  $\geq 100^{\circ}\text{F}$ , cough, shortness of breath, sore throat, congestion/runny nose, muscle aches, fatigue, diarrhea, or loss of taste or smell. If the visitor develops symptoms or temperature  $\geq 100^{\circ}\text{F}$ , they must leave and cannot serve as the designated visitor. All visitors must wear a surgical face mask during their entire visit to the hospital. Visitors must practice hand hygiene before and after donning and doffing their PPE. Visitors' gowns and gloves must be donned before entering the infant's room or bed space and doffed before leaving the infant's room or bed space.

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### **Care of the infant with congenital heart disease born to a COVID-19 positive mother**

As this pandemic spread swiftly across the globe, hospitals have repurposed existing units to meet the surging demand for adult inpatient beds. In cities across the world, pediatric and cardiac intensive care units have been retooled to become adult intensive care units; staff from these units have been redeployed to care for adult patients. This creates logistical issues. Parents expecting to deliver babies with complex congenital heart defects (CHD) at a particular institution may find themselves redirected to other hospitals where care for pediatric patients continues. In such an environment, it is critical that information about the fetus and heart defect is shared with the new team so that adequate preparations can be made for the management of these complex newborns.

During the COVID-19 pandemic, approximately 25% of deliveries are reported to occur prematurely.<sup>11-27</sup> It is unknown whether decisions to deliver early are for maternal health or fetal distress induced by maternal hypoxia. Deliveries at earlier gestation including early term are associated with higher cardiac surgical mortality and morbidity burden.<sup>50</sup>

### **Resuscitation in the delivery room**

Preparations to attend deliveries of COVID positive mothers with fetuses with CHD are by and large no different than described in previous sections. Additional preparations are needed for infants who have critical CHD such as D-Transposition of the great arteries (D-TGA), explained in more detail below. Oxygen saturation by pulse oximetry may be lower than normal in neonates with critical CHD. The delivery team

should be aware of the unique transitional physiology associated with each CHD and the expected oxygen saturation so that interventions which have the potential to generate aerosols- high flow oxygen, NCPAP etc. are avoided if not necessary. After confirmation that oxygen saturations and pulses are adequate, neonates with critical congenital heart disease should be moved into an incubator and transferred to an intensive care unit with appropriate precautions to minimize the risk of viral transmission to health care workers and environmental contamination. A negative pressure room should be ready and prepared to receive the baby, who is considered person under investigation (PUI) until testing at 24 hrs and 14 days excludes infection in the newborn. We recommend that additional interventions including placement of invasive lines for monitoring such as umbilical arterial and venous lines and initiation of PGE-1 be done in the negative pressure room, if available. If apnea occurs secondary to PGE-1 use, CPAP may be utilized with viral/bacterial filter attached within the expiratory limb of the circuit to minimize dispersion of aerosols. Neonates ideally are placed within incubators to minimize exposure to health care workers. For full term infants, hyperthermia may occur in such instances due to environmental reasons in addition to PGE-1.

For neonates with TGA who require balloon atrial septostomy after birth, such procedures should ideally occur in a negative pressure room with the minimal number of providers required to perform the intervention safely. This generally includes a nurse, intensivist, echocardiographer and interventional cardiologist. All individuals within the negative pressure room should wear appropriate PPE including N95 masks if AGPs are going to be performed.

During the pandemic, local and state regulatory bodies are likely to have prohibited elective surgeries. In addition, operating room staff and equipment including ventilators previously reserved for use for pediatric patients may be in short supply. It is likely that each institution has policies or guidelines for surgical procedures with emergency surgeries taking precedence. Collaboration between maternal fetal medicine, fetal cardiologists, intensivists and surgeons should allow pro-active surgical decision making and timing so that surgery is not delayed. We recommend that surgical date be set after the results of the first COVID-19 test on the neonate performed at 24 hrs is available. Transportation to and from the operating room should be done in incubators.

Postoperative care of maternal COVID-19 exposed neonate should be no different from the routine practices of the unit with the exception that these infants will be in closed negative pressure rooms. This environment is certain to pose challenges to the care delivered. Serial bed-side surveillance and frequent examination needed for optimal care of these patients may be difficult with the physical discomfort posed by continual wear of PPE. To limit exposure to health care workers, minimal number of individuals necessary for optimal care should enter the room. Care, diagnostic and laboratory investigations should be clustered to minimize exposure of health care workers. However, although it is unknown, we expect the postoperative course to be no different in the PUI infant.

## Care of the complex neonate with non-cardiac surgical conditions born to a COVID-19 positive mother

### *Pre-delivery planning and postnatal management of surgical infants*

Special precautions are needed when attending the delivery of high-risk neonates born to COVID-19 positive mothers, particularly those that require immediate intervention in the delivery room e.g. congenital diaphragmatic hernia (CDH). PPE precautions and preparations for resuscitation mentioned in previous sections should be followed.

### **Timing of surgery and pre-operative COVID-19 testing**

If surgical intervention is required, a prolonged delay should be avoided. For example, in PUIs who require a surgical procedure such as a CDH repair or a decompression gastrostomy tube placement in a patient with a trachea-esophageal fistula and esophageal atresia, surgery will likely be required in the first week of life, regardless of PUI status. A testing scheme should be established that includes early (~24 hour) PCR testing for virus as well as testing within 24 hrs of any planned surgery.

While the timing of surgery may not be altered for a PUI baby, the surgical approach should be carefully considered. There is currently insufficient data recommending for or against an open versus laparoscopy approach specific to COVID-19.<sup>51</sup> Previous research has suggested a potential increase in aerosolization of blood-borne viruses during laparoscopic procedures, but there has been no consistent evidence that this occurs with COVID-19. Therefore, many surgical guidelines recommend choosing the appropriate surgical method individualized to each patient. If that involves a laparoscopic procedure then surgeons should utilize devices to filter released aerosolized particles. All surgical staff should still be aware of the possibility of viral contamination during an open, laparoscopic or robotic surgery and take all protective measures needed to maintain a safe environment to minimize risk of infection.<sup>52</sup>

Pre-operative COVID-19 testing is recommended in patients preferably within 24 to 72 hrs prior to a known procedure. With improved widespread availability of testing, our institution's turnaround time for the rapid PCR test is less than four hours, but this may be variable at each center. If the patient is transferred from an outside hospital for a surgical emergency, even if the outside institution's test is negative, if feasible, the test should be performed upon arrival given the risk of an invalid sample. If the procedure is emergent, such as a pneumoperitoneum in a neonate with necrotizing enterocolitis or volvulus, the neonate is presumed a PUI and special consideration should be undertaken by all surgical, neonatal and anesthesia staff to minimize viral transmission. Following surgery, the neonate should still be considered a PUI and placed back in a negative pressure room if available and kept in an incubator until his or her day of life 14 swab

returns negative upon which isolation precautions can be lifted.<sup>53</sup>

### *Tracheostomy and other airway procedures*

Although it is well established that SAR-CoV-2 is primarily transmitted via respiratory droplets and contact routes, airborne transmission may be possible in specific circumstances including endotracheal intubation, bronchoscopy, chest tube placement, and tracheostomy—all of which may be required in neonates.<sup>54</sup> Given the asymptomatic nature of the virus in pediatric patients, it is important to recognize that they potentially remain contagious even if asymptomatic. Similar to other surgical groups, the American Academy of Otolaryngology-Head and Neck Surgery recommends limiting care to time-sensitive and emergencies to reduce nosocomial transmission.<sup>55</sup> Similar to above, rapid COVID-19 testing should be performed in the neonate prior to a planned procedure such as a tracheostomy placement or a routine surveillance bronchoscopy.

### *Extracorporeal membrane oxygenation (ECMO)*

Although there have been no reported cases of infants requiring ECMO in the setting of a COVID-19 infection, cannulation is still a possibility in a neonate considered a PUI. In emergent cases such as meconium aspiration syndrome, persistent pulmonary hypertension of the newborn or CDH with refractory respiratory failure that occur early in life, it may not be feasible to obtain testing results in a timely manner. Therefore, providers should undertake extreme precaution, adopting consensus guidelines proposed by the Extracorporeal Life Support Organization (ELSO).<sup>56</sup> It is vital that standard COVID-19 protective measures are followed as recommended by the World Health Organization and other national health organizations during cannulation as well as during ongoing care of an ECMO PUI patient.<sup>57</sup> According to ELSO, standard cannulation techniques should be performed with only essential personnel, ideally in a negative pressure room or at least a single patient room (surgical team, ICU attending and/or fellow, two ICU nurses, one respiratory therapist and one ECMO perfusionist) all wearing standard, contact and airborne PPE. Because electrocautery is an aerosol generating procedure, N95 respirators along with eye protection should be worn by all members present.<sup>56</sup> Following cannulation, bedside care should be performed with as few personnel as safely possible for optimal care and should optimally be timed with blood draws, cannula dressing changes and patient repositioning. If the patient requires re-assessment, one provider, bedside nurse and perfusionist should assess the patient together to limit multiple entries into the room by several providers. Circuit evaluation and maintenance practices should also occur at the time of bedside cares with circuit adjustment parameters discussed with the medical team on rounds in order to minimize multiple providers entering the room. The role of chest physiotherapy and bronchoscopy during ECMO should be determined by patient need. Inline suction catheters are again indicated and used in association with a cuffed endotracheal tube.<sup>56</sup>



In order to ensure safety and success of cannulation in a PUI, following set guidelines and practicing in the form of simulation or video tutorials will aid in minimizing nosocomial transmission.<sup>58</sup> Providers should send rapid PCR testing as soon as possible given likelihood that following cannulation, a patient will remain on ECMO for at least a few days if not longer in order to also preserve PPE if the results are negative. In all these cases, there should be constant professional supervision and guidance as well as monitoring strategies to ensure that healthcare workers are aware of their own personal protection while caring for this high-risk neonatal population during the COVID-19 pandemic.

## Summary

The current COVID-19 pandemic has swiftly surged across the globe. The rapid spread across the world confirms the efficiency with which SARS-CoV-2 is transmitted. It has infected millions including pregnant women, infants and children. Very little is known about the impact of COVID-19 on pregnant women and their newborn infants. Emerging evidence points to a high rate of premature births in women who acquire COVID-19 during pregnancy. We do not yet know the impact of maternal COVID-19 on fetuses with complex cardiac or non-cardiac surgical malformations. As the possibility of vertical transmission exists, providers should exercise caution while caring for these complex newborns until infection has been excluded.

## Declaration of Competing Interest

The authors do not have any conflicts of interest.

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