بسم الله الرحمن الرحيم

COVID19 in NEONATES

Dr. Najib

Associate professor of neonatology

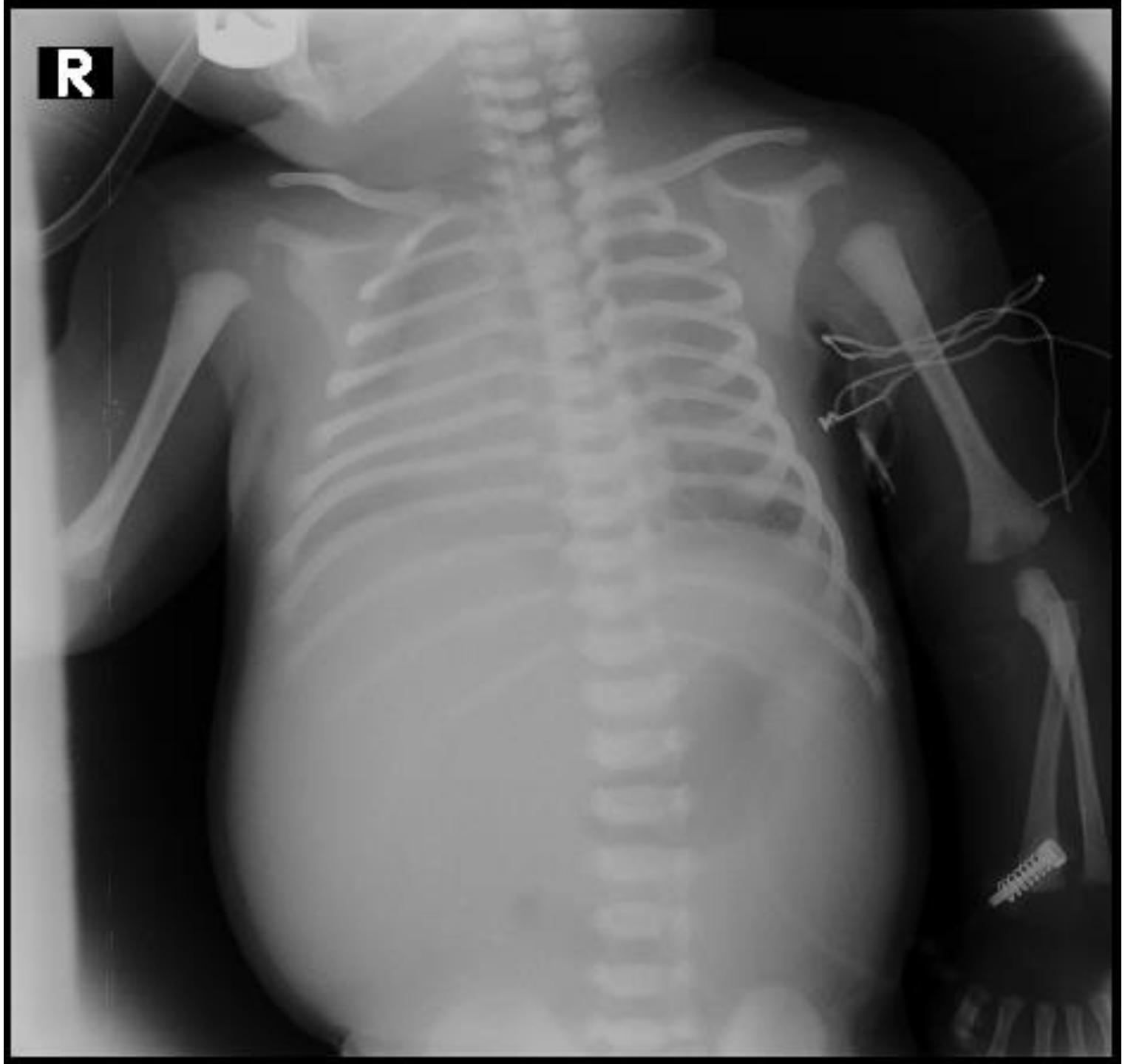
SUMS

1399.10.16

Objectives of this lecture

1. **clinical presentations**, **diagnoses**, and **outcomes** of COVID-19 infection in **neonates**.
2. neonatal **management** of COVID-19
3. the potential for SARS-CoV-2 **transmission during delivery**, **breastfeeding,** and **at-home childcare**.
4. methods to **reduce the horizontal transmission** of SARS-CoV-2 from mother to the neonate.


L


R

Multisystem inflammatory syndrome associated with COVID-19 (MIS-C)

- Multisystem inflammatory syndrome associated with COVID-19 (MIS-C) is a severe inflammatory syndrome occurring after SARS-CoV-2 infection in children and is characterized by inflammation of 2 or more organ systems and can present with severe shock.

Case report

- Infant With SARS-CoV-2 Infection Causing Severe Lung Disease Treated With Remdesivir

Claire Frauenfelder, MBBS, MSurg,[a,b] Joe Brierley, MBChB, FRCPCH, FFICM,[a] Elizabeth Whittaker, MRCPCH, DTM&H, PhD,[c]

Giulia Perucca, MD,[a] Alasdair Bamford, MRCPCH, DTM&H, PhD[a,d]

- PEDIATRICS Volume 146, number 3, September 2020:e20201701

Case report

- We describe an ex-premature infant presenting with severe acute respiratory syndrome coronavirus 2 infection in the fifth week of life.
- In current reports, researchers indicate that acute symptomatic severe acute respiratory syndrome coronavirus 2 infection is relatively rare and much less severe than in adults.

Case report

- This case highlights that infection can be associated with lifethreatening pulmonary disease in young infants and that infection can follow a similar disease course to that described in adults.
- We provide first data on the use of the **novel antiviral remdesivir** in a young child and an innovative approach to expedited **approval from a multidisciplinary clinical team and bioethics committee for compassionate access to the drug.**

Management (UpToDate)

- Antiviral therapy for COVID-19 should be reserved for children with documented severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection if testing is available

Management (UpToDate)

- Remdesivir is dosed according to weight as follows:

  - ≥3.5 to <40 kg: 5 mg/kg intravenous (IV) loading dose on day 1, followed by 2.5 mg/kg IV every 24 hours

Management (UpToDate)

- The usual duration of therapy is up to 5 days for children with severe disease; for children with critical disease who are not improving after 5 days, the duration may be extended to up to 10 days
- Reported adverse effects of remdesivir include nausea, vomiting, and transaminase elevations.

Management (UpToDate)

- We make decisions about the use of glucocorticoids for immune-mediated complications of COVID-19 on a case-by-case basis according to disease severity.
- Although glucocorticoids have been associated with decreased mortality in adult patients, trials in children are ongoing and the benefits and risks are uncertain.
- Pending results of these trials, administration of glucocorticoids ideally should occur in the context of a clinical trial.

Management (UpToDate)

- For select children with severe or critical COVID-19 who cannot participate in a clinical trial (ie, those who require mechanical ventilation or those who require supplemental oxygen and have risk factors for disease progression), low-dose glucocorticoids may be warranted; the duration of therapy is up to 10 days or until discharge, whichever is shorter.

Management (UpToDate)

- Low-dose glucocorticoid regimens include one of the following:
- Hydrocortisone For neonates (<1 month of age): 0.5 mg/kg IV every 12 hours for 7 days followed by 0.5 mg/kg IV once daily for 3 days

ASSESSMENT OF SEVERITY (UpToDate)

I. **Mild or moderate disease** – No new or increased supplemental oxygen requirement

II. **Severe disease** – New requirement for supplemental oxygen or increased requirement from baseline without new or increased need for ventilatory support (noninvasive or invasive)

III. **Critical disease** – New or increased need for noninvasive or invasive mechanical ventilation, sepsis, multiorgan failure, or rapidly worsening clinical trajectory

Clinical Presentation and Diagnosis

- In general, COVID-19 is thought to have a child-sparing pattern, and infected children are largely asymptomatic or have mild symptoms.
- Researchers estimate that only about **1%** of all confirmed or suspected COVID-19 cases have been in children younger than 10 years.

Clinical Presentation and Diagnosis

- It is hypothesized that pediatric populations with COVID-19 infections have milder manifestations compared to adults, because the **ACE2 receptor** in children may be immature and have lower binding affinity than in adults

Clinical Presentation and Diagnosis

- Importantly, infants seem more vulnerable to COVID-19 than other pediatric populations.
- It is estimated that **18%** of all pediatric COVID-19 cases are in infants **younger than 1 year**.

Clinical Presentation and Diagnosis

- manifestations of COVID-19 in neonates are often atypical and insidious.
- Many neonates with COVID-19 present with nonspecific symptoms such as poor feeding, diarrhea, or other mild gastrointestinalsymptoms,making COVID-19 challenging to diagnose in this population.

Clinical Presentation and Diagnosis

- Further, case reports describe that infants with COVID-19 may have more severe symptoms than children older than 1 year, and can present with late-onset sepsis, fever, and leukopenia.
- Because of its atypical presentation, standardized protocols are important for the diagnosis of COVID-19 in neonates.

Clinical Presentation and Diagnosis

- Some found that unlike adults, pediatric patients with COVID-19 did not have systemic inflammation.
- Other studies have reported lymphopenia, neutropenia, and thrombocytosis in neonates and children with COVID-19

Clinical Presentation and Diagnosis

- Thus, potential SARS-CoV-2 infection should be investigated in **neonates** presenting with **sepsis**, **lymphopenia**, or **neutropenia** without an identifiable cause, and neonates with normal proinflammatory cytokine levels should not be excluded from SARS-CoV-2 testing

Clinical Presentation and Diagnosis

- SARS-CoV-2 infection should also be suspected if infants have at least 1 clinical symptom, chest radiographic imaging showing ground glass opacities (in term infants) or pneumonia, or a history of close contact with a relative or caretaker with confirmed COVID-19.

Clinical Presentation and Diagnosis

- The diagnosis of COVID-19 can be made in children using reverse transcriptase polymerase chain reaction (RT-PCR) on nasopharyngeal or nasal samples to detect the presence of SARSCoV-2.

Clinical Presentation and Diagnosis

- ***Outcomes of COVID-19 in Children***: Children appear to be less susceptible to COVID-19 than adults and have good overall outcomes.
- Children are estimated to begin showing **symptoms around 6 days after infection.**

Clinical Presentation and Diagnosis

- Children infected with SARS-CoV-2 may have fevers that typically resolve within 24 hours and other mild symptoms dissipating within 1 to 2 weeks, though fecal viral shedding can persist neonates, children with underlying conditions, and children with coexisting viral infections are especially vulnerable to severe complications associated with COVID-19.

Clinical Presentation and Diagnosis

- **Neonates** may be at an increased risk for COVID-19 symptoms because of underdeveloped immune systems.
- Götzinger et al found that infants younger than 1 month had more severe manifestations of SARS-CoV-2 infections and were more likely to be admitted to the ICU.

Clinical Presentation and Diagnosis

- A recent multicenter, observational cohort study from New York City described 149 maternal-neonatal dyads hospitalized from March 1 to May 10, 2020.
- In this study, **12%** of neonates required admission to the **NICU**, with **10%** of these neonates delivered preterm and 3% requiring mechanical ventilation.
- Of note, neonates born to symptomatic mothers were more likely to be born **preterm** (16% vs 3%) and require **intensive care** (19% vs 2%).

Clinical Presentation and Diagnosis

- The potential complications of COVID-19 in infants make it imperative for physicians to counsel parents and caregivers on the symptoms associated with COVID-19 in neonates and **consider testing for COVID-19 if they have been in close proximity with other infected individuals**

Clinical Presentation and Diagnosis

- Vertical transmission of viruses can occur via **intrauterine** transmission (ie, blood, transplacental), **intrapartum**, or through **breastfeeding**.
- Respiratory viruses also can be transmitted postnatally via droplets from mother to child

Clinical Presentation and Diagnosis

- Although rare, cases of transplacental transmission and reports of SARS-CoV-2 in amniotic fluid, placenta samples, and positive nasopharyngeal swabs at birth indicate that intrauterine transmission may be possible

Clinical Presentation and Diagnosis

- **At birth**, SARS-CoV-2 was identified via **RT-PCR** in samples of **amniotic fluid**, **placental tissue, maternal and neonatal blood**, and **neonatal nasopharyngeal** swab.
- The **viral load** detected in **placental tissue** was substantially **higher** than that found in **amniotic fluid or maternal blood**.

Clinical Presentation and Diagnosis

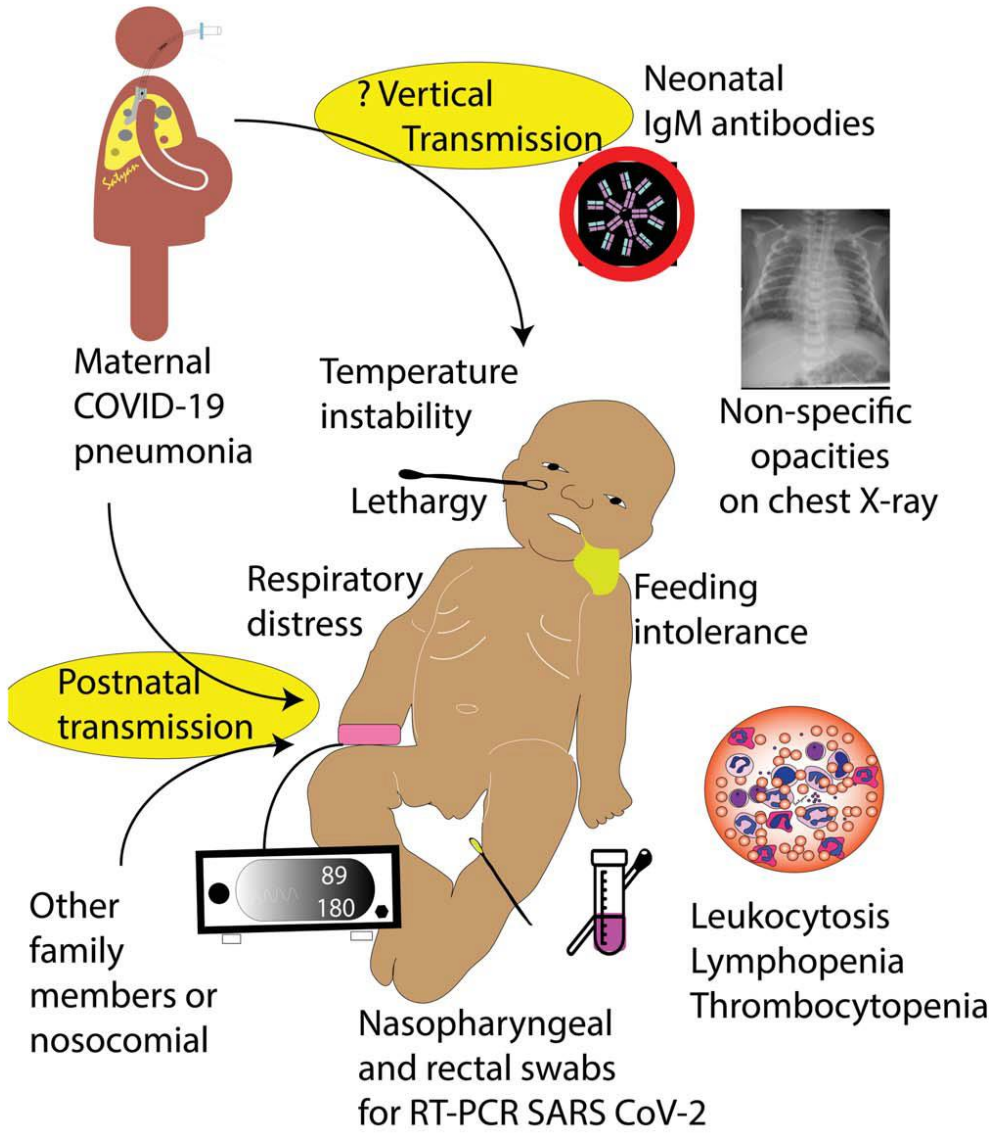
- Immunohistochemistry of placental tissue also showed considerable invasion of trophoblastic cells by SARS-CoV-2 and coexisting placental inflammation.
- Evidence of **high viral load in placental tissue** and **presence of SARS-CoV-2 in trophoblastic cells** support **transplacental transmission** in this case of neonatal congenital infection

Clinical Presentation and Diagnosis

- Neonates who are born to mothers with COVID-19 and test negative for SARS-CoV-2 at birth have promising outcomes. Approximately **2% to 5%** of **infants born to mothers with COVID-19** test **positive** for **SARS-CoV-2** infection within **24 to 96 hours after birth** and most have **favorable outcomes**

Clinical Presentation and Diagnosis

- Although most infants born to mothers with COVID-19 do well, complications such as respiratory distress and low birthweight may be seen at higher proportions in neonates born to mothers with COVID-19 compared with those born to mothers without COVID-19.



Onset: Early - first week
Late - 1 to 3 weeks after birth

Clinical Presentation and Diagnosis

- All neonates born to **mothers** who are **infected with or suspected** to have **COVID-19** should be **tested** for COVID-19 via **nasopharyngeal** or **nasal** swab RT-PCR and monitored for COVID-19 symptoms after delivery

Clinical Presentation and Diagnosis

- The **CDC** recommends testing the neonate at approximately **24 hours of age**, then again at **48 hours** of age **if the initial test results are negative.**

Clinical Presentation and Diagnosis

- Importantly, the optimal timing for testing the neonate remains unclear, and early testing can increase the chances of both **false positives** (ie, contamination of the naso-/oro-pharynx by SARS-CoV-2 RNA in maternal fluids) and **false negatives (RNA may not be immediately detectable after birth).**

Clinical Presentation and Diagnosis

- Caregivers for these neonates should use appropriate personal protective equipment until testing confirms lack of infection.
- Also, large-scale studies need to test amniotic fluid, umbilical cord blood, placental tissue, and neonatal pharyngeal swabs for SARS-CoV-2 to determine the rate of intrauterine transmission

SARS-CoV-2 Transmission During Delivery

- Maternal-neonatal transmission of SARS-CoV-2 is unlikely in both vaginal and cesarean deliveries.
- However, given the **lack of evidence that cesarean delivery is superior to vaginal delivery** for pregnant women with COVID-19

SARS-CoV-2 Transmission During Delivery

- Moreover, cesarean delivery requiring transportation of patients from the ICU to the operating room may increase the risk of SARS-CoV-2 transmission to both hospital workers and other patients.
- **Vaginal delivery has been proven safe for both pregnant women with COVID-19 and their neonates**

SARS-CoV-2 Transmission During Delivery

- **Horizontal Transmission** of SARS-CoV-2 Close contact with an infected person, usually the parent, **is the most likely cause of SARS-CoV-2 transmission to a neonate**
- Wu et al found that **95.6% of COVID-19** cases in children were caused by **transmission from an infected parent**.

Stabilization and Resuscitation of the Neonate

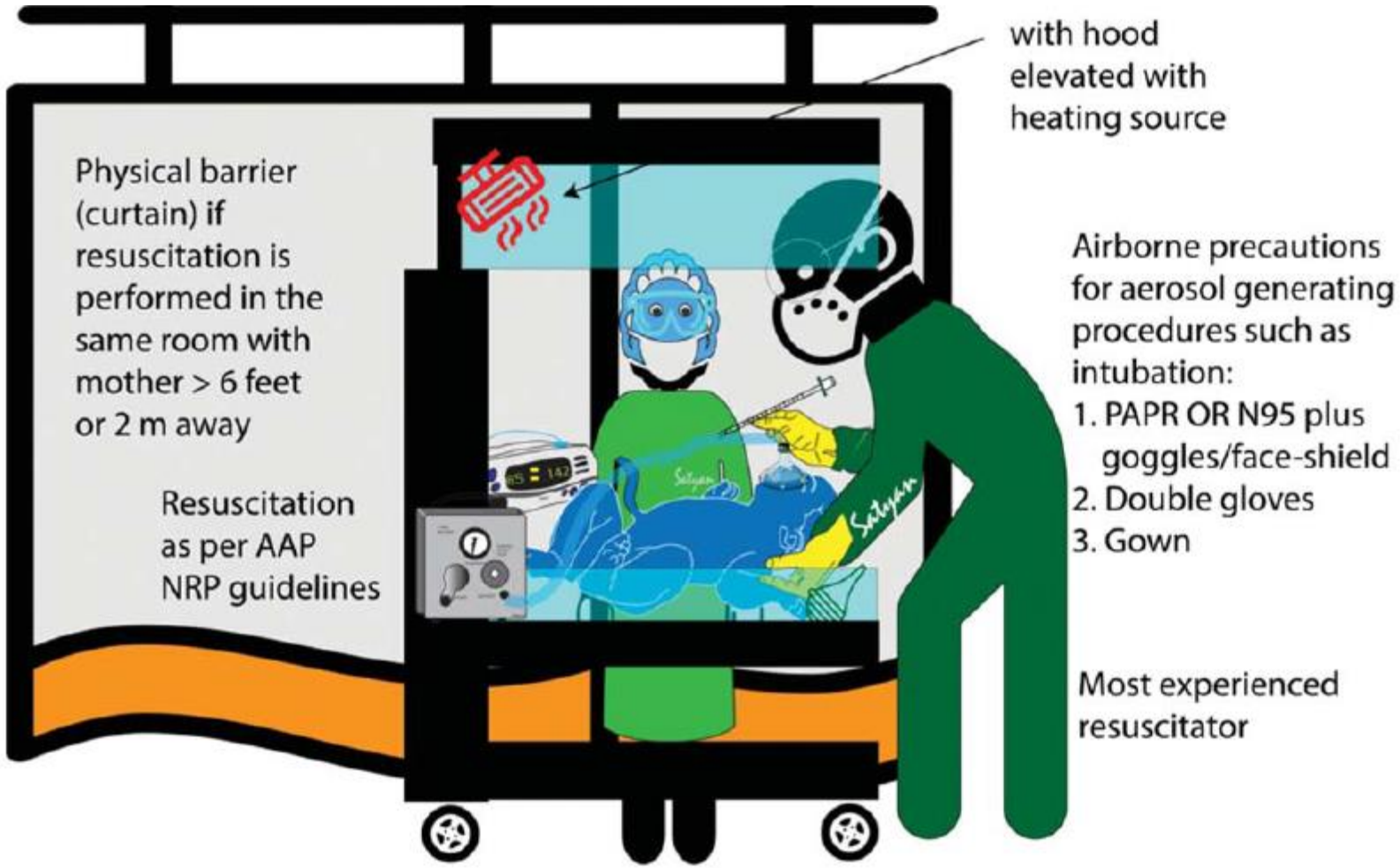
- The neonatology/newborn team should be informed, ideally 30 to 60minutes before delivery.
- Appropriate PPE should be available for the neonatal team.
- Centers could have a PPE grab and go kit containing approximately six facreadily available for the neonatal resuscitation teame shields or goggles, six N95masks and gloves, and gowns, readily available for the neonatal resuscitation team

Stabilization and Resuscitation of the Neonate

- **Minimum number of neonatal resuscitators** should be in the room,with the rest of the team being **available outside the room**

Stabilization and Resuscitation of the Neonate

- The current AAP and NRP recommendations in the delivery room should be followed. The optimal location for neonatal stabilization and resuscitation is not clear. It can be conducted in an adjacent room or the same place at least 6 feet or 2 m away from the mother with a physical barrier such as a curtain.



Limited number of providers in the resucitation room

Stabilization and Resuscitation of the Neonate

- It is preferable to conduct resuscitation in an **isolette with a hood** that can be elevated to provide warmth for resuscitation and then lowered for transport.
- **Regardless of gestational age, the newborn should be transported in a closed isolette and maintained in the isolette for postresuscitation care**.
- In the NICU, these infants should be cared for in an isolette in a negative pressure room

SARS-CoV-2 Transmission of rooming in

- Maternal-neonatal skin contact has lifelong **mental, emotional,** and **physical health benefits**.
- To prioritize skin-to-skin contact while also preventing possible SARSCoV- 2 transmission between the neonate and a mother with a known or suspected SARS-CoV-2 infection in the immediate postpartum period, **we recommend working with parents and the health care team to balance the risks and benefits of various rooming options while the dyad is still hospitalized after delivery.**

SARS-CoV-2 Transmission of rooming in

- To facilitate this decision, the **CDC** recommends that care teams discuss with parents the **benefits of rooming-in**, such as **improved mother-infant bonding, identification of infant feeding behaviors**, and **improved family-centered care**.

SARS-CoV-2 Transmission of rooming in

- Of note, infants rooming- in with mothers with COVID-19 are not at increased risk for contracting SARS-CoV-2 when proper prevention measures are followed **compared with infants who are separated**

SARS-CoV-2 Transmission of rooming in

- If the neonate is healthy and the mother with COVID-19 has mild-to-moderate symptoms, the neonate **can safely room with the infected mother** and the mother should maintain a reasonable distance from the infant when possible.
- The neonate can be placed in a closed isolette at least 6 feet from the mother, if needed, to facilitate distancing

SARS-CoV-2 Transmission During breastfeeding

- When the mother is holding or breastfeeding her neonate, she should wear a mask and practice proper hand hygiene.
- Importantly, **neonates should not wear face shields or masks**. If the neonate requires NICU admission, the neonate should be isolated until **viral tests** are confirmed **negative**, with **consideration to continue isolation practices up to 14 days after birth**

NICU policy

- If the neonate requires NICU admission, **only noninfected parents should be allowed to visit the NICU** if they have not developed symptoms and have not tested positive for COVID-19.
- Visiting parents should practice proper hand hygiene, wear masks, and stay next to their neonate while in the NICU.

NICU policy

- If the neonate requires NICU admission, **only noninfected parents should be allowed to visit the NICU** if they have not developed symptoms and have not tested positive for COVID-19.
- Visiting parents should practice proper hand hygiene, wear masks, and stay next to their neonate while in the NICU.

NICU policy

- **Updated NICU visitor recommendations include the following**:
- People who are not immunocompromised may be considered noninfectious if their symptoms have improved; if they have been afebrile for *24 hours* without use of antipyretics; and at least *10 days* have passed since symptoms first appeared (or, for asymptomatic women identified only by obstetric screening tests, at least 10 days have passed since the positive test result).

NICU policy

- For those who were **severely or critically ill** with COVID-19, and for **immunocompromised** people, the length of time since symptoms first appeared can be extended to **20 days**.

- Centers may choose to extend the amount of time needed to pass before parents with prior infection may safely enter the NICU

SARS-CoV-2 transmission after discharge

- After a mother with COVID-19 and an uninfected neonate are discharged from the hospital, **home isolation** and **physical distancing** should be practiced until the **mother's symptoms have improved** and she remains **afebrile for 24hours** and **has been isolated for 10 days since symptom onset.**

Case 2

- A 2 d/o male neonate, product of NVD (G2L2)
- BW: 3500, HC: 34, Lt: 54
- GA: 40 wks, APGAR: 9, 10
- Breastfeeding
- With CC of poor feeding, lethargy, fever and respiratory distress

Case 2

- WBC: 12100 , RBC: 5.0*10^6 , Hb: 19 , Hct: 55, MCV: 110, Plt: 352,000
- AST: 60, A LT: 39
- LDH: 1187
- BUN: 16, Cr: 0.5, Na: 150, K: 5.3, Ca: 7.2

Case 2

- CRP: 1, 1
- Procalcitonin: 0.2
- B/C: Negative, CSF: Nl
- COVID19 PCR: Positive
- PH: 7.42, PCo2: 32, PO2: 85, HCo2: 20

Case 2

- Echocardiography: Small ASD, VSD, PDA, mild PHTN
- CXR:Abnormal
- AB Rx was done

Case report

- Early Neonatal SARS-CoV-2 Infection Manifesting With Hypoxemia Requiring Respiratory Support

- Mariateresa Sinelli, MD, Giuseppe Paterlini, MD, Marco Citterio, MD, Alessia Di Marco, MD, Tiziana Fedeli, MD,Maria Luisa Ventura, MD

- PEDIATRICS Volume 146, number 1, July 2020:e20201121

Case report

- We describe a case of neonatal SARS-CoV-2 infection, in an **infant diagnosed 3 days after birth**, and manifesting with **silent hypoxemia**, requiring respiratory support

Case report

- In this report, we detail a case of neonatal SARS-CoV-2 infection that presented on day 5 of life with clinically significant hypoxemia **without overt signs of respiratory distress that required oxygen therapy**.
- Although occur in newborns with early SARS-CoV-2 infection.

Case report

- In these cases, diagnosis can be challenging because clinical manifestation of respiratory failure, such as polypnea or respiratory distress, may be absent.

Case report

- Our case report suggests that a newborn infected with SARS-CoV-2 may not demonstrate signs of respiratory distress but may have significant hypoxia that requires treatment.

Case report

- **Pulse oximetry monitoring** may be advisable before the discharge of healthy-appearing infants with positive testing result for SARS-CoV-2.
- In addition, parents should be trained to recognize signs of possible hypoxemia, such as **poor sucking** or **changes in the infant's skin color.**


سپاس از توجه شما