COVID

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PREGNANCY

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VACCINATION

American College of OB/Gyn 2021

JUL 30, 2021

"ACOG encourages its members **to enthusiastically recommend vaccination** to their patients. This means emphasizing the known safety of the vaccines and the increased risk of severe complications associated with COVID-19 infection, including death, during pregnancy."

J. Martin Tucker, MD, FACOG, president of ACOG

"COVID-19 vaccination is the best method to reduce maternal and fetal complications of COVID-19 infection among pregnant people. Maternal-fetal medicine subspecialists—experts in high-risk pregnancy—**strongly recommend that pregnant people get vaccinated**. Vaccination is safe before, during, or after pregnancy.

William Grobman, MD, MBA, president of SMFM

AUG 9, 2021

"As the leading organizations representing experts in maternal care and public health professionals that advocate and educate about vaccination, we ***strongly urge all pregnant individuals***—along with ***recently pregnant, planning to become pregnant, lactating*** and other eligible individuals—to be vaccinated against COVID-19."

"***Pregnant individuals are at increased risk of severe COVID-19 infection, including death***. With cases rising as a result of the Delta variant, the best way for pregnant individuals to protect themselves against the potential harm from COVID-19 infection is to be vaccinated.

"Data from ***tens of thousands*** of reporting individuals have shown that the ***COVID-19 vaccine is both safe and effective when administered during pregnancy***. The same data have been equally reassuring when it comes to infants born to vaccinated individuals. Moreover, *COVID-19 vaccines have no impact on fertility*."

"***Pregnant individuals and those planning to become pregnant should feel confident in choosing vaccination to protect themselves, their infants, their families, and their communities***."

WHO'S WHO?

American College of Obstetricians and Gynecologists | **American Academy of Family Physicians** | American Academy of PAs | **American Academy of Pediatrics** | American Association of Nurse Practitioners | American College of Nurse-Midwives | American College of Osteopathic Obstetricians & Gynecologists | American College of Physicians | American Pharmacists Association | Association of Immunization Managers | Association of State and Territorial Health Officials | Association of Women's Health, Obstetric and Neonatal Nurses | Infectious Diseases Society of America | Infectious Diseases Society for Obstetrics and Gynecology | National Association of Chain Drug Stores | National Association of County & City Health Officials | National Association of Nurse Practitioners in Women's Health | National Foundation for Infectious Diseases | National Hispanic Medical Association | North American Society for Pediatric and Adolescent Gynecology | **Society for Maternal-Fetal Medicine** | Society of OB/GYN Hospitalists | Vaccinate Your Family | Association for Professionals in Infection Control and Epidemiology | Association of PAs in Obstetrics & Gynecology | Society for Healthcare Epidemiology of America | Society of Infectious Diseases Pharmacists.

SEP 29, 2021

"***Our message cannot be stronger or clearer: please get vaccinated today***. Whether you are pregnant, breastfeeding, trying to become pregnant, or plan to get pregnant in the future, vaccination is safe and effective, and is the best way to protect you from severe complications associated with COVID-19 infection. Further, I urge my fellow ACOG members and all maternal health colleagues to strongly, confidently, and clearly recommend COVID-19 vaccination to their pregnant patients."

J. Martin Tucker, MD, FACOG, president, on behalf of the American College of Obstetricians and Gynecologists (ACOG)

SAFETY MOITORING

CDC's V-Safe: A new active surveillance smartphone-based after-vaccination health checker for people who receive COVID-19 vaccines.

Vaccine Adverse Event Reporting System (VAERS): A national early warning system to detect possible safety problems in U.S.-licensed vaccines.

Vaccines and Medications in Pregnancy Surveillance System (VAMPSS): A national surveillance system designed to monitor the use and safety of vaccines and asthma medications during pregnancy

MRNA COVID-19 VACCINES

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PFIZER-BIONTECH & MODERNA

- Messenger RNA (mRNA) encapsulated by a lipid nanoparticle (LNP) for delivery into the host cells.
- These vaccines utilize the body's own cells to generate the coronavirus spike protein.
- These proteins stimulates immune cells to create antibodies against COVID-19.
- The mRNA vaccines are not live virus vaccines.
- These vaccines do not enter the nucleus and do not alter human DNA in vaccine recipients.
- mRNA vaccines cannot cause any genetic changes (CDC, Zhang 2019, Schlake 2012).
- Demonstrated safety and efficacy in Phase II and Phase III clinical trials.
- Safety and efficacy for pregnant and nonpregnant individuals is similar.
- NO identified safety concerns for COVID-19 vaccination during pregnancy.

ADENOVIRUS VECTOR VACCINES

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J&J/JANSSEN BIOTECH

- Monovalent vaccine
- Recombinant human adenovirus type 26 (Ad26) vector
- Constructed to encode a stabilized form of the SARS-CoV-2 Spike (S) protein
- The Ad26 vector cannot replicate in humans
- It is quickly cleared from tissues following injection (FDA 2021)
- Ad26.COV2.S is not a live virus vaccine
- NO preservatives
- Acceptable safety and reactogenicity profile based on data from ongoing and completed clinical trials of Ad26-vectored vaccines including COVID-19, HIV, and Ebola administered to pregnant individuals,
- Available pregnancy data is NOT suggestive of a pregnancy-related safety concern (FDA 2021).

EFFICACY - MRNA COVID-19 VACCINES

Pfizer-BioNTech COVID-19 vaccine was ***95%*** effective at preventing laboratory-confirmed COVID-19 illness in people who received two doses who had no evidence of previous infection (CDC).

Moderna vaccine was ***94.1%*** effective at preventing laboratory-confirmed COVID-19 illness in people who received two doses who had no evidence of being previously infected (CDC).

A *prospective cohort study* from two academic centers found that ***vaccinated pregnant and lactating women produced comparable immune responses to nonpregnant controls and generated higher antibody titers than those observed following SARS-CoV-2 infection in pregnancy***. Further, vaccine-generated ***antibodies were present in umbilical cord blood and breast milk after maternal vaccination*** (Gray 2021, Prabhu 2021, Juncker 2021).

SAFETY - MRNA COVID-19 VACCINES

Typically, mild side effects similar to **influenza-like illness symptoms** following vaccination.

Pfizer-BioNTech study subgroup of persons aged 18–55 years, **fever** greater than 38 °C occurred in 3.7% after the first dose and 15.8% after the second dose (FDA 2020).

Moderna vaccine trials, **fever** greater than 38°C was reported in 0.8% of vaccine recipients after the first dose, and 15.6% of vaccine recipients after the second dose (FDA 2020).

Most of these symptoms resolved by *day 3* after vaccination for both vaccines.

	Injection Site Reactions	Fatigue	Chills	Muscle Pain	Joint Pain	Headaches
Moderna	91.6%	68.5%	43.4%	59.6%	44.8%	63%
Pfizer-BioNTech	84.10%	62.90%	31.90%	38.30%	23.60%	55.10%
J&J/Janssen	48.6%	38.2%	N/A	33.2%	N/A	38.9%

ALLERGIC REACTIONS/ANAPHYLAXIS

- ***Allergic reactions including anaphylaxis*** have been reported to be rare following COVID-19 vaccination in nonpregnant individuals.
- ***Anaphylaxis*** (ACIP August 2021)
  - **Pfizer-BioNTech**: 5 cases per million doses
  - **Moderna**: 4.9 cases per million doses
  - **J&J/Janssen**: 7.6 cases per million doses
- Anaphylaxis should be managed the *same as in nonpregnant individuals*
  - ABC, EMS, supine position, epinephrine (CDC).
- Anaphylaxis may **recur** after the individual begins to recover
  - Monitoring in a medical facility for at least several hours is advised, even after complete resolution of symptoms and signs.

THROMBOSIS WITH THROMBOCYTOPENIA SYNDROME

Most cases of TTS reported to the Vaccine Adverse Event Reporting System (VAERS) following receipt of the J&J/Janssen COVID-19 vaccine to date have occurred in women of reproductive age. None of these individuals were pregnant. While TTS is a clinically serious condition, it is critical to emphasize the rarity of this syndrome, which has occurred in approximately 8.9 out of every million doses of Janssen COVID-19 vaccine administered to females aged 18-49 years (Shimabukuro, 2021).

there is no recommendation to discontinue or change hormonal contraceptive methods in women who have received or plan to receive the J&J/Janssen COVID-19 vaccine. Additionally, people who take aspirin or anticoagulants as part of their routine medications, including during pregnancy, do not need to stop or alter the dose of these medications prior to receipt of the J&J/Janssen COVID-19 vaccine (CDC Clinical Considerations).

Diagnosis and Treatment

Patients receiving the J&J/Janssen COVID-19 vaccine should be informed of symptoms of TTS, including severe headache, visual changes, abdominal pain, nausea and vomiting, back pain, shortness of breath, leg pain or swelling, petechiae, easy bruising, or bleeding. Patients who experience these symptoms should

MYOCARDITIS AND PERICARDITIS

- Myocarditis (1 per 100,000)
- Pericarditis (1.8 per 100,000)
- Particularly in adolescents and young adults (Diaz 2021)
  - -Male adolescents and young adults aged 16 years and older
  - -Onset was typically within several days after mRNA COVID-19 vaccination,
  - -More often after the second dose than the first dose
- Consider the diagnoses of myocarditis and pericarditis in adolescents or young adults with acute chest pain, shortness of breath, or palpitations.

GUILLAIN-BARRÉ SYNDROME

- Multiple safety systems have reported a higher-than expected number of cases of **Guillain-Barré syndrome** following the use of the **J&J/Janssen** COVID-19 vaccine.
- However, investigations into this complex diagnosis are ongoing and additional information is needed to fully understand the ***potential relationship*** between Guillain-Barré syndrome and the J&J/Janssen COVID-19 vaccine.
- **Absolute risk** of Guillain-Barré syndrome following vaccination remains very low (estimated crude reporting rate of **1 per 100,000 doses**)
- *Benefits outweigh risk* regarding prevention of severe COVID-19 illness through vaccination (Woo 2021)

AVAILABLE SAFETY INFORMATION RELATED TO THE USE OF COVID-19 VACCINES IN PREGNANCY

NONE of the COVID-19 vaccines approved under EUA have been tested in pregnant individuals.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY DATA

Data from Developmental and Reproductive Toxicity (DART) studies for the Pfizer-BioNTech COVID-19 vaccine have been reported in Europe

Animal studies using the Pfizer/BioNTech COVID-19 vaccine do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/fetal development, parturition, or postnatal development

DART study of Moderna's mRNA-1273 in rats was submitted to FDA on December 4, 2020. FDA review of this study concluded that mRNA1273 given prior to mating and during gestation periods at dose of 100 µg did not have any adverse effects on female reproduction, fetal/embryonal development, or postnatal developmental except for skeletal variations, which are common and typically resolve postnatally without intervention (FDA)

In a reproductive developmental toxicity study, female rabbits were administered 1 mL of the J&J/Janssen COVID-19 vaccine (a single human dose is 0.5 mL) by intramuscular injection 7 days prior to mating and on gestation days 6 and 20 (ie, one vaccination during early and late gestation, respectively). No vaccine-related adverse effects on female fertility, embryo-fetal or postnatal development up to postnatal day 28 were observed (FDA 2021)

Based on data from ongoing and completed clinical trials of Ad26-vectored vaccines including COVID-19, HIV, and Ebola administered to pregnant individuals, overall, the Ad26-based vaccines have an acceptable safety and reactogenicity profile, without significant safety issues identified to date

Review of the available pregnancy data is not suggestive of a pregnancy-related safety concern (FDA 2021).

POST-ADMINISTRATION PREGNANCY SURVEILLANCE DATA

As of October 25, 2021, there have been nearly **170,000 pregnancies reported in CDC's v-safe post-vaccination health checker** (CDC 2021)

NO SPECIFIC SAFETY SIGNALS have been observed in pregnant people enrolled in v-safe; however longitudinal follow-up is needed

CDC v-safe data **NOT** indicate any safety concerns based on the reactogenicity profile and adverse events observed among more than 5,000 pregnant individuals and side effects were similar in pregnant and nonpregnant populations

Specific neonatal outcomes data published in The New England Journal of Medicine, along with pregnancy complication data from 275 completed pregnancies presented at the March 1, 2021

NO differences have been seen when comparing pregnant individuals participating in the v-safe pregnancy registry with the background rates of adverse pregnancy outcomes

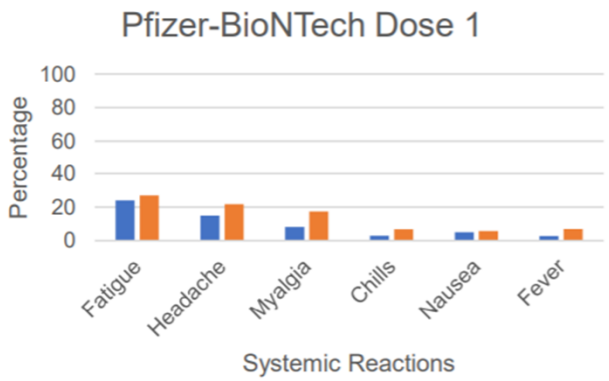
Spontaneous abortion rate following COVID-19 vaccination during pregnancy is consistent with the background rate

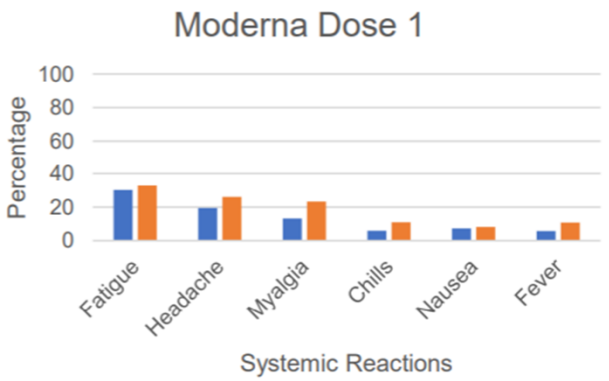
V-safe pregnancy registry outcomes of interest in COVID-19 vaccinated pregnant women as of February 18, 2021*

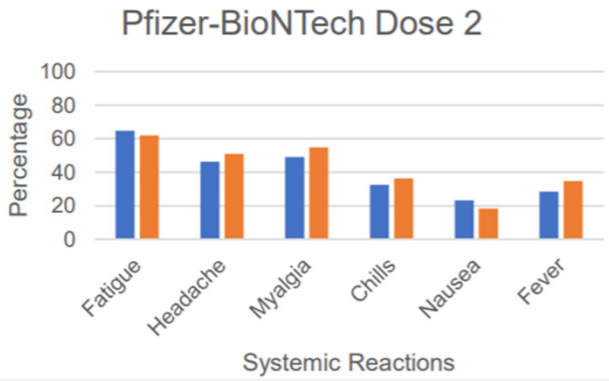
Outcomes	Background rates*	V-safe pregnancy registry overall
Pregnancy outcome		
Miscarriage (<20 weeks)	26%	15%†
Stillbirth (≥ 20 weeks)	0.6%	1%
Pregnancy complications		
Gestational diabetes	7-14%	10%
Preeclampsia or gestational hypertension§	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine growth restriction	3-7%	1%
Neonatal		
Preterm birth	10.1%	10%
Congenital anomalies‡	3%	4%
Small for gestational age^	3-7%	4%
Neonatal death	0.38%	0%

* Sources listed on slide 33; † 93% of these were pregnancy losses <13 weeks of age; § Pre-eclampsia or gestational hypertension diagnosed during pregnancy and/or during delivery; ‡ Congenital anomalies (overall) diagnosed after delivery only; ^ Birthweight below the 10th percentile for gestational age and sex using INTERGROWTH-21st Century growth standards

V-safe: Day 1 post-vaccination local reactions in pregnant and non-pregnant women aged 16-54 years*







Pregnant (self-report)
Not pregnant

v-safe℠
after vaccination
health checker

* Source: CDC unpublished **v-safe** data through January 13, 2021

V-SAFE PREGNANCY REGISTRY OUTCOMES OF INTEREST IN COVID-19-VACCINATED PREGNANT INDIVIDUALS

Pregnancy Complications†	Background Rate	V-safe Pregnancy Registry Overall
Gestational diabetes	7-14%	10%
Preeclampsia or gestational hypertension	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine growth restriction	3-7%	1%
Neonatal Outcomes*	**Background Rate**	**V-safe Pregnancy Registry Overall**
Preterm birth	8-15%	9.4%
Congenital anomalies	3%	2.2%
Small for gestational age	3.5%	3.2%
Neonatal death	0.38%	0%

*Shimabukuro TT, Kim SY, Myers TR, Moro PL, Oduyebo T, Panagiotakopoulos L, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. CDC v-safe COVID-19 Pregnancy Registry Team [published online April 21, 2021]. N Engl J Med. DOI: 10.1056/NEJMoa2104983. Available at: https://www.nejm.org/doi/10.1056/NEJMoa2104983.

†Shimabukuro T. COVID-19 vaccine safety update. Advisory Committee on Immunization Practices (ACIP). Atlanta, GA: Centers for Disease Control and Prevention; 2021. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf. Retrieved March 1, 2021.

COVID-19 BOOSTER PREGNANCY

•Pregnant and recently pregnant people who **received J&J/Janssen** vaccine should receive a COVID-19 **booster** at least 2 months following their initial vaccine

•Pregnant and recently pregnant people who **received an mRNA** vaccine should receive a **booster** at least 6 months following their initial vaccine series

•Pregnant and recently pregnant people can receive any COVID-19 vaccine available to them for their **booster** dose; it does not have to be the same product as their initial vaccine or vaccine series

•These recommendations also **apply to pregnant and recently pregnant** (eg, up to 6 weeks postpartum) individuals who completed their initial COVID-19 vaccine or vaccine series prior to pregnancy

ADDITIONAL VACCINATION CONSIDERATIONS FOR PREGNANT INDIVIDUALS

•Pregnant individuals who experience **fever** following vaccination should be counseled to take **ACETAMINOPHEN**

ACETAMINOPHEN HAS BEEN PROVEN TO BE SAFE FOR USE IN PREGNANCY AND DOES NOT APPEAR TO IMPACT ANTIBODY RESPONSE TO COVID-19 VACCINES

•**Anti-D immunoglobulin** (i.e. Rhogam) should not be withheld from an individual who is planning or has recently received a COVID-19 vaccine as it will not interfere with the immune response to the vaccine

•For patients who **DO NOT** receive the vaccine, the discussion should be ***documented*** in the patient's medical record. During subsequent office visits, obstetrician–gynecologists should *address ongoing questions and concerns and offer vaccination* ***again***

CLINICIANS SHOULD REINFORCE THE IMPORTANCE OF OTHER PREVENTION MEASURES SUCH AS HAND WASHING, PHYSICAL DISTANCING, AND WEARING A MASK

LACTATION

ACOG recommends that **lactating individuals be vaccinated** against COVID-19

While lactating individuals were *not included in most clinical trials*, COVID-19 vaccines should not be withheld from lactating individuals who otherwise meet criteria for vaccination

Theoretical concerns regarding the safety of vaccinating lactating individuals do not outweigh the potential benefits of receiving the vaccine, and a growing body of evidence demonstrates that COVID-19 vaccination is safe during lactation (Bertrand 2021, Kachikis 2021)

There is **NO need to avoid initiation or discontinue breastfeeding** in patients who receive a COVID-19 vaccine (ABM 2020)

Information for pregnant and lactating patients can be found on ACOG's patient website: Coronavirus (COVID-19), Pregnancy, and Breastfeeding: A Message for Patients

CONSIDERING PREGNANCY

Vaccination is strongly recommended for NONPREGNANT individuals

ACOG RECOMMENDS VACCINATION FOR INDIVIDUALS WHO ARE ACTIVELY TRYING TO BECOME PREGNANT OR ARE CONTEMPLATING PREGNANCY

Additionally, **it is NOT necessary to delay pregnancy after completing both doses of the COVID-19 vaccine**

Claims linking COVID-19 vaccines to infertility are unfounded and have no scientific evidence supporting them

mRNA vaccines such as Pfizer and Moderna have **mechanism of action** and **safety profile** in **NONPREGNANT INDIVIDUALS** such that **COVID-19 MRNA VACCINES ARE NOT A CAUSE OF INFERTILITY**

Adenovirus vector vaccines such as the J&J/Janssen COVID-19 vaccine **cannot replicate** following administration, and available data demonstrate that it is **cleared from tissues** following injection, thus the vaccine **cannot cause infection and** cannot alter the DNA of a vaccine recipient and is also **NOT A CAUSE OF INFERTILITY** (Evans, 2021, Morris 2021)

Additionally, a growing body of data demonstrate that **seropositivity to the SARS-CoV-2 spike protein**, whether from vaccination or infection, **DOES NOT PREVENT EMBRYO IMPLANTATION OR INTERFERE WITH EARLY PREGNANCY DEVELOPMENT** (Morris 2021)

If an individual becomes pregnant after the first dose of a COVID-19 vaccine requiring two doses (Pfizer-BioNTech or Moderna), the second dose should be administered as indicated

Finally, routine pregnancy testing is not recommended and should **NOT** be required prior to receiving any EUA-approved COVID-19 vaccine

MAMMOGRAPHY

Reports of some patients developing **temporary contralateral or ipsilateral lymphadenopathy** after a COVID-19 vaccination have raised concerns about the possible effect on interpretation of mammogram screening results

A Radiology Expert Scientific Panel has issued a recommendation that **mammograms should be conducted prior to COVID-19 vaccination or postponed for 4–6 weeks** if possible, following the **second vaccine** dose to avoid uncertainty in interpretation of mammogram results

Screening mammograms are an essential part of preventive care, so postponing screening should only be considered when it does not unduly delay care

If a mammogram is performed fewer than 4–6 weeks after COVID-19 vaccination, patients should inform the mammogram technologist or radiologist **when** the vaccine was administered, **which vaccine** was received, and in **which arm** to aid in interpretation of screening results

MENSTRUAL DISTURBANCES

Anecdotal reports of **temporary changes in menstruation patterns** (eg, heavier menses, early or late onset, and dysmenorrhea) in individuals who have recently been vaccinated for COVID-19

Environmental stresses can temporarily impact menses, however **vaccines have not been previously associated with menstrual disturbances**

ACOG will continue to monitor and evaluate available evidence on this issue. The National Institutes of Health has funded institutions to explore potential links between COVID-19 vaccination and menstrual changes (NIH 2021). Also, an open survey to gather qualitative data on post-vaccination menstrual patterns has been initiated

NO reason for individuals to schedule their vaccinations based on their menstrual cycles; vaccines can be given to those currently menstruating

Information for patients can be found on ACOG's patient website:
Coronavirus (COVID-19) and Women's Health Care: A Message for Patients.

EPIDEMOLOGY

Centers for Disease Control 2021

COVID EPIDEMIOLOGY IN PREGNANCY

- In November 2020, the Centers for Disease Control and Prevention (CDC) released surveillance data on outcomes in approximately 400,000 reproductive-aged women with symptomatic, laboratory-confirmed COVID-19.[1] After adjusting for age, race/ethnicity, and underlying medical conditions, pregnant women had significantly higher rates of intensive care unit (ICU) admission (10.5 vs. 3.9 cases per 1,000 cases; adjusted risk ratio [aRR] 3.0; 95% CI, 2.6–3.4), mechanical ventilation (2.9 vs. 1.1 cases per 1,000 cases; aRR 2.9; 95% CI, 2.2–3.8), extracorporeal membrane oxygenation (0.7 vs. 0.3 cases per 1,000 cases; aRR 2.4; 95% CI, 1.5–4.0), and death (1.5 vs. 1.2 cases per 1,000 cases; aRR 1.7; 95% CI, 1.2–2.4). The increased risk for severe disease was most significant in women aged 35 to 44 years, who were almost four times as likely to be mechanically ventilated and twice as likely to die as nonpregnant women of the same age.

COVID EPIDEMIOLOGY IN PREGNANCY PERINATAL OUTCOMES

- An observational cohort study of all pregnant patients at 33 U.S. hospitals with a singleton gestation and a positive result on a SARS-CoV-2 virologic test evaluated maternal characteristics and outcomes across disease severity.[6] The data suggested that adverse perinatal outcomes were more common in patients with severe or critical disease than in asymptomatic patients with SARS-CoV-2 infection, including an increased incidence of cesarean delivery (59.6% vs. 34.0% of patients; aRR 1.57; 95% CI, 1.30–1.90), hypertensive disorders of pregnancy (40.4% vs. 18.8%; aRR 1.61; 95% CI, 1.18–2.20), and preterm birth (41.8% vs. 11.9%; aRR 3.53; 95% CI, 2.42–5.14). The perinatal outcomes for those with mild to moderate illness were similar to those observed among asymptomatic patients with SARS-CoV2 infection.

COVID EPIDEMIOLOGY IN PREGNANCY RACIAL DISPARITY

- Notably, among Hispanic women, pregnancy was associated with a risk of death that was 2.4 times higher (95% CI, 1.3–4.3) than the risk observed in nonpregnant Hispanic women. Racial and ethnic disparities were also seen in other reports. Among 8,207 pregnant women with COVID-19 who were reported to CDC, the proportion of those who were reported to be Hispanic (46%) and Black (22%) was higher than the proportion of Hispanic and Black women who gave birth in 2019 (24% and 15%, respectively), suggesting that pregnant people who are Hispanic or Black may be disproportionately affected by SARS-CoV-2 infection.[4]

COVID EPIDEMIOLOGY IN PREGNANCY SEVERE DISEASE PREDICTORS

- In an ongoing systematic review that includes 192 studies to date, maternal factors that were associated with severe disease included increased maternal age (OR 1.83; 95% CI, 1.27–2.63; 3,561 women from 7 studies); a high body mass index (OR 2.37; 95% CI, 1.83–3.07; 3,367 women from 5 studies); any pre-existing maternal comorbidity, including chronic hypertension and diabetes (OR 1.81; 95% CI, 1.49–2.20; 2,634 women from 3 studies); pre-eclampsia (OR 4.21; 95% CI, 1.27–14.0; 274 women from 4 studies); and pre-existing diabetes (OR 2.12; 95% CI, 1.62–2.78; 3,333 women from 3 studies).[5] Compared with pregnant women and recently pregnant women without COVID-19, pregnant women with COVID-19 were at a higher risk of any instance of preterm birth (OR 1.47; 95% CI, 1.14–1.91; 8,549 women from 18 studies) and stillbirth (OR 2.84; 95% CI, 1.25–6.45; 5,794 women from 9 studies).

COVID EPIDEMIOLOGY IN PREGNANCY VERTICAL TRANSMISSION

- Although vertical transmission of SARS-CoV-2 is possible, current data suggest that it is rare.[7] A review of 101 infants born to 100 women with SARS-CoV-2 infection at a single U.S. academic medical center found that 2 infants (2%) had indeterminate SARS-CoV-2 polymerase chain reaction (PCR) results, which were presumed to be positive; however, the infants exhibited no evidence of clinical disease. It is reassuring that the majority of the infants received negative PCR results after rooming with their mothers and breastfeeding directly (the mothers in this study practiced appropriate hand and breast hygiene).

MANAGEMENT

Society for Maternal Fetal Medicine 2021

SEVERITY DEFINITIONS

- ***Mild disease***: Flu-like symptoms including fever, cough, myalgias, and anosmia without dyspnea, shortness of breath, or abnormal chest imaging.
- ***Moderate disease***: Lower respiratory tract disease with dyspnea, pneumonia on imaging, abnormal blood gasses, refractory fever of 39.0 °C /**102.2 °F** or greater not alleviated with acetaminophen while maintaining an oxygen saturation of greater than or equal to **94%** on room air at sea level.
- ***Severe disease***: Respiratory rate greater than **30 breaths per minute** (bpm), hypoxia with oxygen saturation less than **94%**, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen of less than 300, or greater than **50% lung involvement** on imaging.
- ***Critical disease***: Multi-organ failure or dysfunction, shock, or respiratory failure requiring mechanical ventilation or high-flow nasal cannula.
- ***Refractory hypoxemia***: Persistent, inadequate oxygenation and/or ventilation despite substantial and appropriate measures to optimize it and represents a further escalation of severity on the spectrum of disease

INPATIENT CRITERIA ..... PREGNANT

Moderate to severe signs and symptoms

Oxygen saturation less than 95%.

Comorbid conditions

- *uncontrolled hypertension, inadequately controlled gestational or pregestational diabetes, chronic renal disease, chronic cardiopulmonary disease, or immunosuppressive states* (intrinsic or medication-related)

Fevers greater than 39 °C despite acetaminophen

Concern for secondary hemophagocytic lymphohistiocytosis (sHLH)

- Cytokine storm syndrome
- Defined by unremitting fever, cytopenia, and high ferritin levels.

OUTPATIENT CARE - PREGNANT

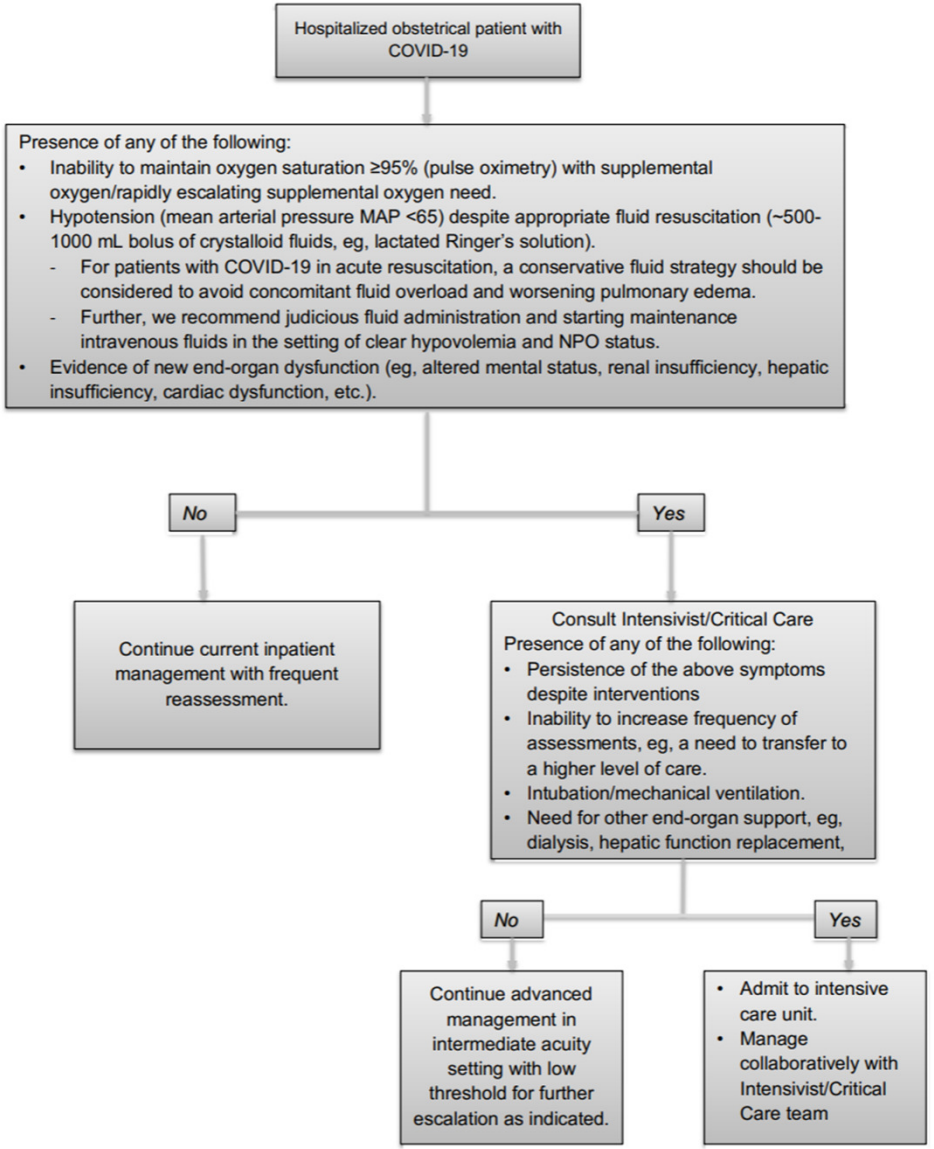
- Monitor closely
- Daily self assessments
- Telehealth is a reasonable option
- Ensure reliable feedback mechanism for early detection of a worsening condition
- **THERE IS NO GUIDANCE ABOUT THE TIMING OF FREQUENCY FOR FOLLOW-UP OUTPATIENT CARE**
- Reasonable to have a follow-up visit at least once within 2 weeks of diagnosis of COVID-19

- CONCERNING PARAMETERS
  - Worsening shortness of breath
  - Tachypnea
  - Unremitting fever (greater than 39 °C) despite appropriate use of acetaminophen
  - Inability to tolerate oral hydration or needed medications
  - Oxygen saturation less than 95% either at rest or on exertion (if home pulse oximetry available)
  - Persistent pleuritic chest pain
  - New-onset confusion or lethargy
  - Cyanotic lips, face, or fingertips
  - Obstetrical complaints, such as preterm contractions, vaginal bleeding, or decreased fetal movement

OXYGEN SATURATION

- Pregnancy: Oxygen saturation is 95% or greater
- Nonpregnant: Oxygen saturation of 92% or greater in COVID patients
- Observe for changes in supplemental oxygen requirements and mode of oxygen delivery (face mask, high-flow nasal cannula)
- Consider targeting an oxygen saturation that is higher than would be used for a nonpregnant patient.
- Exertional oxygen saturation should also be assessed
- Patients whose oxygen saturation is less than or equal to 95% on room air with exertion should be considered for inpatient admission
- Increases in work of breathing could signal a need for a higher level of support and care
  - respiratory rate greater than 30 bpm, accessory muscle use, pursing of lips

ICU ADMISION ALOGRITHM



INTUBATION – TIMING/CRITERIA

- Typically, intubation is considered when oxygen requirements are as follows:
- Greater than 15 L per minute (by common nasal cannula or mask)
- Greater than 40 to 50 L per minute by high-flow nasal cannula
- Greater than 60% fraction of inspired oxygen (FiO2) by Venturi mask to maintain an oxygen saturation of 95% or greater by transcutaneous pulse oximeter
- Inability of a patient to protect the airway due to altered mental status (Glasgow coma scale of less than 8)

INTUBATION - ALTERNATIVES

- Common nasal cannula (maximum of 15 L per minute deliverable)
- Face mask: "Non-rebreather" type; maximum dependent on source, typically up to 15 L per minute (LPN) from wall supply; may be increased to ~50 LPM with an additional source
- Venturi face mask: Supplies support via fraction of inspired oxygen (FiO2); maximum of 60% oxygen delivery
- Use of noninvasive positive-pressure ventilation, eg, bilevel positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP)
- Passive prone positioning
- Alternating lateral decubitus (typically for ~2 hours in each position)

OTHER OPTIONS

- Neuromuscular blockade (paralytics)
  - Benefit in severe ARDS, especially if instituted early (within 12 hours of intubation)
  - Continuous or intermittent paralysis remains an option for moderate to severe ARDS
- Pulmonary vasodilators
  - In general, pulmonary vasodilators do not decrease ventilator-free days, ICU length of stay, or mortality
  - Can be useful in the setting of evolving refractory hypoxemia in the parturient patient
  - Effects may be transient - perform other interventions, transfer, delivery if after 32 weeks of gestation
  - NOT contraindicated during pregnancy
- Inhaled nitric oxide (NO) Inhaled vasodilators
  - Salvage therapy in refractory hypoxemia.
  - Inhaled nitric oxide (NO) and inhaled prostacyclins can dilate well-perfused ventilated lungs
  - Renal impairment and methemoglobinemia
  - Transient, waning effects after 48 to 96 hours

ECMO

- Extracorporeal membrane oxygenation (ECMO) is used to artificially perform the function of the lungs (venovenous; VV ECMO) or the heart as well as the lungs (venoarterial; VA ECMO) in patients with severe ARDS that is refractory to other measures
- ECMO cannulation requires placement of a large central venous or venous and arterial vascular access
- Risks of ECMO, which include stroke (10%), hemorrhage (30%), deep venous thrombosis (70%), pulmonaty embolism (16%), and limb ischemia (<5%)

ECMO

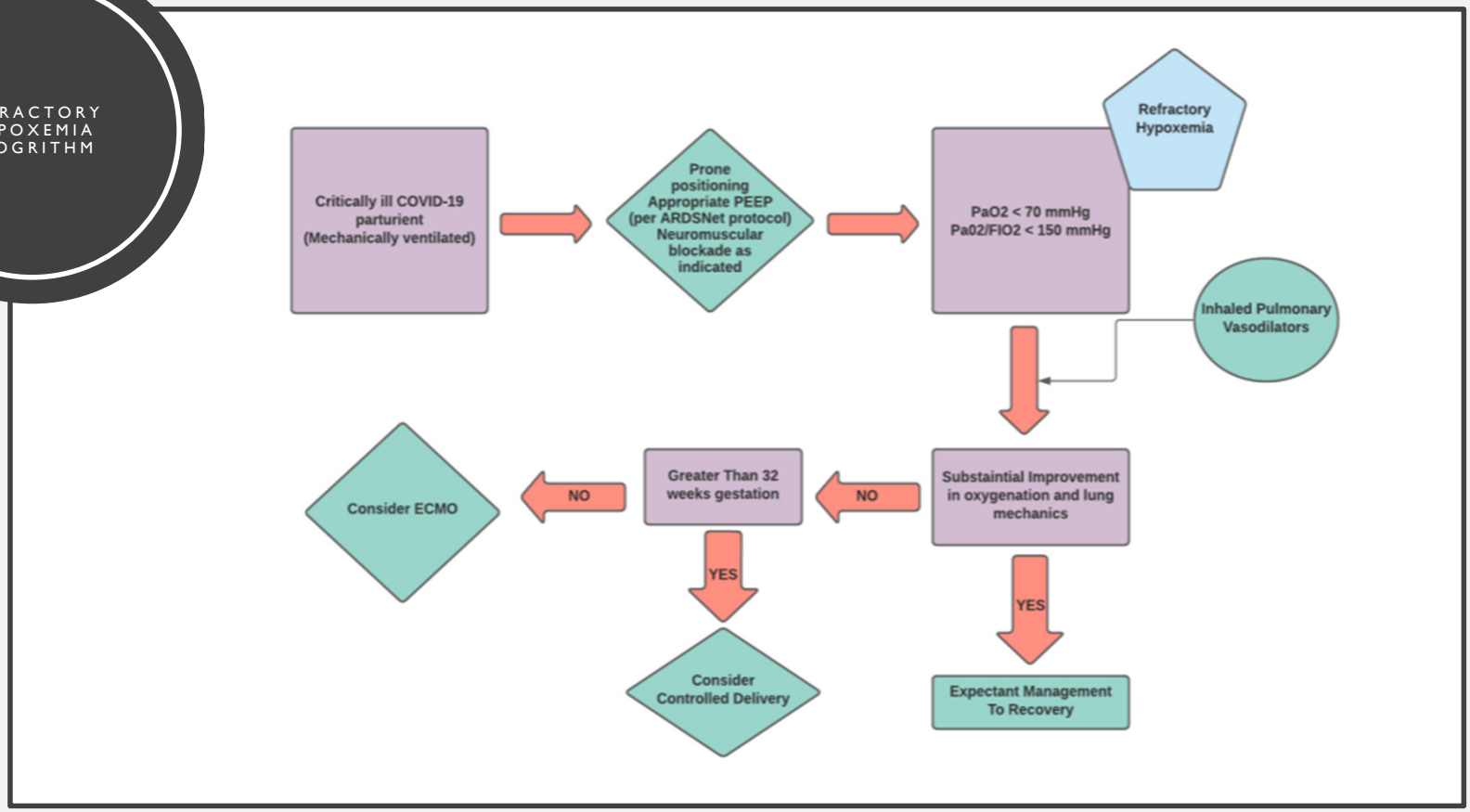
- Hypoxic respiratory failure despite optimal ventilation strategies (as per ELSO guidelines for ARDS)
- Severe hypercapnia (pH <7.2 and $PaCO_2$ >80 mm Hg for >6 hours)
- Prolonged ventilation <7 days
- Cardiogenic shock (refractory to conventional therapy—cardiac index <2 L/min/M^2, central venous oxygen saturation $ScVO_2$ <65%)
- Murray score >3
- Single organ failure with minimal or no comorbidities
- Massive pulmonary embolism
- Bridge to cardiac or lung transplantation
- Cardiac arrest

Murray score components: ratio of arterial oxygen tension to the fraction of inspired oxygen (PaO_2/FiO_2), positive end-expiratory pressure (PEEP), lung compliance, and chest radiograph
Abbreviations: ARDS, acute respiratory distress syndrome; ELSO, Extracorporeal Life Support Organization; $ScVO_2$, central venous oxygen saturation

REFRACTORY HYPOXEMIA

- Inability to maintain **PaO2 > 60 mm Hg** despite maximal FiO2 as well as efforts to optimize PEEP with prone positioning or other measures to improve oxygenation (eg, inhaled vasodilators, neuromuscular blockade)
- Maternal refractory hypoxemia can be expanded to the inability to maintain **PaO2 >70 mm Hg** with maximal FiO2 despite efforts to optimize oxygenation (eg, inhaled vasodilators, neuromuscular blockade)

REFRACTORY HYPOXEMIA ALOGRITHM



- Critical illness, including severe COVID-19 infection, ***increases the risk of thromboembolic events***
- Patients who are critically ill or mechanically ventilated should receive **prophylactic** **UNFRACTIONATED HEPARIN** (UFH) or **LOW-MOLECULAR-WEIGHT HEPARIN** (LMWH) if there are no contraindications to its use

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- There are limited, low-level data on the use of **therapeutic** anticoagulation for severe COVID-19 disease
- C-reactive protein and/or D-dimer may be used to guide management
- In a French study, 16.7% of severe COVID-19 patients had **pulmonary embolism** despite **prophylactic** anticoagulation, and patients with COVID-19 complicated by **ARDS** had an increased risk of thromboembolic events.
- A Dutch study of 184 ICU patients showed similar findings, with a high incidence of **thrombosis** (27%) in patients on prophylaxis
- However, other studies show **lower rates of VTE** and **pulmonary embolism** (3%)

THERAPEUTIC ANTICOAGULATION IN CRITICALLY ILL PREGNANT PATIENTS

THERAPEUTIC ANTICOAGULATION IN CRITICALLY ILL PREGNANT PATIENTS

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ANTENATAL & POSTPARTUM

- **Pregnancy** is an **additional risk factor for thrombosis**, especially in the third trimester and immediately postpartum, and contributes to *severe adverse morbidity and maternal mortality*
- Thus, **ANTICOAGULATION SHOULD BE CONSIDERED FOR IN-HOSPITAL MANAGEMENT OF COVID-19 DISEASE IN PREGNANCY**
- Anticoagulation regimens include both **UFH** and **LMWH**
- Dosing regimens can be delineated into three dosing strategies: **prophylactic**, **intermediate-dose**, and **full** anticoagulation.
- Regimen and dosing may be institution- and medical service-specific
- Prophylaxis and treatment regimens: Expert opinion from the American Society of Hematology recommends **prophylactic** dosing unless otherwise indicated for common conditions, eg, concomitant confirmed venous thromboembolism.
- Risk of **preterm birth** in inflammatory illness (spontaneous or iatrogenic) also places a pregnant patient at **elevated risk of peripartum bleeding**, which may be **worsened by therapeutic anticoagulation**
- **UFH/LMWH** upon discharge: Use of LMWH and UFH after discharge remains controversial, especially in pregnancy, and routine VTE prophylaxis is not recommended after hospital discharge.
- It is reasonable for providers to consider risks such as **obesity, pregnancy, immobility, and inherited thrombophilias** when considering VTE prophylaxis after discharge

REMDESIVIR

- The Adaptive COVID-19 Treatment Trial (ACTT-1) investigated the use of the antiviral agent **REMDESIVIR** among patients requiring oxygen therapy due to COVID-19 infection and demonstrated a **decreased duration of disease in treated patients**
- Because of these promising results, the National Institutes of Health (NIH) COVID-19 Treatment Guidelines Panel recommends **REMDESIVIR** for treatment of COVID-19 in hospitalized patients with **SpO2 ≤94%** on ambient air or those who require **supplemental oxygen**
- The Panel recommends **REMDESIVIR** for treatment of COVID19 in patients who are on mechanical ventilation or extracorporeal membrane oxygenation (ECMO)
- There is **no known fetal toxicity** associated with **REMDESIVIR**.
- **SMFM recommends that REMDESIVIR be offered to pregnant patients with COVID-19 meeting criteria for compassionate use**

https://www.gilead.com/purpose/advancingglobal-health/covid-19/emergency-access-to-remdesivir-outside-of-clinical-trials

DEXAMETHASONE

- RECOVERY trial demonstrated that **DEXAMETHASONE** **was associated with a decreased risk of mortality among people requiring mechanical ventilation** and also demonstrated a small but statistically significant **decrease in mortality risk among those requiring oxygen** for COVID-19
- Because of these promising preliminary results, the NIH COVID-19 Treatment Guidelines Panel recommends using **DEXAMETHASONE** **(6 mg PO or IV per day for up to 10 days)** in patients with COVID-19 who are mechanically ventilated and in patients with COVID-19 who require supplemental oxygen but who are not mechanically ventilated
- The Panel *recommends against* using **DEXAMETHASONE** in patients with COVID-19 who do not require supplemental oxygen
- **THESE RECOMMENDATIONS ARE NOT SPECIFIC TO PREGNANT PATIENTS**
- Since the benefit of mortality reduction outweighs the risk of fetal steroid exposure for this short course of treatment, **SMFM recommends that this treatment should also be offered to pregnant patients with COVID-19 requiring oxygen or mechanical ventilation**
- If glucocorticoids are indicated for fetal lung maturity, **DEXAMETHASONE** 6 mg IM every 12 hours for 48 hours (4 doses) followed by up to a total of 10 days of 6 mg dexamethasone PO/IV daily.
- If glucocorticoids are **NOT** indicated for fetal lung maturity, **DEXAMETHASONE** 6 mg dexamethasone daily (PO/IV) for up to 10 days should be utilized as in nonpregnant patients

MONOCLONAL ANTIBODIES

- **EMERGENCY USE AUTHORIZATIONS** for treatment of ***mild to moderate COVID-19*** in adult and pediatric (>12 years) patients, weighing at least 40kg, and who are at high risk for *progressing to severe COVID-19 and/or hospitalization*
- **HIGH RISK** is defined in these cohorts as patients who meet at least one of the following criteria: **BMI >35, chronic kidney disease, diabetes, and immunosuppressive treatment**
- **BAMLANIVIMAB** (Ly-CoV555), the monoclonal antibody used in clinical trials to treat COVID-19. The FDA has authorized it for emergency use.

THIS MEDICATION HAS NOT SHOWN A BENEFIT FOR PATIENTS WHO ALREADY REQUIRE OXYGEN OR ARE HOSPITALIZED

- **CASIRIVIMAB** (REGN10933) and **IMDEVIMAB** (REGN10987) are ***polyclonal "cocktails" of antibodies*** and are FDA- authorized for emergency use to treat mild to moderate COVID-19. **Exclusion criteria for use include supplemental oxygen requirement, hospitalization, or severe disease.**
- As these medications are used in mild to moderate COVID-19 patients, **risks and benefits** to the pregnant patient and fetus should be assessed by providers
- NIH COVID guidelines state that there is ***inadequate evidence*** for or against use of these agents however, there is ***no absolute contraindication to their use in appropriate pregnant patients***

ANTIBIOTICS

- Use of **antibiotic** is reasonable if **community-acquired pneumonia** coinfection is suspected
- Obtain **culture data** when possible before initiating antibiotics, although **empiric antibiotic treatment** may be given while awaiting these results
- If antibiotics are indicated, clinicians should not wait more than **45 minutes** to start antibiotic therapy
- **CEFTRIAXONE** plus **AZITHROMYCIN** or **CEFTRIAXONE** alone are commonly used to treat community-acquired pneumonia and are not contraindicated in pregnancy
- For patients with severe disease or who have risk factors for **hospital-acquired, ventilator-acquired, and/or drug-resistant types of pneumonia**:
  - broad-spectrum agents should be employed, such as **CEFEPIME**, **MEROPENEM**, **PIPERACILLIN-TAZOBACTAM**, **LINEZOLID**, and **VANCOMYCIN**, all of which are acceptable in pregnancy
- **Procalcitonin** level is not required in the assessment of COVID-19, but it *can be used to help delineate superimposed bacterial pneumonia*. Although an elevated procalcitonin level is suspicious of bacterial infection, **culture data** (eg, sputum, blood, urine) should also be collected with the implementation of antibiotics

TIMING OF DELIVERY

- In pregnant patients at or after ***32 weeks*** of gestation with refractory hypoxemia, delivery may be considered if it will allow for further optimization of care
- The severity of illness may dictate earlier delivery
- **Neonatal mortality is 0.2% at 32 weeks** and remains at this level or lower for each week thereafter.
- **Major morbidity**:
  - 8.7% at 32 weeks
  - 4.2% at 33 weeks
  - 4.4% at 34 weeks
  - 2.8% at 35 weeks
  - 1.8% at 36 weeks

- **COVID-19-POSITIVE STATUS IS NOT AN INDICATION FOR DELIVERY**
- Delivery should be reserved for routine obstetrical indications
- Medically indicated deliveries should not be delayed due to COVID-19- positive status
- In an asymptomatic or mildly symptomatic woman positive for COVID-19 at 37 to 38 6/7 weeks of gestation without other indications for delivery, **expectant management** can be considered until 14 days after the polymerase chain reaction (PCR) result was noted to be positive OR until 7 days after onset of symptoms and 3 days after resolution of symptoms. This option allows for decreased exposure of health care workers and the neonate to SARS-CoV-2 and decreased PPE utilization in areas with supply-chain limitations
- In an asymptomatic or mildly symptomatic woman positive for COVID-19 at 39 weeks of gestation or later, **delivery** can be considered to decrease the risk of worsening maternal status
- **MODE OF DELIVERY SHOULD REMAIN PER ROUTINE INDICATIONS**
- During delivery, *COVID-19 patients should be instructed to wear a mask* throughout labor, delivery, and postpartum, and appropriate personal protective equipment should be utilized by all health care workers

TIMING OF DELIVERY - CRITICALLY ILL

- **MULTI-SPECIALTY APPROACH IS ENCOURAGED**
- Third-trimester **uterus** may account for some mechanical restriction in ventilation, it is unclear whether delivery provides a substantial improvement in every case
- **Mechanical ventilation** alone is not an indication for delivery
- If delivery is considered based on severe hypoxemia, ***other options*** should also be discussed (prone positioning, ECMO, advanced ventilator methods) especially if **the gestational age is less than 30 to 32 weeks**
- If delivery is being considered and ECMO and pulmonary vasodilators are not available, ***transport should also be considered***

THANK YOU