

COVID-19 and Pregnancy Obstetric Considerations

Catherine A. Bigelow, MD
Minnesota Perinatal Physicians
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Disclosure

- I have no financial conflicts of interest.

Objectives

Discuss unique physiology of pregnancy and risks of viral infection

Review the literature on severe COVID-19 in pregnancy

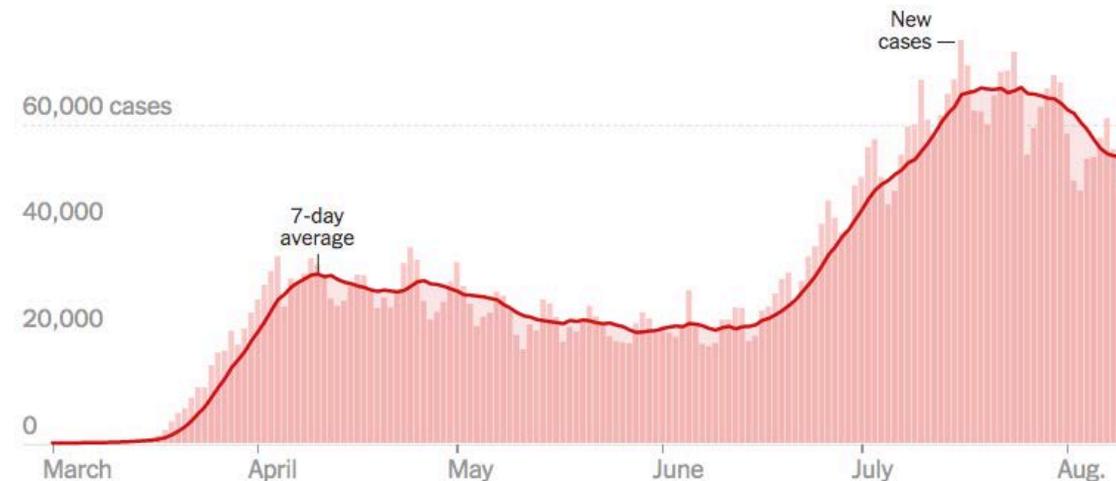
Outline recommendations for hospitalization & transfer in the pregnant patient

Summarize obstetric clinical protocol changes in the era of COVID-19

Novel Coronavirus Disease 2019 – COVID-19

- Caused by ssRNA-virus SARS-CoV-2
 - Originated in Wuhan, Hubei Province, China in late 2019
 - First case in the USA on 1/20/20 in Washington state
 - Pandemic status on 3/11/20 by the WHO
- Current state of the union
[As of 8/10/20]
 - COVID-19 cases: 5,023,649
 - COVID-19 deaths: 161,842
- USA has highest # deaths worldwide
 - Case fatality ratio 3.2%

New reported cases by day in the United States



COVID-19 Cases in Pregnant Women

- Documented COVID-19 in pregnant women
 - 15,735 cases
 - 37 deaths
 - 4,086 hospitalizations
- Limitations
 - Not all pregnancies will be reported
 - No distinction between COVID hospitalization vs. OB hospitalization



COVID-19 in Minnesota

- Current state of affairs [as of 8/10/20]

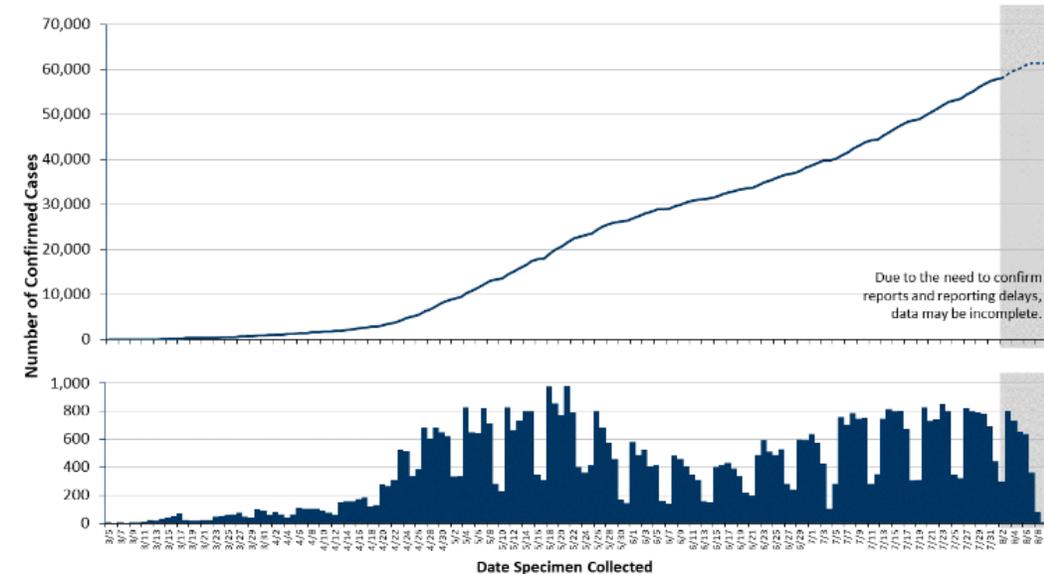
- Number of cases: 61,516
- Number of deaths: 1,660
- Total number hospitalized: 5,606
- Current number hospitalized: 320
- Current number in ICUs: 159

- Statewide response:

- Stay Home order by Gov. Walz 3/27/20-5/18/20
- Phased re-opening plan – last “expansion” 6/10/20

Minnesota Case Overview

- Total positive cases: 61,516
- Number of health care workers: 6,854



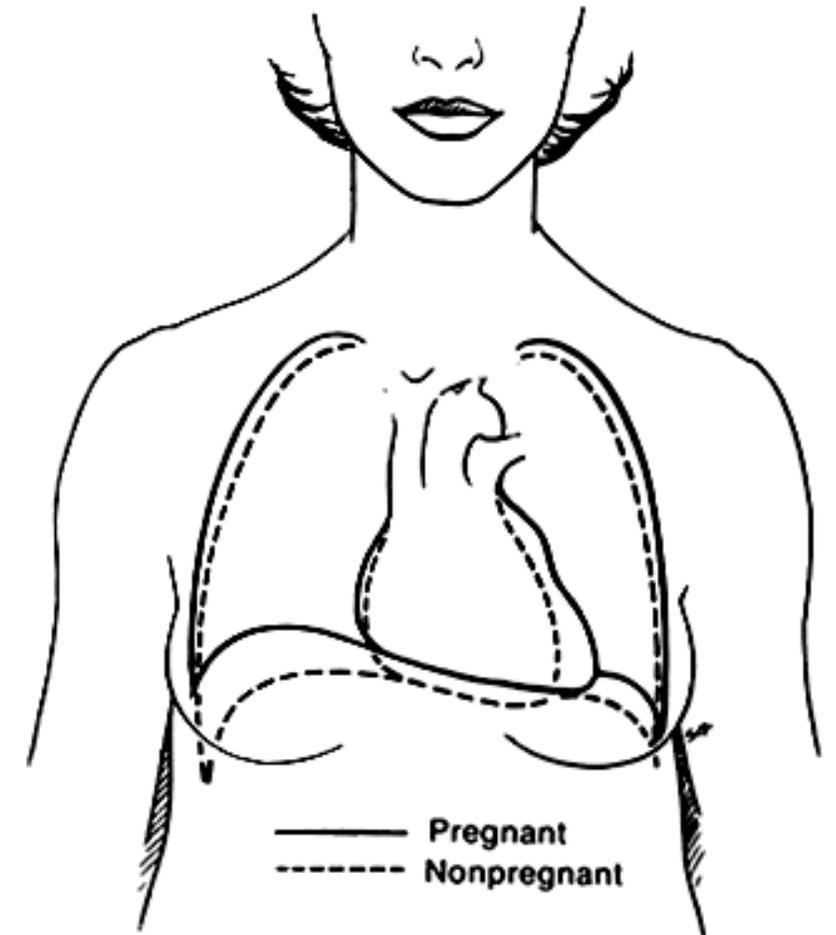
Physiology of Pregnancy

Risks to the Obstetric Patient with
Respiratory Infection

COVID-19 Presentation in Pregnancy

Potential Risks in the Pregnant Patient

- Respiratory
 - Airway edema
 - Decreased chest wall/diaphragmatic compliance
 - Decreased functional residual capacity
 - Baseline increased minute ventilation
 - Respiratory alkalosis
- Cardiovascular
 - Baseline tachycardia
 - Increased plasma volume
- Immunologic
 - Pro-inflammatory state in 3rd trimester
 - Decreased levels of T & B cells (adaptive immunity)
 - Increased NK cells & monocytes (innate immunity)
 - SARS-CoV-2 leads to cytokine storm – interleukins, TNF α , IFN γ



Respiratory Viruses in Pregnancy

- H1N1 Influenza
 - Hospitalization up to 87%, severe disease up to 22%
 - 12% case fatality rate of H1N1 pandemic
 - Increased rates of PTB, SGA, & IUFD
 - Oseltamivir decreases incidence of severe disease
- Other Coronaviruses
 - SARS –15% case fatality rate, 60% ICU admission rate, increased rate of IUGR and placental abnormalities
 - MERS – 27% case fatality rate, 64% ICU admission rate
 - No vertical transmission, regardless of mode of delivery

COVID-19 Presentation in Pregnancy

- Dry cough
- Fever
- Myalgia
- Shortness of breath
- Anosmia, dysgeusia
- Less common: rhinorrhea, sore throat, headache, diarrhea
- Obstetric complaints:
 - Decreased fetal movement
 - Intrapartum or postpartum fever
 - Hypertension, preeclampsia-type picture
 - Postpartum dyspnea, tachypnea, hypoxia

Defining COVID-19 Severity

- **Asymptomatic**: Positive SARS-CoV-2 and no symptoms
- **Mild**: flu-like symptoms (fever, cough myalgia, anosmia)
 - No dyspnea, SOB, abnormal chest imaging
- **Moderate**: evidence of lower respiratory tract disease while maintaining O₂ sat >93%
 - Dyspnea, pneumonia on imaging, abnormal ABG, refractory fever
- **Severe**: RR > 30 breaths/min, hypoxia ≤93%, P:F ratio <300, >50% lung involvement on imaging
- **Critical**: Multiorgan failure or dysfunction, shock, or respiratory failure requiring mechanical ventilation or HFNC

Asymptomatic Infection Rates

- Variable rates cited among institutions
 - 10% in the Newark, NJ area (unpublished data)
 - 14.6% in Marseilles, France (Hydroxychloroquine trial)
 - 32.6% in New York, NY (Columbia University)¹ → 13.7% subsequent data²
 - 16.5% in New York, NY (Mount Sinai)³
 - 42.5% in Vo', Italy⁴
 - 43% in Iceland⁵
- CAVEAT: These institutions are performing universal testing
 - Decisions re: universal testing depend on both disease prevalence and testing availability
 - May not make sense to universally test in all regions/health systems

¹Breslin et al, AJOG MFM, Apr 6 2020

²Sutton et al, NEJM, Apr 13 2020

³Buckley et al, AJOG MFM, May 15 2020

⁴Lavezzo et al, Nature, June 23 2020

⁵Gudbjartsson et al, NEJM June 11 2020

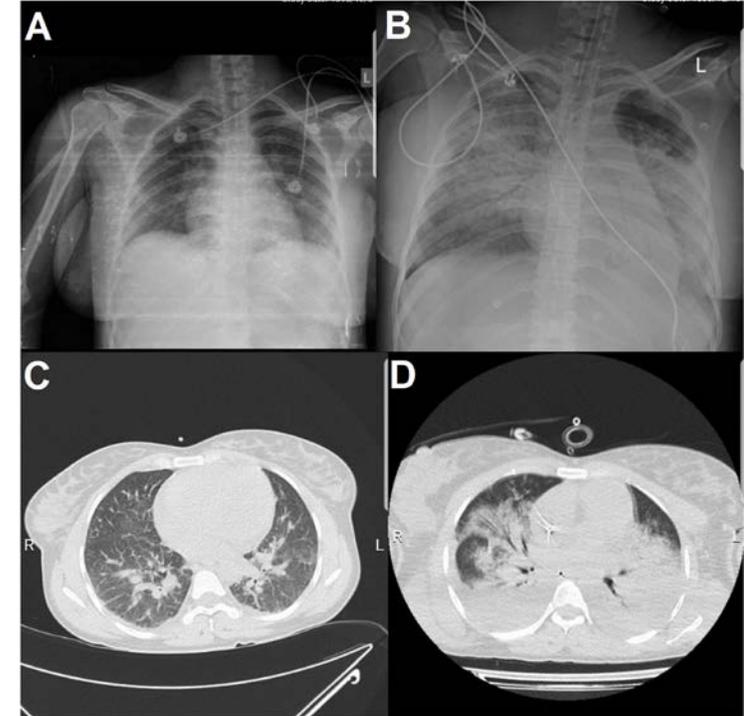
Laboratory Abnormalities in COVID-19

Laboratory Test	Normal Non-Pregnant	Normal Pregnant	COVID-19 Literature
White Blood Cell Count	3500-9100/mL ³	5600-17000/mL ³	Often remains normal
Lymphocyte Count	900-4600/mL ³	1000-3600/mL ³	Lymphopenia <800/mL ³
Creatinine	0.5-1.2 mg/dL	0.4-0.8 mg/dL	May be elevated
D-Dimer	<0.5	Elevated	Elevated
C-Reactive Protein	<0.5 mg/dL	Elevated	Elevated
Troponin-I	<0.3 ng/mL	<0.3 ng/mL	May be elevated
Lactate	0.5-2.0 mmol/L	0.6-1.8 mmol/L	May be elevated
Arterial pH	7.35-7.45	7.4-7.45	-
PCO ₂	32-45 mmHg	30-32 mmHg	-

None of these are a helpful screening tool to guide SARS-CoV-2 PCR testing

Adjunctive Diagnostic Tools & Findings

- Imaging
 - CXR – reticular interstitial opacities
 - CT Chest – multifocal ground glass opacities
 - Chest US – pleural thickening, consolidation
- Cardiac testing
 - TTE – decreased systolic function, global hypokinesis
 - ECG – arrhythmia, ischemic changes
- Considerations: sensitivity/specificity, ability to clean/cohort machines
 - How will the test change your diagnosis? Treatment? Level of care?



Literature Review

US Experience

Severe COVID-19 in Pregnancy

Obstetric Cases of COVID-19 - USA

Source	Location	# Cases	Findings
Breslin, et al. <i>AJOG MFM</i>	New York, NY	43	29/43 (67%) patients presented with symptoms or screen positive 66% dry cough, 48% fever, 38% myalgia 86% mild, 9% severe, 5% critical disease 55% SVD No vertical transmission
Pierce-Williams, et al. <i>AJOG MFM</i>	Multi-institution	64	All cases severe or critical illness Hospitalization day 7 of illness, median hospital duration 6 days 75% PTB in critically ill No maternal or fetal/neonatal deaths
Lokken, et al. <i>AJOG</i>	Seattle, WA	46	93.5% symptomatic 69.8% cough, 51.2% fever/chills 50% 3 rd trimester 15% severe infection – most overweight or obese w comorbidities 1 unexplained IUFD – placenta & fetopsy negative for SARS-CoV-2 1 iatrogenic PTB at 33w for maternal respiratory status

Illness Severity in Pregnancy

Pregnancy Status	Number Cases	Mild	Severe	Critical
Non-Pregnant*	>44,000	81%	14%	5%
Pregnant^	43	86%	9%	5%

*Data from Wu et al, China

^Data from Breslin et al, Columbia University

Illness Severity in Pregnancy

- Initial data from NY suggested no increased rate of ICU admission¹
- CDC MMWR Report: **Pregnant women higher risk**
 - Compared to non-pregnant women ages 15-44 positive for SARS-CoV-2
 - **Hospitalization: 31.5%** (vs. 5.8% non-pregnant, **aRR 5.4**)
 - **ICU admission: 1.5%** (vs. 0.9%, **aRR 1.5**)
 - **Mechanical ventilation: 0.5%** (vs. 0.3%, **aRR 1.7**)
 - Death rate similar: 0.2%
 - All outcomes higher in 35-44yo
 - Higher rates reported in Hispanic & Black women
 - Higher rates of underlying medical conditions: chronic lung disease, diabetes, CV disease
 - Limitations: trimester-specific data not available, unable to distinguish indication for hospitalization (ex: respiratory status vs. delivery), no data on perinatal outcomes (loss, PTB, etc.)
- Despite this MMWR report, CDC has NOT added pregnant patient to its list of high risk populations

¹Blitz et al, AJOG Research Letter, May 2020

²CDC MMWR, June 26 2020

Severe/Critical COVID-19 in Pregnancy

Source	Location	Cases	Findings
Juusela, et al. <i>AJOG MFM</i>	Newark, NJ	7	2/7 (28.5%) of patients developed cardiomyopathy 1/2 patients required intubation for severe hypoxemia, PEA arrest, was resuscitated and remained intubated TTE features: global hypokinesis, EF 40-45%
Schnettler, et al. <i>AJOG MFM</i>	Cincinnati, OH	1	Case of severe ARDS on day 5 of illness (at 31w GA) Required intubation, high PEEP, proning
Karami, et al. <i>Travel Med Infect Dis</i>	Iran	1	Respiratory failure requiring intubation, RV failure, hypotension IUFD and spontaneous PTB at 30w2d Decompensation and death following ARDS with multiorgan failure
Hantoushzadeh, et al. <i>AJOG</i>	Iran	9	7/9 (77.8%) maternal deaths 1 survivor required tracheostomy 5/9 (55.6%) IUFD or neonatal demise
Vallejo & Ilagan. <i>Obstet Gynecol</i>	New York, NY	1	Presented with SOB, cough, fever, sore throat x1 week Rapid respiratory compromise, intubation, delivery via C-section at 37w Death within 36 hours from multiorgan failure and cardiac arrest

Vertical Transmission of COVID-19

- **No proven cases of vertical transmission** during delivery¹
 - Variable reports of PCR+ neonates many hours after delivery
 - Neonatal +IgM at birth thought to be false positive
 - Amniotic fluid, vaginal swab PCR universally negative
- Emerging evidence demonstrates SARS-CoV-2 infection in the placenta²⁻⁴
- No data from first trimester infection on congenital malformation or congenital viral syndrome

¹Lamouroux et al, AJOG

²Penfield et al, AJOG MFM; ³Algarroba et al, AJOG; ⁴Patanè et al, AJOG MFM

Hospitalization in Pregnancy

Recommendations for Hospitalization in Pregnancy for COVID-19+/PUI



- Admission criteria for COVID-19+/PUI in pregnancy
 - O2 sat < 95% on RA
 - Tachypnea > 25 breaths/min or increased work of breathing
 - PCO2 > 32 mmHg on ABG
 - Chest imaging (xray, ultrasound, or CT scan) consistent with COVID-19 pneumonia
 - Cardiac symptoms, cyanosis, or elevated troponin
 - Refractory fever > 39°C not alleviated with antipyretics
 - Inability to tolerate PO hydration or meds
 - New onset confusion or lethargy
 - Non-reassuring fetal testing
 - Obstetric complaints – preterm labor, PPRROM, preeclampsia, decreased fetal movement, etc.

Initial Stabilization & Hospital Management

- Maternal stability
 - Respiratory status
 - Hemodynamics
 - Oxygen requirement, imaging, lab findings
- Fetal stability
 - GA dependent
- Testing
 - SARS-CoV-2 nasopharyngeal or oropharyngeal swab
 - Other pertinent differential dx
- Treatment
 - Symptomatic support
 - Oxygen
 - Therapeutics

Treatments in COVID-19

- Supportive care, acetaminophen, cough suppressants
- Remdesivir (ACTT-1 trial): decreased duration of disease in treated patients
 - Recommended for patients with severe COVID-19
 - No known fetal toxicity
- Convalescent plasma: experimental
 - Likely low risk in pregnancy
- Dexamethasone (RECOVERY trial): decreased mortality among mechanically ventilated patients and those requiring oxygen
 - Benefit outweighs risk of steroid exposure to the fetus¹
- Systemic antibiotics: only if concern for co-infection with CAP
 - Ceftriaxone + azithromycin
 - Broad-spectrum abx acceptable for HAP, VAP, drug-resistant strains
- No longer recommended: hydroxychloroquine (Plaquenil), lopinavir-ritonavir (Kaletra)

Transfer Criteria for COVID-19 in Pregnancy

- **Persistent hypoxia** <93% despite O2 via NC or any need for non-invasive or invasive mechanical ventilation
- **Tachypnea** >30 breaths/min
- **Hypercarbia** on ABG (>34 mmHg)
- Lung imaging with **>50% lung involvement**
- Any signs of **multiorgan failure or dysfunction**

- If unstable, recommend intubation locally prior to transfer
 - Discussion with MPP on call re: utility of delivery for maternal benefit

Regional Care for COVID-19 in Pregnancy

- Asymptomatic or mild COVID-19+ respiratory illness – outpatient care
- Asymptomatic or mild COVID-19+ hospitalized with OB issue
 - Term/preterm labor
 - Pre-eclampsia
 - PPRM
 - Non-reassuring fetal testing
 - Transfer to metro TMBC would be per Allina OB Care Model
- Any patient with worsening respiratory status should be considered for transfer
 - Discussion with MPP on call

Transfer to Metro Hospitals

- Abbott Northwestern or United Hospitals preferred sites of transfer for COVID+ pregnant patients
 - Regardless of location of referring regional hospital
 - Allina Access Center [1-844-725-5462](tel:1-844-725-5462) [1-844-7ALLINA]
 - Transfer call to include: Referring physician, MPP, intensivist, nursing
 - Determination of need for: L&D, ICU, Medicine COVID Unit
 - If no OB concern, recommend Medicine COVID unit
- Consider consultations for COVID+/PUI pregnant patient, as appropriate:
 - Maternal-Fetal Medicine
 - Infectious Disease
 - Internal Medicine
 - Anesthesiology
 - Social Work

Obstetric Protocol Changes in COVID-19

Antenatal Corticosteroids

- Antenatal corticosteroids are a beneficial intervention for the preterm fetus born <34 weeks
- Concern re: systemic corticosteroids in initial COVID-19 literature
 - RECOVERY Trial suggests benefit from systemic dexamethasone
- Protocol changes:
 - If 23w0d-33w6d with severe COVID-19, recommend FLM dosing x48h → lower dose dexamethasone for duration of treatment
 - If 23w0d-33w6d and high likelihood of delivery within 7 days, OK to administer
 - No late preterm steroids >34 weeks' gestation
 - No rescue steroids
 - Individualize management based on risk/benefit for neonate(s) and mother

Magnesium Sulfate

- Check renal function before administration
 - Dose adjustments may be required
- Weigh risk/benefit of maternal respiratory depression or pulmonary edema
- Protocol Changes:
 - For fetal neuroprotection <32 weeks' gestation
 - Only if delivery imminent
 - Consider 4g bolus only
 - For seizure prophylaxis
 - Recommended in severe pre-eclampsia only
- Caution advised in pre-eclampsia
 - Reports of load → infusion have been successful¹

¹Joudi et al, AJOG MFM, May 20 2020

Management of Preterm Labor

- Preterm labor may be increased with severe systemic inflammation
 - Many COVID-19 preterm births have been iatrogenic
- Tocolysis
 - Only for documented cervical change during 48h of betamethasone
 - Nifedipine considered as a first line
 - Unclear impact of NSAIDs in COVID-19
 - For patients with cardiac manifestations of COVID-19: short-acting nifedipine is **CONTRAINDICATED**
 - Potent systemic and pulmonary vasodilation
- Judicious use of IVF – bolus only, no maintenance

Inhaled Agents – Oxygen & Nitrous Oxide

- Oxygen use in labor
 - Use not supported by data to suggest improvement in outcomes
 - SMFM/SOAP guidelines recommend against O₂ for fetal indication¹
 - If fetal indication, must be <4L via nasal cannula, no facemask
 - Recommended for maternal SpO₂ <95%
- Nitrous oxide
 - Not recommended or available at this time at Allina Health
 - Some centers may allow for patients with confirmed negative COVID-19

Postpartum Hemorrhage

- Tranexamic acid
 - Hypercoagulability of pregnancy and COVID-19 of concern
 - May still be used in COVID-19 positive patient with hemorrhage
 - Prophylactic use with risk/benefit of postpartum bleeding vs. severity of COVID-19 illness should be considered
- Methergine
 - Cautious use due to potential cardiovascular effects in COVID-19
- Hemabate, Pitocin, Cytotec recommended as first line

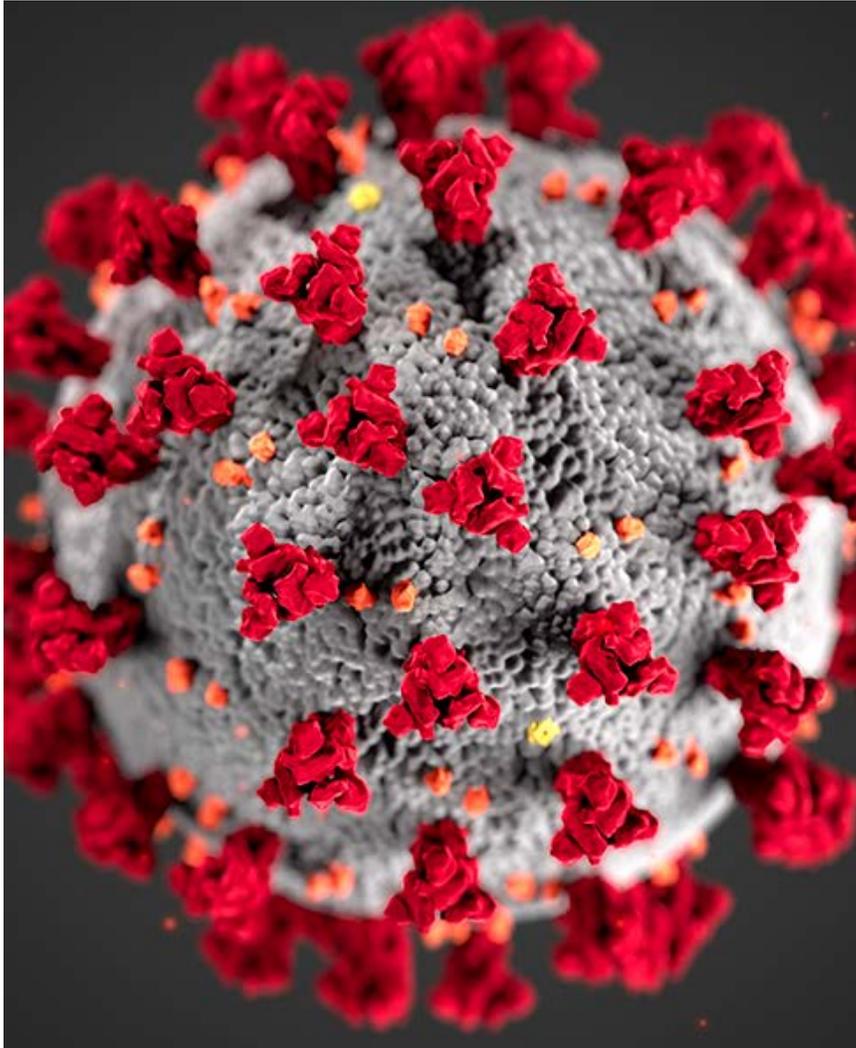
Venous Thromboembolism Prophylaxis

- Hypercoagulability with COVID-19 appears increased
 - May compound with hypercoagulability of pregnancy
- All pregnant patients hospitalized with COVID-19 should receive pharmacologic VTE prophylaxis
 - Agent used (UFH vs. LMWH) depends on GA, likelihood of delivery, bleeding risk
- No data to support therapeutic anticoagulation

Delivery Timing in COVID-19

- Critical illness: individualized
 - Risk/benefit to patient & fetus
 - Communication between MFM & ICU teams
 - Improvement in lung mechanics is theoretical
 - Maximize other options (proning, ECMO, advanced ventilation) particularly if <30-32 weeks' GA
- Asymptomatic or mild illness: COVID-19 positive status is not an indication for delivery
 - If asx or mild at 39+ weeks, can consider delivery to decrease risk of worsening maternal status
 - Mode of delivery per routine OB indication
 - Mask patient throughout labor, delivery, & postpartum

Thank you! Questions?



- Resources for OB Providers
 - smfm.org/covid19
 - acog.org/topics/covid-19
 - cdc.gov/coronavirus
 - health.state.mn.us/diseases/coronavirus
- PRIORITY Study
 - Pregnancy CoRonavirus Outcomes RegIsTrY
 - Nationwide registry of pregnant or recently pregnant women with suspected or confirmed COVID-19
 - priority.ucsf.edu/healthcare-providers

Minnesota Perinatal Physicians – Contact Us

- Contact Information: 612-863-4502, option 2 to be connected with a provider
 - Allinahealth.org/mnperinatal
- Midwest Fetal Care Center: 855-693-3825
 - MWfetalcare@allina.com
- Children's Physician Access: 612-343-2121

