

وبینار کووید 19 و بارداری

اداره مامایی دانشگاه علوم پزشکی تهران



tritapp

Connecting Health Experts

COVID 19 and PREGNANCY

Severity of Illness Categories

Asymptomatic or
Presymptomatic

- Positive PCR
- No symptoms

Mild

- Fever, cough, sore throat, malaise, headache, muscle pain **without** shortness of breath, dyspnea or abnormal chest imaging

Moderate

- Respiratory disease by clinical assessment or imaging + SpO₂ ≥94% on room air at sea level

Severe

- Individuals who have RR >30 /minute, SpO₂ <94% on room air at sea level, PaO₂/FiO₂ <300 mmHg **OR**
- Lung infiltrates >50%

Critical

- Respiratory failure, septic shock, and/or multiple organ dysfunction

Criteria for Inpatient Management

Pregnant COVID-19 patients with



**Moderate to severe category
or
SpO₂ <95%**

Assessment for Pregnant Women With COVID-19

Fever $\geq 38^{\circ}\text{C}$ (100.4°F) or ≥ 1 :

- Cough
- Difficulty breathing or shortness of breath
- Chills
- Headache
- Sore throat
- New loss of taste or smell
- Unprotected exposure to known COVID-positive individual
- Fatigue
- Muscle or body aches
- Congestion or runny nose
- Nausea or vomiting
- Diarrhea

Testing for covid

Any positive answer

Illness Severity Assessment

Elevated Risk

Immediately seek care in an emergency department or equivalent unit that treats pregnant women

Difficulty breathing or shortness of breath

Difficulty completing a sentence without gasping for air or needing to stop to catch breath frequently when walking

Cough with > 1 teaspoon of blood

New pain or pressure in the chest

Unable to keep liquids down

Signs of dehydration such as dizziness when standing

Less responsive than normal or confusion

Assessment for Pregnant Women With COVID-19

If there is no sign of elevated risk



Assess Clinical and Social Risks

- Hypertension
- Diabetes
- Asthma
- HIV
- Chronic heart , liver, kidney, lung disease
- Blood dyscrasia
- Immunosuppressive medications
- Overweight or obesity
- Maternal age >35 y

Comorbidities

Obstetric
issues

Inability to
care for self
or arrange
follow-up

Assessment for Pregnant Women With COVID-19

Any positive answers to clinical risk



Moderate
Risk

- See patient as soon as possible in an ambulatory setting with resources to determine severity of illness.
- Pulse oximetry, chest X-ray, or ABG as clinically indicated.
- Pregnant women (with abdominal shielding) should not be excluded from chest CT if clinically recommended

Outpatient Management

- Pregnant outpatients with COVID-19 should be monitored closely by their obstetric care providers for worsening symptoms
- Patients should perform daily self-assessments

Outpatient Management

Reasons to call a health care provider

Worsening shortness of breath

Tachypnea

Unremitting fever ($>39^{\circ}\text{C}$) despite appropriate use of acetaminophen

Inability to tolerate oral hydration or needed medications

SpO₂ $<95\%$ either at rest or on exertion

Persistent pleuritic chest pain

New-onset confusion or lethargy

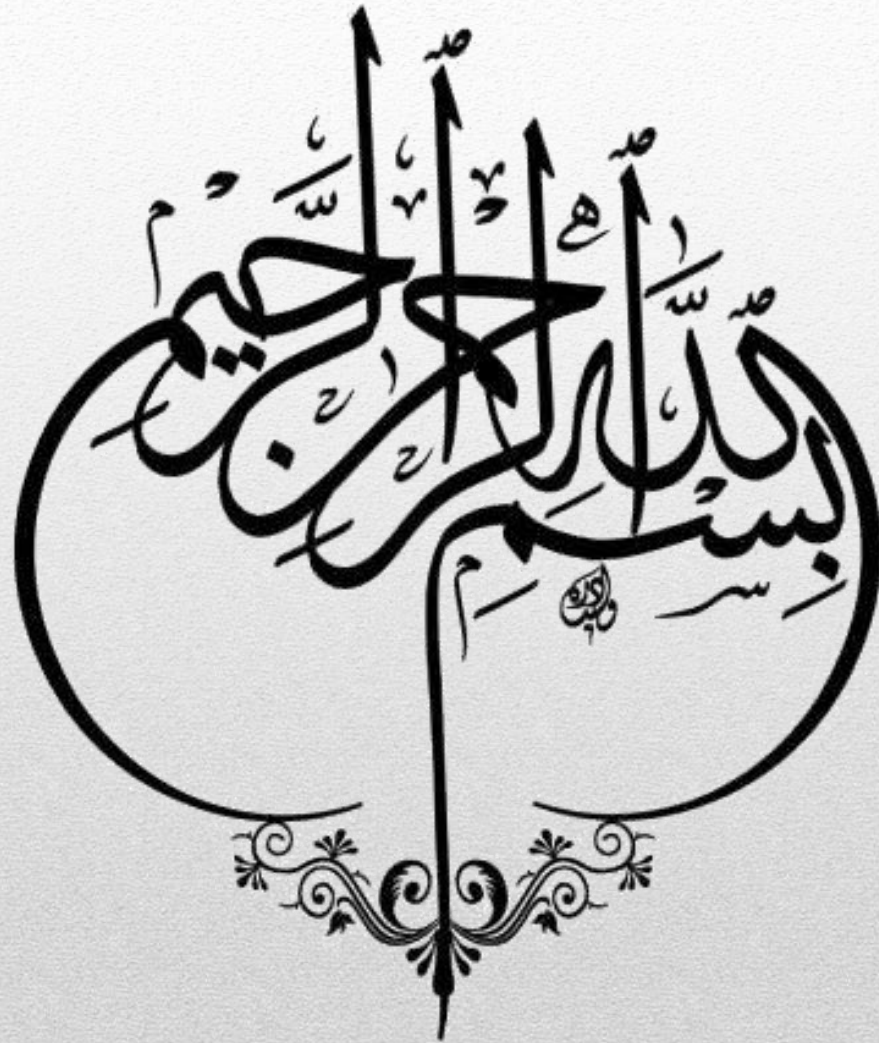
Cyanotic lips, face, or fingertips

Obstetrical complaints, such as preterm contractions, vaginal bleeding, or decreased fetal movement

References

- American College of Obstetricians and Gynecologists. July 14, 2020
- COVID-19 Treatment Guidelines, NIH , July 2020
- COVID-19 Infection in Pregnancy, RCOG 24 July 2020
- Fetal Diagn Ther 2020;47:519–528
- Society for Maternal-Fetal Medicine, Management Considerations for Pregnant Patients With COVID-19, 7.2.2020





Management Considerations for Pregnant Patients With COVID-19

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Identification of Mild, Moderate, and Severe Symptoms of COVID-19

➤ Mild disease

Flu-like symptoms→

fever, cough, myalgias, and anosmia without dyspnea, shortness of breath, or abnormal chest imaging.

➤ Moderate disease

Evidence of lower respiratory tract disease with clinical assessment (dyspnea, pneumonia on imaging, abnormal blood gas results, refractory fever of 39.0°C /102.2 °F or greater not alleviated with acetaminophen) while maintaining an oxygen saturation of greater than 93% on room air at sea level.

➤ Severe disease

- RR>30
- Hypoxia with oxygen saturation less than or equal to 93%, 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

- Is defined as multi-organ failure or dysfunction, shock, or respiratory failure requiring mechanical ventilation or high-flow nasal cannula.
-

Reasons to call a health care provider:



1. Worsening shortness of breath
 2. Tachypnea
 3. Unremitting fever ($>39^{\circ}\text{C}$) despite appropriate use of acetaminophen
 4. Inability to tolerate oral hydration or needed medications
 5. Oxygen saturation less than 95% either at rest or on exertion
 6. Persistent pleuritic chest pain
 7. New-onset confusion or lethargy
 8. Cyanotic lips, face, or fingertips
 9. Obstetrical complaints, such as preterm contractions, vaginal bleeding, or decreased fetal movement
- follow-up visit at least once within 2 weeks of diagnosis of COVID-19.
 - Antenatal testing should be performed for the usual indications, with consideration of consolidating these tests as feasible, eg, a once-weekly full or modified biophysical profile instead of twice-weekly nonstress tests.
-

Inpatient monitoring:

1. With moderate to severe signs, $O_2\text{Sat} < 95\%$
 2. With comorbid conditions, eg, uncontrolled hypertension, inadequately controlled (GDM or DM), chronic renal disease, chronic cardiopulmonary disease, or immunosuppressive states.
 3. With fevers $>39^\circ\text{C}$ despite acetaminophen.
 4. raising concern for secondary hemophagocytic lymphohistiocytosis (sHLH) or "cytokine storm syndrome."
 5. respiratory rate greater than 30 bpm, use of accessory muscles, pursing of lips, and need for oxygen supplementation.
-

Pregnant patients, have mild or no symptoms:

- **Outpatient** monitoring with a 14-day self-quarantine
 - Exertional SO_2 should also be assessed with a walking SO_2 test. Patients whose SO_2 is less than or equal to 95% on room air with exertion should be considered for inpatient admission.
-

O₂Sat in pregnancy:



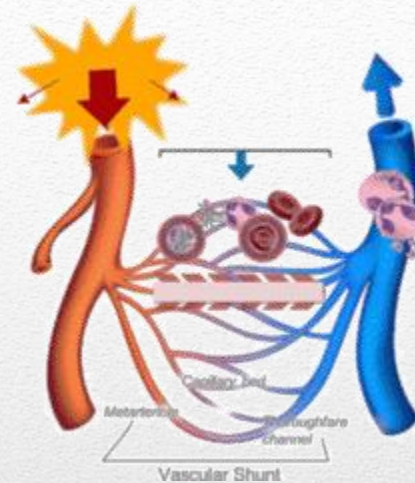
- In general, the recommended oxygen saturation is 95% or greater in pregnancy.
-

Protocols for inpatient care:

1. vital sign → q 4 to 8 hours and as needed: temperature, heart rate, respiratory rate, blood pressure, and pulse oximetry.
 2. **Severe** disease → q 2 to 4 hours. To reduce exposure to health care workers, continuous pulse oximetry and/or telemetry.
 3. **Critical** illness, continuous pulse oximetry and telemetry should be utilized. Noninvasive and invasive cardiovascular monitoring can be considered as indicated. Vital signs, including respiratory support as needed, should be recorded every 1 to 2 hours.
 4. Fetal and tocodynamometer monitoring should also be performed when fetal needed.
-

Anticoagulation:

Patients who are critically ill or mechanically ventilated should receive prophylactic heparin or low-molecular-weight heparin if there are no contraindications to its use.



Treatment options:

Antibiotics and plasma therapy:

- ✓ **Azithromycin, Remdesivir, Tocilizumab, Bacillus Calmette–Guérin vaccine, and convalescent plasma.**

None of these therapies are contraindicated in pregnancy.

Use of antibiotics:

- ❖ Ceftriaxone plus azithromycin or ceftriaxone , cefepime, meropenem, piperacillin-tazobactam, linezolid, and vancomycin can be used to treat community-acquired pneumonia and are not contraindicated in pregnancy.
 - ❖ Procalcitonin can be used to help delineate superimposed bacterial pneumonia.
 - ❖ Although a procalcitonin level is not required in the assessment of COVID-19, it can be used to help delineate superimposed bacterial pneumonia.
 - ❖ Many COVID-19 patients without bacterial pneumonia will have normal procalcitonin levels (less than 0.1 ng/mL).
 - ❖ It should be noted that a high procalcitonin level does not rule out COVID-19 infection.
-

Timing of Delivery for Critically Ill Pregnant Patients:

- Should be individualized. Decisions should be based on maternal status, concurrent pulmonary disease.
- Critical illness.
- Ability to wean off the ventilator \ ventilator mechanics.
- Gestational age at time of delivery
- Shared decision-making with the patient or healthcare proxy.

Mechanical ventilation alone is not an indication for delivery.

- If delivery is considered based on severe hypoxemia, other options should also be discussed, including prone positioning, extracorporeal membrane oxygenation (ECMO), and the use of other advanced ventilator methods, especially if the gestational age is less than 30 to 32 weeks.
 - Though the late third-trimester uterus may account for some mechanical restriction in ventilation, it is unclear whether delivery provides a substantial improvement in every case.
-

Timing of Delivery in Asymptomatic or Mildly Symptomatic Pregnant Patients

- ❖ **COVID-19-positive status is not an indication for delivery, and delivery should be reserved for routine obstetrical indications.**
 - ❖ 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.
-

Fetal concerns:

- Limited data are currently reassuring regarding fetal risks in the setting of maternal COVID-19 infection.
-

Preterm labor:

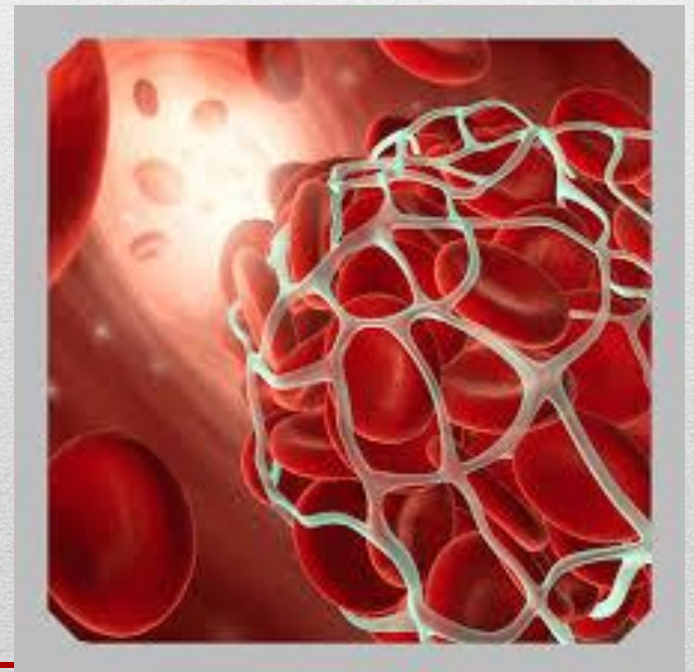
- ❖ **Tocolysis** → our preferred tocolytic is **nifedipine**. It is a suitable alternative to indomethacin, which is subject to the concerns and to beta sympathomimetics, which can further increase the maternal heart rate.
 - ❖ **Mgso4** → The use of magnesium sulfate should be individualized based on at risk of preterm birth at less than 32 weeks of gestation.
 - ❖ With severe respiratory compromise or COVID-19-related acute renal injury, it is reasonable to consider **withholding or dose-adjusting magnesium sulfate, particularly in the intubated patient already receiving benzodiazepine.**
 - ❖ I/O chart
 - ❖ In COVID-19 pregnant patients, it is unclear whether the use of magnesium sulfate increases the risk of pulmonary edema due to limited data and potential confounding of disease process overlap.
-

Preeclampsia:

- ❖ Laboratory findings for COVID-19 can overlap with those found in HELLP syndrome and preeclampsia with severe features.
 - ❖ The diagnostic criteria for preeclampsia remain unchanged during the pandemic, and management should be dictated by established guidelines.
 - ❖ However, it is reasonable to consider PCR testing for SARS-CoV-2 if a patient with transaminitis and thrombocytopenia has additional risk factors for COVID-19.
-

Thromboprophylaxis:

- ✓ Aspirin and indomethacin may be used for their respective common obstetrical indications.



Postpartum Care Considerations:

- Women who are asymptomatic/presymptomatic or women with mild symptoms without comorbid conditions may be able to recover at home after a normal postpartum recovery. Those with severe or critical disease require ongoing hospitalization.
- Venous thromboembolism (VTE) prophylaxis should be considered in postpartum women with COVID-19, with the decision based on individual risk assessment.
- For patients who did not receive antepartum pharmacologic prophylaxis because of COVID-19, we would not administer postpartum prophylaxis if they remain asymptomatic or mildly symptomatic and have an uncomplicated delivery, with no standard indications for postpartum VTE prophylaxis.

Outpatient

- It should be emphasized that patients can clinically worsen after several days of apparently mild illness, and women should be instructed to call or be seen for care if symptoms worsen.

Breastfeeding:

- There is no evidence of COVID-19 in the breast milk → breast and hand hygiene
-

Postpartum pain management considerations

- ◆ For women who are asymptomatic, mildly symptomatic, or moderately symptomatic who require analgesic medication beyond acetaminophen, nonsteroid anti-inflammatory drugs (NSAIDs) should be used because opioids likely pose more clinical risks. For women with acute kidney injury, this decision must be individualized.

contraception considerations:

- ▶ Immediate postpartum insertion (defined as insertion within 10 minutes of delivery of the placenta up to hospital discharge) of an IUD or implant placement can be considered.
 - ▶ postpartum tubal ligation in the setting of SARS-CoV-2 infection should be avoided. Obstetric clinicians should ensure that safe and effective contraception options remain available to all postpartum women.
-



postpartum depression:

- Universal screening for perinatal depression both during pregnancy and the postpartum period has been recommended





In the Name of GOD



Imaging indication in COVID 19 in **Pregnancy** and diagnosis of severity of disease in CT Scan

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Proposed Imaging Guidelines for Pregnant Women Suspected of Having COVID-19

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Letter to the Editor

1. It is prudent to avoid radiation imaging modalities such as chest x-ray or CT scans in pregnant women suspected of having COVID-19, as much as possible.
2. Chest x-ray or CT scan requests must be based on thorough examination, in case of investigating differential diagnoses of respiratory problems during the COVID-19 pandemic, along with other conditions like pulmonary edema etc. or appraisalment of COVID-19 pulmonary infection in case of clinical indications.
3. The patient must be well informed of the necessity, benefits and possible risks of the imaging procedures (chest radiography or CT scan), by the attending physician.
4. If requested by the physician, the imaging procedure (chest x-ray or CT scan) maybe done if the following conditions apply from the admitted ward to the imaging department: The CT scan request in the hospital information system is marked in red, and in coordination with the radiology department admission, the pregnant patient is transferred to the ward when no other patient is there and the ward is disinfected. Also, the patients' files should be placed in the red cover and the patient's clothing should be marked with a sign related to high-risk patients, so that maximum protec-

Proposed Imaging Guidelines for Pregnant Women Suspected of Having COVID-19

[Iranian Society of Radiology]

- CT scan has been considered as a necessary part of the evaluation in
 - most suspected subjects
 - in patients with respiratory complications in order to rule out a wide spectrum of diseases in the differential diagnosis.
- Because of the associated higher risk of COVID-19 in pregnancy and the defined constraints for use of ionizing radiation in pregnant women indication are challenging but

- *The Iranian Society of Radiology* devised the following guidelines to gain the maximum benefit from imaging techniques along with optimal protection and safety for pregnant women
- In general, ionizing radiation must be avoided in pregnant women as much as possible.
- Its utilization must be narrowed to limited indications with a high level of protection.
- The maximum permitted dose of radiation exposure is below 50 mGy in pregnant women.
- The absorbed dose of radiation for a fetus whose mother undergoes chest x-ray and chest CT scan are 0.002 mGy and 0.2 mGy respectively, which are not associated with known adverse effects on fetal health and thus are safe

- ❖ 1. It is prudent to avoid radiation imaging modalities such as chest x-ray or CT scans in pregnant women suspected of having COVID-19, as much as possible.
- ❖ 2. Chest x-ray or CT scan requests must be based on thorough examination, in case of investigating differential diagnoses
 - Respiratory problems,
 - Other conditions like pulmonary edema
 - Appraisalment of COVID-19 pulmonary infection in case of clinical indications.
- ❖ 3. **The patient must be well informed** of the necessity, benefits and possible risks of the imaging procedures (chest radiography or CT scan), by the attending physician.

❖4. *If requested by the physician, the imaging procedure (chest x-ray or CT scan) maybe done if the following conditions apply from the admitted ward to the imaging department:*

- The CT scan request in the hospital information system is marked in red
- in coordination with the radiology department admission
- the pregnant patient is transferred to the ward when no other patient is there
- the ward is disinfected.
- Also, the patients' files should be placed in the red cover-
- the patient's clothing should be marked with a sign related to high-risk patients
- so that maximum protection measures can be implemented as soon as they enter the imaging section and eliminate any possible errors.

- ❖ 5. To minimize the dose of exposure, the minimum possible dose for radiography must be utilized with the low dose CT protocol.
- ❖ 6. When chest CTs and chest x-rays are indicated, local protection for the fetus (abdominal lead shields) must be utilized.
- ❖ 7. Standard personal protection equipment for the corona virus like masks, gloves, gowns, goggles, and disinfectants must be available for the patients, the accompanying people and all other personnel who are involved in the procedure, in accordance with the relevant protection protocols.

- ❖ 8. During the **first trimester of pregnancy**, the decision to proceed with chest x-ray or CT scan must be made with meticulous consideration of the risks involved. It is advisable to initially perform chest x-ray with abdominal shield and then proceed to CT only if the chest X-ray turns out to be inconclusive.
- ❖ 9. During the **2nd and 3rd trimesters**, low dose stage. CT may be requested in the first
- ❖ 10. The attending physician is responsible for making decisions on requesting or repeating imaging procedures and continuation or termination of pregnancy
- ❖ 11. It is compulsory to use lead abdominal shields especially in the 1st trimester, even if it hampers visualization of the sub-diaphragmatic areas in the imaging field

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INTERIM GUIDANCE

ISUOG Interim Guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium: information for healthcare professionals – an update

ISOUG

- Fetal growth restriction (FGR), microcephaly and intellectual disability are the most common adverse effects from high-dose (> 610 mGy) radiation exposure
- According to the American College of Radiology and American College of Obstetricians and Gynecologists, when a pregnant woman undergoes a single chest X-ray examination, the radiation dose to the fetus is 0.0005-0.01 mGy, which is negligible, while the radiation dose to the fetus is 0.01-0.66 mGy from a single chest CT scan or CT pulmonary angiogram
- **Chest CT scanning has high sensitivity (97%) for diagnosis of COVID-19.** In a pregnant woman with suspected COVID-19, a chest CT scan may be considered as a primary tool for the detection of COVID-19 in epidemic areas
- **Informed consent** should be acquired (shared decision-making and a radiation shield applied over the gravid uterus)
- Because of the logistics involved in performing a CT scan on critically ill patients, and the need for thorough cleaning of the CT unit after imaging a COVID-19 patient, a portable chest X-ray is an acceptable alternative to a CT scan.
- A CT pulmonary angiogram is generally used in preference to a ventilation/perfusion scan on clinical suspicion of pulmonary embolus and should not be withheld during pregnancy.

- It has been proposed that ultrasound examination of the lungs of a pregnant woman with suspected COVID-19 could be carried out at the same time as the obstetric scan, in order to minimize the risk of radiation as well as streamline the clinical assessment of these patients. This mode of lung imaging could also be considered when chest X-ray and CT scan are not available
- However, management should be determined by the clinical features and severity of the disease, and not be based merely on diagnostic imaging.
- Detailed guidance regarding cleaning of ultrasound equipment and transducers in the context of COVID-19 has been provided in the article

Please Write

Low dose CT scan or Chest CT scan for COVID 19

Remind and report The History of probable COVID for radiology department and
Consider accurate arrangement

NOT *HRCT or Routine Chest CT scan*

CT can play an important role in

Triage of patients:

- COVID-19 yes or no
- possible or most likely COVID-19
- severity of the disease
- Prediction of worsening
- Prediction of improvement
- Problem solver

CT-changes over time

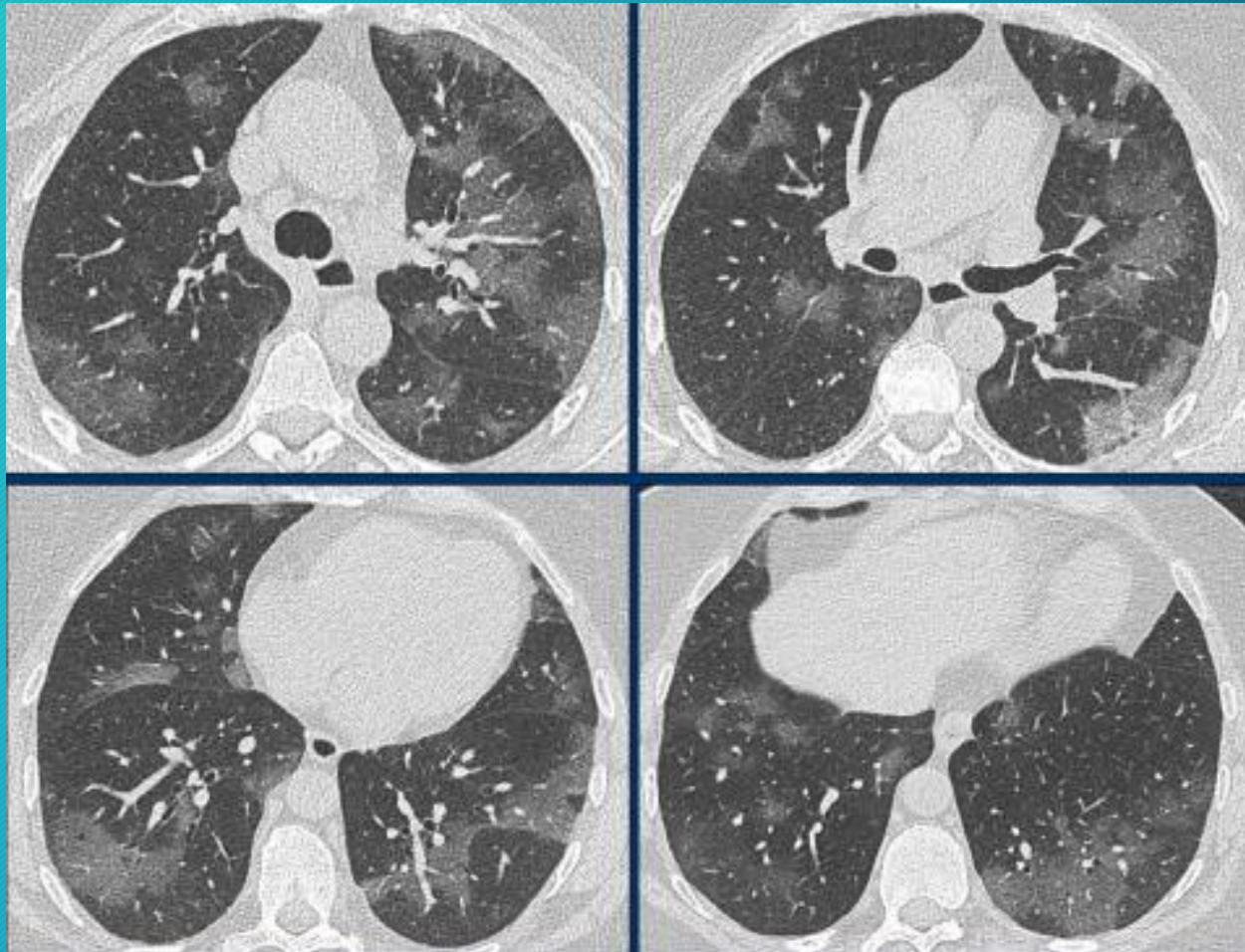
Early stage	0-4 days	GGO, partial crazy paving, lower number of involved lobes
Progressive stage	5-8 days	Progressive (5-8 days): Extension of GGO, increased crazy paving pattern
Peak stage	10-13 days	Consolidation
Absorption stage	≥14 days	Gradual resolution

Radiology assistant

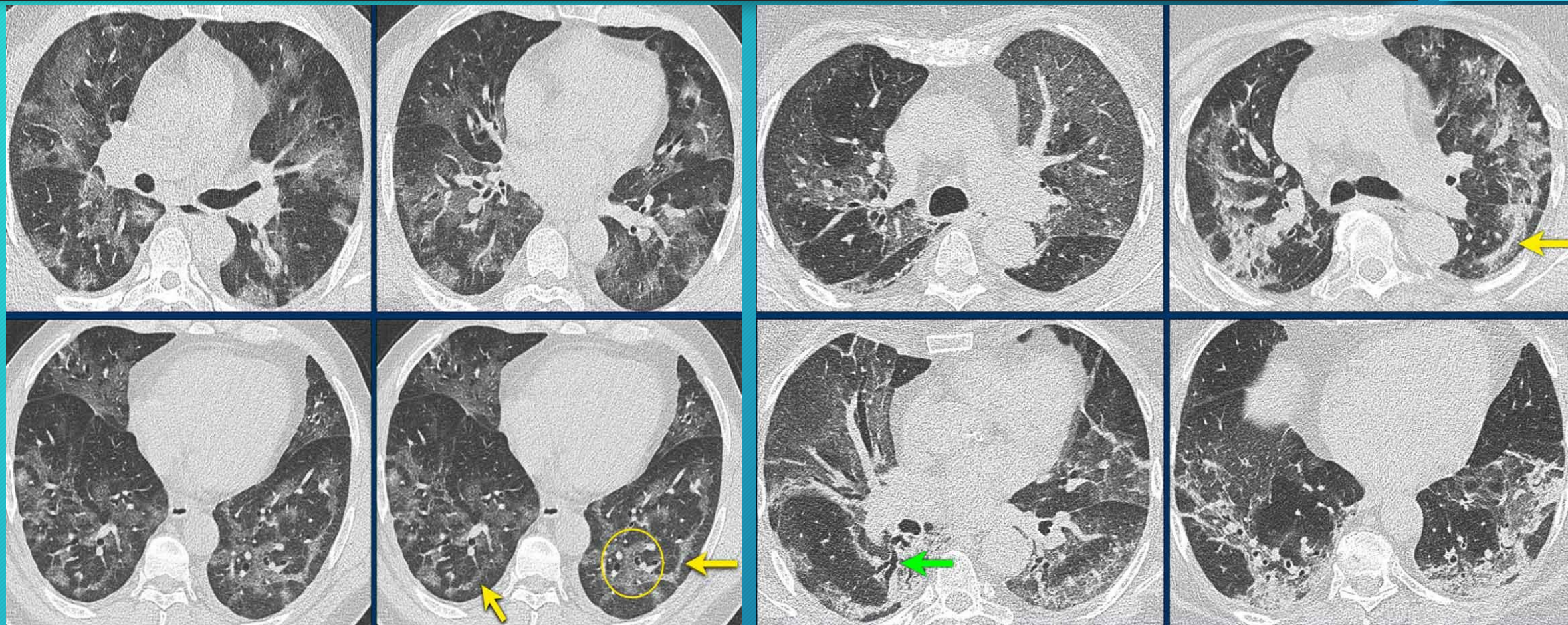
Advanced-phase disease increased frequency of:

- ---GGO plus a reticular pattern (crazy paving) , Vacuolar sign, Fibrotic streaks, Air bronchogram , Bronchus distortion, Subpleural line or a subpleural transparent line, Pleural effusion

Early Stage



Late Stage



CT involvement score: The severity of the lung involvement on the CT correlates with the severity of the disease.

Visual assessment

The severity on CT can be estimated by visual assessment. (easiest way)

Severity score

Another method is by scoring the percentages of each of the five lobes that is involve

< 5% involvement

-5%-25% involvement

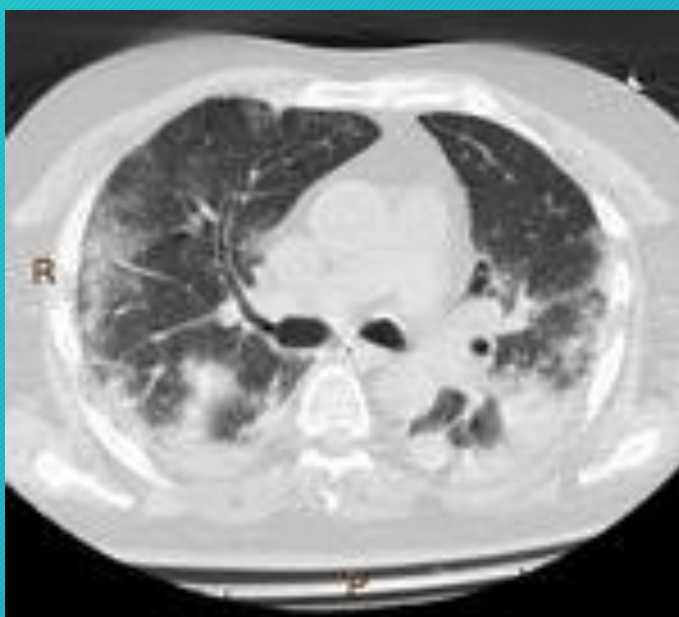
- 26%-49% involvement

-50%-75% involvement

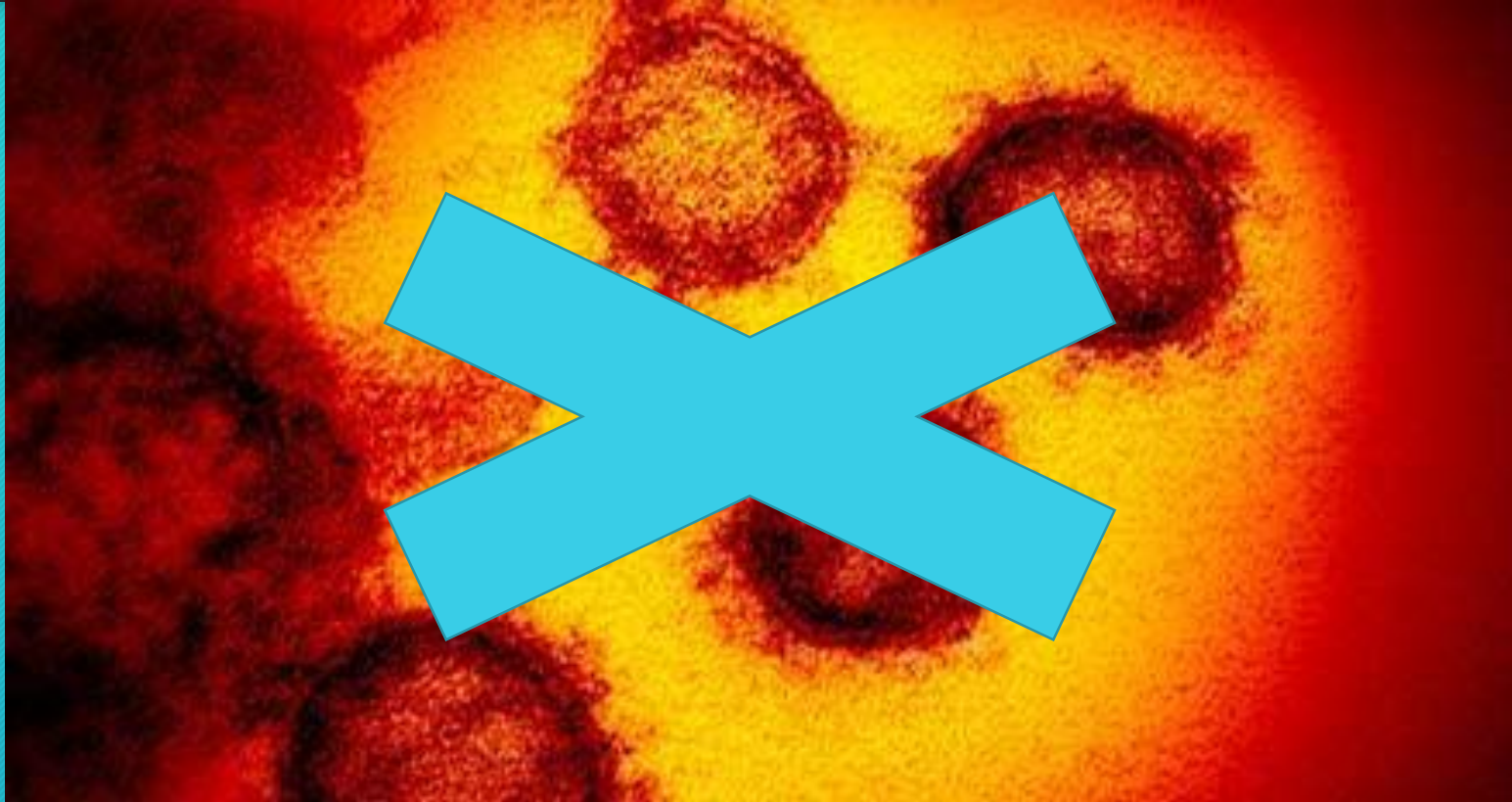
- > 75% involvement.

The total CT score is the sum of the individual lobar scores and can range from 0 (no involvement) to 25 (maximum involvement), when all the five lobes show more than 75% involvement.

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Thanks for your attention



Hope To Overcome in the world



IN THE NAME OF GOD



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**PREGNANT WOMEN ARE MORE SUSCEPTIBLE TO
THE VIRUS AND SHOW A WORSE PROGNOSIS
THAN NON-PREGNANT WOMEN SARS. H1N1**

CHANGES IN RESPIRATORY SYSTEM 1

- **Anatomically**, the effects of **progesterone** and relaxants in the first trimester of pregnancy can lead to the **relaxation of ligaments in the ribs**.
- And **the diaphragm will move up as the uterus grows**.
- Besides, the subcostal angle and transverse diameter of the thoracic cavity will increase further in the third trimester.
- The above anatomical factors, together with the decreased compliance of chest wall, eventually lead to a **20 to 30% reduction in functional residual capacity (FRC)** which makes **the mother prone to hypoxia, subsequently compensated by increased tidal volume and hyperventilation**.

2

- **elevated progesterone** can be transmitted through estrogen-dependent progesterone receptors in **the hypothalamus, thus stimulating the respiratory center** and increasing tidal volume by **50%** compared with non-pregnancy
- **.Hyperventilation** causes **pregnant women to inhale more air within the same period of time.** If SARS- CoV-2 is in the air, pregnant women are more likely to get the disease than ordinary people and are infected by droplets, aerosols, and other means.
- In addition, the **changes of nasal mucosa mediated by progesterone** during pregnancy may lead to the adhesion of the virus in the upper respiratory tract and make it difficult to be cleared

CHANGES IN THE IMMUNE SYSTEM 1

- A successful pregnancy is the mother's tolerance to the allogeneic fetus. Because nearly half of the embryo's genome comes from the father, which are then expressed as paternal antigens that can be recognized by the maternal immune system as foreign antigens. Therefore, the mother will undergo a series of complicated processes to ensure the acceptance of fetus and these immune changes may increase the mother's susceptibility to certain infectious disease herefore, the mother will undergo a series of complicated processes to ensure the acceptance of fetus ,and these immune changes may increase the mother's susceptibility to certain infectious diseases

2

- during pregnancy, Th2/Th1 is deviated to Th2, while in abortion, it is reversed .The transfer of immunity to Th2 is the cause of changes in the peripheral response to respiratory virus infection
- in addition to a decrease in the number of T cells in the blood during pregnancy, the activity of these cells was significantly reduced even in the absence of a significant preference for the Th2 phenotype ,all of which contributes to the susceptibility of pregnant women to the virus.

THE EXPRESSION OF **ACE2** IS INCREASED DURING PREGNANCY

- **ACE2** is the “doorknob” for SARS-CoV-2 entering the door of the host cells ,and the upregulation of ACE2 is likely to increase the susceptibility of COVID-19.
- Studies have shown that smoking is also a susceptibility factor for SARS-CoV-2, and analysis of gene chips in smoking patients has found that **ACE2 expression is upregulated when comparing with non-smoking patients**, which is consistent with clinical evidence. In the same way, a **high expression of ACE2 in pregnant women** also in- creases the susceptibility of pregnant women to SARS- CoV-2.

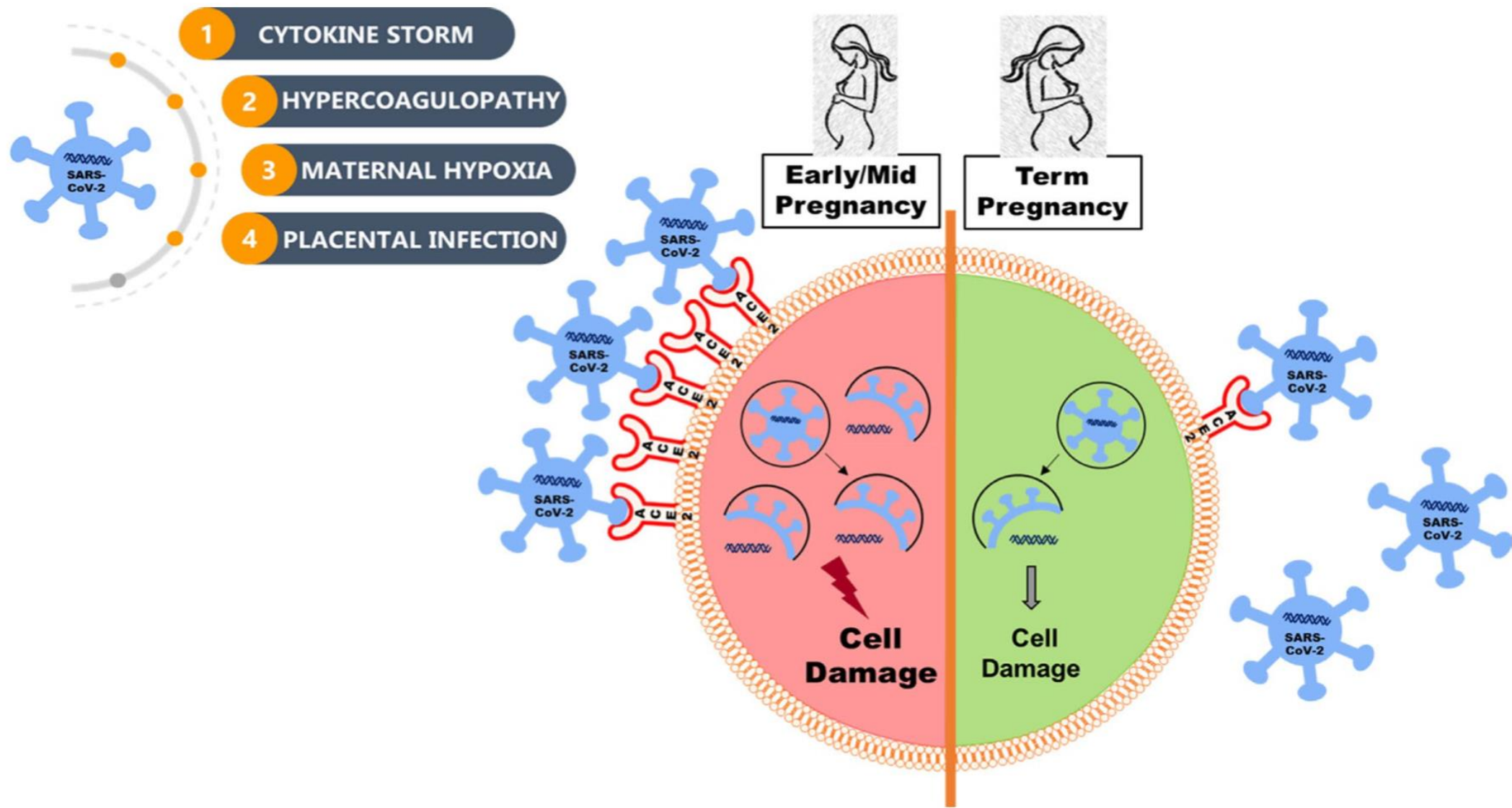


FIGURE 1 COVID-19 and placental ACE2 expression and its possible consequences. The SARS-CoV-2 can cause placental dysfunction by inducing systemic inflammation (cytokine storm), oxygenation abnormalities within the intervillous space (COVID 19-associated coagulopathy and maternal pneumonia), or by directly infecting the placenta causing cell damage. Since ACE2 expression is highly expressed in early/mid-pregnancy compared to term placentas, the viral entry and trophoblasts cell damage is more extensive in early/mid-pregnancy compared to term

EFFECTS OF VIRAL INFECTION ON THE FETUS

- No evidence has been found that the development of COVID-19 in the third trimester of pregnancy can lead to severe adverse outcomes in fetus and the newborn arose from infections that may be caused by vertical intrauterine transmission. Chen et al.
- SARS-CoV-2 test of amniotic fluid, umbilical cord blood, neonatal throat swabs, and breast milk samples of 6 patients were negative.
- even if we do not find proofs of vertical transmission, it is not enough to make us relax. Because the present study shows that even if the virus infection is absent in the placenta, the mother's response to infection tends to promote the fetus inflammatory response, which is defined as the fetal inflammatory response syndrome (FIRS), characterized by high levels of inflammatory cytokines in placenta, such as IL-1, IL-6, IL-8, and TNF- α but a lack of culturable microorganisms. These cytokines have been shown to affect the central nervous system and circulatory system and tend to cause fetal abnormal morphology in animal models, including
- ventricular expansion and bleeding . In addition to the morphological effects on the fetal brain, the presence of FIRS has been associated with an increased risk of diagnosis of autism, schizophrenia, neurosensory deficits, and late-stage psychosis .

CYTOKINE STORM SYNDROME IN COVID-19:

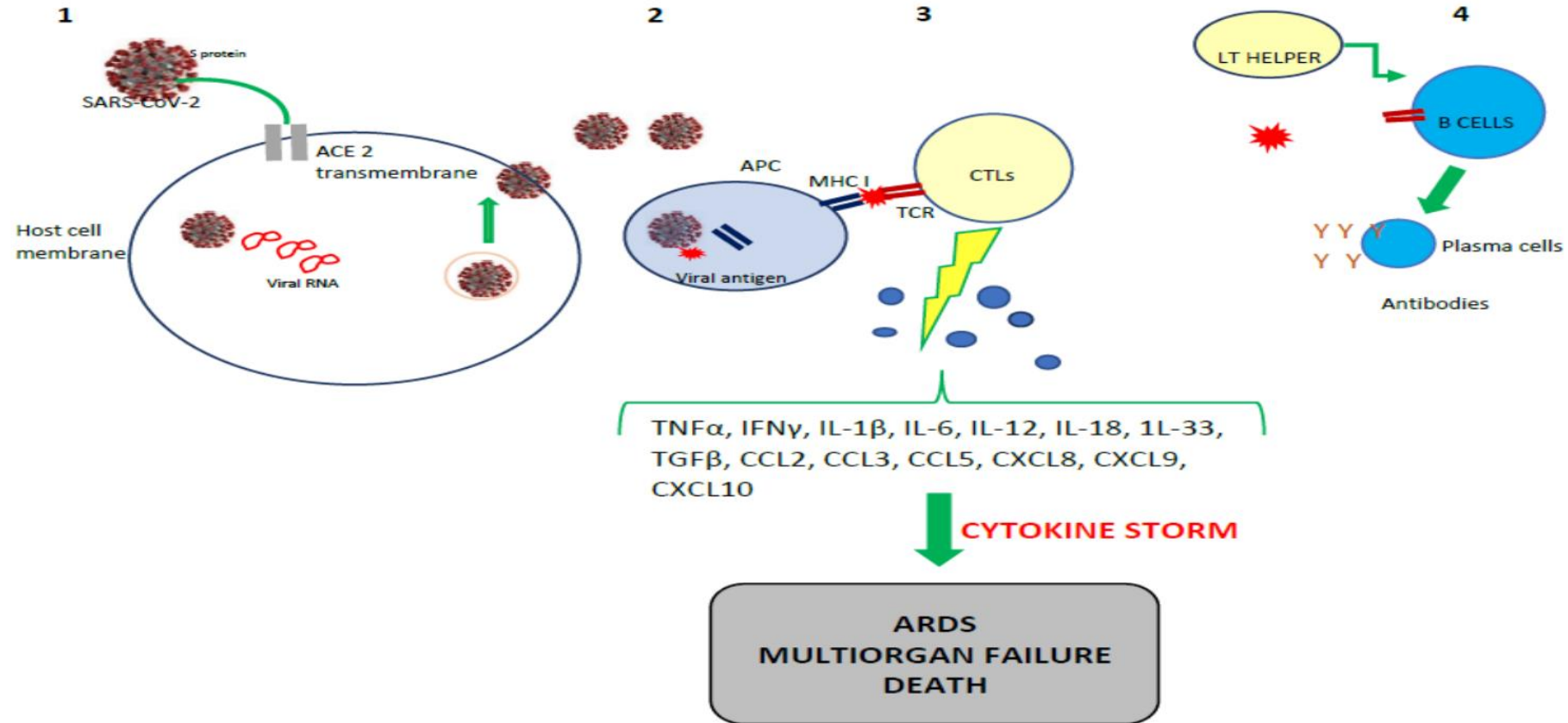
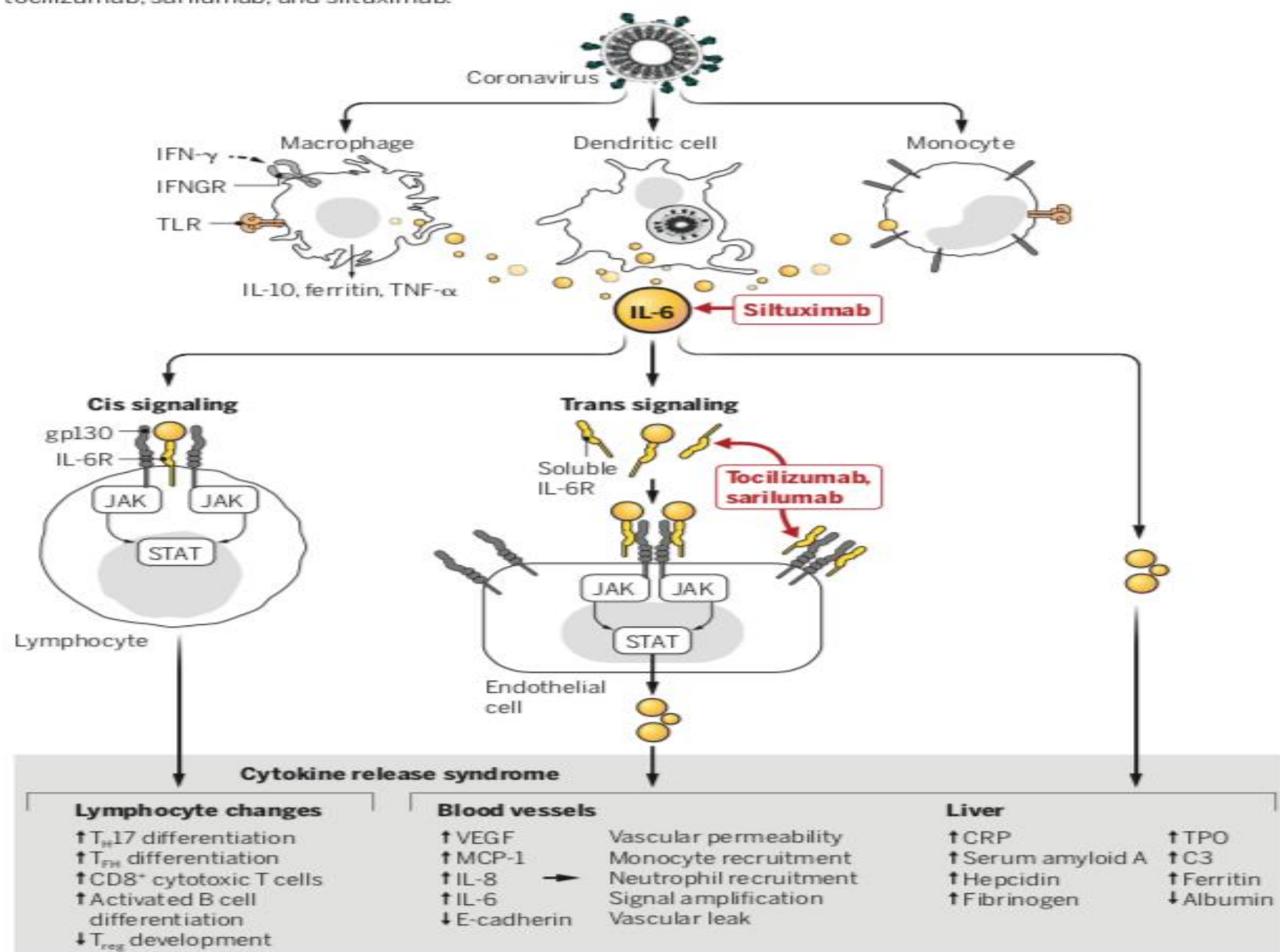
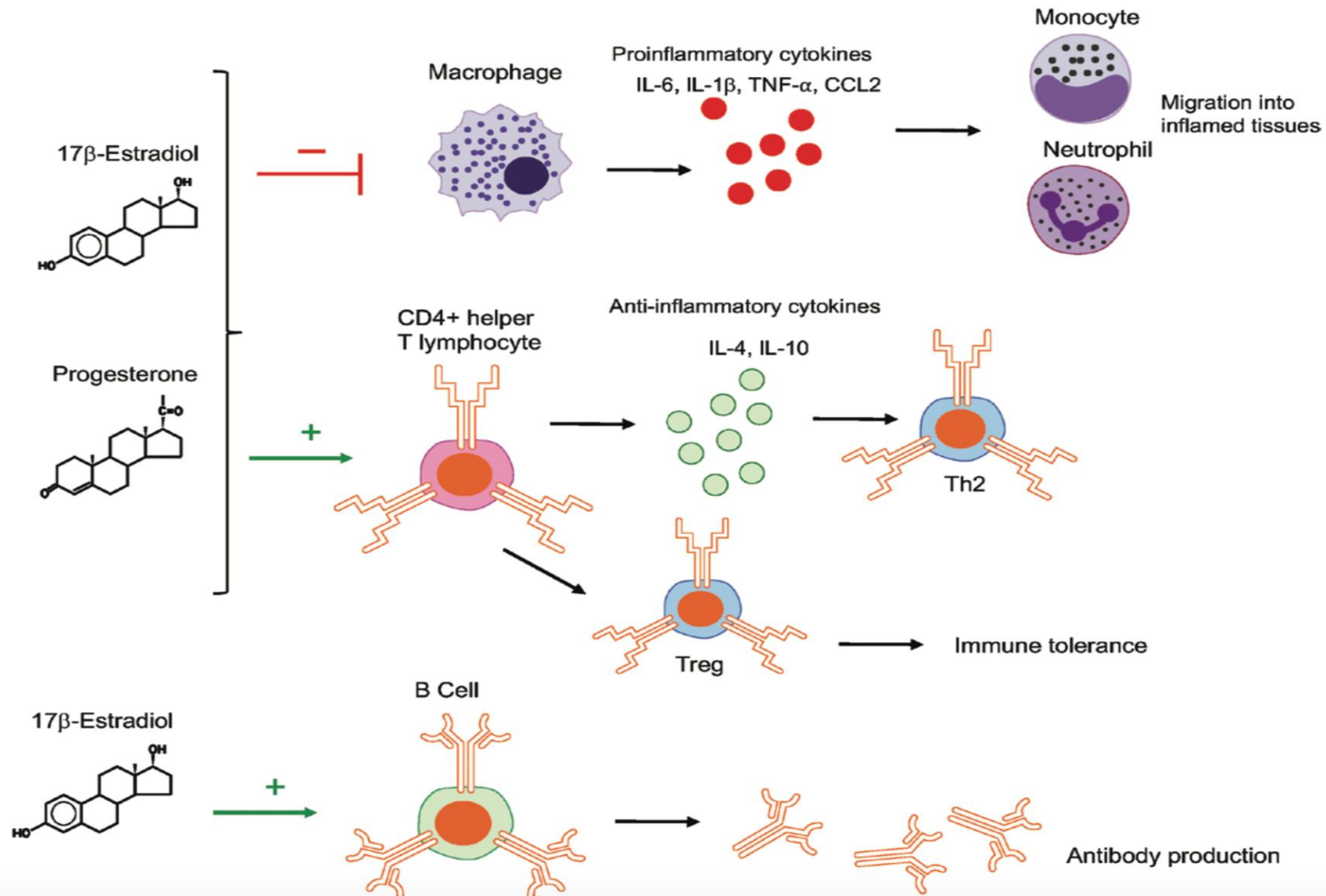


Fig. 1. Pathogenesis of COVID-19: 1. SARS-COV2 entry, replication and release. The virus binds to its ACE2 cell receptor by means of its spike glycoprotein (S protein) and then enters the cell cytoplasm where it releases its RNA genome, begins to replicate, and forms and releases new viral particles. 2. Antigen presentation. The viral antigen is presented to antigen-presenting cells (APCs) that present the antigenic peptides by means of the major histocompatibility complex (MHC). Antigen presentation stimulates both (3) cellular and (4) humoral immunity. 3. Immune effector cells release large amounts of cytokines and chemokines (a cytokine storm) that may rapidly provoke acute respiratory distress syndrome (ARDS), single or multiple organ failure, and eventually death.

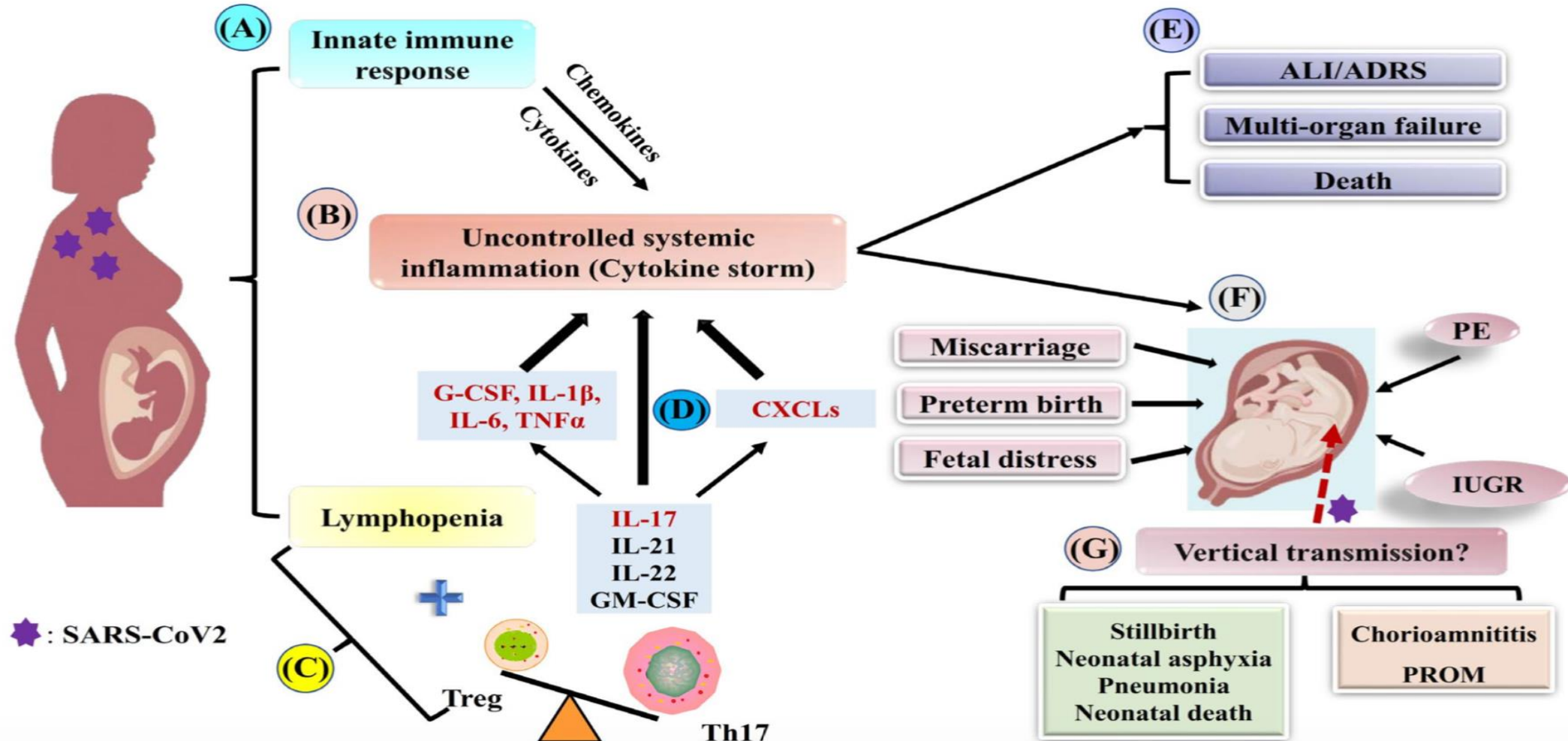


C3, complement 3; CRP, C reactive protein; IFN- γ , interferon- γ ; IFNGR, IFN- γ receptor; IL, interleukin; IL-6R, IL-6 receptor; JAK, Janus kinase; MCP-1, monocyte chemoattractant protein-1; STAT3, signal transducer and activator of transcription 3; T_{FH} , T follicular helper cell; T_H17 , T helper 17 cell; TNF- α , tumor necrosis factor- α ; TLR, Toll-like receptor; TPO, thrombopoietin; T_{reg} , T regulatory cell; VEGF, vascular endothelial growth factor.

ESTRADIOL, PROGESTERONE, IMMUNOMODULATION, AND COVID-19 OUTCOMES

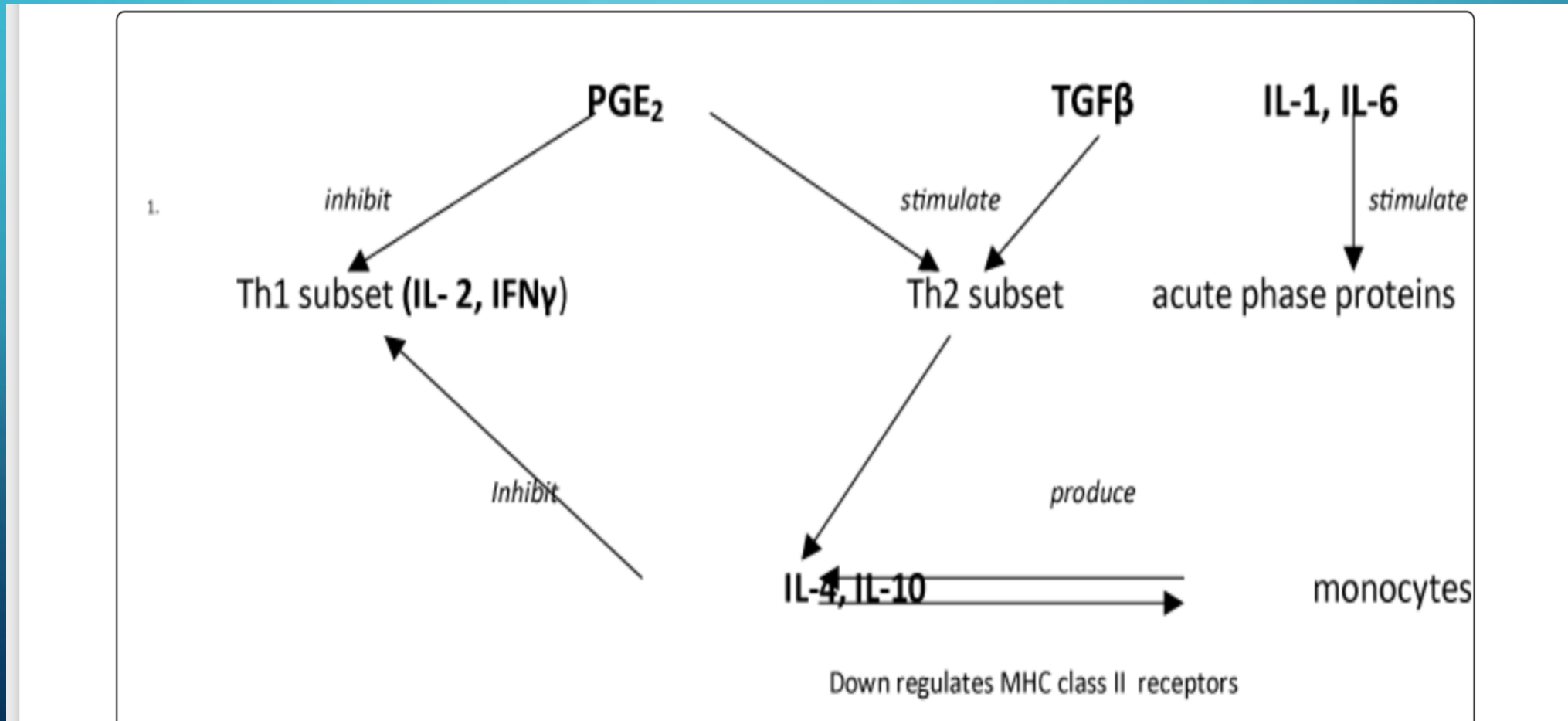


TREG/TH17 CELL IMBALANCE AND RELATED OUTCOMES IN SEVERE COVID-19 PREGNANT WOMEN



CYTOKINES AND THE METABOLIC RESPONSE TO SURGERY

1



Stress of surgery- vicious cycle

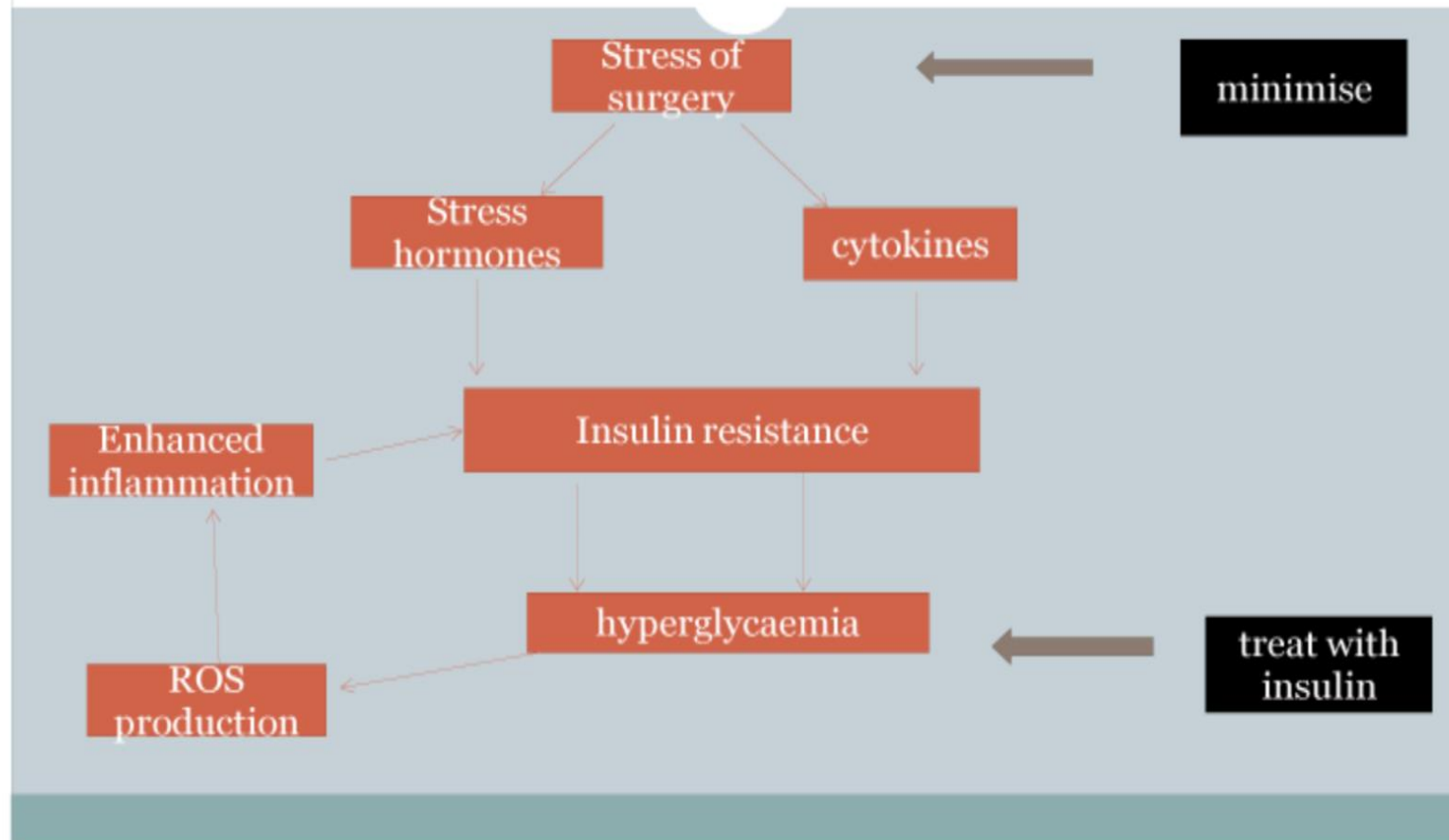


Figure 3: The vicious cycle of the stress of surgery.

IMMUNE-BASED THERAPY UNDER EVALUATION

- these agents include human blood-derived products and immunomodulatory .Some human blood-derived products are obtained from individuals who have recovered from SARS-CoV-2 infection (e.g., convalescent plasma, immunoglobulin products) These heterogenous products are postulated to have either direct antiviral properties, such as with convalescent plasma, and/or immunomodulatory effects like those noted with mesenchymal stem cells. Additionally, neutralizing monoclonal antibodies directed against SARS-CoV-2 have been developed and are under investigation in clinical trials.
- Other agents in this group include therapeutics currently approved for the treatment of other immune and/or inflammatory syndromes. These agents include corticosteroids (e.g., glucocorticoids), which as a class possess a broad array of mechanisms to abrogate systemic inflammation, and more targeted anti-inflammatory treatments such as interleukin inhibitors, interferons, kinase inhibitors, and others.

BLOOD-DERIVED PRODUCTS UNDER EVALUATION 1

- **Convalescent Plasma**
- Plasma from donors who have recovered from COVID-19 may contain antibodies to SARS-CoV-2 that may help suppress the virus and modify the inflammatory response.²
- The risks associated with convalescent plasma transfusion include TRALI, TACO, and allergic transfusion reactions.
- Rare **complications** include the transmission of infectious pathogens and red cell alloimmunization. There is a theoretical risk of antibody-mediated enhancement of infection.
- Several ongoing clinical trials evaluating COVID-19 convalescent plasma include **pregnant women**.

2

- **Immunoglobulins: Non-SARS-CoV-2 Specific**
- The COVID-19 Treatment Guidelines Panel **recommends against** the use of non-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-specific **intravenous immunoglobulin (IVIG)** for the treatment of COVID-19, **except in a clinical trial (AIII)**. This recommendation **should not preclude** the use of IVIG when otherwise **indicated for the treatment of complications that arise during the course of COVID-19**.
- IVIG is commonly used in **pregnancy** for other indications such as **immune thrombocytopenia** with an acceptable safety profile.

MESENCHYMAL STEM CELLS. 3

- The COVID-19 Treatment Guidelines Panel **recommends against** the use of **mesenchymal stem cells (MSCs)** for the treatment of COVID-19, except in a **clinical trial (All)**.
- **Risks associated** with MSC transfusion appear to be uncommon. The potential risks include failure of the cells to work as expected, potential for MSCs to multiply or change into inappropriate cell types, **product contamination**, **growth of tumors**, **infections**, **thrombus formation**, and administration site reactions.
- There are insufficient data to assess the risk of MSC use during **pregnancy**.

IMMUNOMODULATORS UNDER EVALUATION 1

- **Corticosteroids**
- On the basis of the preliminary report from the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial (discussed below), the COVID-19 Treatment Guidelines Panel (the Panel) **recommends** using **dexamethasone** 6 mg per day for **up to 10 days** for the treatment of **COVID-19** in patients who are mechanically ventilated **(AI)** and in patients who require supplemental oxygen but who are not mechanically ventilated **(BI)**.
- The Panel **recommends against** using **dexamethasone** for the treatment of **COVID-19** in patients who do not require supplemental oxygen **(AI)**.
- If **dexamethasone is not available**, the Panel recommends using alternative glucocorticoids such as **prednisone**, **methylprednisolone**, or **hydrocortisone** (see Additional Considerations below for dosing recommendations) **(AIII)**.

CORTICOSTEROIDS 2

- Whether use of other corticosteroids (e.g., prednisone, methylprednisolone, hydrocortisone) for the treatment of COVID-19 provides the same benefit as dexamethasone is unclear. The total daily dose equivalencies to dexamethasone 6 mg (oral or intravenous [IV])¹⁶ for these drugs are:
 - Prednisone 40 mg
 - Methylprednisolone 32 mg
 - Hydrocortisone 160 mg
- Half-life, duration of action, and frequency of administration vary among corticosteroids.
 - *Long-Acting Corticosteroid:* Dexamethasone; half-life: 36 to 72 hours, administer once daily.
 - *Intermediate-Acting Corticosteroids:* Prednisone and methylprednisolone; half-life: 12 to 36 hours, administer once daily or in two divided doses daily.
 - *Short-Acting Corticosteroid:* Hydrocortisone; half-life: 8 to 12 hours, administer in two to four divided doses daily.
- A short course of betamethasone and dexamethasone, which are known to cross the placenta, is routinely used to decrease neonatal complications of prematurity in women with threatened preterm delivery.^{17,18}
- Given the potential benefit of decreased maternal mortality, and the low risk of fetal adverse effects for this short course of therapy, the Panel recommends using **dexamethasone** in pregnant women with COVID-19 who are mechanically ventilated (**AIII**) or who require supplemental oxygen but who are not mechanically ventilated (**BIII**).

INTERFERONS (ALFA, BETA)

- The COVID-19 Treatment Guidelines Panel **recommends against** the use of **interferons** for the treatment of patients with severe and critical COVID-19, except in a **clinical trial (AIII)**. There are insufficient data to recommend either for or against the use of **interferon-beta for the treatment of early (i.e., <7 days from symptom onset) mild and moderate COVID-19**.
- The most frequent adverse effects of interferon-alfa include flu-like symptoms, nausea, fatigue, weight loss, hematological toxicities, elevated transaminases, and psychiatric problems (depression and suicidal ideation). Interferon-beta is better tolerated than interferon-alfa.
- Data from several large **pregnancy** registries did not demonstrate an association between exposure to interferon beta-1b preconception or during pregnancy and an increased risk of adverse birth outcomes (e.g., spontaneous abortion, congenital anomaly), and exposure did not influence birth weight, height, or head circumference.

INTERLEUKIN-6 INHIBITORS

- There are insufficient data to recommend either for or **against** the use of **interleukin-6 (IL-6) inhibitors** (e.g., **sarilumab, siltuximab, tocilizumab**) for the treatment of COVID-19.
- There are insufficient data to determine whether there is a drug-associated risk for major birth defects or miscarriage. **Monoclonal antibodies are actively transported across the placenta as pregnancy progresses (with greatest transfer during the third trimester) and may affect immune responses *in utero* in the exposed fetus.**

- Timing of Delivery: • In most cases, the timing of delivery should be dictated by obstetric indications rather than maternal diagnosis of COVID-19.
- For women with suspected or confirmed COVID-19 early in pregnancy who recover, no alteration to the usual timing of delivery is indicated. •
- For women with suspected or confirmed COVID-19 in the third trimester, it is reasonable to attempt to postpone delivery (if no other medical indications arise) until a negative test result is obtained or quarantine restrictions are lifted in an attempt to avoid virus transmission to the neonate. •
- In general, a diagnosis of COVID-19 in pregnancy is not an indication for early delivery.¹¹ • Based on limited data on primarily cesarean deliveries, there appears to be no clear evidence of vertical transmission of SARS-CoV-2 via the transplacental route, but this has not been definitively ruled out.

POST-DELIVERY:

- Currently the CDC recommends that the determination of whether or not to **separate a mother with** known or suspected COVID-19 and her infant should be made on a **case-by-case** basis using shared decision-making between the mother and the clinical team.
- ACOG supports breastfeeding for infants. They recommend that, for women who are PUI or confirmed to have SARS-CoV-2 infection, the decision about whether and how to start or continue breastfeeding be made by the mother in coordination with her family and health care practitioners.
- CDC has developed interim guidance on breastfeeding, recommending that women who intend to breastfeed and who are temporarily separated from their infants express their breastmilk, ideally from a dedicated pump, practice good hand hygiene before and after pumping, and consider having a healthy person feed the infant.
- CDC advises that women with COVID-19 who choose to room-in with their infants and feed them at the breast should practice good hand hygiene and wear a facemask to prevent transmission of the virus to the infant via respiratory droplets during breastfeeding.¹ **SARS-CoV-2 has not been isolated from breast milk.**

THANK YOU



LESSONS LEARNED ON COVID-19 IN PREGNANCY FROM THE 7 LAST MONTHS

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Vital signs

- Even with a chief complaint of dyspnea the RR is not recorded in the documents.
- With an O₂ sat of 98% RR may be 20 or 40, but the management differs and the patient may require supplemental O₂.
- When the O₂ sat is < 95% measure ABG, the SpO₂ should be > 70% to ensure fetal oxygenation.
- After fetal viability CTG is helpful.

Happy Hypoxemia (silent hypoxemia)

- O₂ saturation < 90% causes dyspnea, but in Covid-19 it occurs with lower saturation, therefore using pulse oximeter is helpful for early diagnosis & timely O₂ supplement.
- Patients whose oxygen saturation is less than or equal to 95% on room air with exertion should be considered for inpatient admission.

Cytokine storm

- Pregnant COVID-19 patients with fevers $>39^{\circ}\text{C}$ despite acetaminophen, raising concern for “cytokine storm syndrome”.
- It is a fulminant and often **fatal hypercytokinemia** associated with **multi-organ failure**.
- The disease is defined by **unremitting fever**, **cytopenia**, and **high ferritin** levels.
- Delivery may induce cytokine storm.

Prone positioning

- Prone positioning is feasible in pregnant as well as postpartum patients, including the recently delivered.
- Padding and/or support devices (eg, pillows, padding from the operating room, etc) may need to be utilized to position the patient properly.
- The most important aspect of this maneuver is to **ensure that the endotracheal tube remains in place** throughout rotation and positioning and that it is secured afterward.
- "Passive prone positioning," in which the patient is not intubated and positions herself in either the lateral decubitus (typically for ~2 hours in each position) or fully prone position, may aid in patient comfort and theoretically help avoid intubation.

Lab in critical patients

- PCT, CRP, IL-6, BNP, Troponins, Ferritin, Neutrophil-Lymphocyte ratio, D-dimer & Mg.
- D-dimer is the most important prognostic marker.
- The Hb level should be kept @ 10g/dl.
- Mg level should not be < 3 mg/dl.
- Beware of hyperglycemia with dexamethasone prescription & treat it.
- There is LFT rise with Covid 19, antiviral treatment & preeclampsia.

Drugs

- Proposed therapies have included azithromycin, remdesivir, tocilizumab, Bacillus Calmette–Guérin vaccine, and convalescent plasma.
-
- None of these therapies are contraindicated in pregnancy.

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**.
- Therefore, the National Institutes of Health (NIH) COVID-19 Treatment Guidelines Panel (the Panel) recommends remdesivir for treatment of COVID-19 in **hospitalized patients**:
 - 1) with $\text{SpO}_2 \leq 94\%$ on ambient air (at sea level)
 - 2) who require supplemental oxygen (AI).
 - 3) who are on mechanical ventilation or
 - 4) extracorporeal membrane oxygenation (ECMO) (BI).
- 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.

Dexamethasone

- The NIH COVID-19 Treatment Guidelines Panel (the Panel) recommends using dexamethasone (at a dose of 6 mg PO or IV per day for up to 10 days) in patients with COVID-19 who are **mechanically ventilated** (AI) and in patients with COVID-19 who **require supplemental oxygen** but who are not mechanically ventilated (BI). (due to decreased risk of mortality)
- The Panel recommends **against** using dexamethasone in patients with COVID-19 who do not require supplemental oxygen (AI).
- SMFM recommends that this treatment should also be offered to pregnant patients with COVID-19.

Antibiotics

- If clinicians suspect community-acquired pneumonia co-infection, the use of antibiotics is reasonable.
- Ceftriaxone plus azithromycin or ceftriaxone alone are commonly used to treat community-acquired pneumonia and are not contraindicated in pregnancy.
- Clinicians should obtain culture data when possible before initiating antibiotics, although empirical antibiotic treatment may be given while awaiting these results.

Antibiotics

- Broad-spectrum agents should be employed, such as cefepime, meropenem, piperacillin-tazobactam, linezolid, and vancomycin for patients with:
 - 1) severe disease
 - 2) risk factors for hospital-acquired pneumonia
 - 3) ventilator-acquired pneumonia
 - 4) drug resistant types of pneumonia
- All of which are acceptable in pregnancy.
- Although a procalcitonin level is not required in the assessment of COVID-19, it can be used to help delineate superimposed bacterial pneumonia.

Fever

- Beware of fever differential diagnosis even in Covid-19 pandemic.
- Consider chorioamnionitis, sepsis or

Preeclampsia

- With proteinuria and raised LFT: Only if there is hypertension, it is preeclampsia.

Clinical deterioration

- The diagnoses of pulmonary embolism and heart failure should be considered in women:
 - 1) with chest pain
 - 2) worsening hypoxia
 - 3) a RR >22 breaths/min (particularly if there is a sudden increase in O2 requirements)
 - 4) in women whose breathlessness persists or worsens after expected recovery from COVID-19.

Timing of delivery in Asymptomatic or Mildly Symptomatic Pregnant Patients

- COVID-19 positive status is not an indication for delivery, and delivery should be reserved for routine obstetrical indications.
- 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.

Timing of delivery in Asymptomatic or Mildly Symptomatic Pregnant Patients

- In an asymptomatic or mildly symptomatic woman positive for COVID-19 at 37 - 38 6/7 weeks of gestation without other indications for delivery, expectant management can be considered:
 - 1) until 14 days after the PCR result was noted to be positive **OR**
 - 2) 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.

Timing of delivery in critically ill pregnant patients

- Timing of delivery in critically ill pregnant women should be individualized.
- Decisions should be based on maternal status, concurrent pulmonary disease), critical illness, ability to wean off the ventilator and ventilator mechanics, gestational age at time of delivery, and shared decision-making with the patient or healthcare proxy.
- Septic shock, acute organ failure or fetal distress should prompt emergency Cesarean delivery (or termination, if legal, before fetal viability).

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Timing of delivery in critically ill pregnant patients

- Disease progression in COVID-19 can be protracted, and maternal-fetal medicine and critical care teams should discuss **individualized delivery criteria** in the setting of:
 - 1) worsening maternal status
 - 2) worsening fetal status
 - 3) limited or no improvement in maternal status
- Although the late 3rd 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.

Miscellaneous

- Do not forget anticoagulation unless contraindicated.
-
- Vitamin D deficiency predisposes to ARDS in Covid-19.
- Other medications: methylprednisolone, anticoagulation, Pantoprazole, vitamin C, Zinc, vitamin D3, Melatonin, Thiamine, Mg.
- Mg may dampen the storm.
- FGR may occur after severe disease.(needs U/S evaluation later)
- Avoid postpartum hypervolemia.
- Beware of domestic violence.

Thank you