I hope everyone had a wonderful weekend. For my colleagues in the NE stay safe.

For those who did not receive the Daily Briefing last Friday I want to explain. My computer crashed last Monday, and I am trying over time to rebuild my distribution list. If you did not receive Friday's Daily Briefing (or last Monday's) please let me know and I will resend.

Under COVID-19 News, the CDC is requiring people in the United States to wear masks when they travel by plane, ship, ferry, train, subway, bus, taxi, and ride-share. People must also wear masks in travel hubs like airports or subway stations. The mask must cover the nose and mouth and can be reusable or disposable, but bandanas, shirt collars, scarves, face shields alone, and masks with valves do not satisfy the requirement. The order goes into effect tomorrow. The second is the announcement of the J&J vaccine. The preliminary results are better than some news reported-see comment.

Under Journal Reviews the first article demonstrates infants born to women with SARS-CoV-2 antibodies often have the antibodies themselves whether the mother had symptoms or not. The second article is the SSC update on COVID-19. For severe or critical coronavirus disease 2019, the panel strongly recommends using systemic corticosteroids and venous thromboprophylaxis and suggests using remdesivir in nonventilated patients with COVID-19 and suggests against starting remdesivir in patients with critical coronavirus disease (MV or vapotherm). What has become clear we need better antivirals.

Have a wonderful day

Ed

COVID-19 News

CDC/DHS Requirement for Persons to Wear Masks While on Conveyances and at Transportation Hubs
January 29, 2021

1. Persons must wear masks (a material covering the nose and mouth of the wearer-masks do not include face shields) over the mouth and nose when traveling on conveyances (aircraft, train, road vessel) into and within the US.
2. A conveyance operator transporting persons into and within the US must require all persons onboard to wear masks for the duration of travel.
    a. Boarding only those persons who wear a mask.
    b. Instructing persons that Federal law requires wearing a mask on the conveyance and failure to comply constitutes a violation of Federal law.
    c. Monitoring persons onboard the conveyance for anyone who is not wearing a mask and seeking compliance for such persons.
    d. At the earliest opportunity, disembarking any person who refuses to comply.
3. Operators of transportation hubs (airport, marina, seaport, subway station, terminal, train station) must use best efforts to ensure that any person entering or on the premises of the transportation hub wears a mask.

Comment: Most of this is already in place in many areas, but now it is covered under section 361 of the Public Health Service Act and code of Federal Regulations. This order starts February 2, 2021.

J&J Vaccine

Results from an international phase 3 trial of Johnson & Johnson's single-dose COVID-19 vaccine show it is overall 66% effective in preventing moderate to severe symptoms of COVID-19. The vaccine was 85% effective in preventing COVID-19-related hospitalizations and deaths. After day 28 after vaccination no one needed hospitalization or died regardless of strain. The vaccine appears to be 72% effective at preventing moderate to severe disease among US trial participant, 66% in Latin America participants, and 57% in South African participants 28 days post-vaccination. When one looks at potential impact for severe disease there were no hospitalizations or deaths recorded among South African study participants who received the vaccine. Overall, the vaccine proved to be 57% effective in preventing moderate to severe COVID-19 in South Africa, where the dominant strain of the virus is variant B1351.

Comment: The reason for differences in efficacy in different geographic areas probably reflect what variant was circulating in those areas. The current Pfizer and Moderna vaccine trial were done before significant penetration of the UK and South African variant. 85 plus percent protection in South Africa against severe disease is very encouraging. The J&J vaccine has potential advantages over the existing two-dose Pfizer and Moderna mRNA vaccines because it is single-dose and has less stringent storage requirements — only regular refrigeration is needed versus a need to freeze the two-dose Pfizer and Moderna COVID-19 vaccines. The J&J vaccine can be refrigerated for up to 3 months at 36°- 46°F (2°- 8°C). Bottom line the J&J vaccine is an important addition to our vaccine toolkit. The more people we can immunize the faster we can suppress transmission and replication and the less likely the virus will mutate.

Journal Review

Assessment of Maternal and Neonatal Cord Blood SARS-CoV-2 Antibodies and Placental Transfer Ratios

JAMA Pediatrics published online January 29, 2021
doi:10.1001/jamapediatrics.2021.0038

Investigators report on a large study including 1714 pregnant women who delivered newborns in the northeastern United States during the early stages of the COVID-19 pandemic, from April to August 2020. Maternal and cord blood sera were available for antibody measurement for 1471 mother/newborn dyads. Investigators collected discarded maternal and cord blood sera from 1471 eligible mother-newborn pairs to measure IgG and IgM antibodies to the receptor-binding domain of the SARS-CoV-2 spike protein by enzyme-linked immunosorbent assay and assess antibody concentrations and transplacental transfer, contributing useful data to assess the potential for protection of infants in early life. The study cohort consisted of 1714 parturient women, with median (interquartile range) age of 32 (28-35) years, of whom 450 (26.3%) identified as Black/non-Hispanic, 879 (51.3%) as White/non-Hispanic, 203 (11.8%) as Hispanic, 126 (7.3%) as Asian, and 56 (3.3%) as other race/ethnicity. Among 1471 mother/newborn dyads for which matched sera were available, SARS-CoV-2 IgG and/or IgM antibodies were detected in 83 of 1471 women (6%; 95% CI, 5%-7%) at the time of delivery, and IgG was detected in cord blood from 72 of 83 newborns (87%; 95% CI, 78%-93%). While only 83 women (6% of the study population) had detectable IgG and/or IgM antibodies at delivery, most infants born to seropositive mothers (72 of 83 [87%]) had detectable IgG antibody at birth. As expected, given the process of active IgG transplacental transfer during pregnancy, transfer ratios were more than 1.0, and there was a positive correlation between maternal and infant antibody titers. However, infants born to mothers with very low IgG levels were seronegative at birth. Interestingly, transplacental transfer was

efficient regardless of the presence of symptoms in the mother or the severity of disease. This unique observation was possible because of the use of serologic testing for the diagnosis of infection, which allowed the ascertainment of asymptomatic infection at any time during pregnancy, independently from molecular testing at the time of symptoms or admission for delivery. As has been reported elsewhere most seropositive women (50 of 83 [60%]) were asymptomatic. Transplacental transfer was more likely when the time between maternal infection and delivery was longer. This finding is consistent with similar observations on the transfer of antibodies in recent studies of an RSV vaccine given during pregnancy, where an interval of 30 days or more from vaccination to delivery was significantly associated with higher antibody transfer. [N Engl J Med. 2020;383(5):426-439] Interestingly, the transfer ratio of SARS-CoV-2 antibodies was not affected by premature delivery (gestational age at birth, <37 weeks). In this study, the most preterm infant was born at 31 weeks of gestation.

Comment: In this cohort study, maternal IgG antibodies to SARS-CoV-2 were transferred across the placenta after asymptomatic as well as symptomatic infection during pregnancy. The findings demonstrate the potential for maternally derived SARS-CoV-2 specific antibodies to provide neonatal protection from coronavirus disease 2019. In an editorial Dr. Munoz asked the following questions worth considering: "Could maternal antibodies help delay the onset of infection or protect the infant from becoming infected, having severe disease, or dying of COVID-19? To what extent can antibodies transferred through breast milk protect lactating newborns? Should infants be vaccinated regardless of maternal infection, and if so, what is the best timing to initiate infant vaccines? Is there a potential detrimental effect of maternal antibodies on infant responses to active immunization? And what would be the optimal vaccine and vaccination regimen for infants, considering their risk and unique immunologic needs?" I agree with her final statement that "critical information needs to be collected through carefully designed prospective or longitudinal clinical studies to inform and implement safe and effective maternal and infant vaccination strategies".

Surviving Sepsis Campaign Guidelines on the Management of Adults with Coronavirus Disease 2019 (COVID-19) in the ICU: First Update

Crit Care Med published online January 2021

Highlights [brackets are my comments]

DOI: 10.1097/CCM.0000000000004899

Summary: For severe or critical coronavirus disease 2019, the panel strongly recommends using systemic corticosteroids and venous thromboprophylaxis but strongly recommends against using hydroxychloroquine. In addition, the panel suggests using dexamethasone (compared with other corticosteroids) and suggests against using convalescent plasma and therapeutic anticoagulation outside clinical trials. The Surviving Sepsis Campaign Coronavirus Disease 2019 panel suggests using remdesivir 2019 in nonventilated patients with severe coronavirus disease 2019 and suggests against starting remdesivir in patients with critical coronavirus disease outside clinical trials.

1. There is insufficient evidence to issue recommendation on the use of awake prone positioning in nonintubated adults with severe COVID-19.
    a. Uncertainty about the balance between benefit and harm. Await results of RCTs.
2. For adults with severe or critical COVID-19, we recommend against using hydroxychloroquine (strong recommendation).
3. For adults with severe or critical COVID-19, we recommend using a short course of systemic corticosteroids over not using corticosteroids (strong recommendation).
4. For adults with severe or critical COVID-19, we suggest against the use of convalescent plasma outside clinical trials (weak recommendation).

a. Low-quality evidence from RCTs showed no improvement in outcomes.
b. [recent article on use as outpatient with early symptoms in high-risk patients may prevent progression and need for hospitalization similar to combination monoclonals]

5. For adults with severe COVID-19 who do not require mechanical ventilation, we suggest using IV remdesivir over not using it (weak recommendation).
   a. *Remark*: Remdesivir should *ideally* be started within 72 hours of positive SARS-CoV-2 with severe disease confirmed by PCR or antigen testing.
   b. [ACTT-1 Trial post hoc analysis]
      i. The benefit of remdesivir for reducing time to recovery was clearest in the subgroup of hospitalized patients who required supplemental oxygenation (<15 liters) at study enrollment (ordinal scale 5, n = 435; recovery rate ratio 1.45; 95% CI, 1.18–1.79). In a post hoc analysis of deaths by Day 15, remdesivir appeared to confer a survival benefit in this subgroup (HR for death 0.28; 95% CI, 0.12–0.66).
      ii. In patients who required high-flow oxygen or noninvasive ventilation at study enrollment (ordinal scale 6, n = 193), there was no observed difference in time to recovery between the remdesivir and placebo groups (recovery rate ratio 1.09, 95% CI, 0.76–1.57). In a post hoc analysis of deaths by Day 15, there was no evidence that remdesivir had an impact on the mortality rate in this subgroup (HR 0.82; 95% CI, 0.40–1.69).
      iii. Among the patients who were on mechanical ventilation or ECMO at study enrollment (ordinal scale 7, n = 285), there was no observed difference in time to recovery between the remdesivir and placebo groups (recovery rate ratio 0.98; 95% CI, 0.70–1.36). In a post hoc analysis of deaths by Day 15, there was no evidence that remdesivir had an impact on the mortality rate in this subgroup (HR 0.76; 95% CI, 0.39–1.50).
6. For adults undergoing mechanical ventilation for critical COVID-19, we suggest against starting IV remdesivir (weak recommendation). [see above]
7. For adults with severe or critical COVID-19, we recommend using pharmacologic VTE prophylaxis over not using prophylaxis (strong recommendation).
   a. VTE rates are higher in COVID-19 population
8. Infection Control and Testing
   a. For healthcare professionals performing aerosol-generating procedures on patients with COVID-19 in the ICU, we recommend using fitted respirator masks (N95 respirators, filtering facepiece 2, or equivalent) as opposed to surgical/medical masks, in addition to other PPE (e.g., gloves, gown, and eye protection, such as a face shield or safety goggles). -Best practice
   b. We recommend performing aerosol-generating procedures on ICU patients with COVID-19 in a negative-pressure room. -Best Practice
   c. For healthcare professionals providing usual care for nonventilated COVID-19 patients, we suggest using surgical/medical masks as opposed to respirator masks, in addition to other PPE (e.g., gloves, gown, and eye protection, such as a face shield or safety goggles). -Weak
   d. For healthcare professionals performing non-aerosol-generating procedures on mechanically ventilated (closed circuit) patients with COVID-19, we suggest using surgical/medical masks as opposed to respirator masks, in addition to other PPE (e.g., gloves, gown, and eye protection, such as a face shield or safety goggles). -Weak
   e. For COVID-19 patients requiring endotracheal intubation, we recommend that endotracheal intubation be performed by the healthcare professional who is most experienced with airway management to minimize the number of attempts and risk of transmission. -Best Practice
   f. For intubated and mechanically ventilated adults with suspicion of COVID-19: For diagnostic testing, we suggest obtaining lower respiratory tract samples in preference to upper respiratory tract (nasopharyngeal or oropharyngeal) samples. -Weak

g. For intubated and mechanically ventilated adults with suspicion of COVID-19: With regard to lower respiratory samples, we suggest obtaining endotracheal aspirates in preference to bronchial wash or bronchoalveolar lavage samples. -Weak

Comments: There is growing consensus that use of RDV should be reserved for nonventilated patients with COVID-19 requiring <15 liters and against starting remdesivir in patients with critical coronavirus disease requiring vapotherm or mechanical ventilation. The European Society of Intensive Medicine (ESICM) does not recommend RDV in COVID-19 patients in the ICU. IDSA, NIH, and NHS all comment on weak evidence for using RDV in the ICU and support its use early in patients <15 liters. Dexamethasone is now SOC for COVID-19 patients requiring supplemental oxygen including patients on vapotherm and mechanical ventilation. Enthusiasm for convalescent plasma has decreased. The use of convalescent plasma may have a role early as an outpatient intervention or early for hospitalized patients given high titered plasma. VTE prophylaxis continues to be recommended.