Neonatal management and outcomes during the COVID-19 pandemic: an observation cohort study
Lancet Child Adolesc Health published online July 23, 2020

This is an observational cohort study. All neonates were identified between March 22 to May 17, 2020 at three hospitals in New York City to mothers positive for SARS-CoV-2 at delivery. Mothers could practice skin-to-skin care and breastfeed in the delivery room but had to wear a surgical mask when near their neonate and practice proper hand hygiene before skin-to-skin contact, breastfeeding, and routine care. Unless medically required, neonates were kept in a closed isolette in the same room as their mothers and were held by mothers for feeding after appropriate hand hygiene, breast cleansing, and placement of a surgical mask. Neonates were tested for SARS-CoV-2 by use of real-time PCR on nasopharyngeal swabs taken at 24 h, 5–7 days, and 14 days of life, and were clinically evaluated by telemedicine at 1 month of age.

Of 1481 deliveries, 116 (8%) mothers tested positive for SARS-CoV-2; 120 neonates were identified. All neonates were tested at 24 h of life and none were positive for SARS-CoV-2. 82 (68%) neonates completed follow-up at day 5–7 of life. Of the 82 neonates, 68 (83%) roomed in with the mothers. All mothers were allowed to breastfeed; at 5–7 days of life, 64 (78%) were still breastfeeding. 79 (96%) of 82 neonates had a repeat PCR at 5–7 days of life, which was negative in all; 72 (88%) neonates were also tested at 14 days of life and none were positive. None of the neonates had symptoms of COVID-19.

Comment: The study is limited by the sample size and a follow-up period of only 1 month. In addition, some of neonates were lost to follow-up. Lastly, they were unable to screen for presence of the virus in blood, urine, or stool due to absence of approved testing for these samples during the study period. Nonetheless, this study is very reassuring. Perinatal transmission of COVID-19 is unlikely to occur if infection precautions are followed. It also supports allowing neonates to room in with their mothers and direct breastfeeding if appropriate precautions are taken.

Characteristics and Outcomes of 241 Births to Women with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection at Five New York City Medical Centers
Ob Gyn 2020; 136:273-282

The investigators performed a prospective cohort study of pregnant women with laboratory-confirmed SARS CoV-2 infection who gave birth from March 13 to April 12, 2020, identified at five New York City medical centers.

Among this cohort 61.4% of women were asymptomatic for COVID-19 at the time of admission. Throughout the delivery hospitalization, 26.5% of women met World Health Organization criteria for mild COVID-19, 26.1% for severe, and 5% for critical. Cesarean birth was the mode of delivery for 52.4% of women with severe and 91.7% with critical COVID-19. The singleton preterm birth rate was 14.6%. Admission to the intensive care unit was reported for 17 women (7.1%), and nine (3.7%) were intubated during their delivery hospitalization. There were no maternal deaths. Body mass index (BMI) 30 or higher was associated with COVID-19 severity (P5.001). Nearly all newborns tested negative for SARS-CoV-2 infection immediately after birth (97.5%).

Comment: Most women with laboratory-confirmed infection admitted for delivery did not have symptoms of COVID-19. Almost one third of women who were asymptomatic on admission became symptomatic during their delivery hospitalization. Obesity was associated with COVID-19 severity like non-pregnant patients. The question of vertical transmission of SARS CoV-2 infection from mother to

fetus was beyond the scope of this report, but almost all newborns tested were negative after delivery. Testing availability and reliability, as well as testing protocols, were not uniform across study sites and changed over the course of the study period.

Remdesivir for Severe COVID-19 versus a Cohort Receiving Standard of Care
Clin Infect Dis published online July 27, 2020

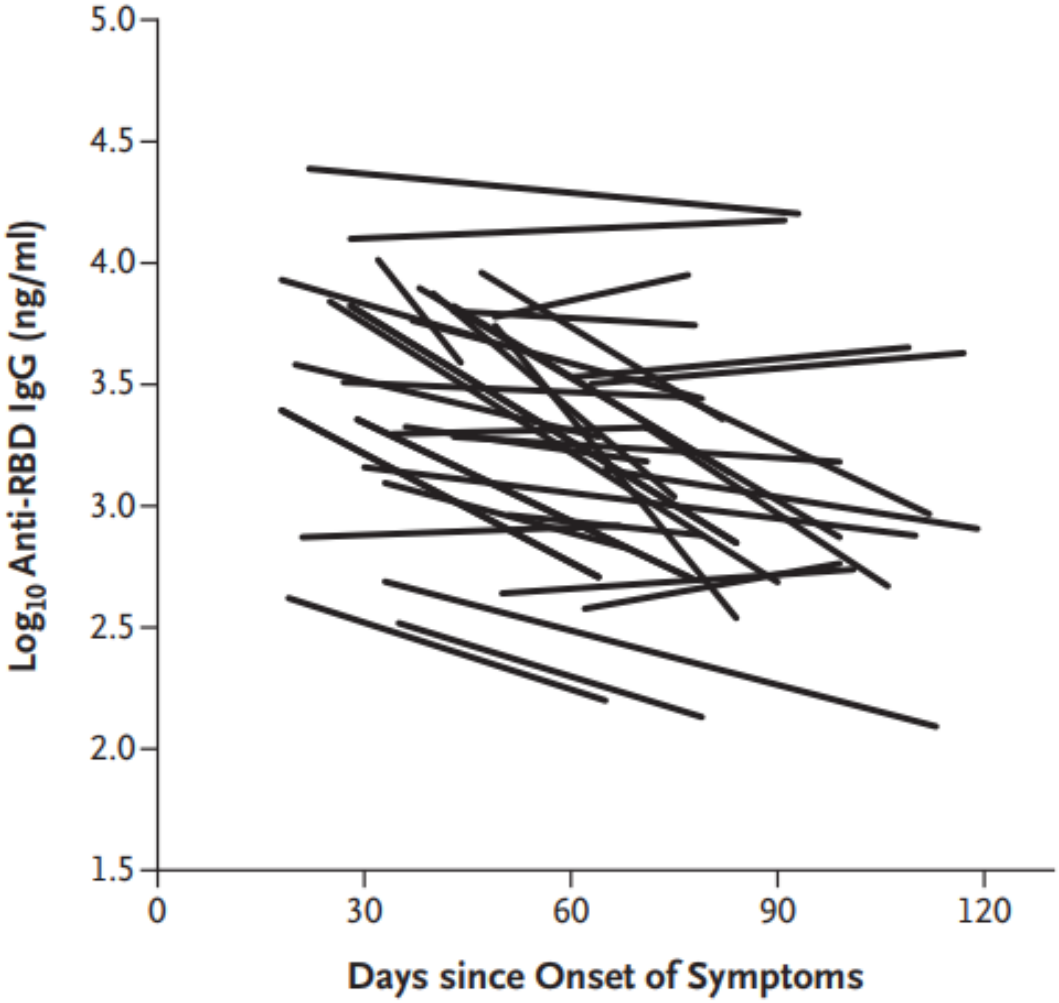
This is an ongoing phase 3, randomized open labeled trials (2 studies) comparing remdesivir to standard of care in an ongoing retrospective cohort study. Inclusion criteria was confirmed SARS-CoV-2 infection requiring hospitalization, had O_2 saturation ≤94% on RA or requiring supplemental oxygen, and had pulmonary infiltrates. Patients on mechanical ventilation were excluded. (therefore, not critically ill) 312 and 818 patients were included in the remdesivir and non-remdesivir arms, respectively. At day 14, 74% of patients given remdesivir recovered versus 59% in the non-remdesivir arm ($p<0.001$). At day 14, 7.6% of patients in the remdesivir arm died versus 12.5% in the non-remdesivir arm ($p=0.001$).

Comment: There were several important limitations of this paper. Most importantly, the comparison was not randomized or blinded, and although there were efforts made to balance the two studies for known factors associated with poor COVID-19 prognosis using IPTW and multivariable regression, there were some factors that could not be well balanced. Some patients in the remdesivir arm did receive other potential COVID-19 treatments. Both trials are still ongoing. Despite these limitations remdesivir is associated with higher recovery rates and lower mortality in patients with severe SARS-CoV-2 infections and currently is the anti-viral drug of choice for patients with severe SARS-CoV-2 infections.

Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild Covid-19
N Engl J Med published online July 23, 2020

The investigators evaluated persons who had recovered from Covid-19 and referred themselves to our institution for observational research. Blood samples were analyzed by enzyme-linked immunosorbent assay (ELISA) to detect anti– SARS-CoV-2 spike receptor-binding domain IgG. Infection had been confirmed by PCR in 30 of the 34 participants. The other 4 participants had had symptoms compatible with Covid-19 and were household contacts with persons who were known to have Covid-19 but were not tested because of mild illness and the limited availability of testing. Most of the participants had mild illness; 2 received low flow supplemental oxygen and leronlimab (a CCR5 antagonist), but they did not receive remdesivir. There were 20 women and 14 men. The mean age was 43 years (range, 21 to 68). A total of 31 of the 34 participants had two serial measurements of IgG levels, and the remaining 3 participants had three serial measurements. The first measurement was obtained at a mean of 37 days after the onset of symptoms, and the last measurement was obtained at a mean of 86 days after the onset of symptoms.

The initial mean IgG level was 3.48 log10 ng per milliliter (range, 2.52 to 4.41). On the basis of a linear regression model that included the participants' age and sex, the days from symptom onset to the first measurement, and the first log10 antibody level, the estimated mean change (slope) was -0.0083 log10 ng per milliliter per day (range, -0.0352 to 0.0062), which corresponds to a half-life of approximately 36 days over the observation period.



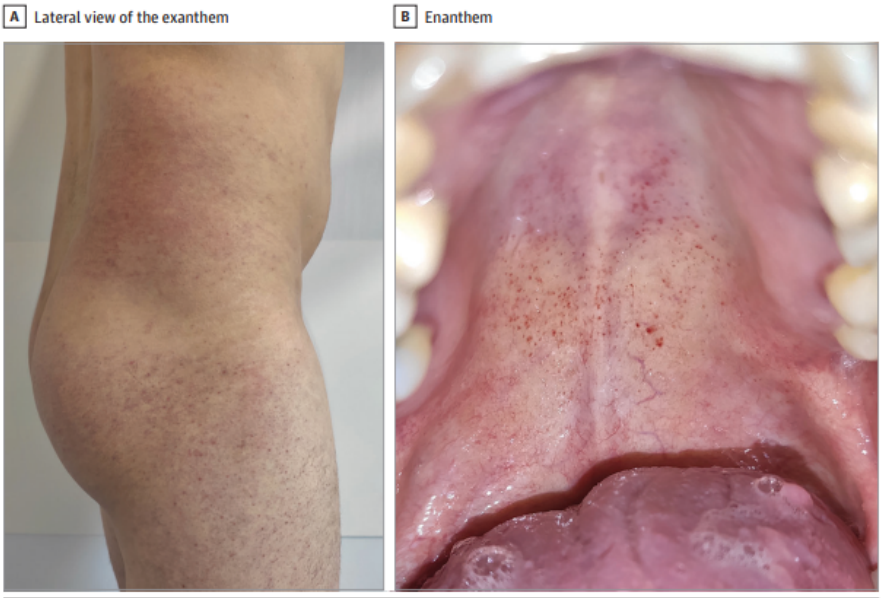
Comments: This paper highlights the knowledge gap around protective immunity. The protective role of antibodies against SARS-CoV-2 is unknown, but these antibodies are usually a reasonable correlate of antiviral immunity, and anti–receptor-binding domain antibody levels correspond to plasma viral neutralizing activity. This is a small study with only 34 participants. Given that early antibody decay after acute viral antigenic exposure is approximately exponential, they found antibody loss that was quicker than that reported for SARS-CoV-1. Their findings raise concern that humoral immunity against SARS-CoV-2 may not be long lasting in persons with mild illness, who compose ~80% of persons infected with SAR-CoV-2. They do not comment on T-cell response. [current vaccine candidates stimulate both humeral and T-cell responses] Still, the results call for caution regarding antibody-based herd immunity, and perhaps vaccine durability, especially considering short-lived immunity against other common human coronaviruses. Like influenza we may need yearly vaccination. What if the virus mutates?

Enanthem in Patients With COVID-19 and Skin Rash
JAMA Dermatology published online July 15, 2020

The authors included 21 consecutive patients from a tertiary care hospital who had skin rash and COVID-19, confirmed by PCR from a nasopharyngeal swab, and who required dermatology consultation from

March 30 to April 8, 2020. The oral cavities of patients presenting with skin rash were systematically examined. Enanthems [a rash on mucous membranes] were classified into 4 categories: petechial, macular, macular with petechiae, or erythematovesicular. Of 21 patients with COVID-19 and skin rash, 6 patients (29%) had enanthem. The morphology of the skin rash was papulovesicular, purpuric periflexural, and erythema multiforme–like in 1, 2, and 3 patients, respectively. The enanthem was macular in 1 patient, petechial in 2 patients, and macular with petechiae in 3 patients, and was located in the palate in all patients.

Figure. Clinical Presentation of Exanthem and Enanthem in a Patient With Severe Acute Respiratory Syndrome Coronavirus 2 Infection



This patient presented with coalescing purpuric macules distributed in a periflexural pattern, mainly around the buttocks and inguinal area (A), and enanthem on hard and soft palate consisting of millimetric petechiae without erythema (B).

Comment: This work describes preliminary observations and is limited by the small number of cases. The skin is just another manifestation of the organs involved with SARS-CoV-2 which has been reviewed in the Daily Briefing, but this is the first report I have seen regarding enanthems.

Therapeutic Plasma Exchange in Adults with Severe COVID-19 Infection
Int J Infect Dis published online June 2020 article provided by Vishal Demla

This is a case series of critically ill adult men and non-pregnant women, ³18 years of age, with laboratory confirmed COVID-19, from April 17th to May 11th, 2020. Therapeutic plasma exchange (TPE) was performed on patients admitted to intensive care unit (ICU) with severe SARS-CoV-2 infection. A total of 31 COVID-19 patients were included with an overall mean age of 51 ± 15 years (range: 27-76 years), 90% (n = 28) were males, and 35% (n = 11) of the patients had TPE as a mode of treatment. The TPE group was associated with higher extubation rates than the non TPE cohort (73% *versus* 20%; $p = 0.018$). Additionally, patients on TPE had a lower 14 days (0 *versus* 35%; $p = 0.033$) and 28 days (0 *versus* 35%; $p = 0.033$) all-cause mortality compared to patients not on TPE. However, all-cause mortality was only marginally lower in the TPE group compared to the non-TPE group (9.1% *versus* 45%; $p = 0.055$; *power* = 66%). Laboratory (absolute lymphocytic count (ALC), CRP, LDH, ferritin, D-dimer, IL-6, PH and lactate) and ventilatory parameters also improved with the TPE. Just over

half of our patients in the TPE group and one third in the control group received tocilizumab, after plasma exchange and this might additionally have contributed to the decrease in the cytokine storm.

Comment: This is a small single center study done early in the pandemic. The use of tocilizumab may have also influenced the results. Doing TPE logistically can also be challenging. CytoSorb Extracorporeal Cytokine Absorber has been advocated by some as well. It is used to decrease elevated cytokine levels in conditions including critical illness, sepsis, and cardiac surgery. There is currently limited published evidence evaluating the use of CytoSorb to treat cytokine storm in COVID-19. Although these are interesting approaches, it is not clear these would significantly add to the current therapeutic agents we now have such as remdesivir, plasma, steroids, and IL-6 inhibitors.