Reference(s) of the Week

- Villar J. Maternal and Neonatal Morbidity and Mortality among Pregnant Women with and Without COVID-19 Infection. JAMA Pediatrics. 04.22.2021. https://jamanetwork.com/journals/jamapediatrics/fullarticle/2779182 pdf
  Premise/Methods: 1. SARS-CoV-1 and MERS are coronavirus infections that have a deleterious effect upon pregnant women and their offspring. **2.** To what extent SARS-CoV-2 has on pregnant women and their offspring though smaller initial studies suggested problematic maternal and neonatal outcomes. **3.** This is a prospective, longitudinal, observational study (INTERCOVID), involving 43 hospitals in 18 countries to assess the association between COVID-19 and maternal and neonatal outcomes in pregnant women with COVID-19 diagnosis, compared with concomitantly enrolled pregnant women without COVID-19 diagnosis. Pregnant women with COVID-19 were enrolled 1:2 with uninfected pregnant women at the time of enrollment.
  Findings: 1. 706 and 1424 women with and without COVID-19 were enrolled: 287 COVID-19 patients were asymptomatic; COVID-19 48.6% /non-COVID-19 40.2% were overweight; multiple other features were compared as well.

  2. Women with COVID-19 had higher rates of the following conditions:
  - pregnancy-induced hypertension
  - preeclampsia/eclampsia
  - infections requiring antibiotics
  - risk of ICU admission
  - referral to higher level of care
  - preterm delivery
  - both neonatal and maternal morbidity indicies were higher
  - 22 times more likely to die (11 deaths vs 1)

  3. Among test positive women with test-positive neonates, the cesarean delivery rate was 72.2 %(n = 39) and among test positive women with test-negative neonates was 47.9 %(n = 173). The rate in women without COVID-19 diagnosis was 39.4 %(n = 568). **4.** Only cesarean delivery was independently associated with the risk of a test-positive neonate and there was no association between exclusive breastfeeding and neonatal test positivity.

Other References:

- Shimabukuro TT. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. NEJM. 04.21.2021. https://www.nejm.org/doi/full/10.1056/NEJMoa2104983 pdf
  Premise/Methods: 1. Studies relating to the safety of mRNA vaccines in pregnant persons were not performed prior to EUA, but pregnant persons have been vaccinated either knowingly or unknowingly in prioritized populations such as health care workers. **2.** Vaccine safety surveillance is provided by the following mechanisms: self-reported V-safe health checker, V-safe pregnancy registry, and the Vaccine Adverse Event Reporting Systems (VAERS). **3.** This study reports the safety of mRNA vaccines administered during pregnancy from the aforementioned monitoring systems from December 14, 2020 to February 28, 2021.
  Findings: 1. 35,691 pregnant recipients of an mRNA vaccine (Pfizer, Moderna) were identified through the V-safe system: for both products, age 25-34 years (~60%); non-Hispanic white (~75%); pregnant at the time of vaccination (~86%). The pattern of adverse reactions and vaccine reactogenicity were similar to those reported from non-pregnant individuals. **2.** 3,719 individuals were identified through the V-safe pregnancy registry: age 25-44 years (~99%); non-Hispanic white (79%). Calculated proportions of pregnancy and neonatal outcomes appeared similar to incidences published in the peer-reviewed literature. **3.** VAERS received 221 reports involving Covid-19 vaccination among pregnant persons with miscarriage being the most common. Comparison rates are not possible through VAERS limiting its usefulness. **4.** This preliminary study that suffers from limitations of self-reporting in V-safe and under-reporting in VAERS does not indicate any obvious safety signals with respect to pregnancy or neonatal outcomes associated with Covid-19 vaccination in the third trimester of pregnancy.

- Mack CD. Risk Among National Basketball Association Players, Staff, and Vendors Exposed to Individuals With Positive Test Results After COVID-19 Recovery During the 2020 Regular and Postseason. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2779287 pdf
  Premise/Methods: 1. Limited evidence exists regarding the infectious nature of persons who have recovered from COVID-19 yet remain persistent PCR + up to 105 days after diagnosis. **2.** Current CDC guidance indicates that immunocompetent individuals with improving or resolved symptoms following COVID-19 are no longer infectious 10 days after symptom onset or their first positive RT-PCR test result and may discontinue isolation precautions as replication virus is not likely to be isolated. **3.** The 2020

NBA playoffs were performed from June 11 through October 19 within a closed campus ("NBA bubble") in Orlando during which time protocols required routine testing for 2 weeks before arrival at the campus, with a mandatory quarantine that ended on receipt of 2 negative PCR test results at least 24 hours apart on arrival and mandatory testing was performed daily for individuals who were living on campus, while regular testing for local personnel who resided off campus was available before or on each day they worked on campus. **4.** The hypothesis of this retrospective cohort observational study was that these individuals with persistently positive high cycle time RT-PCR results presented a low probability of SARSCoV-2 transmission.
Results: 1. 3648 individuals (2915 men [79.9%]; age <30 years, 956[26.2%]) participated in the NBA Orlando campus program, 36 individuals (1.0%) met inclusion criteria as a persistent positive case (34 men [94.4%]; age <30 years, 24 [66.7%] and no individual was hospitalized or thought to have reinfection. **2.** Persistent positive individuals continued to have intermittent detectable SARS-CoV-2 RNA for a mean (SD) of 31(11) days (median, 30 days [range, 14-68 days]) from the date of initial infection. **3.** Twenty-nine individuals (81%) with persistent positive test results participated in unmasked activities on campus, such as officiating, coaching, meals, on-court training, and basketball games. **4.** No transmission events or secondary infections were detected following contact, despite daily RT-PCR testing on the Orlando campus.
This "natural experiment" validates the CDC symptom and time-based strategy to determine infectivity rather than relying on PCR testing. The latter, however, coupled to antibody testing can differentiate persistent infection if cycle time threshold breeches the upper limit threshold.

- Letizia AG. SARS-CoV-2 seropositivity and subsequent infection risk in healthy young adults: a prospective cohort study. Lancet Resp Med. 04.15.2021. www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00158-2/fulltext pdf
Premise/Methods: 1. The risk of re-infection following natural infection to SARS-CoV-2 is unknown but case reports have identified re-infection occurring. **2.** Knowledge of reinfection risk can help inform vaccination strategies and estimating herd immunity. **3.** This study utilized the COVID-19 Health Action Response for Marines (CHARM) study, a longitudinal prospective cohort study, to examine the effect of SARS-CoV-2 seropositivity on the risk of developing SARS-CoV-2 infection in young (18–20 years), healthy, adult Marine recruits. **4.** Marine recruits had baseline serologic status obtained, underwent a supervised quarantine for 2 weeks which included SARS-CoV-2 PCR testing at 0, 1, and 2 weeks, and had subsequent PCR testing at 2, 4, and 6 weeks with a second assessment for serology as well as a symptom questionnaire.
Results: 1. 3,076 recruits were eligible for the study: 225 (7%) were baseline seropositive; 2851 (93%) were baseline seronegative; participants were 18-20 years old. **2.** A total of 19 (10%) of 189 seropositive participants and 1,079 (48%) seronegative participants had at least one positive SARS-CoV-2 PCR during the 6 week follow-up period. **3.** Neutralizing antibody activity was detected in 45 (83%) of 54 seropositive participants who never became PCR positive and in 6 (32%) of 19 participants infected during the 6 weeks of observation. **4.** Of those participants who developed a positive PCR, viral load was estimated to by 10 fold higher in the seronegative group; PCR positivity was more prolonged in the seronegative group; and more seronegative participants had symptomatic infection compared to seropositive participants.

- Ohlsen EC. Airport Traveler Testing Program for SARS-CoV-2 — Alaska, June–November 2020. MMWR Morb Mortal Wkly Rep 2021. 04.23. vol 70 (16):583–588. https://www.cdc.gov/mmwr/volumes/70/wr/mm7016a2.htm pdf
Premise/Methods: 1. Alaska implemented a program to reduce importation of SARS-CoV-2 in June 2020 requiring individuals arriving from air, sea, and road to have pre-arrival testing within 72 hours, or PCR testing upon arrival, and/or self-quarantine for 14 days after arrival. **2.** Data from the 10 participating Alaska airports is reviewed in this report and the logistical requirements and cost of such a program are explained. **3.** Rules changed during the pandemic: March 2020, all travelers were required to self-quarantine for 14 days; June 2020, testing pre-arrival, testing within 7-14 days after arrival were implemented to reduce self-quarantine; August 2020, 14 day quarantine without testing was removed for non-residents; and October 2020, the requirement for a second test 7-14 days after arrival was removed.
Findings: 1. From June 6 – November 14, 2020, a total of 386,435 air travelers were screened for symptoms. **2.** 184,438 (48%) arrived with proof of a negative or pending PCR; 111,370 (29%) chose to be tested on arrival; 39,685 (10%) chose to self-quarantine without testing; 50,942 were exempt; and an additional 15,112 persons obtained a second test within 7-14 days at airport testing sites. **3.** Of the 126,482 airport tests performed in Alaska, 951 (0.8%) results were positive, or one per 406 arriving travelers. **4.** The program was resource intense and the cost substantial, with a budget of $26 million for June–December.