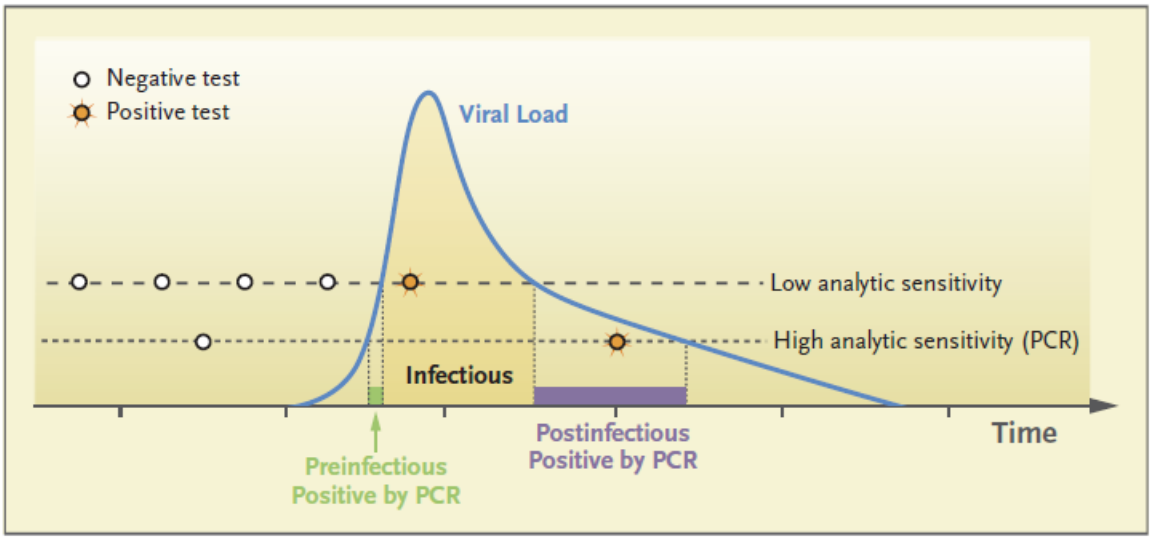
COVID-19 LITERATURE BRIEFING
October 7th, 2020

Children's MINNESOTA

Reference of the Week

- Mina MJ. Rethinking Covid-19 Test Sensitivity — A Strategy for Containment. NEJM. 09.30.2020. (perspective) https://www.nejm.org/doi/full/10.1056/NEJMp2025631 pdf
  Challenge: 1. Rapidly and cheaply identifying people who are transmitting the virus increases the effectiveness of contact tracing. **2.** The high analytic sensitivity (the lower limit of its ability to correctly detect small concentrations of molecules of current PCR testing in a sample) does not measure infectivity and the long tail of PCR positivity past the infection period has consequences: quarantine may be assigned when unnecessary; economic consequences of wrongful quarantine; mental health issues from COVID-19 in general and quarantine in particular; cost and turn-around time of PCR testing limits the effectiveness of contact tracing. **3.** What is required is an inexpensive SARS-CoV-2 test with rapid turn-around time that has less analytical sensitivity but identifies individuals who are infectious. **4.** Rapid lateral-flow antigen tests fulfill these criteria and could be performed at home.



High-Frequency Testing with Low Analytic Sensitivity versus Low-Frequency Testing with High Analytic Sensitivity.

A person's infection trajectory (blue line) is shown in the context of two surveillance regimens (circles) with different analytic sensitivity. The low-analytic-sensitivity assay is administered frequently and the high-analytic-sensitivity assay infrequently. Both testing regimens detect the infection (orange circles), but only the high-frequency test detects it during the transmission window (shading), in spite of its lower analytic sensitivity, which makes it a more effective filter. The window during which polymerase chain reaction (PCR) detects infections before infectivity (green) is short, whereas the corresponding postinfectious but PCR-detectable window (purple) is long.

Other References:

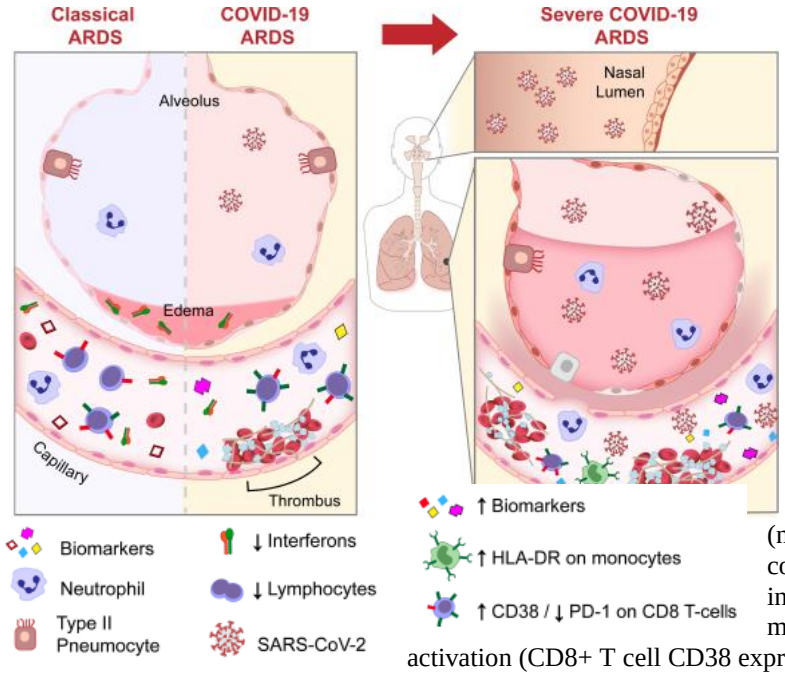
- Alexander GC. Use and Content of Primary Care Office-Based vs Telemedicine Care Visits during the COVID-19 Pandemic in the US. JAMA. 10.02.2020. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2771191 pdf
  Premise/Methods: 1. The impact of COVID-19 on primary care visits (all age groups) and the characteristics of those visits is largely unknown. **2.** Health outcomes and patient experience of telemedicine are fertile areas of investigation. **3.** Data from 4,000 physicians is collected through a national database during a two day period each quarter from patients in the continental US utilizing a standardized data entry form. **4.** Regional differences in COVID-19 were determined by deaths due to COVID-19 per 100,000 individuals as of 07/28/2020.

Results: 1. Office based average quarterly visits from 2018-2019 decreased 50.2% compared to Q2 2020. **2.** Telemedicine visits increased from 1.1% to 35.3% during the two intervals but there was significant regional variation not associated with local COVID-19 numbers. **3.** Telemedicine visit accounted for 19.3% and 20.5% among White and Black individuals respectively and predictably assessment of BP and cholesterol levels declined during telemedicine visits. **4.** Office based pediatric visits declined 28% from 2018 to 2020 while telemedicine visits increased 24 fold during the same interval.

The authors point out the explosion but emerging limitations of telemedicine visits (BP and cholesterol levels) amongst adults. More healthcare outcomes require assessment for telemedicine to find its niche in outpatient care.

- Hue S. Uncontrolled Innate and Impaired Adaptive Immune Responses in Patients with COVID-19 ARDS. Amer J of Resp and Crit Care Med. 08.31.2020 (online). https://www.atsjournals.org/doi/abs/10.1164/rccm.202005-1885OC pdf

Premise/Methods: 1. Assumptions: 50% of the 200,000 COVID-19 deaths are due to ARDS; mortality from COVID-19 ARDS is 25% - at least 400,000 COVID-19 ARDS cases to date; COVID-19 ARDS exceeds ARDS from other reasons by 2 fold. **2.** Single center prospective, observational study comparing COVID-19 ARDS and "regular" ARDS. **3.** Immunologic phenotype and chemokine signature determined. **4.** Nasopharyngeal viral loads related to immune and clinical outcome.
Results: 1. COVID-19 has impaired adaptive immune response with lymphopenia and delayed lymphocyte activation. **2.** Cytokine responses in COVID-19 ARDS showed no difference than "regular"ARDS with regard to IL-6, IL-8, and IL-Ra but findings associated with mortality included an increase in serum interferon gamma-induced protein 10 and granulocyte-macrophage colony-stimulating factor. **3.** SARS-CoV-2 NP loads were higher in patients with COVID-19 who died. **4. Figure:**



Airway and Alveolar biology during classical and COVID-19 ARDS. The alveolar-interstitial-capillary unit is similarly affected during classical and COVID-19 ARDS (left panel). In both types of ARDS, there is a marked upregulation of pro-inflammatory biomarkers, increase in capillary endothelial permeability, and an increase in inflammatory cells (neutrophils, monocytes/macrophages) in the vascular and alveolar compartments. There are, however, notable differences in the types of upregulated biomarkers, with lower expression levels of interferons and an increase in thrombotic mediators in COVID-19 relative to classical ARDS. Relative to milder forms of COVID-19 ARDS, significant alterations in severe COVID-19 ARDS (right panel) include a higher SARS-CoV-2 viral load in both the upper airways (nasal lumen) and in the circulation, a higher neutrophil count and activity (i.e., NET formation), increase in inflammatory biomarkers and thrombosis, greater monocyte (HLA-DR expression) and lymphocyte activation (CD8+ T cell CD38 expression), as well as more damage to the alveolar-interstitial-capillary unit. [from Matthay MA. AJRCCM].

- Makaronidis J. Seroprevalence of SARS-CoV-2 antibodies in people with an acute loss in their sense of smell and/or taste in a community-based population in London, UK: An observational cohort study. PLoS Med. 10.01.2020;17(10):e1003358. https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003358https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003358 pdf

Premise/Methods: 1. COVID-19 can cause loss or reduced ability to smell or taste. How frequent this occurs is unknown. **2.** The proportion of people with AB evidence of COVID-19 with newly developed loss of smell or taste was determined.
Findings: 1. A total of 78% of 567 people with acute smell and/or taste loss had SARS-CoV-2 antibodies; of these, 40% had neither cough nor fever; and participants with loss of smell were 3 times more likely to have SARS-CoV-2 antibodies, compared

with those with loss of taste. **2.** Loss of smell is a highly specific symptom of COVID-19. **3.** COVID-19 can present with loss of smell and/or taste without cough or fever.

SEE THE ARTICLE CABINET ON THE S: DRIVE, "COVID-19 ARTICLE RESOURCE CABINET" FOR CHILDREN'S FULL COLLECTION