Reference of the Week

- Jackson LA. An mRNA Vaccine against SARS-CoV-2 — Preliminary Report. NEJM. 07.14.2020.
  https://www.nejm.org/doi/pdf/10.1056/NEJMoa2022483?articleTools=true pdf
  Methods: 1. Phase 1 safety trial of mRNA-1273 vaccine (encodes the SARS-CoV-2 spike glycoprotein) to determine the optimum dose with the least side effects. **2.** Adult study with participants receiving 2 vaccinations 28 days apart at 25ug, 100ug, and 250ug doses. **3.** Primary outcome: immunogenicity, measurement of neutralizing SARS-CoV-19 antibody. **4.** Second primary outcome: safety, distribution of adverse effects across dosing regimens.
  Findings: 1. 15 adult patients received 2 vaccines at the aforementioned three doses with F/U at 57 days. **2.** No serious adverse effects noted though 1 subject developed transient urticaria following the 25ug dose. **3.** At least one-half of subjects had limited systemic and local reactions across both vaccinations. **4.** Dose dependent seroconversion occurred in all participants by day 15 and the vaccine induced "robust binding" AB in all participants as well as neutralizing AB (augmented by the second dose) comparable to convalescent plasma.
  This study is currently being followed by an active phase 2 trial in 600 adults at the 50ug and 100ug doses.

Other References:

- Havers FP. Seroprevalence of Antibodies to SARS-CoV-2 in 10 Sites in the United States, March 23-May 12, 2020. JAMA. 07.21.2020. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2768834?guestAccessKey=7a5c32e6-3c2741b3b46c43c4a38bbe00&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=072120 pdf
  Methods: 1. Confirmed case reporting of COVID-19 underestimates the true prevalence of disease in the community. **2.** Serologic testing can provide population-based estimates of infection. **3.** Convenience samples of residual plasma from primarily outpatient general health screening was used to assess for serologic evidence of COVID-19 in 10 geographic areas. **4.** Results from serologic prevalence was compared to PCR positive incidence and an estimate of local population prevalence was made.
  Findings: 1. 16 025 residual sera specimens from 10 sites collected from March 23 through May 12 were tested for serologic evidence of COVID-19 (1,205 pediatric age patients). **2.** Seroprevalence estimates ranged between 1% and 6.9% across all sites and were 6 – 23.8 times greater than PCR positive patients. **3.** The seroprevalence results for each site suggest that the number of infections was much greater than the number of reported cases reflecting asymptomatic, mildly symptomatic, and untested individuals. **4.** For most sites, it is likely that greater than 10 times more SARS-CoV-2 infections occurred than the number of reported COVID-19 cases; most persons in each site, however, likely had no detectable SARS-CoV-2 antibodies.

- Kamrath C. Ketoacidosis in Children and Adolescents With Newly Diagnosed Type 1 Diabetes During the COVID-19 Pandemic in Germany. JAMA. 07.20.2020 (Research Letter). https://jamanetwork.com/journals/jama/fullarticle/2768716 pdf
  Methods: 1. The pandemic has resulted in a reduction in healthcare use by individuals who fear contracting the disease at a health care facility. **2.** In Germany, a data registry exists across diabetic F/U sites. **3.** The registry was accessed to ascertain the frequency of DKA and severe DM during the COVID-19 period compared to similar periods during 2018 and 2019.
  Findings: 1. 532 children from 216/217 diabetes centers were retrospectively assessed (median age 9.9 yrs, IQR 5.8-12.9 years). **2.** During the COVID-19 period the frequency of both DKA and severe DKA were significantly higher compared with previous years. **3.** The increase in illness frequency and severity appear to be due to reduced utilization of healthcare resources that may be generated by fear of contracting COVID-19 at a healthcare facility.

- Bellino S. COVID-19 disease severity risk factors for pediatric patients in Italy. Pediatrics. 07.17.2020
  https://pediatrics.aappublications.org/content/early/2020/07/16/peds.2020-009399 pdf
  Methods: 1. Retrospective national study of COVID-19 children <18 years extracted from the Italian integrated COVID-19 surveillance system. **2.** Three regions of data were inputted into a single on line database. **3.** Details of the four deaths were abstracted from the medical records. **4.** The primary outcomes were to outline the epidemiological and clinical characteristics of

COVID-19 pediatric patients in Italy, investigate the disease severity risk factors, and compare children and adolescents to adults and the elderly.

Findings: 1. 3,836 patients accounted for 1.8% of all COVID-19 patients reported on a national level, median age 11 yrs: 0-1 yrs, 13.8%; 2-6 yrs, 17.2%; 7-12 yrs, 12.8%; and 13-17 yrs, 40.1%. **2.** 13.3% of the total COVID-19 pediatric patients were hospitalized: 0-1 yrs, 36.6%; 2-6 yrs, 12.8%; 7-12 yrs, 8.8%; and 13-17 yrs, 8.9% *and* 3.5% were admitted to PICUs. **3.** 9.8% of hospitalized patients had an underlying condition and the 0-1 yr age group had the highest proportion of severe/critical patients (10.8%). **4.** The four deaths included: 1 patient with mucolipidosis, 1 patient with Williams syndrome, 1 patient with aggressive cancer, and 2 patients with congenital heart disease. **5.** Compared to adult and elderly patients: hospitalization – children 3.5%, adults 17.2%, elderly 41.1%; 63.4% of children were asymptomatic/mild compared to adults 44% and elderly 27.3%; and mortality was much higher in adults and the elderly.

- Gupta S. Factors Associated With Death in Critically Ill Patients With Coronavirus Disease 2019 in the US. JAMA. 07.15.2020. https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2768602 pdf
Methods: 1. Retrospective multicenter ICU study of adult patient to examine the demographics, comorbidities, organ dysfunction, treatment, and outcomes of patients with COVID-19. **2.** Standardized case report forms were submitted electronically from each study site. **3.** Patient, outcome, and hospital level data were included on the case report form. **4.** The primary outcome was to describe demographic, treatment, and outcomes or ICU patients and to assess interhospital variation in treatments and outcomes.

Findings: 1. 2,215 adult patients from 65 US sites met inclusion criteria: mean age 60.5 yrs; 64.8% men; 78.5% of patients had at least 1 co-morbidity (hypertension, diabetes, and chronic lung disease); cough, dyspnea, and fever were the most common presenting symptoms. **2.** Organ dysfunction after ICU admission: acute respiratory failure (84%); 74% ARDS; acute kidney injury (43%); and 10% had detectable thrombosis. **3.** Considerable variability in supportive and medicinal therapies characterized treatment options. **4.** Rate of death ranged from 12% to 63% with 28 day mortality risk being higher for a variety of co-morbid conditions including hospitals with < 50 ICU beds (OR, 3.28; 95% CI, 2.16-4.99).

- **WHY IS WEARING A MASK SO HARD?**
During the 1918 influenza pandemics even animals wore a mask:

https://www.atlasobscura.com/articles/pets-during-1918-influenza-epidemic

COVID-19 LITERATURE BRIEFING

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