COVID-19 LITERATURE BRIEFING
July 29 , 2020

Children's MINNESOTA

Reference of the Week

- DeFilippis EM. Trends in US Heart Transplant Waitlist Activity and Volume During the Coronavirus Disease 2019 (COVID-19) Pandemic. JAMA. 07.22.2020. https://jamanetwork.com/journals/jamacardiology/fullarticle/2768735 pdf
  Method: 1. Descriptive cross-sectional study of public data across the US regarding adult heart transplant activity. **2.** Transplantation has been effected by COVID-19: ICU beds may not be available; hospital personnel may be in short supply or repurposed to care for COVID patients; testing of donor and recipient not available; and the safety of transporting personnel as well as organ recipients. **3.** Data assessed: deactivation (patients not sick enough); new waitlist patients; and heart transplant recipients. **4.** The primary outcome was to assess the state of heart transplantation in the US during the pandemic.
  Findings: 1. Waitlist inactivations: 75% increase with the majority due to COVID-19 precautions. **2.** Waitlist additions: 38% decrease with reductions increasing during the pandemic. **3.** Decreased donor recovery: a 26% decline in donor heart recovery across all sections of the US. **4.** Heart transplant volume decline 26% nationally. **5.** The collective effect of these trends is likely to increase mortality in the prospective heart transplant population. Although not addressed, the situation for pediatric heart transplantation may not be any better.

Other References:

- Walker D. The Work of Philanthropy in Responding to COVID-19 and Addressing Inequality - A New Foundation. JAMA 07.23.2020 (Viewpoint). https://jamanetwork.com/journals/jama/fullarticle/2768893 pdf
  Messages: 1. COVID-19 has revealed how structural racism is tightly woven into the fabric of America and the consequence has been disparity in public health outcomes, the economy, education, criminal justice system, and policing. **2.** Philanthropic foundations (Ford, Carnegie, MacArthur, Gates, Rockefeller, etc) *exist due to the very unequal system that created them:* and they have an obligation to address the imbalance of wealth at the root of many societal problems. **3.** Tangible interventions: sustain the multi-foundation relief organization for the current crisis; reimagine healthcare and fund the vision; use debt not for acquisitions/construction but as a means to fund targeted grants; demand that well-endowed colleges/universities support the endowments of traditionally black institutions; and direct philanthropic support for rural communities and communities of color. **4.** Now is the time to rebuild a world filled with equality and justice for all.

- Patel BV. Pulmonary Angiopathy in Severe COVID-19: Physiologic, Imaging and Hematologic Observations. AJRCCM. 07.15.2020. (pre-print). https://www.atsjournals.org/doi/10.1164/rccm.202004-1412OC pdf
  Methods: 1. Enroll COVID-19 adults with severe disease and define their underlying pathophysiology. **2.** Respiratory mechanics were defined by PaO2/FiO2, ventilation ratio (VR) as a surrogate for physiologic dead space, and dynamic compliance (DC). **3.** Coagulation status was measured by the usual coagulation parameters plus thromboelastography (TEG). **4.** Imaging was performed by CT, CTpulmonary angiogram (CTPA), and dual energy CT (DECT) to further define pulmonary vascular changes.
  Findings: 1. 39 mechanically ventilated adults: male 79.5%, persons of color 64%, co-morbid condition 80%, 100% received at least prophylactic heparin, and 20 required ECMO. **2.** Respiratory parameters: PaO2/FiO2 = 114.9 $\pm$ 74.2; DC = 33.7 $\pm$ 14.7mls/cm H20; VR increased and PaO2/FiO2 decreased with PEEP. **3.** Imaging findings: dilated (tortuous and branching) peripheral vessels (Figure 2) on CT in 21 out of 33 (63.6%) patients; arterial filling defects on CTPA, consistent with acute pulmonary emboli (PE) were present in 15/39 (38%) patients; perfusion defects were present in 100% of patients by DECT (n=18); vascular "tree and bud" formation suggests in situ thrombosis. **4.** Coagulation findings: despite the use of heparin, TEG data showed hypercoagulability; all patients showed absent fibrinolysis. **5.** Mechanically ventilated patients with severe COVID-19 pneumonia present with hypercapnic respiratory failure and initial relatively preserved respiratory system compliance, reflecting increased pulmonary dead space and a predominant defect in pulmonary perfusion consistent with the respiratory mechanics, hematological, and morphological findings in this study.

- Weisberg SP. Antibody responses to SARS-CoV2 are distinct in children with MIS-C compared to adults with COVID-19. medRxiv. 07.14.2020 (preprint). https://www.medrxiv.org/content/10.1101/2020.07.12.20151068v1 pdf
  Methods: 1. Antibody (AB) responses to COVID-19 from patients in New York were compared among children with MIS-C, adults with mild disease who were convalescent plasma donors (CPD), and adults with severe disease (COVID-ARDS). **2.** Samples from

MIS-C were obtained at a shorter interval between symptom-onset and disease than the other cohorts. **3.** ABs measured in the three cohorts include: anti-S ABs including IgM, IgG, and IgA; anti-N IgG; and neutralizing AB production. **4.** Primary outcome: determine whether a difference occurs in AB production and neutralizing function occurs among the aforementioned three cohorts.
Findings: 1. COVID-ARDS patients had the highest levels of anti-S ABs for immunoglobulin classes; MIS-C patients and CPD patients had predominantly IgG anti-S ABs; MIS-C patients had IgM ant-S ABs at a level similar to pre-pandemic controls. **2.** MIS-C patients had significantly lower anti-N IgG levels compared with COVID-ARDS and CPD patients. **3.** Highest neutralizing AB titers were found in the COVID-ARDS patients compared to MIS-C and CPD. **4.** Clear quantitative and qualitative differences in AB production exists across the three cohorts and inefficient neutralizing AB in MIS-C suggests that neutralizing AB products may have a role in treatment (current therapy for MIS-C is steroids and IgG).

- He J. Proportion of asymptomatic coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. J of Medical Virology. 07.21.2020 (pre-print). https://onlinelibrary.wiley.com/doi/10.1002/jmv.26326 pdf
  Methods: 1. Electronic databases were searched to determine the characteristics of asymptomatic infection. **2.** Definitions included asymptomatic, pre-symptomatic, and asymptomatic at the point of testing (including patients who were either asymptomatic or pre symptomatic. **3.** Primary outcome: Determine the rate of asymptomatic infection at the time of testing and other characteristics of COVID-19.
  Findings: 1. 41 studies including 50,155 patients were included (25 studies from China and 16 from other countries). **2.** The pooled percentage of asymptomatic infection from all studies was 15.6%. **3.** 10 studies contained information regarding pre-symptomatic infection- the pooled percentage of pre-symptomatic infection was 48.9%. **4.** In the 11 pediatric articles, a 27.65% of cases were asymptomatic.

- Abolghasemi H. Clinical efficacy of convalescent plasma [CP] for treatment of COVID-19 infections: Results of a multicenter clinical study. Transfusion and Apheresis Science. 07.2020 (pre-print).
  Method: 1. Retrospective Iranian adult study from 7 hospitals with a hospital case fatality rate of 8.06% (extraordinarily low??). **2.** Convalescent plasma tested for COVID-19 antibody by a semi-quantitative method (no testing for neutralizing antibody). **3.** Recipients were hospitalized, required oxygen, and were early in the course of their disease ($\leq$ 7 days since illness onset) and did not require intubation. **4.** Primary outcomes: mortality and length of hospital stay. Secondary outcomes: progression to intubation, improvement in clinical score, and adverse effects of plasma infusion.
  Findings: 1. 189 patients: 115 CP with 75 controls; matching of individuals between group by gender, age, and co-morbidities. **2.** All patients received similar pharmacologic therapy (hydroxychloroquine, Lopinavir/Ritonavir, and an anti-inflammatory agent [?]). **3.** Mortality: 0.08% in CP group vs 21.3% in the control group. **4.** Hospital LOS and intubation requirement were significantly better in the CP group. *There are limitations to this study from many perspectives but it adds to the literature a positive CP study.*

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