



Reference of the Week

- Kox M. Cytokine Levels in Critically Ill Patients with COVID-19 and Other Conditions. JAMA. 09.03.2020 (research letter). <https://jamanetwork.com/journals/jama/fullarticle/2770484> pdf
Premise/Methods: **1.** “Cytokine storm” is a poorly defined term used to identify an exuberant pro-inflammatory state. **2.** COVID-19 has elevated pro-inflammatory cytokines compared to baseline levels. **3.** This study compares cytokine levels in mechanically ventilated COVID-19 patients with ARDS (COVID) to other disorders: septic shock without ARDS (SS-) septic shock with ARDS (SS+); out-of-hospital cardiac arrest (CA); and multiple trauma (MT). **4.** Cytokine levels were determined by the same assay, by the same technician, and within a predetermined time interval for all conditions.
Findings: **1.** Subjects: 46 COVID; 51 SS; 30 CA; and 62 MT. **2.** Levels of TNF, IL-6, and IL-8 were all lower for COVID compared to SS+ and limited differences occurred compared to other conditions. **3.** The findings of this preliminary analysis suggest COVID-19 may not be characterized by excessive “cytokine storm”. *This limited study suggests that anti-cytokine therapy may have only a limited role in treatment of COVID-19 and that the key identifying feature of the disease remains the pro-thrombotic changes in the lung.*

Other References:

- REACT-WHO. Association between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A meta-analysis. JAMA. 09.02.2020. <https://pubmed.ncbi.nlm.nih.gov/32876694/> pdf
Premise/Methods: **1.** At one time, there were 55 registered trials addressing the efficacy of corticosteroids in COVID-19. **2.** The benefit of mortality reduction in one study resulted in the suspension of most other trials. **3.** The objective of this prospective meta-analysis of randomized trials was to estimate the association between administration of corticosteroids, compared with usual care or placebo, and 28-day all-cause mortality in hospitalized, critically ill patients with suspected or confirmed COVID-19.
Findings: **1.** 7 clinical trials recruiting 1,703 patients from multiple countries were included. **2.** The studies used dexamethasone, hydrocortisone, and methylprednisolone at both low and high doses. **3.** There were 222 deaths among 678 patients randomized to corticosteroids and 425 deaths among 1025 patients randomized to usual care or placebo. **4.** Mortality at 28 days after randomization was reduced compared to controls or placebo in all 7 studies and no major adverse effects were noted. *Timing, dosing, delivery, steroid preparation, and days of therapy were not addressed in this study. Corticosteroids are clearly of benefit and currently are considered standard of care for the treatment of COVID-19.*
- Broadhurst R. Asthma in COVID-19 Hospitalizations: An Overestimated Risk Factor? Annals ATS. 09.2020 (Research letter). <https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.202006-613RL> pdf
Premise/Methods: **1.** Asthma prevalence in COVID-19 in multiple international studies appears to be low and does not stand out as a risk factor. **2.** In this study, asthma prevalence among hospitalized COVID-19 patients in 15 studies was compared to the corresponding population asthma prevalence. **3.** The four year asthma prevalence in hospitalized influenza in the USA was compared to asthma prevalence in COVID-19. **4.** The likelihood of intubation of COVID-19 patients with and without asthma at the University of Colorado Hospital was determined.
Findings: **1.** 15 studies were included in the study. **2.** The proportion of asthmatics among hospitalized patients with COVID-19 is similar to that of each study site’s population asthma prevalence. **3.** Asthmatics make up more than 20% of hospitalized influenza patients in the USA. **4.** At the University of Colorado asthma COVID-19 patients were no more likely to be intubated than non-asthma patients.
At first glance this article appears counter-intuitive but the absence of risk imparted by asthma may be related to the reduction of ACE2 expression in the population and the effect of inhaled corticosteroids ACE2 expression.
- Alsayegh F. Challenges in the Management of Sickle Cell Disease During SARS-CoV-2 Pandemic. Clin Appl Throm/Hemo. 09.02.2020 . <https://journals.sagepub.com/doi/full/10.1177/1076029620955240> pdf
Premise/Review: **1.** Both sickle cell disease (SCD) and COVID-19 are thrombogenic disorders. **2.** Limited published data exists



on how to care for SCD in COVID-19. **3.** SCD complicates SARS-CoV-1 and influenza pneumonia suggesting that similar challenges are likely to occur with SARS-CoV-2.

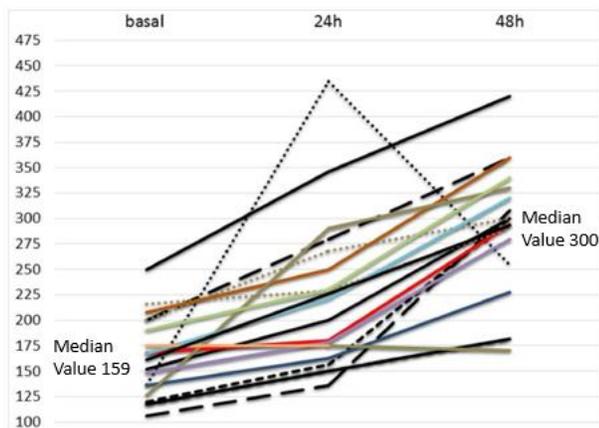
Findings: **1.** 19 patients with SCD or Hb S β have been reported in the literature: various interventions were utilized including exchange transfusion, prophylactic LMWH, full heparinization, and tocilizumab. **2.** This article provides a review of current treatments available for patients with SCD. **3.** Recommendations for the following conditions are provided for SCD and COVID-19: asymptomatic patients; mildly symptomatic with an oxygen requirement; severe disease but not requiring mechanical ventilation; severe disease requiring mechanical ventilation and/or ECMO; vaso-occlusive crisis or hemolytic crisis; acute chest syndrome; and splenic sequestration crisis. *This thoughtful and comprehensive review provides a quick resource to help guide therapy in the event a patient with SCD contracts COVID-19.*

- Capochiani E. Ruxolitinib Rapidly Reduces Acute Respiratory Distress Syndrome in COVID-19 Disease. Analysis of Data Collection From RESPIRE Protocol. *Frontiers in Med.* 08.04.2020.

<https://www.frontiersin.org/articles/10.3389/fmed.2020.00466/full> pdf

Premise/Methods: **1.** Janus kinase family of enzymes (JAK) are important in cytokine signaling once a cytokine binds to a cell receptor and drugs such as ruxolitinib block JAK signal transduction. **2.** Immunomodulation in COVID-19 by blocking cytokines such IL-6 and IL-1 have demonstrated efficacy in preliminary studies. **3.** This was a multi-center retrospective cohort study in three Italian hospitals where patients with progressive ARDS on NIV or mechanical ventilation were enrolled. **4.** This study sought to determine the effect of ruxolitinib on respiratory function, respiratory support, and inflammatory measures.

Findings: **1.** 18 patients were enrolled: median age 62.5 yrs; 6 patients had comorbidities (18%); median onset of treatment from the onset of symptoms was 9 days; median PaO₂/FiO₂ was 159; and all patients received the local standard of care. **3.** Sixteen out of 18 patients showed a significant improvement in respiratory response within the first 48 hrs. **4.** At day 14 of ruxolitinib treatment, 16/18 patients showed complete recovery of respiratory function.



PaO₂/FiO₂ values during the first 48 hours of ruxolitinib treatment

- Goldstrom N. Neonates With Complex Cardiac Malformation and Congenital Diaphragmatic Hernia Born to SARS-CoV-2 Positive Women—A Single Center Experience. *World J Ped and Congenital Heart Surg.* 08.27.2020.

Premise/Methods: **1.** Little is known about the outcome of pregnant women and their newborn infants with congenital heart disease and pulmonary malformations. **2.** Miscarriage, intrauterine fetal demise, and premature birth have been reported with COVID-19 while most neonates who acquire SARS-CoV-2 infections have either been asymptomatic or experienced a mild course. **3.** This is a single center case series on the outcomes of mothers with COVID-19 and their newborn infants. **4.** The latter were minimally tested for SARS-CoV-2 (PCR) at 24 hours and at 14 days.

Findings: **1.** This case series included neonates with prenatal diagnosis of complex congenital malformations of the heart (6) or lung (1) born to women who tested positive by nasopharyngeal swab for SARSCoV-2. **2.** Visitation of the newborns was



restricted to the mothers until cleared by infection control but expression of breast milk was encouraged. **3.** All 7 infants had unremarkable courses comparable to the outcomes expected in the pandemic era.

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