



## Reference of the Week

- Cytokine profiling in COVID-19:  
McElvaney OJ. Characterization of the inflammatory response to severe COVID-19 illness. AJRCCM 07.2020 (pre-publication). <https://pubmed.ncbi.nlm.nih.gov/32584597/> pdf

**Methods:** **1.** This is a serologic study comparing adult patients with stable hospitalized COVID-19 (CO<sub>STABLE</sub>), ICU COVID-19 (CO<sub>ICU</sub>), healthy controls (HC), and severe community acquired pneumonia (CAP<sub>ICU</sub>). **2.** Cytokine levels, including pro- vs anti-inflammatory cytokines, and immunomodulatory assays are performed. **3.** The purpose of this study is to determine the differences in assays between study groups. **4.** Preliminary rationale for different therapies is explored.

**Findings:** **1.** Significant differences are revealed between the study groups with COVID-19 patients having a distinctive profile and CO<sub>STABLE</sub> and CO<sub>ICU</sub> being clearly different as well. **2.** Pro-inflammatory markers, IL-1B, IL-6, and sTNFR1 are higher in COVID-19 and anti-inflammatory markers IL-10 and relative alpha-1-antitrypsin (AAT) levels are decreased compared to CAP<sub>ICU</sub>. **3.** In CO<sub>ICU</sub> patients increases in IL-6:AAT predicted prolonged ICU stay and mortality, while improvement in IL-6:AAT was associated with clinical resolution. **4.** IL-1 and IL-6 blockers and supplementation with AAT may have a role in treatment.

Figure 1: The ratio of IL-6 to AAT comparisons between CO<sub>ICU</sub> and CAP<sub>ICU</sub> and outcome suggests that anti-inflammatory defense is overwhelmed by the pro-inflammatory cytokine IL-6. It should be noted, however, that IL-6 levels in non-COVID-19 ARDS are substantially higher than what we observe with COVID-19 ARDS.

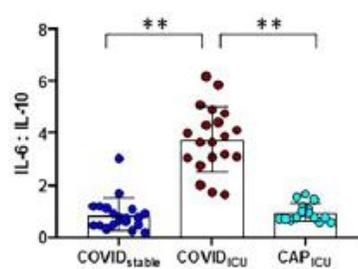
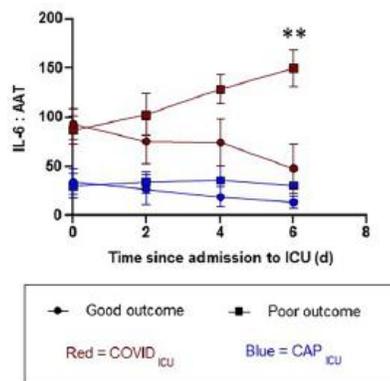


Figure 2:  
CO<sub>ICU</sub> and CAP<sub>ICU</sub> have distinctly different cytokine profiles.

## Other References:

- Blocking IL-6 production in COVID-19:  
Roschewski M. Inhibition of Bruton tyrosine kinase [BTK] in patients with severe COVID-19. Science Immunology.06.05.2020;5(48). <https://immunology.sciencemag.org/content/5/48/eabd0110> pdf
- Methods:** **1.** BTK participates in the triggering the production of multiple inflammatory cytokines including IL-6. **2.** Acalabrutinib (ALA) inhibits BTK and is licensed for use in treating lymphoid malignancies. **3.** Off-label use of ALA in adults with severe COVID-19 (100 mg BID enteral for 10-14 days). **4.** Outcomes of interest: clinical and laboratory effect of inhibiting BTK.
- Findings:** **1.** 19 patients with severe COVID-19 (11 increasing supplemental oxygen [GRP<sub>OXY</sub>], 8 mechanical ventilation[GRP<sub>MV</sub>]). **2.** Oxygenation improved; 8/11 in the GRP<sub>OXY</sub> discharged; 4/8 GRP<sub>MV</sub> extubated. **3.** Levels of CRP normalized or diminished rapidly, monocyte IL-6 levels declined and lymphocyte counts improved. **4.** This very preliminary study has led to a larger clinical trial that is ongoing.

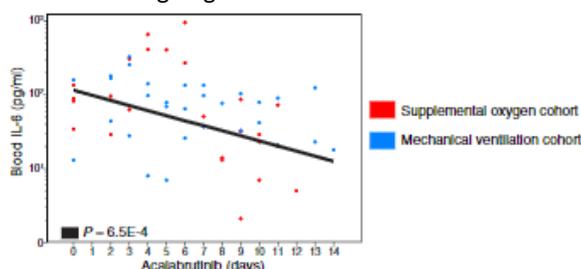


Figure.  
Plot of IL-6 on a log scale versus days of acalabrutinib treatment in whom there were at least two IL-6 measurements during the time course.



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

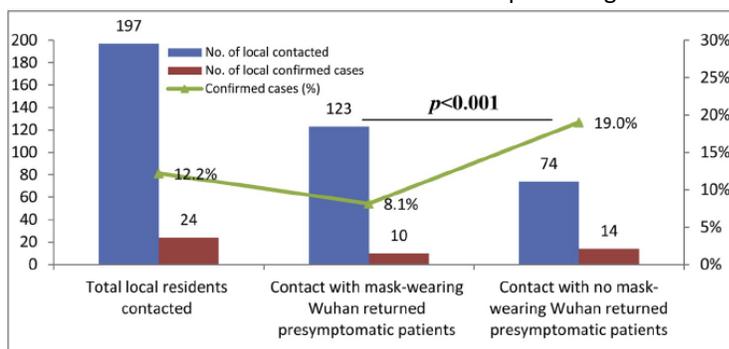
- Colchicine for COVID-19:  
Deftereos SG. Clinical Outcomes in Patients Hospitalized With Coronavirus Disease 2019 The GRECCO-19 Randomized Clinical Trial. JAMA.06.24.2020;3(6):e2013136. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2767593> pdf  
**Methods:** 1. Colchicine is an anti-inflammatory agent with unique properties including inhibition of inflammasome signaling and production of IL-1B. 2. Prospective, multi-Greek center, open-label, RCT adult study comparing standard of care (SOC) and SOC with colchicine. 3. Exclusion criteria included COVID-19 patients receiving mechanical ventilation. 4. Primary outcome: biochemical- difference in maximal troponin level and clinical- improvement by defined scale; secondary outcomes- progression to mechanical ventilation, mortality, and adverse effects.  
**Findings:** 1. 105 patients randomized: 50 SOC and 55 colchicine group; study halted due to limited number of eligible patients (flattening of curve). 2. Significant clinical benefit was observed in the colchicine group. 3. Troponin and CRP levels did not change significantly between the two groups though D-dimers were less in the colchicine group. 4. No major adverse events were encountered.
- PPE: A refresher!**  
Ortega R. Personal protective equipment and COVID-19. NEJM. 05.19.2020.



NEJMdo005771\_download.mp4

Additional protections not emphasized in the video include:

1. Consider disinfection of PPE in a "doffing room" prior to removal.
  2. Following removal of the face shield (which may be contaminated) wash hands before touching the mask and/or face.
  3. Consider donning two sets of gloves which allows removal of a contaminated outer glove and the second pair of gloves is used to remove the gown . . . and then hand washing afterwards.
  4. Providers should follow **local instructions** to the letter to confer the greatest protection possible depending on institutional capability.
- Hong LX. Mask wearing in pre-symptomatic patients prevents SARS-CoV-2 transmission: An epidemiological analysis. Travel Med and Infect Dis. 06.2020. <https://www.sciencedirect.com/science/article/pii/S1477893920302994> pdf  
**Methods:** 1. Retrospective evaluation of Zhejiang residents who returned from Wuhan prior to lockdown of Hubei province. 2. Contact tracing questionnaire with questions directed at the use of masks performed upon hospitalization.  
**Findings:** 1. 127 patients with SARS-CoV-2 including 64 Zhejiang residents and 63 travelers from Wuhan; 41 had completed information. 2. 41 pre-symptomatic patients (28 wearing face masks, 13 without face masks) had close contact with 197 local residents and 24 became infected. 3. The percentage of local residents who became infected from mask wearing individuals (8.1%) was significantly lower than the number infected from non-mask wearing individuals (19%),  $p < 0.001$ .



4. The authors conclude, "In our opinion, universal use of masks in general public and community should be recommended if supply permits." Figure.

Comparison of the incidence of local COVID-19 patients after close-contact between mask-wearing and without mask-wearing Wuhan returned COVID-19 pre-symptomatic patients ( $p < 0.001$ ).



# COVID-19 LITERATURE BRIEFING

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