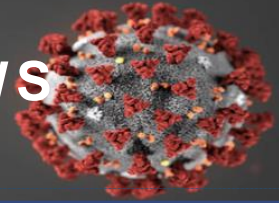


WEEK IN REVIEW

COVID-19 SCIENTIFIC NEWS

MAY 11 – 15, 2020



MS Literature Review Task Force: Sherry Chao, Michael Galie, Mary Chandler Gwin, Tin Phan, Feiyun Ma, Laiken Price, Cath Rueckeis, Chris Sefton, Peter Triggiani, and Laurel Wood
Faculty Advisor: Louise King, MD

The MS Literature Review Task Force is a group of UNC medical and pharmacy students who conduct daily literature searches for scientific updates on COVID-19. Contact Mary Chandler Gwin, mary_gwin@med.unc.edu for any comments, questions, etc.

LATEST ARTICLES:

CLINICAL INFORMATION

[Coronavirus Disease-19 \(COVID-19\) associated with severe acute pancreatitis: Case report on three family members.](#)

Hadi, A. et al., *Pancreatology*, 05 May 2020.

- A case report of 3 family member in Denmark who contracted SARS-CoV-2 reported 2 out of 3 family members were diagnosed with acute pancreatitis (Modified Glasgow Acute Pancreatitis Score of 5) with other causes of acute pancreatitis excluded. The researchers suggest that physicians should consider ordering pancreas-specific plasma amylase in patients with COVID-19 and abdominal pain, especially as COVID-19 and acute pancreatitis can induce multiorgan failure.

[Characteristics and Clinical Outcomes of Adult Patients Hospitalized with COVID-19 – Georgia, March 2020.](#) Gold, J. A. W. et al., *CDC Morbidity and Mortality Weekly Report*. 08 May 2020.

- Data was abstracted for laboratory confirmed COVID-19 patients hospitalized from March 1 – 30, 2020 from 8 hospitals in Georgia: 7 Atlanta Metropolitan hospitals and 1 community hospital in Southern Georgia. Of the 305 patients, 297 (93%) had race and ethnicity data, which was categorized as black non-Hispanic (247, 83.2%) and nonblack patients (50, 16.8%). The proportion of hospitalized patients who were black was higher than expected based on overall hospitalization. At four affiliated hospitals which had 67% of the patients in this cohort, 80% of the patients were black compared to the 47% of patients hospitalized overall during March.

[Characteristics and Outcomes of Recipients of Heart Transplant with Coronavirus Disease 2019.](#) Farhana, L. et al. *JAMA Cardiology*. May 13, 2020.

- A single-center case series characterized 28 heart transplant recipients' disease courses after infection with COVID-19. Prior to this case series, preliminary case reports had not indicated a higher incidence of infections within the posttransplant population. Comorbid conditions of the 28 patients included diabetes, hypertension and cardiac allograft vasculopathy. 25% required mechanical ventilation, while 76% had evidence of myocardial injury and elevated inflammatory markers (CRP and interleukin 6). For the management of the immunosuppression, mycophenolate mofetil was discontinued in 70% of patients and 26% had a reduction in the dose of their calcineurin inhibitor. 78% of patients were treated with hydroxychloroquine, while 47% were given high-dose corticosteroids. 26% of patients were given interleukin 6 receptor antagonists. The mortality rate for the 28 patients was 25%, as 7 patients had died.

[COVID-19: How to Recognize and Manage Kawasaki-like Syndrome.](#) Lecrubier, A. *Medscape Medical News*. 08 May 2020.

- There is a syndrome very similar to Kawasaki disease but not quite “classic Kawasaki” that has increased, with 25 cases in the Paris area over three weeks. There is a large variability in presentation; however, most are associated with circulatory failure and myocarditis. Patients in France were initially described as having a respiratory, hemodynamic, septic, or digestive presentation. Cardiac collapse is common +/- LV systolic dysfunction. The treatment is the exact same as for Kawasaki (aspirin+IVIG) and patients typically respond well to treatment.

Hyperbaric oxygen therapy in preventing mechanical ventilation in COVID-19 patients: a retrospective case series.

Thibodeaux, K. et al., *Journal of Wound Care*. May 2020.

- In this retrospective case series, 5 patients were given hyperbaric oxygen therapy (HBOT) instead of mechanical ventilation. A decrease in oxygen requirement below an FiO₂ of 50% took an average of 5 treatment sessions. All patients recovered (increased oxygen saturation, tachypnoea improved, and inflammatory markers decreased) without requiring mechanical ventilation.

[Hypoxaemia related to COVID-19: vascular and perfusion abnormalities on dual-energy CT](#). Lang et al., *Lancet Infectious Diseases*. April 30, 2020

- Dual-energy CT was performed on three COVID-19 positive patients with severe hypoxemia, elevated D-dimer, and clinical suspicion for PE. Imaging showed striking perfusion abnormalities without evidence of PE. Pulmonary vessels were dilated proximal to and surrounding the ground-glass opacity consolidation, suggesting a failure of hypoxic vasoconstriction secondary to underlying inflammatory process that causes over-activation of vasodilation. This pathophysiology is rarely seen typical ARDS. These results suggest hypoxia in COVID-19 is due to intrapulmonary shunting secondary to endothelial dysfunction, rather than intrinsic airway disease.

[Review article: COVID-19 and liver disease - what we know on 1st May 2020](#) . Garrido, I., et al. *Alimentary Pharmacology & Therapeutics*. 13 May 2020.

- COVID-19 is frequently associated with abnormal LFTs, particularly mildly elevated transaminases. Clinically significant liver impairment is rare. Children with COVID19 do not typically have increased LFTs. Patients with chronic liver disease seem not to be at increased risk of contracting COVID19

[Risk Factors for Mortality in 244 Older Adults With COVID-19 in Wuhan, China: A Retrospective Study](#). Sun, H, et al., *Journal of American Geriatrics*. 08 May 2020.

- Older age and lower lymphocyte count on admission were associated with death in hospitalized COVID-19 patients. Multivariable logistic regression analysis revealed that lymphocyte count (odds ratio [OR] = 0.009; 95% confidence interval [CI] = 0.001-0.138; *P* = .001) and older age (OR = 1.122; 95% CI = 1.007-1.249; *P* = .037) were independently associated with hospital mortality. Risk factors for in-hospital death were similar between older men and women.

[Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019 \(COVID-19\)](#). Alipio. *SSRN*. May 7, 2020

- A retrospective multicenter study of 212 cases from three hospitals in Southern Asian countries with confirmed COVID-19 was done to investigate the association between serum 25(OH)D level and clinical outcomes. Serum 25(OH)D levels were lowest in the critical cases and highest in the mild cases (17.1 vs 31.2 ng/mL, *p*<0.001). Severe cases also had higher proportion of vitamin D deficiency compared to mild cases (31% vs 1.4%, *p*<0.001). For each standard deviation increase in serum 25(OH)D, the odds of having a mild clinical outcome rather than a critical outcome were increased approximately 19.61 times (OR=0.051, *p*<0.001).

[Hyperinflammatory shock in children during COVID-19 pandemic](#). Riphagen et al., *The Lancet*. 7 May 2020.

- The first retrospective case report of a cluster of 8 Kawasaki-like disease cases in England examined clinical presentation of disease. All children were prior well except one well above the 75th percentile for weight. 4 had known familial exposure to COVID-19. Ages ranged from 4-14 years with median. Symptoms included unrelenting fever, variable rash, conjunctivitis, peripheral edema, and extremity pain. Untypically, all patients presented with significant gastrointestinal symptoms (vomiting, diarrhea). All patients progressed to warm, vasoplegic shock refractory to volume resuscitation, needing noradrenaline and milrinone. All patients presented with echobright coronary vessels and one patient expired due to progression to giant coronary aneurysm.

[An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study.](#) Verdoni *et al.*, *The Lancet*. May 13, 2020.

- A retrospective cohort study examined the change in incidence and presentation of Kawasaki-like diseases in a Bergamo, Italy hospital PICU. In the 5 years leading up to February 17, 2020, the beginning of the epidemic, 19 cases of Kawasaki-like disease were reported—incidence 0.019%. From February 17, 2020 to April 20, 2020, 10 cases were reported—incidence 3.5%. This marks a statistically significant ($p < 0.00001$) 30-fold increase in incidence within two months. Epidemic term Kawasaki-like disease patients also presented more severely and atypically than pre-epidemic patients in ways such as: incomplete type disease (50%), cardiac issues (40%), needing inotropic support (20%), and KDSS and/or MAS development (70%). RT-PCR testing for SARS-CoV-2 was positive among 30% but serology was IgG positive among 80% and IgM positive among 30%. This is strong evidence for Kawasaki-like disease as a secondary morbidity of COVID-19. IgG positivity suggests late presentation. More research is needed on the timing post COVID-19 exposure until presentation of disease.

PUBLIC HEALTH/EPIDEMIOLOGY

[Characteristics of Health Care Personnel with COVID-19 — United States, February 12–April 9, 2020.](#) *CDC MMWR*. 14 May 2020

- Between Feb 12 and Apr 9, 49,370 of the confirmed cases included a form indicating if the patient was a HCP. 9,282 (19%) were identified as HCP. Median age was 42 years and 38% reported at least one underlying health condition. 55% reported known exposure to COVID-19 only in health care settings. 8% of the HCP who tested positive reported no symptoms. 90% of HCP with COVID-19 were not hospitalized; however, the 10% with more severe disease included HCP in all age groups; death was more likely in HCP aged ≥ 65 years.

[The Disproportionate Burden of COVID-19 for Immigrants in the Bronx, New York.](#) Ross, J. *et al.*, *JAMA Internal Medicine*. May 8, 2020.

- Due to a disproportionate number of comorbidities among immigrants in the Bronx, New York, the population is predisposed to a greater risk of COVID-19 infection. The Bronx currently has the highest rate of COVID-19 diagnoses. Most immigrants in this area already experienced a lack of access to healthcare before the pandemic and are now experiencing even higher levels of stress as well as lack of care. Important considerations are accommodations for non-English speaking patients to understand their plans of care while admitted to the hospital in addition to literature that ensures immigrant populations are informed about safety precautions.

[Knowledge and Behaviors Toward COVID-19 Among US Residents During the Early Days of the Pandemic: Cross-Sectional Online Questionnaire.](#) Clements, J.M. *JMIR Public Health Surveillance*. 08 May 2020.

- Lower knowledge was associated with self-reports of engaging in purchasing more goods than necessary, attending gatherings of more than 50 people, and wearing medical masks outside the house. Differences in knowledge about COVID-19 based on age group: baby boomers in this sample were more knowledgeable about COVID-19 than all other age groups and were less likely to engage in purchasing behavior while people attending large gatherings and wearing masks in public were younger on average.

[Race, Socioeconomic Deprivation, and Hospitalization for COVID-19 in English participants of a National Biobank.](#) Patel, A. P. et al., *MedRxiv*. 02 May 2020.

- Both black participants (odds ratio 3.4; 95%CI 2.4–4.9) and Asian participants (odds ratio 2.1; 95%CI 1.5–3.2) were at substantially increased risk as compared to white participants. We further observed a striking gradient in COVID–19 hospitalization rates according to the Townsend Deprivation Index – a composite measure of socioeconomic deprivation – and household income. Adjusting for such factors led to only modest attenuation of the increased risk in black participants, adjusted odds ratio 3.1 (95%CI 2.0–4.8)

[School Closure and Management Practices During Coronavirus Outbreaks Including COVID-19: A Rapid Systematic Review](#) . Viner, R. M. et al., *Lancet Child & Adolescent Health*. May 2020.

- Review of 16 school closures during the SARS outbreak in China, Hong Kong, and Singapore suggest that complete school closures did not contribute to the control of the epidemic. “Recent modelling studies of COVID-19 predict that school closures alone would prevent only 2–4% of deaths, much less than other social distancing interventions.” School officials and policy makers should consider other less disruptive strategies such keeping students to one classroom, practicing good sanitation and hygiene, allowing for greater spacing of students, etc. It is also beneficial for schools to allow children of healthcare workers to attend school, as 29% of health-care workers have childcare obligations.

[Humoral immune response and prolonged PCR positivity in a cohort of 1343 SARS-CoV 2 patients in the New York City region.](#) Wajnberg, A. et al., *BMJ preprint*. 05 May 2020.

- Nearly all PCR confirmed cases of COVID-19 developed a strong IgG antibody response to SARS-CoV-2. Only 35% of self-reported COVID-19 cases (had consistent signs and symptoms and either a) lived with someone with a PCR confirmed diagnosis, b) was told by a doctor they likely had COVID-19, or c) was a healthcare worker) developed strong antibody response, suggesting either overdiagnosis of COVID-19 clinically, or possibly an underwhelming immune response in mild cases. Based on the timeline of presence of antibodies on ELISA testing, authors suggest ideal time to test for antibodies is 3-4 weeks after symptom onset or 2 weeks after symptom resolution. Study did not address IgG status of asymptomatic carriers; appropriate immune response in this population still needs to be studied.

THERAPEUTIC DEVELOPMENTS

[Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study.](#) Cavalli, G. et al., *The Lancet*. May 7, 2020.

- A retrospective cohort study from a single center in Italy that studied adult COVID-19 patients with moderate-severe-ARDS and hyperinflammation (C-reactive protein at least 100mg/L, ferritin at least 900ng/ml or both). No patients were admitted to the ICU. Sixteen patients received “standard treatment” – hydroxychloroquine and lopinavir/ritonavir. Seven patients received low dose anakinra via SQ plus standard treatment (cohort ended early due to lack of effect on CRP levels). Finally, 29 patients received high-dose anakinra via IV plus standard treatment. All patients were in the hospital concurrently and outcomes were assessed at 21 days. The high-dose group was found to have 90% survival compared to 56% in standard treatment only, as well as greater likelihood of avoiding mechanical ventilation.

[Observational Study of Hydroxychloroquine in Hospitalized Patients with Covid-19](#) New England Journal of Medicine May 7, 2020

- This observational study was a single center (NY) and had 1376 COVID-19 patients involved. During a median follow-up of 22.5 days, 811 (58.9%) patients received hydroxychloroquine (600 mg twice on day 1, then 400 mg daily for a median of 5 days). In the main analysis, there was no significant association between

hydroxychloroquine use and intubation or death (hazard ratio, 1.04, 95% confidence interval, 0.82 to 1.32). Results were similar in multiple sensitivity analyses. The author concluded that in patients with Covid-19 who had been admitted to the hospital, hydroxychloroquine administration was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death.

[A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe Covid-19](#). Cao, B. et al., *NEJM*. 18 May 2020.

- Open label RCT with n=199 (n=160 needed for 80% power) with no placebo group due to the emergency nature of the trial. Looked at as ITT. Time to clinical improvement: 16 day vs. 16 days; hazard ratio for clinical improvement, 1.31; 95% confidence interval [CI], **0.95 to 1.85**; P=**0.09**. No benefit in severe COVID19 compared to standard care. However, 3 pts died within 24hrs after randomization in the Lopinavir/Ritonavir group. With a modified ITT primary endpoint analysis excluding those three patients showed 15d compared to 16d (hazard ratio, 1.39; 95% CI, **1.00** to 1.91) [statistically significant, but not clinically significant].

[Triple combination of interferon beta-1b, lopinavir-ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomized, phase 2 trial](#) The Lancet May 8,2020

- A multicenter, prospective, open-label, randomized, phase 2 trial with COVID-19 who were admitted to six hospitals in Hong Kong. 86 pts in combination group were given 14-day combination of lopinavir 400 mg and ritonavir 100 mg every 12 h, ribavirin 400 mg every 12 h, and three doses of 8 million international units of interferon beta-1b on alternate days. The control group (41 pts) was given 14 days of lopinavir 400 mg and ritonavir 100 mg every 12 h. The author concluded that triple antiviral therapy with interferon beta-1b, lopinavir-ritonavir, and ribavirin were safe and superior to lopinavir-ritonavir alone in shortening virus shedding, alleviating symptoms, and facilitating discharge of patients with mild to moderate COVID-19 in the early stage.

BASIC SCIENCE

[Host-viral infection maps reveal signatures of severe COVID-19 patients](#). Bost, P. et al., *Cell*. 07 May 2020.

- Viral-Track offers an unsupervised pipeline for characterization of viral infections in scRNA-seq data by identifying infected versus bystander cells and uncovering virus-induced pathways. They identified dramatic differences between the mild and severe COVID-19 patients, including an inflammatory signature and a perturbed immune response associated with the severe manifestation of the COVID-19 disease. They also identified co-infection of SARS-CoV-2 with the human Metapneumovirus

[A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2](#). Wu, Y. et al., *Science*. 13 May 2020.

- Of the four antibodies isolated from a covid-19 patient's peripheral blood mononuclear cells, two of them B38 and H4 block the binding between virus S-protein RBD and cellular receptor ACE2 with different epitopes on the RBD. A mouse model study showed that B38 and H4 decrease virus titers in infected lungs. The structure of RBD-B38 complex structure showed that most residues on the epitope overlap with the RBD-ACE2 binding interface.

[Structural basis for the inhibition of SARS-Co-V-2 main protease by antineoplastic drug carmofur](#). Zhenming, J. et al., *Nature*. 07 May 2020

- The antineoplastic drug carmofur has been shown to inhibit the SARS-CoV-2 main protease (EC50 = 24.30 μ M). The mechanism of this action had not previously been elucidated. Typically, carmofur is thought to target thymidylate synthase. The X-ray crystal structure of the main protease binds to the reactive carbonyl group of carmofur with its catalytic Cys145 residue. This information serves to continue the investigation of possible antiviral therapy for COVID-19.

Circulating plasma concentrations of angiotensin-converting enzyme 2 in men and women with heart failure and effects of renin–angiotensin–aldosterone inhibitors. Sama, IE., et al. *European Heart Journal*. 10 May 2020.

- Two large, European, CHF cohorts were used to measure circulating plasma ACE2 levels. Men were shown to have higher levels than women (5.38 vs. 5.09 (p<0.001); 5.46 vs 5.16 (p<0.001)), and no significant differences were seen between patients on RAAS blocking therapies and those who were not. Notably, plasma ACE2 was measured rather than membrane bound ACE2, and the relationship between these two levels is not fully understood. These results suggest taking RAAS blocking therapies does not alter ACE2 expression, and, by extension, may not change susceptibility to SARS-CoV-2 infection.

GUIDELINES AND FIGURES:

FROM CDC

May 12 – [Guidelines updated](#)

- Communication Toolkit for Airlines to Inform Travelers and Crew
- Cruise Ship Crew Member Disembarkations
- Testing in the U.S.
- Groups at Higher Risk for Severe Illness
- COVID-19 Travel Recommendations by Country

May 13 -

- [COVID-19 Travel Recommendations by Country](#)
 - Interactive Map
- [Guidelines for pregnant and breastfeeding women or those caring for young children](#)
 - Practice social distancing, wash hands often, use face masks (unless child is under 2 y/o)
 - Properly launder toys
- [Updates on guidelines on unsheltered homelessness and coronavirus disease 2019 for Homeless Service Providers and Lead Officials](#)
 - Revisions to document organization
 - Description of “whole community” approach

May 14

- [Guideline Added for Disaster Shelters During Covid-19](#)

FROM WHO

May 11 – [Situation Report 112](#)

- Guidance on [Surveillance strategies for COVID-19 human infection](#)
- New guidance on [Contact tracing in the context of COVID-19](#)

May 12 - [Situation Report 113](#)

- New guidance on school-related public health measures
- Issued statement on tobacco use and COVID-19
- Director-General Dr. Tedros held media briefing urging slow, steady lifting of social distancing measures

May 13 – [Situation Report 114](#)

- Guidance on adjusting public health and social measures (PHSM) and guidance on how countries can adapt PHSM according to their own epidemiological and public health data
- WHO is joining with the UK to run an awareness campaign specifically about the risks of inaccurate and false information regarding the pandemic
- Dr. Carissa F. Etienne (Regional director for the WHO Regional Office for the Americas) called on countries to “support their economies while building strong social protection networks and embracing evidence-based public health measures that are essential to saving lives”
- New WHO guidelines for school-related public health measures

May 14 - [Situation Report 115](#)

- New guidance released for countries on adjusting public health and social measures.

FROM JOHNS HOPKINS

[John Hopkins Testing Comparison by State – Updated May 11, 2020](#)

CASES/DEATHS: WORLD/US/NC/ORANGE COUNTY as of 12:30pm 05/15/2020

- World: 4,483,864/303,825
- US:1,420,299/85,992
- North Carolina: 16,968/641
- Orange County, NC: 263/34