

COVID-19 Research Watch

July 26, 2020

CLINICAL PRESENTATION AND MANAGEMENT

[Extrapulmonary manifestations of COVID-19](#)¹

(Part 1 of 4; 2 systems will be summarized per week)

Hematologic manifestations: Patients who are positive for COVID-19 may present with thromboembolic complications and laboratory abnormalities. Studies show that lymphopenia is a common laboratory finding in 67-90% of patients with COVID-19. Data suggest that decreased CD8⁺ T cells and CD4⁺ T cells are associated with severe COVID-19. Although thrombocytopenia is often mild in 5-36% of admissions, it is associated with worse outcomes in patients. Coagulopathy is marked by elevated levels of D-dimer and fibrinogen. Smaller studies where critically ill COVID-19 patients were screened for thrombotic disease, found high rates of thrombotic complications despite given thromboprophylaxis (69% to 85%). COVID-19 specific considerations include evaluation of inflammatory markers, cell counts, and coagulation indices in hospitalized patients. Routine risk assessment for venous thromboembolism and strongly consider prophylaxis in the absence of contraindications.

Cardiovascular manifestations: In 20-30% of COVID-19 hospitalized patients, myocardial injury with elevated biomarkers was found, and those with pre-existing cardiovascular disease had higher rates (55%). A larger magnitude and frequency of troponin elevations is associated with worse outcomes and more severe disease in hospitalized patients. Biventricular cardiomyopathy has been reported in 7–33% of critically ill patients. Cardiac arrhythmias are also prevalent, occurring in 17% of hospitalized patients and 44% of patients in the ICU setting in a study of 138 patients from Wuhan. An increase of out-of-hospital cardiac arrest has also been found in some studies. A study in New York City of 4,250 patients with COVID-19, 6% had prolonged QTc (corrected QT; >500 ms) during admission. COVID-19 specific considerations: do not discontinue ACE inhibitors or ARBs in patients already on them at home, assess each case.

[Characteristics of Persons Who Died with COVID-19 — United States, February 12–May 18, 2020](#)²

Analyzing supplementary data from 16 public health departments in the United States, Wortham et al. sought to understand the demographic and clinical characteristics of 10,647 COVID-19 deaths between February 12 and April 24, 2020. Of the 10,647 decedents, 76.4% reported at least one underlying medical condition. 58.7% identified as racial minorities, and the median age among Hispanic patients (71 years, IQR = 59–81 years) and nonwhite non-Hispanic patients (72 years, IQR = 62–81 years) was markedly lower than among white patients (81 years, IQR = 71–88 years). Notably, more than one third (34.9%) of Hispanic patients and nearly one third (29.5%) of nonwhite patients were aged <65 years,

while only around one eighth (13.2%) of white patients were aged <65 years. The median interval from illness onset to death was 10 days (IQR = 6–15 days), and the median interval from hospital admission to death was 5 days (IQR = 3–8 days). Among patients, 62.0% died in hospitals, and the age group with the highest percentage of deaths in the emergency department (6.8%) or at home (1.0%) was <65 years (combined total = 7.8%), with the percentage decreasing as age group increased.

[Deep immune profiling of COVID-19 patients reveals distinct immunotypes with therapeutic implications³](#)

This study performed a deep immune profiling of individual B and T cell populations in a cohort of over 120 COVID-19 patients using high dimensional flow cytometry and investigated the relationship between immune responses and disease severity. In hospitalized patients, immune responses have been found to vary and three immunotypes have been identified. Immunotype 1 is characterized by robust CD4 T cell activation and proliferation, highly activated or exhausted CD8 T cells, and a signature of T-bet⁺ plasmablasts. Immunotype 2 had Tbet^{bright} effector-like CD8 T cell responses with less robust CD4 T cell responses. Immunotype 3 lacked detectable lymphocyte response. Via Uniform Manifold Approximation and Projection (UMAP) embedding, an association was found between immunotype 1 and increased severity score. Authors suggest using an immune topology map to determine the most useful interventions for patients.

[NON-CLINICAL TRENDS](#)

[Routine childhood immunisation during the COVID-19 pandemic in Africa: a benefit-risk analysis of health benefits versus excess risk of SARS-CoV-2 infection⁴](#)

In this study, Abbas et al. used previous estimates of country-specific child mortality rates for vaccine-preventable diseases to model the potential effect of suspending routine childhood immunisation programs in Africa. The authors found that if vaccines for diphtheria, tetanus, pertussis, hepatitis B, *H. influenzae type b*, *S. pneumoniae*, rotavirus, measles, meningitis A, rubella and yellow fever were suspended, an estimated 84 children would die before age 5 due to the suspension for every one excess COVID-19 death attributable to SARS-CoV-2 infection acquired during routine vaccination visits. This benefit was greatest for the vaccinated child, and secondarily their siblings, parents/adult carers and surrounding older adults. Overall, authors do not recommend suspending routine childhood immunisations in Africa during the COVID-19 pandemic, as the risks of mortality from vaccine-preventable diseases, far outweigh the benefits.

[Factors Associated with Cloth Face Covering Use Among Adults During the COVID-19 Pandemic — United States, April and May 2020](#)⁵

Following the US CDC's recommendation on April 3rd to use a cloth face covering in public, Fisher et al. sampled 1,005 U.S. adults aged 18 or older between April 7th-9th and May 11th-13rd to understand behavioural and sociodemographic factors that may facilitate or discourage use of face coverings in public settings requiring interaction with others. Of the 839 participants who reported leaving their homes the week before completing the survey, 61.9% of participants reported use of a cloth mask in April, compared to 76.4% in May. The increase in face covering usage occurred across all sociodemographic groups; however, the greatest increase in use between April and May occurred among non-Hispanic white persons (54% to 75%), those persons 65 years of age or older (37% to 79%), and those residing in the Midwest (44% to 74%). Non-Hispanic black persons, Hispanic or Latino persons, younger participants (18-39 years old) and those residing in the Northeast reported high rates of cloth face use in April (all >70%), though usage prevalence also increased in May. Among those participants who reported wearing a facemask, 83% reported receiving information about cloth facemask coverings from newspapers, 81% from healthcare providers, and 80% from the radio.

NON-PHARMACEUTICAL INTERVENTIONS

[Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries](#)⁶

Using data reported to the European Centre for Disease Prevention and Control and the Oxford covid-19 Government Response Tracker between January 1 and May 30, 2020, Nazrul et al. used an interrupted time series analysis to calculate incidence rate ratios of covid-19 infection pre- and post-physical distancing interventions. The distancing measures evaluated were school, work, and public transport closures, as well as restrictions on mass/public gathering or general movement (e.g. lockdowns). The authors found that initiation of any physical distancing intervention was associated with a 13% reduction in the incidence of covid-19, though closure of public transport did not provide further reduction in the incidence when school and workplace closures, as well as mass gatherings and population movement measures were already in place. Acknowledging the study's limitations, the authors suggest that physical distancing measures enacted in many countries, particularly workplace and school closures in combination with restrictions on mass gatherings, allow for the continued use of public transport for essential workers, though further research is needed to better understand the different physical distancing combinations during the pandemic.

[Assessing the impact of coordinated COVID-19 exit strategies across Europe](#)⁷

This study used mobility data to evaluate the impact of Non-Pharmaceutical Interventions (NPIs) on the resurgence of COVID-19 in Europe. The authors used a series of simulations to predict the effect of coordinated versus uncoordinated reopening strategies and found that coordinated efforts across countries could lead toward the mitigation of community transmission and that the premature ending of existing NPIs could lead to the resurgence of COVID-19 earlier by 5 weeks. The authors also note that these results may also be applicable in the United States due to the interconnectedness of the states, each with their own uncoordinated reopening strategy.

[Contact Tracing during Coronavirus Disease Outbreak, South Korea, 2020](#)⁸

Park et al. analyzed data from 59,073 contacts of 5,706 COVID-19 index patients reported in South Korea from January 20 to March 27, 2020. An index case was defined as the first lab-confirmed case in an investigation within a cluster, and a detected case was defined as a contact with symptom onset after that of an index patient. Of 10,592 household contacts, 11.8% (95% CI = 11.2%–12.4%) tested positive for COVID-19, and for the 48,481 non-household contacts, the positivity rate was 1.9% (95% CI = 1.8%–2.0%). Overall, clusters with a household index patient aged 10-19 years had the highest detection rate (18.6% [95% CI = 14.0%–24.0%]), and those with an index patient aged 0-9 years had the lowest (5.3% [95% CI 1.3%–13.7%]). Detection of COVID-19 contacts was significantly higher for index patients >40 years of age in nonhousehold settings.

PHARMACEUTICAL INTERVENTIONS

[Dexamethasone in Hospitalized Patients with COVID-19- Preliminary Report](#)⁹

The study authors performed a controlled, open-label trial to assess the impact of dexamethasone on 28-day mortality from COVID-19. A total of 2104 patients were randomly assigned into two groups: dexamethasone (6mg QD for 10 days, oral or IV) or usual standard of care. Results showed that 22.9% of patients who received dexamethasone died, compared with 25.7% of patients who received standard of care treatment. In parallel, respiratory support conferred a greater reduction in mortality incidence among those who received both dexamethasone and respiratory support together. This effect was more pronounced in patients who received invasive mechanical ventilation compared to those who received oxygen only. This preliminary report provides important insight into the utility of dexamethasone, a widely available steroid, for hospitalized patients with COVID-19.

[Encouraging results from phase 1/2 COVID-19 vaccine trials](#)¹⁰

There are two vaccines in the early phase of the COVID-19 vaccine trials from [CanSino](#) (Wuhan, China) and [AstraZeneca/Oxford University](#) (Oxford, UK). An adenoviral vector was used for both vaccines, and by day 28, they were achieving humoral responses to the SARS-CoV-2 spike glycoprotein receptor binding domain along with T cell responses. Both vaccines reported only mild adverse events such as fatigue, fever, and pain at injection site. During the UK phase 1/2 trial of one injection of chimpanzee adenovirus-vectored COVID-19 vaccine, neutralizing antibodies were generated in more than 90% of the 1077 healthy participants in the study. A second-dose, among a small sample, showed strong neutralizing responses and mild adverse events. In China, the phase 2 randomized trial of non-replicating adenovirus-vectored COVID-19 vaccine showed seroconversion in more than 96% of participants and neutralizing antibodies in 85%. T-cell responses were found in more than 90% of participants and no serious adverse events. Those who were 55 years of age and older had lower humoral responses but higher than the placebo group. These two vaccines will head into phase 3 trial where they will be tested on larger samples and assessed for efficacy and safety. However, inferential caution is warranted due to the small trial size.

NATURAL HISTORY OF INFECTION

[Longitudinal evaluation and decline of antibody responses in SARS-CoV-2 infection](#)^{11*}

In order to evaluate the antibody (Ab) response to SARS-CoV-2, Seow et al. took a series of serum samples from 65 health care workers and hospitalized patients who tested positive for COVID-19 up to 94 days post onset of symptoms. The investigators found that the level of neutralizing antibodies (nAb) were dependent on the severity of disease and that nAb levels declined over the follow up period. The results of this study suggest that nAb response to SARS-CoV-2 infection may last only a short period of time, similar to that of nAb responses to coronaviruses associated with common colds.

*Please note all studies published in medRxiv and bioRxiv are preprints and have not yet undergone a rigorous peer review process.

ADDITIONAL RESOURCES

[UCSF Library COVID-19 Research and Information Resources](#)
[UCSF Institute for Global Health Sciences COVID-19 Resources](#)
[UC Davis One Health Institute COVID-19 FAQs](#)
[Harvard Viswanath Lab Myths vs Facts](#)

Note on this Document: This document was assembled by graduate and doctoral students attending the University of California, San Francisco with the intent of facilitating the rapid dissemination of information to the global community in order to help during this time. Hannah Thomas, Canice Christian, Sigal Maya, Micaela Reyna, and Jane Fieldhouse contributed to these summaries. This work is volunteer based.

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