

COVID-19 Resource Desk

#20 | 9.2.2020 to 9.8.2020

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New Research

*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see [Digital Commons](#)

Basic Science / Virology / Pre-clinical

1. **Broad and strong memory CD4(+) and CD8(+) T cells induced by SARS-CoV-2 in UK convalescent individuals following COVID-19.** Peng Y, Mentzer AJ, Liu G, et al. *Nat Immunol.* 2020 Sep 4. doi: 10.1038/s41590-020-0782-6. <https://www.nature.com/articles/s41590-020-0782-6>

Findings: We studied T cell memory in 42 patients following recovery from COVID-19 (28 with mild disease and 14 with severe disease) and 16 unexposed donors, using interferon- γ -based assays with peptides spanning SARS-CoV-2 except ORF1. The breadth and magnitude of T cell responses were significantly higher in severe as compared with mild cases. Total and spike-specific T cell responses correlated with spike-specific antibody responses. We identified 41 peptides containing CD4+ and/or CD8+ epitopes, including six immunodominant regions. Six optimized CD8+ epitopes were defined, with peptide-MHC pentamer-positive cells displaying the central and effector memory phenotype. In mild cases, higher proportions of SARS-CoV-2-specific CD8+ T cells were observed. The identification of T cell responses associated with milder disease will support an understanding of protective immunity and highlights the potential of including non-spike proteins within future COVID-19 vaccine design.

2. **SARS-CoV-2 infection of human iPSC-derived cardiac cells predicts novel cytopathic features in hearts of COVID-19 patients.** Pérez-Bermejo JA, Kang S, Rockwood SJ, et al. *bioRxiv PREPRINT.* doi: <https://doi.org/10.1101/2020.08.25.265561> <https://www.biorxiv.org/content/10.1101/2020.08.25.265561v1>

Findings: COVID-19 causes cardiac dysfunction in up to 50% of patients, but the pathogenesis remains unclear. Infection of human iPSC-derived cardiomyocytes with SARS-CoV-2 revealed robust transcriptomic and morphological signatures of damage in cardiomyocytes. These morphological signatures include a distinct pattern of sarcomere fragmentation, with specific cleavage of thick filaments, and numerous iPSC-cardiomyocytes that lacked nuclear DNA. Human autopsy specimens from COVID-19 patients also displayed marked sarcomeric disruption and similar fragmentation, as well as prevalently enucleated cardiomyocytes. These striking transcriptomic and cytopathic changes provide a roadmap to understand the

mechanisms of COVID-19 cardiac damage, search for potential treatments, and determine the basis for prolonged cardiac morbidity observed in this pandemic.

Clinical Syndrome

3. **Acute arterial thromboembolism in patients with COVID-19 in the New York City area.** Etkin Y, Conway AM, Silpe J, et al. *Ann Vasc Surg.* 2020 Aug 28:S0890-5096(20)30765-2. doi: 10.1016/j.avsg.2020.08.085. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7455233/>
Findings: Over the 11-week period, Northwell Health System cared for 12,630 hospitalized patients with COVID-19. A total of 49 patients with arterial thromboembolism and confirmed COVID-19 were identified. Median age was 67 years (58-75) and 37 (76%) were male. The most common preexisting conditions were hypertension (53%) and diabetes (35%). Median D-dimer level was 2673 ng/mL (723-7139). The distribution of thromboembolic events included upper 7 (14%) and lower 35 (71%) extremity ischemia, bowel ischemia 2 (4%), and cerebral ischemia 5 (10%). Six patients (12%) had thrombus in multiple locations. Concomitant deep vein thrombosis was found in 8 patients (16%). Twenty-two (45%) patients presented with signs of acute arterial ischemia and were subsequently diagnosed with COVID-19. The remaining 27 (55%) developed ischemia during hospitalization. Revascularization was performed in 13 (27%) patients, primary amputation in 5 (10%), administration of systemic tissue plasminogen activator in 3 (6%), and 28 (57%) were treated with systemic anticoagulation only. The rate of limb loss was 18%. Twenty-one patients (46%) died in the hospital. Twenty-five (51%) were successfully discharged and 3 patients are still in the hospital. While the mechanism of thromboembolic events in patients with COVID-19 remains unclear, the occurrence of such complication is associated with acute arterial ischemia which results in a high limb loss and mortality.
4. **AKI in Hospitalized Patients with COVID-19.** Chan L, Chaudhary K, Saha A, et al. *J Am Soc Nephrol.* 2020 Sep 3:ASN.2020050615. doi: 10.1681/ASN.2020050615. <https://jasn.asnjournals.org/content/early/2020/09/02/ASN.2020050615>
Findings: Of 3993 hospitalized patients with COVID-19, AKI occurred in 1835 (46%) patients; 347 (19%) of the patients with AKI required dialysis. The proportions with stages 1, 2, or 3 AKI were 39%, 19%, and 42%, respectively. A total of 976 (24%) patients were admitted to intensive care, and 745 (76%) experienced AKI. Of survivors with AKI who were discharged, 35% had not recovered to baseline kidney function by the time of discharge. An additional 28 of 77 (36%) patients who had not recovered kidney function at discharge did so on posthospital follow-up. AKI is common among patients hospitalized with COVID-19 and is associated with high mortality. Of all patients with AKI, only 30% survived with recovery of kidney function by the time of discharge.
5. **A systematic review and meta-analysis of the COVID-19 associated liver injury.** Wong YJ, Tan M, Zheng Q, et al. *Ann Hepatol.* 2020 Aug 31:S1665-2681(20)30161-7. doi: 10.1016/j.aohep.2020.08.064. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7458067/>
Findings: Among 1543 citations, there were 24 studies (5961 subjects) which fulfilled our inclusion criteria. The pooled odds ratio for elevated ALT, AST, hyperbilirubinemia and

hypoalbuminemia were higher subjects in critical COVID-19. COVID-19 associated liver injury is more common in severe COVID-19 than non-severe COVID-19. Physicians should be aware of possible progression to severe disease in subjects with COVID-19-associated liver injury.

Diagnostics & Screening

6. **A Direct Comparison of Enhanced Saliva to Nasopharyngeal Swab for the Detection of SARS-CoV-2 in Symptomatic Patients.** Procop GW, Shrestha NK, Vogel S, et al. *J Clin Microbiol.* 2020 Sep 3:JCM.01946-20. doi: 10.1128/JCM.01946-20.

<https://jcm.asm.org/content/early/2020/09/03/JCM.01946-20>

Findings: Of the 216 patients included in the final analysis, there was a 100% Positive Percent Agreement (38/38 positive specimens) and 99.4% Negative Percent Agreement (177/178 negative specimens). The one discrepant specimen had the presence of SARS-CoV-2 confirmed in the saliva specimen using an alternate FDA EUA assay. The overall mean difference in crossing threshold (Ct) values for the positive NPS and saliva specimens was -3.61 (95% C.I. - 5.78 to -1.44, p = 0.002). An enhanced saliva specimen performed as well as NPS for the qualitative detection of SARS-CoV-2 in symptomatic patients, albeit the overall mean viral load in saliva was lower.

7. **A Simple Algorithm for Return to Workplace Employer Antibody Testing.** Shrunk WH, Caveney B, Miller S, Rhonda M Medows [PSJH author] *Popul Health Manag.* 2020 Aug 26. doi: 10.1089/pop.2020.0136. <https://www.liebertpub.com/doi/full/10.1089/pop.2020.0136>

Epidemiology & Public Health

8. **Temporal profile and determinants of viral shedding and of viral clearance confirmation on nasopharyngeal swabs from SARS-CoV-2-positive subjects: a population-based prospective cohort study in Reggio Emilia, Italy.** Mancuso P, Venturelli F, Vicentini M, et al. *BMJ Open* 2020;10:e040380. doi: 10.1136/bmjopen-2020-040380

<https://bmjopen.bmjjournals.org/content/bmjopen/10/8/e040380.full.pdf>

Findings: Viral clearance was achieved by 60.6% of patients, with a median time of 30 days from diagnosis and 36 days from symptom onset. Of those negative and retested, 78.7% had viral clearance confirmation, suggesting one in five false negative tests. The time from symptom onset to viral clearance slightly increased with age, from 35 days under age 50 to 38 in over age 80, and with disease severity, from 33 days in non-hospitalised subjects to 38 days in hospitalised patients. The probability of confirmed viral clearance reached 86.8% after 34 days from symptom onset and increased with time, even when adjusting for age and sex. Postponing follow-up testing of clinically recovered COVID-19 patients could increase the efficiency and performance of testing protocols. Understanding viral shedding duration also has implications for containment measures of pauci-symptomatic subjects.

9. **Renin-angiotensin-aldosterone System Inhibitors and Risks of SARS-CoV-2 Infection: A Systematic Review and Meta-analysis.** Chan CK, Huang YS, Liao HW, et al. *Hypertension.* 2020

Sep 1. doi: 10.1161/HYPERTENSIONAHA.120.15989.

<https://www.ahajournals.org/doi/abs/10.1161/HYPERTENSIONAHA.120.15989>

Findings: We systematically assessed case-population and cohort studies from MEDLINE (Ovid), Cochrane Database of Systematic Reviews PubMed, Embase, medRXIV, the World Health Organization database of COVID-19 publications and ClinicalTrials.gov through Jun 1, 2020, with planned ongoing surveillance. After pooling the adjusted odds ratios from the included studies, no significant increase was noted in the risk of SARS-CoV-2 infection by the use of ACEi or ARBs. However, the random-effects meta-regression revealed that age may modify the SARS-CoV-2 infection risk in subjects with the use of ARBs, as opposed to ACEi, specifically augmented the risk of SARS-CoV-2 infection in younger subjects (< 60 years-old). The use of ACEi might not increase the susceptibility of SARS-CoV-2 infection, severity of disease and mortality in case-population and cohort studies. Additionally, we found for the first time that the use of ARBs, as opposed to ACEi, specifically augmented the risk of SARS-CoV-2 infection in younger subjects; without obvious effects on COVID-19 outcomes.

- 10. Cell Phone Activity in Categories of Places and Associations with Growth in Cases of COVID-19 in the US.** Sehra ST, George M, Wiebe DJ, Fundin S, Baker JF. *JAMA Intern Med.* 2020 Aug 31. doi: 10.1001/jamainternmed.2020.4288.

<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2769771>

Findings: Our findings support the hypothesis that greater reductions in cell phone activity in the workplace and retail locations, and greater increases in activity at the residence, are associated with lesser growth in COVID-19 cases. These data provide support for the value of monitoring cell phone location data to anticipate future trends of the pandemic.

Healthcare Delivery & Healthcare Workers

- 11. SARS-CoV-2 Testing and Changes in Primary Care Services in a Multistate Network of Community Health Centers during the COVID-19 Pandemic.** Heintzman J, O'Malley J, Marino M, et al. *JAMA.* 2020 Aug 31. doi: 10.1001/jama.2020.15891.

<https://jamanetwork.com/journals/jama/article-abstract/2770242>

Findings: Despite limited test availability, CHCs reported thousands of SARS-CoV-2 tests, underscoring their important role in serving vulnerable populations. The 75,053 patients seen for the first time after the pandemic started suggests that CHCs were an access point in the midst of the crisis. Small differences in testing and positive rates by race, and larger differences by ethnicity, preferred language, and insurance status, suggest ongoing need for targeted, language-concordant testing strategies. In the pandemic's initial weeks, delivery of common services in CHCs declined, possibly due to in-person care reductions. Although these changes may have been necessary and unavoidable, the potential consequences are concerning because reductions in preventive/chronic disease care may affect population health.

- 12. Telemedicine and Healthcare Disparities: A cohort study in a large healthcare system in New York City during COVID-19.** Chunara R, Zhao Y, Chen J, et al. *J Am Med Inform Assoc.* 2020 Aug 31:ocaa217. doi: 10.1093/jamia/ocaa217.

<https://academic.oup.com/jamia/advance-article/doi/10.1093/jamia/ocaa217/5899729>

Findings: There are disparities for Black patients accessing telemedicine, however increased uptake by young, female Black patients. Mean income and decreased mean household size of Zip code were also significantly related to telemedicine use. Telemedicine access disparities reflect those in in-person healthcare access. Roots of disparate use are complex and reflect individual, community, and structural factors, including their intersection; many of which are due to systemic racism. Evidence regarding disparities that manifest through telemedicine can be used to inform tool design and systemic efforts to promote digital health equity.

13. Symptoms of Anxiety, Depression and Peritraumatic Dissociation in Critical Care Clinicians

Managing COVID-19 Patients: A Cross-Sectional Study. Azoulay E, Cariou A, Bruneel F, et al. *Am J Respir Crit Care Med.* 2020 Aug 31. doi: 10.1164/rccm.202006-2568OC.

<https://www.atsjournals.org/doi/abs/10.1164/rccm.202006-2568OC>

Findings: 1058 HCW responded (median age 33 y, 71% women, 68% nursing staff). The prevalence of symptoms of anxiety, depression, and peritraumatic dissociation was 50.4%, 30.4%, and 32%, respectively, with the highest rates in nurses. Male sex was independently associated with lower prevalence of symptoms of anxiety, depression, and peritraumatic dissociation. HCPs working in non-university-affiliated hospitals and nursing assistants were at high risk of symptoms of anxiety and peritraumatic dissociation. Importantly, we identified six modifiable determinants of symptoms of mental health disorders: fear of being infected, inability to rest, inability to care for family, struggling with difficult emotions, regret about the restrictions in visitation policies, and witnessing hasty end-of-life decisions. HCPs experience high levels of psychological burden during the COVID-19 epidemic. Hospitals, ICU directors, and ICU staff must devise strategies to overcome the modifiable determinants of adverse mental illness symptoms.

14. Impact of the COVID-19 Pandemic on Healthcare Workers' Risk of Infection and Outcomes in a Large, Integrated Health System. Misra-Hebert AD, Jehi L, Ji X, et al. *J Gen Intern Med.* 2020

Sep 1. doi: 10.1007/s11606-020-06171-9.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7462108/>

Findings: Of 72,909 individuals tested, 9.0% (551) of 6145 HCW tested positive for SARS-CoV-2 compared to 6.5% (4353) of 66,764 non-HCW. The HCW were younger than the non-HCW (median age 39.7 vs. 57.5, p < 0.001) with more females, higher reporting of COVID-19 exposure, and fewer comorbidities. Among those testing positive, weighted proportions for hospitalization were 7.4 vs. 15.9 for HCW vs. non-HCW with OR of 0.42 (CI 0.26-0.66) and for ICU admission: 2.2 vs. 4.5 for HCW vs. non-HCW with OR of 0.48 (CI 0.20-1.04). Those HCW identified as patient facing compared to not had increased odds of a positive SARS-CoV-2 test, but no statistically significant increase in hospitalization and ICU admission. In a large healthcare system, HCW had similar odds for testing SARS-CoV-2 positive, but lower odds of hospitalization compared to non-HCW. Patient-facing HCW had higher odds of a positive test. These results are key to understanding HCW risk mitigation during the COVID-19 pandemic.

Laboratory Results

15. **Humoral Immune Response to SARS-CoV-2 in Iceland.** Gudbjartsson DF, Nordahl GL, Melsted P, et al. *N Engl J Med.* 2020 Sep 1. doi: 10.1056/NEJMoa2026116.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2026116>

Findings: Of the 1797 persons who had recovered from SARS-CoV-2 infection, 1107 of the 1215 who were tested (91.1%) were seropositive; antiviral antibody titers assayed by two pan-Ig assays increased during 2 months after diagnosis by qPCR and remained on a plateau for the remainder of the study. Of quarantined persons, 2.3% were seropositive; of those with unknown exposure, 0.3% were positive. We estimate that 0.9% of Icelanders were infected with SARS-CoV-2 and that the infection was fatal in 0.3%. Our results indicate that antiviral antibodies against SARS-CoV-2 did not decline within 4 months after diagnosis. We estimate that the risk of death from infection was 0.3% and that 44% of persons infected with SARS-CoV-2 in Iceland were not diagnosed by qPCR.

16. **Cytokine Levels in Critically Ill Patients with COVID-19 and Other Conditions.** Kox M, Waalders NJB, Kooistra EJ, et al. *JAMA.* 2020 Sep 3. doi: 10.1001/jama.2020.17052.

<https://jamanetwork.com/journals/jama/fullarticle/2770484?resultClick=1>

Findings: In this study, critically ill patients with COVID-19 with ARDS had circulating cytokine levels that were lower compared with patients with bacterial sepsis and similar to other critically ill patients. These findings are in line with lower leukocyte counts observed in patients with COVID-19, and are possibly due to lower overall disease severity, despite the presence of severe pulmonary injury. The findings of this preliminary analysis suggest COVID-19 may not be characterized by cytokine storm. Whether anticytokine therapies will benefit patients with COVID-19 remains to be determined.

Prognosis

17. **Initial MEWS score to predict ICU admission or transfer of hospitalized patients with COVID-19: a retrospective study.** Barnett WR, Radhakrishnan M, Macko J, et al. *J Infect.* 2020 Sep 1:S0163-4453(20)30583-1. doi: 10.1016/j.jinf.2020.08.047.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7462753/>

Findings: A retrospective study was conducted at the University of Toledo Medical Center on COVID-19 positive patients hospitalized from late March to the end of May 2020. All patients were confirmed for COVID-19 by real-time reverse transcription polymerase chain reaction. Patient demographics, biometrics, and comorbidities were gathered from the electronic medical record. The highest level of hospital disposition was used to create the medical floor and ICU groups. The MEWS scores were retrieved from an electronic database. Initial MEWS scores were considered either at admission or prior to ICU transfer. Sequential organ failure assessment (SOFA) scores were manually calculated and included as a point of comparison. As a validated scoring system, SOFA scores are used to determine a patient's prognosis and have been considered for use in hospitalized COVID-19 patients.

18. Outpatient management or hospitalization of patients with proven or suspected SARS-CoV-2 infection: the HOME-CoV rule. Douillet D, Mahieu R, Boiveau V, et al. *Intern Emerg Med.* 2020 Sep 4. doi: 10.1007/s11739-020-02483-0. <https://link.springer.com/article/10.1007/s11739-020-02483-0>

Findings: Our aim was to define an easy-to-use clinical rule aiming to help emergency physicians in hospitalization or outpatient management decision-making for patients with suspected or confirmed SARS-CoV-2 infection (the HOME-CoV rule). Eight criteria constituting the HOME-CoV were selected: six correspond to the severity of clinical signs, one to the clinical course (clinically significant worsening within the last 24 h), and the last corresponds to the association of a severe comorbidity and an inadequate living context. Hospitalization is deemed necessary if a patient meets one or more of the criteria. In the end, 94.4% of the experts agreed with the defined rule.

19. SARS-CoV-2 RNA in plasma is associated with ICU admission and mortality in patients hospitalized with COVID-19. Prebensen C, Hre PLM, Jonassen C, et al. *Clin Infect Dis.* 2020 Sep 5:ciaa1338. doi: 10.1093/cid/ciaa1338. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1338/5901727>

Findings: The clinical significance of SARS-CoV-2 RNA in the circulation is unknown. In this prospective cohort study, we detected viral RNA in the plasma of 58/123 (47%) patients hospitalized with COVID-19. RNA was detected more frequently, and levels were higher, in patients who were admitted to the ICU and/or died.

20. Association of Vitamin D Status and Other Clinical Characteristics With COVID-19 Test Results. Meltzer DO, Best TJ, Zhang H, et al. *JAMA Netw Open.* 2020 Sep 1;3(9):e2019722. doi: 10.1001/jamanetworkopen.2020.19722. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770157>

Findings: In this single-center, retrospective cohort study, likely deficient vitamin D status was associated with increased COVID-19 risk, a finding that suggests that randomized trials may be needed to determine whether vitamin D affects COVID-19 risk.

21. Infection Fatality Ratios for COVID-19 among Noninstitutionalized Persons 12 and Older: Results of a Random-Sample Prevalence Study. Blackburn J, Yiannoutsos CT, Carroll AE, Halverson PK, Menachemi N. *Ann Intern Med.* 2020 Sep 2. doi: 10.7326/M20-5352. <https://www.acpjournals.org/doi/10.7326/M20-5352>

Findings: To calculate a true IFR, population prevalence data are needed from large geographic areas where reliable death data also exist. Most previous IFR estimates came from non-U.S. populations, including a cruise ship, or were calculated by using simulation techniques. Previous estimates also are not age specific, are relatively ungeneralizable, and are unsuitable for making clinical or policy decisions. By using SARS-CoV-2 population prevalence data, we found that the risk for death among infected persons increased with age. Indiana's IFR for noninstitutionalized persons older than 60 years is just below 2% (1 in 50). In comparison, the ratio is approximately 2.5 times greater than the estimated IFR for seasonal influenza, 0.8% (1 in 125), among those aged 65 years and older. Of note, the IFR for non-Whites is more than 3 times that for Whites, despite COVID-19 decedents in that group being 5.6 years younger on average.

Therapeutics

- 22. Association between Administration of Systemic Corticosteroids and Mortality among Critically Ill Patients with COVID-19: A Meta-analysis.** The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group. *JAMA*. September 2, 2020.

doi:10.1001/jama.2020.17023 <https://jamanetwork.com/journals/jama/fullarticle/2770279>

Findings: In this prospective meta-analysis of clinical trials of critically ill patients with COVID-19, administration of systemic corticosteroids, compared with usual care or placebo, was associated with lower 28-day all-cause mortality.

*see also [Effect of Hydrocortisone on 21-Day Mortality or Respiratory Support Among Critically Ill Patients With COVID-19: A Randomized Clinical Trial.](#) | [Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients with Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19: The CoDEX Randomized Clinical Trial.](#) | [Effect of Hydrocortisone on Mortality and Organ Support in Patients with Severe COVID-19: The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial.](#)

- 23. Percutaneous and Open Tracheostomy in Patients with COVID-19: Comparison and Outcomes of an Institutional Series in New York City.** Long SM, Chern A, Feit NZ, et al. *Ann Surg*. 2020 Sep 1. doi: 10.1097/SLA.0000000000004428.

<https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=ovft&AN=00000658-90000000-94238&PDF=y>

Findings: During the study period, 67 consecutive patients underwent tracheostomy, including 48 males and 19 females with a median age of 66 years. Two surgeons alternated techniques, with 35 tracheostomies performed percutaneously and 32 via an open approach. The median time from intubation to tracheostomy was 23 days. At a median follow-up of 26 days, 52 patients (78%) no longer required mechanical ventilation and 58 patients (87%) were off continuous sedation. There were 11 total complications (16%) in 10 patients, most of which involved minor bleeding. There were no significant differences in outcomes between percutaneous and open methods. Tracheostomy under apneic conditions by either percutaneous or open technique can be safely performed in patients with respiratory failure due to COVID-19. Tracheostomy facilitated weaning from continuous intravenous sedation and mechanical ventilation. Continued follow-up of these patients to ascertain long-term outcome data is ongoing.

- 24. Anticoagulant interventions in hospitalized patients with COVID-19: A scoping review of randomized controlled trials and call for international collaboration.** Tritschler T, Mathieu ME, Skeith L, et al. *J Thromb Haemost*. 2020 Sep 5. doi: 10.1111/jth.15094.

<https://onlinelibrary.wiley.com/doi/10.1111/jth.15094>

Findings: A total of 20 trials were included in the review. With individual target sample sizes ranging from 30 to 3,000 participants, the pooled sample size of all included trials is 12,568 participants. Several trials evaluate different dose regimens of anticoagulant interventions in hospitalized patients with COVID-19. Since these trials compete for sites and study participants,

a collaborative effort is needed to complete trials faster, conduct pooled analyses and bring effective interventions to patients more quickly.

- 25. Ventilatory Mechanics in Early vs Late Intubation in a Cohort of COVID-19 Patients with Acute Respiratory Distress Syndrome: A Single Center's Experience.** Pandya A, Kaur NA, Sacher D, et al. *Chest*. 2020 Aug 31:S0012-3692(20)34314-2. doi: 10.1016/j.chest.2020.08.2084.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456835/pdf/main.pdf>

Findings: Our study found late intubation (>1.27 days; median day 4) was associated with longer ICU length of stay and longer duration of mechanical ventilation than early intubation (≤ 1.27 days; median day 0). We found non-survivors had a longer time to intubation than survivors in our cohort. Patients intubated later had higher driving pressures, lower static compliance, and higher ventilator ratios. By day 6, static compliance improved in the late intubation group while it declined in the early intubation group. This may be partially explained by disease improvement over time. Additionally, not all patients were included in the static compliance measures by day 6 as several patients had been extubated or expired. Low static compliance was seen in both groups of patients albeit at varying times during the mechanical ventilation course. We did not find distinct ARDS phenotypes as previously suggested in line with other cohort studies, suggesting a majority of patients have low compliance.

Transmission / Infection Control

- 26. Probable Evidence of Fecal Aerosol Transmission of SARS-CoV-2 in a High-Rise Building.** Kang M, Wei J, Yuan J, et al. *Ann Intern Med*. 2020 Sep 1. doi: 10.7326/M20-0928.
<https://www.acpjournals.org/doi/10.7326/M20-0928>

Findings: 9 infected patients in 3 families were identified. The first family had a history of travel to the COVID-19 epicenter Wuhan, whereas the other 2 families had no travel history and a later onset of symptoms. No evidence was found for transmission via the elevator or elsewhere. The families lived in 3 vertically aligned flats connected by drainage pipes in the master bathrooms. Both the observed infections and the locations of positive environmental samples are consistent with the vertical spread of virus-laden aerosols via these stacks and vents. On the basis of circumstantial evidence, fecal aerosol transmission may have caused the community outbreak of COVID-19 in this high-rise building.

- 27. Community Outbreak Investigation of SARS-CoV-2 Transmission Among Bus Riders in Eastern China.** Shen Y, Li C, Dong H, et al. *JAMA Intern Med*. 2020 Sep 1. doi: 10.1001/jamainternmed.2020.5225.
<https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2770172>

Findings: In this cohort study and case investigation of a community outbreak of COVID-19 in Zhejiang province, individuals who rode a bus to a worship event with a patient with COVID-19 had a higher risk of SARS-CoV-2 infection than individuals who rode another bus to the same event. Airborne spread of SARS-CoV-2 seems likely to have contributed to the high attack rate in the exposed bus. Future efforts at prevention and control must consider the potential for airborne spread of the virus.

28. The use of germicidal ultraviolet light, vaporised hydrogen peroxide and dry heat to decontaminate face masks and filtering respirators contaminated with a SARS-CoV-2 surrogate virus. Ludwig-Begall LF, Wielick C, Dams L, et al. *J Hosp Infect*. 2020 Sep 1:S0195-6701(20)30413-8. doi: 10.1016/j.jhin.2020.08.025.

<https://www.sciencedirect.com/science/article/pii/S0195670120304138>

FINDINGS: UV irradiation, vaporised H₂O₂ and dry heat reduced infectious PRCV by more than three orders of magnitude on mask and respirator coupons and rendered it undetectable in all decontamination assays. This is the first description of stable disinfection of face masks and filtering facepiece respirators contaminated with an infectious SARS-CoV-2 surrogate using UV irradiation, vaporised H₂O₂ and dry heat treatment. The three methods permit demonstration of a loss of infectivity by more than three orders of magnitude of an infectious coronavirus in line with the FDA policy regarding face masks and respirators. It presents advantages of uncomplicated manipulation and utilisation in a BSL2 facility, therefore being easily adaptable to other respirator and mask types.

Vaccine

29. Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia. Logunov, D. Y., Dolzhikova, I. V., et al. *Lancet*. September 4, 2020.

[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31866-3/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31866-3/fulltext)

Findings: Between June 18 and Aug 3, 2020, we enrolled 76 participants to the two studies (38 in each study). In each study, nine volunteers received rAd26-S in phase 1, nine received rAd5-S in phase 1, and 20 received rAd26-S and rAd5-S in phase 2. Both vaccine formulations were safe and well tolerated. The most common adverse events were pain at injection site (44 [58%]), hyperthermia (38 [50%]), headache (32 [42%]), asthenia (21 [28%]), and muscle and joint pain (18 [24%]). Most adverse events were mild and no serious adverse events were detected. All participants produced antibodies to SARS-CoV-2 glycoprotein. At day 42, receptor binding domain-specific IgG titres were 14 703 with the frozen formulation and 11 143 with the lyophilised formulation, and neutralising antibodies were 49·25 with the frozen formulation and 45·95 with the lyophilised formulation, with a seroconversion rate of 100%. Cell-mediated responses were detected in all participants at day 28, with median cell proliferation of 2·5% CD4+ and 1·3% CD8+ with the frozen formulation, and a median cell proliferation of 1·3% CD4+ and 1·1% CD8+ with the lyophilised formulation. The heterologous rAd26 and rAd5 vector-based COVID-19 vaccine has a good safety profile and induced strong humoral and cellular immune responses in participants. Further investigation is needed of the effectiveness of this vaccine for prevention of COVID-19.

30. Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. Cheryl Keech, M.D., Ph.D., Gary Albert, M.S., Iksung Cho, et al. *NEJM*. September 2, 2020 DOI: 10.1056/NEJMoa2026920 <https://www.nejm.org/doi/full/10.1056/NEJMoa2026920>

Findings: NVX-CoV2373 is a recombinant severe acute respiratory syndrome coronavirus 2 nanoparticle vaccine composed of trimeric full-length SARS-CoV-2 spike glycoproteins and Matrix-M1 adjuvant. We initiated a randomized, placebo-controlled, phase 1–2 trial to evaluate

the safety and immunogenicity of the rSARS-CoV-2 vaccine (in 5- μ g and 25- μ g doses, with or without Matrix-M1 adjuvant, and with observers unaware of trial-group assignments) in 131 healthy adults. At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype.

31. **A SARS-CoV-2 vaccine candidate would likely match all currently circulating variants.** Dearlove B, Lewitus E, Bai H, et al. *Proc Natl Acad Sci U S A*. 2020 Aug 31;202008281. doi:

10.1073/pnas.2008281117. <https://www.pnas.org/content/early/2020/08/28/2008281117>

Findings: Here we investigate the diversity seen in SARS-CoV-2 sequences and compare it to the sequence on which most vaccine candidates are based. Using 18,514 sequences, we perform phylogenetic, population genetics, and structural bioinformatics analyses. We find limited diversity across SARS-CoV-2 genomes: Only 11 sites show polymorphisms in >5% of sequences; yet two mutations, including the D614G mutation in Spike, have already become consensus. Because SARS-CoV-2 is being transmitted more rapidly than it evolves, the viral population is becoming more homogeneous, with a median of seven nucleotide substitutions between genomes. There is evidence of purifying selection but little evidence of diversifying selection, with substitution rates comparable across structural versus nonstructural genes. Finally, the Wuhan-Hu-1 reference sequence for the Spike protein, which is the basis for different vaccine candidates, matches optimized vaccine inserts, being identical to an ancestral sequence and one mutation away from the consensus. While the rapid spread of the D614G mutation warrants further study, our results indicate that drift and bottleneck events can explain the minimal diversity found among SARS-CoV-2 sequences. These findings suggest that a single vaccine candidate should be efficacious against currently circulating lineages.

32. **National Academies of Sciences, Engineering, and Medicine. 2020. Discussion Draft of the Preliminary Framework for Equitable Allocation of COVID-19 Vaccine.** Washington, DC: The National Academies Press. <https://doi.org/10.17226/25914>.

<https://www.nap.edu/catalog/25914/discussion-draft-of-the-preliminary-framework-for-equitable-allocation-of-covid-19-vaccine>

On September 1, 2020, the National Academies of Sciences, Engineering, and Medicine invited public comment on the Discussion Draft of the Preliminary Framework for Equitable Allocation of COVID-19 Vaccine, commissioned by the Centers for Disease Control and the National Institutes of Health. Input from the public, especially communities disproportionately affected by the COVID-19 pandemic, is essential to produce a final report that is objective, balanced, and inclusive. The public comment period was open for 4 days, from Tuesday, September 1 until Friday, September 4.

33. **An ethical framework for global vaccine allocation.** Emanuel EJ, Persad G, Kern A, et al. *Science*. 2020 Sep 3. 2020;eabe2803. doi:10.1126/science.abe2803

<https://science.sciencemag.org/content/early/2020/09/02/science.abe2803.long>

The Fair Priority Model is the best embodiment of the ethical values of limiting harms, benefiting the disadvantaged, and recognizing equal concern. The responsibility for implementing the model rests with countries, international organizations, and vaccine

producers. Ultimately, the model offers governments, international organizations, and vaccine producers a practical way to fulfill their pledges to distribute vaccine fairly and equitably and make their words a reality.

34. Attitudes toward a Potential SARS-CoV-2 Vaccine: A Survey of U.S. Adults. Fisher KA,

Bloomstone SJ, Walder J, et al. *Ann Intern Med.* 2020 Sep 4. doi: 10.7326/M20-3569.

<https://www.acpjournals.org/doi/10.7326/M20-3569>

Findings: A total of 991 AmeriSpeak panel members responded. Overall, 57.6% of participants ($n = 571$) intended to be vaccinated, 31.6% ($n = 313$) were not sure, and 10.8% ($n = 107$) did not intend to be vaccinated. Factors independently associated with vaccine hesitancy included younger age, Black race, lower educational attainment, and not having received the influenza vaccine in the prior year. Reasons for vaccine hesitancy included vaccine-specific concerns, a need for more information, antivaccine attitudes or beliefs, and a lack of trust. **LIMITATIONS:** Participants' intent to be vaccinated was explored before a vaccine was available and when the pandemic was affecting a narrower swath of the United States. Questions about specific information or factors that might increase vaccination acceptance were not included. The survey response rate was 16.1%. This national survey, conducted during the coronavirus pandemic, revealed that approximately 3 in 10 adults were not sure they would accept vaccination and 1 in 10 did not intend to be vaccinated against COVID-19. Targeted and multipronged efforts will be needed to increase acceptance of a COVID-19 vaccine when one becomes available.

35. Ad26 vaccine protects against SARS-CoV-2 severe clinical disease in hamsters. Tostanoski LH,

Wegmann F, Martinot AJ, et al. *Nat Med.* 2020 Sep 3. doi: 10.1038/s41591-020-1070-

6. <https://www.nature.com/articles/s41591-020-1070-6>

Findings: Studies of SARS-CoV-2 infection in hamsters and nonhuman primates have generally reported mild clinical disease, and preclinical SARS-CoV-2 vaccine studies have demonstrated reduction of viral replication in the upper and lower respiratory tracts in nonhuman primates. Here we show that high-dose intranasal SARS-CoV-2 infection in hamsters results in severe clinical disease, including high levels of virus replication in tissues, extensive pneumonia, weight loss and mortality in a subset of animals. A single immunization with an adenovirus serotype 26 vector-based vaccine expressing a stabilized SARS-CoV-2 spike protein elicited binding and neutralizing antibody responses and protected against SARS-CoV-2-induced weight loss, pneumonia and mortality. These data demonstrate vaccine protection against SARS-CoV-2 clinical disease. This model should prove useful for preclinical studies of SARS-CoV-2 vaccines, therapeutics and pathogenesis.

36. Phase 1-2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine. Keech C,

Albert G, Cho I, et al. *N Engl J Med.* 2020 Sep 2. doi: 10.1056/NEJMoa2026920.

<https://www.nejm.org/doi/full/10.1056/NEJMoa2026920>

Findings: After randomization, 83 participants were assigned to receive the vaccine with adjuvant and 25 without adjuvant, and 23 participants were assigned to receive placebo. No serious adverse events were noted. Reactogenicity was absent or mild in the majority of participants, more common with adjuvant, and of short duration (mean, ≤ 2 days). One

participant had mild fever that lasted 1 day. Unsolicited adverse events were mild in most participants; there were no severe adverse events. The addition of adjuvant resulted in enhanced immune responses, was antigen dose-sparing, and induced a T helper 1 (Th1) response. The two-dose 5- μ g adjuvanted regimen induced geometric mean anti-spike IgG (63,160 ELISA units) and neutralization (3906) responses that exceeded geometric mean responses in convalescent serum from mostly symptomatic Covid-19 patients (8344 and 983, respectively). CONCLUSIONS: At 35 days, NVX-CoV2373 appeared to be safe, and it elicited immune responses that exceeded levels in Covid-19 convalescent serum. The Matrix-M1 adjuvant induced CD4+ T-cell responses that were biased toward a Th1 phenotype.

Whole Person Care

37. Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic.

Ettman CK, Abdalla SM, Cohen GH, et al. *JAMA Netw Open*. 2020;3(9):e2019686.

doi:10.1001/jamanetworkopen.2020.19686

<https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2770146>

Findings: In this survey study that included 1441 respondents from during the COVID-19 pandemic and 5065 respondents from before the pandemic, depression symptom prevalence was more than 3-fold higher during the COVID-19 pandemic than before. Lower income, having less than \$5000 in savings, and having exposure to more stressors were associated with greater risk of depression symptoms during COVID-19. These findings suggest that there is a high burden of depression symptoms in the US associated with the COVID-19 pandemic and that this burden falls disproportionately on individuals who are already at increased risk.

Women & Children

38. COVID-19 and Parent-Child Psychological Well-being. Gassman-Pines A, Ananat EO, Fitz-Henley J 2nd. 2020 Aug 6. *Pediatrics*. 2020;e2020007294. doi:10.1542/peds.2020-007294

<https://pediatrics.aappublications.org/content/early/2020/08/31/peds.2020-007294>

Findings: The frequency of parent-reported daily negative mood increased significantly since the start of the crisis. Many families have experienced hardships during the crisis, including job loss, income loss, caregiving burden, and illness. Both parents' and children's well-being in the postcrisis period was strongly associated with the number of crisis-related hardships that the family experienced. Consistent with our hypotheses, in families that have experienced multiple hardships related to the coronavirus disease 2019 crisis, both parents' and children's mental health is worse. As the crisis continues to unfold, pediatricians should screen for mental health, with particular attention to children whose families are especially vulnerable to economic and disease aspects of the crisis.

39. Echocardiographic Findings in Pediatric Multisystem Inflammatory Syndrome Associated with COVID-19 in the United States. Matsubara D, Kauffman HL, Wang Y, et al. *J Am Coll Cardiol*.

2020 Aug 31:S0735-1097(20)36488-3. doi: 10.1016/j.jacc.2020.08.056.

<https://www.onlinejacc.org/content/early/2020/08/29/j.jacc.2020.08.056>

Findings: Multisystem inflammatory syndrome in children (MIS-C) is an illness that resembles Kawasaki Disease (KD) or toxic shock, reported in children with a recent history of COVID-19 infection. This study analyzed echocardiographic manifestations of this illness. In our cohort of 28 MIS-C patients, left ventricular systolic and diastolic function were worse than in classic KD. These functional parameters correlated with biomarkers of myocardial injury. However, coronary arteries were typically spared. The strongest predictors of myocardial injury were global longitudinal strain, right ventricular strain, and left atrial strain. During subacute period, there was good recovery of systolic function, but diastolic dysfunction persisted.

40. Characteristics of Newborns Born to SARS-CoV-2-Positive Mothers: A Retrospective Cohort

Study. Farghaly MAA, Kupferman F, Castillo F, Kim RM. *Am J Perinatol.* 2020 Sep 3. doi: 10.1055/s-0040-1715862. <https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0040-1715862>

Findings: For SARS-CoV-2-positive mothers, reducing transmission of infection to newborns is crucial. Newborns of SARS-CoV-2-positive mothers are usually asymptomatic and may not be easily infected. Critical illness in the newborn may still happen, so monitoring is needed.

41. Quantitative SARS-CoV-2 Serology in Children with Multisystem Inflammatory Syndrome (MIS-C).

(MIS-C). Rostad CA, Chahroudi A, Mantus G, et al. *Pediatrics.* 2020 Sep 2:e2020018242. doi: 10.1542/peds.2020-018242.

<https://pediatrics.aappublications.org/content/pediatrics/early/2020/08/31/peds.2020-018242.full.pdf>

Findings: All children with MIS-C had high titers of SARS-CoV-2 RBD IgG antibodies, which correlated with full-length spike IgG antibodies, nucleocapsid protein antibodies, and neutralizing antibodies. Children with MIS-C had significantly higher SARS-CoV-2 RBD IgG antibody titers than children with COVID-19, KD and hospitalized controls. All children with MIS-C also had detectable RBD IgM antibodies, indicating recent SARS-CoV-2 infection. RBD IgG titers correlated with erythrocyte sedimentation rate and with hospital and ICU lengths of stay. Quantitative SARS-CoV-2 serology may have a role in establishing the diagnosis of MIS-C, distinguishing it from similar clinical entities, and stratifying risk for adverse outcomes.

42. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus

disease 2019 in pregnancy: living systematic review and meta-analysis. Allotey J, Stallings E, Bonet M, et al. *BMJ.* 2020 Sep 1;370:m3320. doi: 10.1136/bmj.m3320.

<https://www.bmjjournals.org/content/370/bmjjournals.m3320>

Findings: 77 studies were included. Overall, 10% of pregnant and recently pregnant women attending or admitted to hospital for any reason were diagnosed as having suspected or confirmed covid-19. The most common clinical manifestations of covid-19 in pregnancy were fever (40%) and cough (39%). Pregnant and recently pregnant women are less likely to manifest covid-19 related symptoms of fever and myalgia than non-pregnant women of reproductive age and are potentially more likely to need intensive care treatment for covid-19. Pre-existing comorbidities, high maternal age, and high body mass index seem to be risk factors for severe covid-19. Preterm birth rates are high in pregnant women with covid-19 than in pregnant women without the disease.

GUIDELINES & CONSENSUS STATEMENTS

[**ASHP principles for COVID-19 vaccine distribution, allocation, and mass immunization.**](#) *Am J Health Syst Pharm.* 2020 Sep 1:zxa311. doi: 10.1093/ajhp/zxa311.

[**A living WHO guideline on drugs for covid-19.**](#) Lamontagne F, Agoritsas T, Macdonald H, et al. *BMJ.* 2020 Sep 4;370:m3379. doi: 10.1136/bmj.m3379.

[**Summary of respiratory rehabilitation and physical therapy guidelines for patients with COVID-19 based on recommendations of World Confederation for Physical Therapy and National Association of Physical Therapy.**](#) Zhu Y, Wang Z, Zhou Y, et al. *J Phys Ther Sci.* 2020;32(8):545-549. doi: 10.1589/jpts.32.545.

FDA / CDC / NIH / WHO Updates

CDC - [**How to Make 0.1% Chlorine Solution to Disinfect Surfaces in Healthcare Settings.**](#) August 31, 2020.

CDC - [**Interim Guidance for Rapid Antigen Testing for SARS-CoV-2.**](#) September 3, 2020.

GAO - [**COVID-19 : Brief Update on Initial Federal Response to the Pandemic.**](#)

NIH - [**The COVID-19 Treatment Guidelines Panel's Statement on the Emergency Use Authorization of Convalescent Plasma for the Treatment of COVID-19.**](#)

WHO - [**Corticosteroids for COVID-19**](#) : Living Guidance, 2 September 2020.

Commentary / Press Releases

[**AstraZeneca Covid-19 vaccine study put on hold due to suspected adverse reaction in participant in the U.K.**](#) *Stat,* September 8, 2020.

*on hold, *Phase III Double-blind, Placebo-controlled Study of AZD1222 for the Prevention of COVID-19 in Adults.* ClinicalTrials.gov Identifier: NCT04516746

[**Facial Masking for Covid-19 — Potential for “Variolation” as We Await a Vaccine.**](#) *NEJM* Sept 8, 2020.

[**Roche receives FDA Emergency Use Authorization for the cobas SARS-CoV-2 & Influenza A/B Test.**](#)

[**Regulatory Decision-making on COVID-19 Vaccines during a Public Health Emergency.**](#) *JAMA* August 31, 2020.

[**Emergency Use Authorizations during the COVID-19 Pandemic: Lessons From Hydroxychloroquine for Vaccine Authorization and Approval.**](#) *JAMA* August 31, 2020.

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