

COVID-19 Resource Desk

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Retraction Watch

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

 In Vitro Efficacy of a Povidone-Iodine Nasal Antiseptic for Rapid Inactivation of SARS-CoV-2.
 Frank S, Brown SM, Capriotti, JA, et al. JAMA Otolaryngol Head Neck Surg. September 17, 2020. doi:10.1001/jamaoto.2020.3053
 https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2770785
 Findings: Povidone-iodine nasal antiseptic solutions at concentrations as low as 0.5% rapidly

Findings: Povidone-iodine nasal antiseptic solutions at concentrations as low as 0.5% rapidly inactivate SARS-CoV-2 at contact times as short as 15 seconds. Intranasal use of PVP-I has demonstrated safety at concentrations of 1.25% and below and may play an adjunctive role in mitigating viral transmission beyond personal protective equipment.

*See also: Efficacy of Povidone-Iodine Nasal and Oral Antiseptic Preparations Against Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2). Pelletier JS, Tessema B, Frank S, et al. Ear Nose Throat J. 2020 Sep 21:145561320957237. doi: 10.1177/0145561320957237

Clinical Syndrome

2. Stroke Risk, phenotypes, and death in COVID-19: Systematic review and newly reported cases. Fridman S, Bullrich MB, Jimenez-Ruiz A, et al. Neurology. 2020 Sep 15:10.1212/WNL.000000000000010851. doi: 10.1212/WNL.000000000000010851. https://n.neurology.org/content/early/2020/09/15/WNL.00000000000010851
Findings: The proportion of COVID-19 patients with stroke (1.8%) and in-hospital mortality (34.4%) were exceedingly high. Mortality was 67% lower in patients <50 years-old relative to those >70 years-old. Large vessel occlusion was twice as frequent (46.9%) as previously reported and was high across all age groups, even in the absence of risk factors or comorbidities. A clinical phenotype characterized by older age, a higher burden of comorbidities, and severe COVID-19 respiratory symptoms, was associated with the highest inhospital mortality (58.6%) and a 3x higher risk of death than the rest of the cohort. Stroke is relatively frequent among COVID-19 patients and has devastating consequences across all ages. The interplay of older age, comorbidities, and severity of COVID-19 respiratory symptoms is associated with an extremely elevated mortality.

3. Characteristics of Acute Kidney Injury in Hospitalized COVID-19 Patients in an Urban Academic Medical Center. Lee JR, Silberzweig J, Akchurin O, et al. *Clin J Am Soc Nephrol*. 2020 Sep 18:CJN.07440520. doi: 10.2215/CJN.07440520.

https://cjasn.asnjournals.org/content/early/2020/09/18/CJN.07440520.long

Findings: In this study, we found several laboratory parameters that are significantly different between patients with AKI and patients without AKI. d-dimer level was significantly higher in patients with AKI without kidney function recovery than in patients with AKI and kidney function recovery. Our study identified a high incidence of AKI in hospitalized patients with COVID-19. We found that a significant proportion did not have complete kidney function recovery, supporting the importance of CKD follow-up in patients with COVID-19.

*see also <u>Prevalence of Kidney Injury and Associations with Critical Illness and Death in Patients with COVID-19.</u> Zheng X, Yang H, Li X, et al. *Clin J Am Soc Nephrol*. 2020 Sep 17:CJN.04780420. doi: 10.2215/CJN.04780420.

4. Thrombotic and haemorrhagic complications in critically ill patients with COVID-19: a multicentre observational study. Shah A, Donovan K, McHugh A, et al. *Crit Care*. 2020 Sep 18;24(1):561. doi: 10.1186/s13054-020-03260-3.

https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03260-3

Findings: A total of 187 patients were included. Eighty-one (43.3%) patients experienced one or more clinically relevant thrombotic complications, which were mainly pulmonary emboli (n = 42 (22.5%)). Arterial embolic complications were reported in 25 (13.3%) patients. ICU length of stay was longer in patients with thrombotic complications when compared with those without. Fifteen (8.0%) patients experienced haemorrhagic complications, of which nine (4.8%) were classified as major bleeding. Thromboelastography demonstrated a hypercoagulable profile in patients tested but lacked discriminatory value between those with and without thrombotic complications. Patients who experienced thrombotic complications had higher D-dimer, ferritin, troponin and white cell count levels at ICU admission compared with those that did not. Critically ill patients with COVID-19 experience high rates of venous and arterial thrombotic complications. The rates of bleeding may be higher than previously reported and re-iterate the need for randomised trials to better understand the risk-benefit ratio of different anticoagulation strategies.

Diagnostics & Screening

 Clinical Impact, Costs, and Cost-Effectiveness of Expanded SARS-CoV-2 Testing in Massachusetts. Neilan AM, Losina E, Bangs AC, et al. Clin Infect Dis. 2020 Sep 18:ciaa1418. doi: 10.1093/cid/ciaa1418. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1418/5908298

Findings: Testing people with any COVID-19-consistent symptoms would be cost-saving compared to testing only those whose symptoms warranting hospital care. Expanding PCR testing to asymptomatic people would decrease infections, deaths, and hospitalizations. Despite modest sensitivity, low-cost, repeat screening of the entire population could be cost-effective in all epidemic settings.

 Probative Value of the D-Dimer Assay for Diagnosis of Deep Venous Thrombosis in the Coronavirus Disease 2019 Syndrome. Gibson CJ, Alqunaibit D, Smith KE, et al. Crit Care Med. 2020 Sep 15. doi: 10.1097/CCM.0000000000004614. https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=ovft&AN=0000

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=ovft&AN=0000 3246-90000000-95512&PDF=y

Findings: Lower extremity deep venous thrombosis is prevalent in coronavirus disease 2019 disease and can be present on ICU admission. Screening has been recommended in the context of the pro-inflammatory, hypercoagulable background milieu. D-dimer concentrations are elevated in nearly all coronavirus disease 2019 patients, and the test appears reliable for screening for lower extremity deep venous thrombosis at or above a concentration of 3,000 ng/mL (more than 13-fold above the normal range). Full anticoagulation is indicated if the diagnosis is confirmed, and therapeutic anticoagulation should be considered for prophylaxis, as all coronavirus disease 2019 patients are at increased risk.

- 7. **Detection of SARS-CoV-2 with SHERLOCK One-Pot Testing.** Joung J, Ladha A, Saito M, et al. *N Engl J Med.* 2020 Sep 16. doi: 10.1056/NEJMc2026172. https://www.nejm.org/doi/full/10.1056/NEJMc2026172
 - Findings: Here, we describe a simple test for detection of SARS-CoV-2. The sensitivity of this test is similar to that of reverse-transcription—quantitative polymerase-chain-reaction (RT-qPCR) assays. STOP (SHERLOCK testing in one pot) is a streamlined assay that combines simplified extraction of viral RNA with isothermal amplification and CRISPR-mediated detection. This test can be performed at a single temperature in less than an hour and with minimal equipment.
- 8. Assessing the Dilution Effect of Specimen Pooling on the Sensitivity of SARS-CoV-2 PCR Tests. Bateman AC, Mueller S, Guenther K, Shult P. *J Med Virol*. 2020 Sep 16. doi: 10.1002/jmv.26519. https://onlinelibrary.wiley.com/doi/10.1002/jmv.26519
 - Findings: The SARS-CoV-2 pandemic has led to an unprecedented demand for diagnostic tests. Many studies have modeled the efficiency gains of specimen pooling, but few have systematically evaluated the dilution effect of pooling on the sensitivity of tests. Using the frequency distribution of Ct values of our first 838 SARS-CoV-2 positive specimens, we modeled 100 specimens on the same frequency distribution. Given this distribution, we then tested dilutions of 1:5, 1:10, and 1:50 to find the percentage of specimens positive at each Ct value with each pool size. Using the frequency distribution and the percentage of specimens positive at each Ct value, we estimate that pools of 5 lead to 93% sensitivity, pools of 10 lead to 91% sensitivity, and pools of 50 lead to 81% sensitivity. Pools of 5 and 10 lead to some specimens with Ct values of ≥32 becoming negative, while pools of 50 lead to some specimens with Ct values of ≥28 becoming negative. These sensitivity estimates can inform laboratories seeking to implement pooling approaches as they seek to balance test efficiency with sensitivity. This article is protected by copyright. All rights reserved.
- Comparison of eight commercial, high-throughput, automated or ELISA assays detecting SARS-CoV-2 IgG or total antibody. Trabaud MA, Icard V, Milon MP, et al. J Clin Virol. 2020 Sep 7;132:104613. doi: 10.1016/j.jcv.2020.104613. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7476603/

Findings: The positivity rate varied depending on the assay but was greater for all assays in hospitalized than non-hospitalized patients. Despite a good correlation between the assays, discrepancies occurred, without a systematic origin, even for samples taken more than 20 days after symptom onset. These discrepancies were linked to low antibody levels in paucisymptomatic patients. Whichever assay is chosen, a false negative result may need to be ruled out with another test in a risk situation.

10. Evaluation of performance of two SARS-CoV-2 Rapid IgM-IgG combined antibody tests on capillary whole blood samples from the fingertip. Prazuck T, Colin M, Giachè S, et al. PLoS One. 2020 Sep 17;15(9):e0237694. doi: 10.1371/journal.pone.0237694. eCollection 2020. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0237694
Findings: COVID-PRESTO® and DUO® POC tests turned out to be very specific (none false positive) and to be sensitive enough after 15 days from onset of symptom. These easy to use IgG/IgM combined test kits are the first ones allowing a screening with CWB sample, by typing from a finger prick. These rapid tests are particularly interesting for screening in low resource settings.

Epidemiology & Public Health

11. COVID-19-Associated Deaths in San Francisco: The Important Role of Dementia and Atypical Presentations in Long-term Care Facilities. Louie JK, Scott HM, Lu W, et al. *J Gen Intern Med.* 2020 Sep 15. doi: 10.1007/s11606-020-06206-1.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7491360/

Findings: Consistent with other reports, older adults in San Francisco remain the most likely to die due to COVID-19. In San Francisco, as of July 30, 2020, persons ≥ 60 years comprise 14% of COVID-19 infections, yet 90% of deaths. Most decedents had multiple co-morbidities reported by others, including diabetes and chronic cardiac and lung disease. However, we found dementia was the most frequent co-morbidity, driven predominantly by LTCF residents who comprised nearly half of our decedents. Additionally, LTCF decedents were more likely to present with altered mental status; nearly half did not present with any typical COVID-19 symptoms of fever, cough, or dyspnea. Presentation with altered mental status has also been reported in older COVID-19 patients presenting to emergency medical services. Although we found that LTCF cases were less likely to be hospitalized, receive aggressive medical interventions, or develop complications of sepsis or acute renal failure, they progressed more rapidly to death after symptom onset, likely reflecting the frail, debilitated state of many LTCF residents who are near end-of-life and have a DNR/DNI or comfort care status.

12. SARS-CoV-2-Associated Deaths among Persons Aged <21 Years - United States, February 12-July 31, 2020. Bixler D et al. MMWR Morb Mortal Wkly Rep. 2020 Sep 18;69(37):1324-1329. doi: 10.15585/mmwr.mm6937e4.

https://www.cdc.gov/mmwr/volumes/69/wr/mm6937e4.htm

Findings: Persons aged <21 years constitute 26% of the U.S. population, and this report describes characteristics of U.S. persons in that population who died in association with SARS-CoV-2 infection, as reported by public health jurisdictions. Among 121 SARS-CoV-2-associated

deaths reported to CDC among persons aged <21 years in the United States during February 12-July 31, 2020, 63% occurred in males, 10% of decedents were aged <1 year, 20% were aged 1-9 years, 70% were aged 10-20 years, 45% were Hispanic persons, 29% were non-Hispanic Black (Black) persons, and 4% were non-Hispanic American Indian or Alaska Native (AI/AN) persons. Among these 121 decedents, 91 (75%) had an underlying medical condition, 79 (65%) died after admission to a hospital, and 39 (32%) died at home or in the ED. These data show that nearly three quarters of SARS-CoV-2-associated deaths among infants, children, adolescents, and young adults have occurred in persons aged 10-20 years, with a disproportionate percentage among young adults aged 18-20 years and among Hispanics, Blacks, AI/ANs, and persons with underlying medical conditions. Careful monitoring of SARS-CoV-2 infections, deaths, and other severe outcomes among persons aged <21 years remains particularly important as schools reopen in the United States. Ongoing evaluation of effectiveness of prevention and control strategies will also be important to inform public health guidance for schools and parents and other caregivers.

13. Decreased Influenza Activity During the COVID-19 Pandemic - United States, Australia, Chile, and South Africa, 2020. Olsen SJ, Azziz-Baumgartner E, Budd AP, et al. MMWR Morb Mortal Wkly Rep. 2020 Sep 18;69(37):1305-1309. doi:10.15585/mmwr.mm6937a6. https://www.cdc.gov/mmwr/volumes/69/wr/mm6937a6.htm?s cid=mm6937a6 w Findings: After recognition of widespread community transmission of SARS-CoV-2, the virus that causes COVID-19, by mid- to late February 2020, indicators of influenza activity began to decline in the Northern Hemisphere. These changes were attributed to both artifactual changes related to declines in routine health seeking for respiratory illness as well as real changes in influenza virus circulation because of widespread implementation of measures to mitigate transmission of SARS-CoV-2. Data from clinical laboratories in the United States indicated a 61% decrease in the number of specimens submitted and a 98% decrease in influenza activity as measured by percentage of submitted specimens testing positive. Interseasonal (i.e., summer) circulation of influenza in the United States (May 17-August 8, 2020) is currently at historical lows (median = 0.20% tests positive in 2020 versus 2.35% in 2019, 1.04% in 2018, and 2.36% in 2017). Influenza data reported to the World Health Organization's FluNet platform from three Southern Hemisphere countries that serve as robust sentinel sites for influenza from Oceania (Australia), South America (Chile), and Southern Africa (South Africa) showed very low influenza activity during June-August 2020, the months that constitute the typical Southern Hemisphere influenza season. In countries or jurisdictions where extensive community mitigation measures are maintained (e.g., face masks, social distancing, school closures, and teleworking), those locations might have little influenza circulation during the upcoming 2020-21 Northern Hemisphere influenza season. The use of community mitigation measures for the COVID-19 pandemic, plus influenza vaccination, are likely to be effective in reducing the incidence and impact of influenza, and some of these mitigation measures could have a role in preventing influenza in future seasons. Influenza vaccination of all persons aged ≥6 months remains the best method for influenza prevention and is especially important this season when SARS-CoV-2 and influenza virus might cocirculate.

- 14. COVID-19 Racial Disparities in Testing, Infection, Hospitalization, and Death: Analysis of Epic Patient Data. Rubin-Miller L, Alban C, Sullivan S, et al. *Epic Health Research Network*, Sept. 16, 2020. https://www.ehrn.org/covid-19-racial-disparities-in-testing-infection-hospitalization-death/
- 15. Frequency of Children vs Adults Carrying Severe Acute Respiratory Syndrome Coronavirus 2
 Asymptomatically. Milani GP, Bottino I, Rocchi A, et al. *JAMA Pediatr*. September 14, 2020. doi:10.1001/jamapediatrics.2020.3595
 https://jamanetwork.com/journals/jamapediatrics/fullarticle/2770117
 Findings: In this study conducted among individuals hospitalized in Milan, one of the cities with the highest SARS-CoV-2 burden in the world, about 1% of children and 9% of adults without any symptoms or signs of SARS-CoV-2 infection tested positive for the virus. It has been estimated that approximately 80% of adults with SARS-CoV-2 are asymptomatic. The few available reports on children are from China and suggest that children who are asymptomatic might be 15% of individuals positive for SARS-CoV-2. In this study, children without symptoms and signs of SARS-CoV-2 carried the virus less frequently than adults, suggesting that their role as facilitators of the spreading of SARS-CoV-2 infection could be reconsidered.
- 16. Relationship between Influenza Vaccination Coverage Rate and COVID-19 Outbreak: An Italian Ecological Study. Amato M, Werba JP, Frigerio B, et al. Vaccines (Basel). 2020 Sep 16;8(3):E535. doi: 10.3390/vaccines8030535. https://www.mdpi.com/2076-393X/8/3/535/htm Results: In the Italian population, the coverage rate of the influenza vaccination in people aged 65 and over is associated with a reduced spread and a less severe clinical expression of COVID-19. This finding warrants ad hoc studies to investigate the role of influenza vaccination in preventing the spread of COVID-19.
- 17. Risk Factors for COVID-19-associated hospitalization: COVID-19-Associated Hospitalization Surveillance Network and Behavioral Risk Factor Surveillance System. Ko JY, Danielson ML, Town M, et al. Clin Infect Dis. 2020 Sep 18:ciaa1419. doi: 10.1093/cid/ciaa1419. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1419/5908300 Findings: Among 5,416 adults, hospitalization rates were higher among those with ≥3 underlying conditions, severe obesity, chronic kidney disease, diabetes, obesity, hypertension, and asthma, after adjusting for age, sex, and race/ethnicity. Adjusting for the presence of an individual underlying medical condition, higher hospitalization rates were observed for adults aged ≥65, 45-64 (versus 18-44 years), males (versus females), and non-Hispanic black and other race/ethnicities (versus non-Hispanic whites). Our findings elucidate groups with higher hospitalization risk that may benefit from targeted preventive and therapeutic interventions.
- 18. SARS-CoV-2 seroprevalence and neutralizing activity in donor and patient blood. Ng DL, Goldgof GM, Shy BR, et al. *Nat Commun*. 2020 Sep 17;11(1):4698. doi: 10.1038/s41467-020-18468-8. https://www.nature.com/articles/s41467-020-18468-8
 Findings: Given the limited availability of serological testing to date, the seroprevalence of SARS-CoV-2-specific antibodies in different populations has remained unclear. Here, we report very low SARS-CoV-2 seroprevalence in two San Francisco Bay Area populations. Seroreactivity

was 0.26% in 387 hospitalized patients admitted for non-respiratory indications and 0.1% in 1,000 blood donors in early April 2020. We additionally describe the longitudinal dynamics of immunoglobulin-G (IgG), immunoglobulin-M (IgM), and in vitro neutralizing antibody titers in COVID-19 patients. The median time to seroconversion ranged from 10.3-11.0 days for these 3 assays. Neutralizing antibodies rose in tandem with immunoglobulin titers following symptom onset, and positive percent agreement between detection of IgG and neutralizing titers was >93%. These findings emphasize the importance of using highly accurate tests for surveillance studies in low-prevalence populations and provide evidence that seroreactivity using SARS-CoV-2 anti-nucleocapsid protein IgG and anti-spike IgM assays are generally predictive of in vitro neutralizing capacity.

19. Analysis of Drug Test Results before and After the US Declaration of a National Emergency Concerning the COVID-19 Outbreak. Wainwright JJ, Mikre M, Whitley P, et al. *JAMA*. September 18, 2020. doi:10.1001/jama.2020.17694 https://jamanetwork.com/journals/jama/fullarticle/2770987

Findings: This study demonstrated that urine drug test positivity in a population diagnosed with or at risk of substance use disorders increased significantly for illicit cocaine, fentanyl, heroin, and methamphetamine from the 4 months before the COVID-19 emergency declaration to the 4 months after the COVID-19 declaration. Compared with the period before COVID-19, the proportion of specimens testing positive during the COVID-19 period increased from 3.59% to 4.76% for cocaine, from 3.80% to 7.32% for fentanyl, from 1.29% to 2.09% for heroin, and from 5.89% to 8.16% for methamphetamine.

*See also: Nonfatal Opioid Overdoses at an Urban Emergency Department during the COVID-19 Pandemic. Ochalek TA, Cumpston KL, Wills BK, Gal TS, Moeller FG. JAMA. Published online September 18, 2020. doi:10.1001/jama.2020.17477

Healthcare Delivery & Healthcare Workers

20. Guiding Principles for the Conduct of Observational Critical Care Research for Coronavirus Disease 2019 Pandemics and Beyond: The Society of Critical Care Medicine Discovery Viral Infection and Respiratory Illness Universal Study Registry. Walkey AJ, Sheldrick RC, Kashyap R, et al. Crit Care Med. 2020 Sep 15. doi: 10.1097/CCM.0000000000004572. https://journals.lww.com/ccmjournal/Abstract/9000/Guiding Principles for the Conduct of.9 5513.aspx

Findings: Large-scale observational data collection requires 1) quality assurance and harmonization across many sites; 2) a transparent process for selecting from among many potential research questions; 3) the use of best practices in design of descriptive, predictive, and inferential studies; (4) innovative approaches to characterize random error in the setting of constantly updated data; (5) rapid peer-review and reporting; and (6) transitions from a focus on discovery to implementation. Herein, we describe the guiding principles to best practices and suggestions for innovations to study design and reporting within the coronavirus disease 2019 Viral Infection and Respiratory Illness Universal Study pandemic registry.

21. The Association between Symptoms and COVID-19 Test Results among Healthcare Workers. Sacks CA, Dougan M, McCoy TH Jr, et al. *Ann Surg*. 2020 Sep 15. doi: 10.1097/SLA.000000000004483.

https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=ovft&AN=0000 0658-900000000-94202&PDF=v

Findings: Nearly 10% of a symptomatic health care worker cohort tested in the outpatient setting had a positive NP-PCR for SARS-CoV-2. Fever, myalgias and anosmia were associated with an increased odds of a positive test. Although some symptoms — such as sore throat — were associated with decreased odds of a positive test, no singular symptom seemed likely to effectively exclude a diagnosis of COVID-19 given the relatively small magnitude of an effect that each symptom had on the odds of a positive test. Those with a positive test reported a greater number of symptoms, though whether this difference is clinically meaningful is unclear. Given the guidance by the WHO that a positive test rate below 10% indicates adequate testing, these data also demonstrate the ability of a large employer to develop and implement a mandatory, large-scale program with onsite capacity to test all symptomatic health care workers.

22. Change in Antibodies to SARS-CoV-2 Over 60 Days Among Health Care Personnel in Nashville, Tennessee. Patel MM, Thornburg NJ, Stubblefield WB, et al. JAMA. 2020 Sep 17. doi: 10.1001/jama.2020.18796. https://jamanetwork.com/journals/jama/fullarticle/2770928 Findings: Anti–SARS-CoV-2 antibodies to the spike protein, which have correlated with neutralizing antibodies, decreased over 60 days in health care personnel, with 58% of seropositive individuals becoming seronegative. These results suggest that cross-sectional seroprevalence studies to evaluate population immunity may underestimate rates of prior infections because antibodies may only be transiently detectable following infection. The window after recovering from SARS-CoV-2 infection when people could donate serum that has sufficiently high antibody levels may be limited.

Prognosis

23. Patient characteristics and admitting vital signs associated with COVID-19 related mortality among patients admitted with non-critical illness. Sands K, Wenzel R, McLean L, et al. *Infect Control Hosp Epidemiol*. 2020 Sep 15:1-20. doi: 10.1017/ice.2020.461. https://tinyurl.com/yy4vrebg

Findings: A total of 6180 COVID-19+ patients were identified as of May 12, 2020. The majority of COVID-19+ patients (77.8%, 4808) were admitted directly to a medical/surgical unit with no documented critical care or mechanical ventilation within 8 hours of admission. After adjusting for demographic characteristics, comorbidities, and vital signs at admission in this subgroup, the largest driver of the odds of mortality was patient age. Decreased oxygen saturation at admission was associated with increased odds of mortality as was diabetes. The identification of factors observable at admission that are associated with mortality in COVID-19 patients who are initially admitted to non-critical care units may help care providers, hospital epidemiologists, and hospital safety experts better plan for the care of these patients.

- 24. High levels of SARS-CoV-2 specific T-cells with restricted functionality in severe course of COVID-19. Schub D, Klemis V, Schneitler S, et al. *JCI Insight*. 2020 Sep 16:142167. doi: 10.1172/jci.insight.142167. https://insight.jci.org/articles/view/142167/pdf
 Findings: Despite severe lymphopenia affecting all major lymphocyte subpopulations, patients with severe disease mounted significantly higher levels of SARS-CoV-2 specific T-cells as compared to convalescent individuals. SARS-CoV-2 specific CD4 T-cells dominated over CD8 T-cells and closely correlated with the number of plasmablasts and SARS-CoV-2 specific IgA- and IgG-levels. Unlike in convalescents, SARS-CoV-2 specific T-cells in patients with severe disease showed marked alterations in phenotypical and functional properties, which also extended to CD4 and CD8 T-cells in general. Given the strong induction of specific immunity to control viral replication in patients with severe disease, the functionally altered characteristics may result from the need for contraction of specific and general immunity to counteract excessive immunopathology in the lung.
- 25. Biomarkers and outcomes of COVID-19 hospitalisations: systematic review and meta-analysis. Malik P, Patel U, Mehta D, et al. *BMJ Evid Based Med.* 2020 Sep 15:bmjebm-2020-111536. doi: 10.1136/bmjebm-2020-111536. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7493072/ Findings: 32 studies with 10,491 confirmed COVID-19 patients were included. We found that lymphopenia, thrombocytopenia, elevated D-dimer, elevated CRP, elevated PCT, elevated CK, elevated AST, elevated ALT, elevated creatinine and LDH were independently associated with higher risk of poor outcomes. The results have the potential to be used as an early biomarker to improve the management of COVID-19 patients, by identification of high-risk patients and appropriate allocation of healthcare resources in the pandemic.
- 26. Impact of Vitamin D Deficiency on COVID-19-A Prospective Analysis from the CovILD Registry. Pizzini A, Aichner M, Sahanic S, et al. Nutrients. 2020 Sep 11;12(9):E2775. doi: 10.3390/nu12092775. https://www.mdpi.com/2072-6643/12/9/2775 Findings: We aimed to investigate associations of VITD status to disease presentation within the CovILD registry. This prospective, multicenter, observational study on long-term sequelae includes patients with COVID-19 after hospitalization or outpatients with persistent symptoms. A total of 109 patients were included in the analysis (60% males, 40% females), aged 58 ± 14 years. Eight weeks after the onset of COVID-19, a high proportion of patients presented with impaired VITD metabolism and elevated parathyroid hormone (PTH) levels. PTH concentrations were increased in patients who needed ICU treatment, while VITD levels were not significantly different between disease severity groups. Low VITD levels at disease onset or at eight-week follow-up were not related to persistent symptom burden, lung function impairment, ongoing inflammation, or more severe CT abnormalities. VITD deficiency is frequent among COVID-19 patients but not associated with disease outcomes. However, individuals with severe disease display a disturbed parathyroid-vitamin-D axis within their recovery phase. The proposed significance of VITD supplementation in the clinical management of COVID-19 remains elusive.
- 27. A granulocytic signature identifies COVID-19 and its severity. Vitte J, Diallo AB, Boumaza A, et al. *J Infect Dis*. 2020 Sep 17:jiaa591. doi: 10.1093/infdis/jiaa591. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa591/5907982

Findings: Granulocytic (neutrophil, eosinophil and basophil) markers were enriched during COVID-19 and discriminated between mild and severe patients. Increased counts of CD15 +CD16 + neutrophils, decreased granulocytic expression of integrin CD11b, and Th2-related CRTH2 downregulation in eosinophils and basophils established a COVID-19 signature. Severity was associated with the emergence of PDL1 checkpoint expression in basophils and eosinophils. This granulocytic signature was accompanied by monocyte and lymphocyte immunoparalysis. Correlation with validated clinical scores supported pathophysiological relevance. Phenotypic markers of circulating granulocytes are strong discriminators between infected and uninfected individuals as well as between severity stages. COVID-19 alters the frequency and functional phenotypes of granulocyte subsets with the emergence of CRTH2 as a disease biomarker.

- 28. COVIDTrach; the outcomes of mechanically ventilated COVID-19 patients undergoing tracheostomy in the UK: Interim Report. COVIDTrach collaborative. *Br J Surg.* 2020 Sep 17. doi: 10.1002/bjs.12020. https://bjssjournals.onlinelibrary.wiley.com/doi/10.1002/bjs.12020 COVIDTrach is a UK multidisciplinary collaborative project that evaluates the outcomes of tracheostomy in patients diagnosed with COVID-19 who are receiving invasive mechanical ventilation. In parallel, data is collected on the use of personal protective equipment (PPE) and rates of COVID-19 infection amongst operators. Between 6th April and 11th May 2020, data was received on 564 tracheostomies from 78 UK NHS hospitals. See URL for full results.
- 29. Predictors of Outcomes of COVID-19 in Patients with Chronic Liver Disease: US Multi-center Study. Kim D, Adeniji N, Latt N, et al. *Clin Gastroenterol Hepatol.* 2020 Sep 17:S1542-3565(20)31288-X. doi: 10.1016/j.cgh.2020.09.027. https://www.cghjournal.org/article/S1542-3565(20)31288-X/fulltext
 - Findings: Of the 978 patients in our cohort, 867 patients (mean age 56.9±14.5 years, 55% male) met inclusion criteria. The overall all-cause mortality was 14.0% (n = 121), and 61.7% (n = 535) had severe COVID-19. Patients presenting with diarrhea or nausea/vomiting were more likely to have severe COVID-19. The liver-specific factors associated with independent risk of higher overall mortality were alcohol-related liver disease, decompensated cirrhosis and hepatocellular carcinoma. Other factors were increasing age, diabetes, hypertension, chronic obstructive pulmonary disease and current smoker. Hispanic ethnicity and decompensated cirrhosis were independently associated with risk for severe COVID-19. The risk factors which predict higher overall mortality among patients with CLD and COVID-19 are ALD, decompensated cirrhosis and HCC. Hispanic ethnicity and decompensated cirrhosis are associated with severe COVID-19. Our results will enable risk stratification and personalization of the management of patients with CLD and COVID-19.
- 30. Relation of Statin Use Prior to Admission to Severity and Recovery Among COVID-19 Inpatients. Daniels LB, Sitapati AM, Zhang J, et al. Am J Cardiol. 2020 Sep 15:S0002-9149(20)30947-4. doi: 10.1016/j.amjcard.2020.09.012. https://www.ajconline.org/article/S0002-9149(20)30947-4/fulltext

Findings: We studied the association between use of statin/ACEi/ARB in the month before hospital admission, with risk of severe outcome, and with time to severe outcome or disease recovery, among patients hospitalized for COVID-19. We performed a retrospective single-

center study of all patients hospitalized at UCSD Health between February 10-June 17, 2020 (n=170 hospitalized for COVID-19, n=5281 COVID-negative controls). Severe disease occurred in 53% of COVID-positive inpatients. Median time from hospitalization to severe disease was 2 days; median time to recovery was 7 days. Statin use prior to admission was associated with reduced risk of severe COVID-19 (adjusted OR 0.29, 95% CI 0.11-0.71, p<0.01) and faster time to recovery among those without severe disease (adjusted HR for recovery 2.69, 95% CI 1.36-5.33, p<0.01). The association between statin use and severe disease was smaller in the COVID-negative cohort. There was potential evidence of faster time to recovery with ARB use. In conclusion, statin use during the 30 days prior to admission for COVID-19 was associated with a lower risk of developing severe COVID-19, and a faster time to recovery among patients without severe disease.

31. Characteristics of a Diverse Cohort of Stroke Patients with SARS-CoV-2 and Outcome by Sex.

Trifan G, Goldenberg FD, Caprio FC, et al. *J Stroke Cerebrovasc Dis.* 2020 Sep 11:105314. doi: 10.1016/j.jstrokecerebrovasdis.2020.105314.

https://www.sciencedirect.com/science/article/pii/S1052305720307321

Findings: The study included 83 patients, 47% of which were Black, 28% Hispanics/Latinos, and 16% whites. Median age was 64 years. Approximately 89% had at least one preexisting vascular risk factor (VRF). When divided by stroke subtype, there were 77% ischemic, 19% intracerebral hemorrhage and 3% subarachnoid hemorrhage. The most common ischemic stroke etiologies were cryptogenic (39%) and cardioembolic (27%). Compared with females, males had higher mortality (38% vs. 13%; p = 0.02) and were less likely to be discharged home (12% vs. 33%; p = 0.04). In this cohort of SARS-CoV-2 stroke patients, most had clinical evidence of coronavirus infection on admission and preexisting VRFs. Severe in-hospital complications and worse outcomes after ischemic strokes were higher in males, than females.

Survivorship & Rehabilitation

32. Short- and Potential Long-term Adverse Health Outcomes of COVID-19: A Rapid Review.

Leung T, Chan A, Chan EW, et al. *Emerg Microbes Infect*. 2020 Sep 17:1-19. doi: 10.1080/22221751.2020.1825914.

https://www.tandfonline.com/doi/full/10.1080/22221751.2020.1825914

Findings: Emerging evidence suggests that COVID-19 adversely affects different systems in the human body. This review summarizes the current evidence on the short-term adverse health outcomes and assesses the risk of potential long-term adverse outcomes of COVID-19. Major adverse outcomes were found to affect different body systems: immune system (including but not limited to Guillain-Barré syndrome and paediatric inflammatory multisystem syndrome), respiratory system (lung fibrosis and pulmonary thromboembolism), cardiovascular system (cardiomyopathy and coagulopathy), neurological system (sensory dysfunction and stroke), as well as cutaneous manifestations, impaired hepatic and renal function. Mental health in patients with COVID-19 was also found to be adversely affected. The burden of caring for COVID-19 survivors is likely to be huge. Therefore, it is important for policy makers to develop comprehensive strategies in providing resources and in the healthcare system. Future

epidemiological studies are needed to further investigate the long-term impact on COVID-19 survivors.

Therapeutics

- 33. Successful awake proning is associated with improved clinical outcomes in patients with COVID-19: single-centre high-dependency unit experience. Hallifax RJ, Porter BM, Elder PJ, et al. BMJ Open Respir Res. 2020 Sep;7(1):e000678. doi: 10.1136/bmjresp-2020-000678. https://bmjopenrespres.bmj.com/content/bmjresp/7/1/e000678.full.pdf Findings: This single-centre retrospective study aimed to assess whether successful awake proning of patients with COVID-19, requiring respiratory support (CPAP) or high-flow nasal oxygen (HFNO) on a respiratory high-dependency unit (HDU), is associated with improved outcomes. HDU care included awake proning by respiratory physiotherapists. Of 565 patients admitted with COVID-19, 71 (12.6%) were managed on the respiratory HDU, with 48 of these (67.6%) requiring respiratory support. Patients managed with CPAP alone 22/48 (45.8%) were significantly less likely to die than patients who required transfer onto HFNO 26/48 (54.2%): CPAP mortality 36.4%; HFNO mortality 69.2%, (p=0.023); however, multivariate analysis demonstrated that increasing age and the inability to awake prone were the only independent predictors of COVID-19 mortality. The mortality of patients with COVID-19 requiring respiratory support is considerable. Data from our cohort managed on HDU show that CPAP and awake proning are possible in a selected population of COVID-19 and may be useful.
- 34. Convalescent plasma treatment of severe COVID-19: a propensity score-matched control study. Liu STH, Lin HM, Baine I, et al. *Nat Med.* 2020 Sep 15. doi: 10.1038/s41591-020-1088-9. https://www.nature.com/articles/s41591-020-1088-9
 Findings: Convalescent plasma, donated by persons who have recovered from COVID-19, is the acellular component of blood that contains antibodies, including those that specifically recognize SARS-CoV-2. This retrospective, propensity score-matched case-control study assessed the effectiveness of convalescent plasma therapy in 39 patients with severe or life-threatening COVID-19 at The Mount Sinai Hospital in New York City. Oxygen requirements on day 14 after transfusion worsened in 17.9% of plasma recipients versus 28.2% of propensity score-matched controls who were hospitalized with COVID-19 (adjusted odds ratio (OR), 0.86; 95% confidence interval (CI), 0.75-0.98; chi-square test P value = 0.025). Survival also improved in plasma recipients (adjusted hazard ratio (HR), 0.34; 95% CI, 0.13-0.89; chi-square test P = 0.027). Convalescent plasma is potentially against COVID-19, but adequately powered, randomized controlled trials are needed.
- 35. Critically Ill Adults with COVID-19 in New Orleans and Care with an Evidence-based Protocol.

 Janz DR, Mackey S, Patel N, et al. Chest. 2020 Sep 14:S0012-3692(20)34493-7. doi:
 10.1016/j.chest.2020.08.2114. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7487861/
 Findings: The initial 147 patients admitted to any ICU and tested positive for SARS-CoV-2 comprised the cohort for this study. In the entire network, exposure to an evidence-based protocol was associated with more ventilator-free days compared with non-protocolized ICUs, including in adjusted analyses. Twenty patients (37%) admitted to protocolized ICUs died

compared with 51 (56%) in non-protocolized ICUs. Among 82 patients admitted to the academic safety net hospital's ICUs, the median number of ventilator-free days was 22 and mortality rate was 39%. Care of critically ill COVID-19 patients with an evidence-based protocol is associated with increased time alive and free of invasive mechanical ventilation. In-hospital survival occurred in the majority of critically ill adults with COVID-19 admitted to an academic safety net hospital's ICUs despite a high rate of co-morbidities.

36. Factors Associated with Good Patient Outcomes Following Convalescent Plasma in COVID-19: A Prospective Phase II Clinical Trial. Ibrahim D, Dulipsingh L, Zapatka L, et al. *Infect Dis Ther*. 2020 Sep 20. doi: 10.1007/s40121-020-00341-2.

https://link.springer.com/article/10.1007/s40121-020-00341-2

Findings: Of the 38 patients included in the analysis, 24 (63%) recovered and were discharged, and 14 (37%) died. Patients who received convalescent plasma early in the disease course (severe illness group) as compared to the patients that received convalescent plasma later in the disease progression (critical illness group) had significantly lower hospital mortality 13% vs 55% and shorter mean hospital length of stay 15.4 vs 33 days. One patient experienced a transient transfusion reaction. No other adverse effects of plasma infusion were observed. Our results suggest that convalescent plasma with adequate anti-SARS-CoV-2 antibody titer is safe and has the potential for positive impact on clinical outcomes including recovery and survival if given to patients early in the course of COVID-19 disease.

- 37. Intravenous methylprednisolone pulse as a treatment for hospitalised severe COVID-19 patients: results from a randomised controlled clinical trial. Edalatifard M, Akhtari M, Salehi M, et al. *Eur Respir J.* 2020 Sep 17:2002808. doi: 10.1183/13993003.02808-2020. https://erj.ersjournals.com/content/early/2020/09/09/13993003.02808-2020
 Findings: Sixty-eight eligible patients underwent randomisation (34 patients in each group) from April 20, till Jun 20, 2020. In the standard care group, six patients received corticosteroids by the attending physician during treatment and excluded from the ITT population. Patients with clinical improvement were higher in the methylprednisolone group than in the standard care group (94·1% versus 57·1%), and the mortality rate was numerically lower in the methylprednisolone group (5·9% versus 42.9%; p <0·001). We demonstrated that patients in the methylprednisolone intervention group had a significantly increased survival time compared with the patients in the standard care group. A total of two patients in each group (5·8% and 7·1% respectively) showed severe adverse events between initiation of treatment and the end of the study. Our results suggested that methylprednisolone pulse could be an efficient therapeutic agent for hospitalised severe COVID-19 patients at the pulmonary phase.
- 38. Treatment of COVID-19 Patients with Prolonged Post-Symptomatic Viral Shedding with Leflunomide -- a Single-Center, Randomized, Controlled Clinical Trial. Wang M, Zhao Y, Hu W, et al. Clin Infect Dis. 2020 Sep 21:ciaa1417. doi: 10.1093/cid/ciaa1417. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1417/5909448

 Findings: A total of 50 COVID-19 patients with prolonged PCR positivity were randomized into 2 groups; 26 were assigned to the leflunomide group, and 24 were assigned to the interferon alone group. Treatment with leflunomide was not associated with a difference from the

interferon alone group in the duration of viral shedding. In addition, the patients given leflunomide did not have a substantially shorter length of hospital stay than patients treated with interferon alone, with median durations of 29.0 (19.3-47.3) days and 33.0 (29.3-42.8) days, respectively. Two leflunomide recipients were unable to complete the full 10-day course of administration due to adverse events.

Transmission / Infection Control

- 39. **Seasonal coronavirus protective immunity is short-lasting.** Edridge AWD, Kaczorowska J, Hoste ACR, et al. *Nat Med.* 2020 Sep 14. doi: 10.1038/s41591-020-1083-1. https://www.nature.com/articles/s41591-020-1083-1
 - Findings: A key unsolved question in the current coronavirus disease 2019 (COVID-19) pandemic is the duration of acquired immunity. Insights from infections with the four seasonal human coronaviruses might reveal common characteristics applicable to all human coronaviruses. We monitored healthy individuals for more than 35 years and determined that reinfection with the same seasonal coronavirus occurred frequently at 12 months after infection.
- 40. Association of Daily Wear of Eyeglasses with Susceptibility to Coronavirus Disease 2019 Infection. Zeng W, Wang X, Li J, et al. JAMA Ophthalmol. September 16, 2020. doi:10.1001/jamaophthalmol.2020.3906 https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2770872
 Findings: In this cohort study of patients hospitalized with COVID-19 in Suizhou, China, the proportion of inpatients with COVID-19 who wore glasses for extended daily periods (>8 h/d) was smaller than that in the general population, suggesting that daily wearers of eyeglasses may be less susceptible to COVID-19.
- 41. Use of antimicrobial mouthwashes (gargling) and nasal sprays by healthcare workers to protect them when treating patients with suspected or confirmed COVID-19 infection. Burton MJ, Clarkson JE, Goulao B, et al. *Cochrane Database Syst Rev.* 2020 Sep 16;9:CD013626. doi: 10.1002/14651858.CD013626.pub2. https://www.cochrane.org/CD013626/ENT what-are-benefits-and-risks-healthcare-workers-using-antimicrobial-mouthwashes-or-nasal-sprays
 Findings: We identified no studies for inclusion in this review. This is not surprising given the relatively recent emergence of COVID-19 infection. It is promising that the question posed in this review is being addressed by two RCTs and a non-randomised study. We are concerned that only one of the ongoing studies specifically states that it will evaluate adverse events and it is not clear if this will include changes in the sense of smell or to the oral and nasal microbiota, and any consequences thereof. Very few interventions have large and dramatic effect sizes. If a positive treatment effect is demonstrated when studies are available for inclusion in this review, it may not be large. In these circumstances in particular, where those receiving the intervention are otherwise fit and well, it may be a challenge to weigh up the benefits against the harms if the latter are of uncertain frequency and severity.

^{**}see two new articles in Basic Science section above **

*see also: Antimicrobial mouthwashes (gargling) and nasal sprays to protect healthcare workers when undertaking aerosol-generating procedures (AGPs) on patients without suspected or confirmed COVID-19 infection. Burton MJ, Clarkson JE, Goulao B, et al. Cochrane Database Syst Rev. 2020 Sep 16;9:CD013628. doi: 10.1002/14651858.CD013628.pub2.

Antimicrobial mouthwashes (gargling) and nasal sprays administered to patients with suspected or confirmed COVID-19 infection to improve patient outcomes and to protect healthcare workers treating them. Burton MJ, Clarkson JE, Goulao B, et al. Cochrane Database Syst Rev. 2020 Sep 16;9:CD013627. doi: 10.1002/14651858.CD013627.pub2.

42. Transmission of SARS-CoV-2: A Review of Viral, Host, and Environmental Factors. Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. *Ann Intern Med.* 2020 Sep 17. doi: 10.7326/M20-5008. https://www.acpjournals.org/doi/10.7326/M20-5008

Findings: This article presents a comprehensive review of the evidence on transmission of this virus. Although several experimental studies have cultured live virus from aerosols and surfaces hours after inoculation, the real-world studies that detect viral RNA in the environment report very low levels, and few have isolated viable virus. Strong evidence from case and cluster reports indicates that respiratory transmission is dominant, with proximity and ventilation being key determinants of transmission risk. In the few cases where direct contact or fomite transmission is presumed, respiratory transmission has not been completely excluded. Infectiousness peaks around a day before symptom onset and declines within a week of symptom onset, and no late linked transmissions (after a patient has had symptoms for about a week) have been documented. The virus has heterogeneous transmission dynamics: Most persons do not transmit virus, whereas some cause many secondary cases in transmission clusters called "super-spreading events." Evidence-based policies and practices should incorporate the accumulating knowledge about transmission of SARS-CoV-2 to help educate the public and slow the spread of this virus.

43. Viable SARS-CoV-2 in the air of a hospital room with COVID-19 patients. Lednicky JA, Lauzardo M, Hugh Fan Z, et al. *Int J Infect Dis.* 2020 Sep 16:S1201-9712(20)30739-6. doi: 10.1016/j.ijid.2020.09.025. https://www.ijidonline.com/article/S1201-9712(20)30739-6/fulltext

Findings: Viable SARS-CoV-2 was isolated from air samples collected 2 to 4.8 m away from the patients. The genome sequence of the SARS-CoV-2 strain isolated from the material collected by the air samplers was identical to that isolated from the newly admitted patient. Estimates of viable viral concentrations ranged from 6 to 74 TCID50 units/L of air. Patients with respiratory manifestations of COVID-19 produce aerosols in the absence of aerosol-generating procedures that contain viable SARS-CoV-2, and these aerosols may serve as a source of transmission of the virus.

44. A Case of Early Re-infection with SARS-CoV-2. Larson D, Brodniak SL, Voegtly LJ, et al. *Clin Infect Dis.* 2020 Sep 19:ciaa1436. doi: 10.1093/cid/ciaa1436. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1436/5908892

A 42-year-old healthy male military healthcare provider presented with cough, subjective fever, and myalgias on 21 March following a workplace COVID-19 exposure and tested positive by SARS-CoV-2 RT-PCR. Physical examination was unrevealing and supportive outpatient management was pursued. Clinical resolution of illness occurred by day 10, and he returned to baseline excellent health for the following 51 days.

45. In-Flight Transmission of Severe Acute Respiratory Syndrome Coronavirus 2. Choi EM, Chu DKW, Cheng PKC, et al. *Emerg Infect Dis.* 2020 Sep 18;26(11). doi: 10.3201/eid2611.203254. https://wwwnc.cdc.gov/eid/article/26/11/20-3254 article

Findings: Four persons with severe acute respiratory syndrome coronavirus 2 infection had traveled on the same flight from Boston, Massachusetts, USA, to Hong Kong, China. Their virus genetic sequences are identical, unique, and belong to a clade not previously identified in Hong Kong, which strongly suggests that the virus can be transmitted during air travel.

See also: <u>Transmission of Severe Acute Respiratory Syndrome Coronavirus 2 During Long Flight.</u> Khanh NC, Thai PQ, Quach HL, et al. *Emerg Infect Dis.* 2020 Sep 18;26(11). doi: 10.3201/eid2611.203299.

- 46. **Droplets and Aerosols generated by singing and the risk of COVID-19 for choirs.** Bahl P, de Silva C, Bhattacharjee S, et al. *Clin Infect Dis.* 2020 Sep 18:ciaa1241. doi: 10.1093/cid/ciaa1241. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1241/5908276
 Findings: Choral singing has become a major risk during COVID-19 pandemic due to high infection rates. Our visualisation and velocimetry results reveal that majority of droplets expelled during singing follow the ambient airflow pattern. These results points toward the possibility of COVID-19 spread by small airborne droplets during singing.
- 47. Cardiopulmonary exercise and the risk of aerosol generation while wearing a surgical mask. Helgeson SA, Taylor BJ, Lim KG, et al. *Chest*. 2020 Sep 18:S0012-3692(20)34508-6. doi: 10.1016/j.chest.2020.09.088. https://www.sciencedirect.com/science/article/pii/S0012369220345086?via%3Dihub Findings: This study suggests that when wearing a type II procedural mask, light exercise is not associated with an increase in particulate generation, but there is a trend to increasing particles with hard exercise. Very hard exercise, similar to what is performed during clinical treadmill stress tests and many workouts performed at gyms, significantly increased particle generation. This is the first study to quantify this particle generation with exercise. The exercise component of most cardiopulmonary rehabilitation classes is generally performed at a light to hard exertion, during which particle generation is negligible. If strenuous exertion is to be performed, then proper room clearance measures would need to be in place before someone else enters the room or should not be performed at all. This study provides valuable information guiding infection control measures for healthcare workers and participants during
- 48. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. Buitrago-Garcia D, Egli-Gany D, Counotte MJ, et al. *PLOS Medicine*. September 22, 2020

cardiopulmonary rehabilitation, interval training, and symptom limited exercise testing.

https://doi.org/10.1371/journal.pmed.1003346

https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1003346

Findings: The findings of this living systematic review suggest that most people who become infected with SARS-CoV-2 will not remain asymptomatic throughout the course of the infection. The contribution of presymptomatic and asymptomatic infections to overall SARS-CoV-2 transmission means that combination prevention measures, with enhanced hand hygiene, masks, testing tracing, and isolation strategies and social distancing, will continue to be needed.

Women & Children

- 49. Antivirals for COVID-19 and Breastfeeding. Anderson PO. Breastfeed Med. 2020 Sep 4. doi: 10.1089/bfm.2020.0268. https://www.liebertpub.com/doi/10.1089/bfm.2020.0268
 Many drugs are being investigated for treatment of COVID-19. The Medical Letter on Drugs and Therapeutics maintains an excellent, periodically updated and well-referenced table of anti-COVID-19 drugs that is free to download. Additional information about ongoing trials can be found at clinicaltrials.gov. This column will review the use in breastfeeding of the most prominent drugs that might be active against the SARS-CoV-2 virus that causes the disease. See URL for list.
- 50. Management of Multisystem Inflammatory Syndrome in Children Associated with COVID-19:

 A Survey from the International Kawasaki Disease Registry. Elias MD, McCrindle BW, Larios G, et al. CJC Open. 2020 Sep 11. doi:10.1016/j.cjco.2020.09.004.

 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7484693/
 Findings: Among the respondents, 56% reported using immunomodulatory treatment for all MIS-C patients, regardless of presentation. Every respondent reported use of intravenous immunoglobulin (IVIG), including 53% administering IVIG in all patients. Steroids were most often used for patients with severe clinical presentation or lack of response to IVIG, and only a minority used steroids in all patients (14%). ASA was frequently used among respondents (91%), including anti-inflammatory and/or anti-platelet dosing. Respondents reported use of prophylactic anticoagulation, especially in patients at higher risk for venous thromboembolism, and therapeutic anticoagulation, particularly for patients with giant coronary artery aneurysms. There is variation in management of MIS-C patients with suboptimal evidence to assess superiority of the various treatments; evidence-based gaps in knowledge should be addressed through worldwide collaboration to optimize treatment strategies.
- 50. Characteristics and Maternal and Birth Outcomes of Hospitalized Pregnant Women with Laboratory-Confirmed COVID-19 COVID-NET, 13 States, March 1—August 22, 2020. Delahoy MJ, Whitaker M, O'Halloran A, et al. MMWR Morb Mortal Wkly Rep. ePub: 16 September 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6938e1
 Findings: Among 598 hospitalized pregnant women with COVID-19, 55% were asymptomatic at admission. Severe illness occurred among symptomatic pregnant women, including intensive care unit admissions (16%), mechanical ventilation (8%), and death (1%). Pregnancy losses occurred for 2% of pregnancies completed during COVID-19-associated hospitalizations and were experienced by both symptomatic and asymptomatic women. Pregnant women and

health care providers should be aware of potential risks for severe COVID-19, including adverse pregnancy outcomes. Identifying COVID-19 during birth hospitalizations is important to guide preventive measures to protect pregnant women, parents, newborns, other patients, and hospital personnel.

- 51. SARS-CoV-2 Infection Among Hospitalized Pregnant Women: Reasons for Admission and Pregnancy Characteristics Eight U.S. Health Care Centers, March 1—May 30, 2020.

 Panagiotakopoulos L, Myers TR, Gee J, et al. MMWR Morb Mortal Wkly Rep. ePub: 16
 September 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6938e2
 Findings: Prevalences of pre-pregnancy obesity and gestational diabetes were higher among pregnant women hospitalized for COVID-19—related illness (e.g., worsening respiratory status) than among those admitted for pregnancy-related treatment or procedures (e.g., delivery) and found to have COVID-19. Intensive care was required for 30% (13 of 43) of pregnant women admitted for COVID-19, and one pregnant woman died from COVID-19. Antenatal counseling emphasizing preventive measures, including use of masks, frequent hand washing, and social distancing, might help prevent COVID-19 among pregnant women, especially those with prepregnancy obesity and gestational diabetes.
- 52. Infant Outcomes Following Maternal Infection with SARS-CoV-2: First Report from the PRIORITY Study. Flaherman VJ, Afshar Y, Boscardin J, et al. Clin Infect Dis. 2020 Sep 18:ciaa1411. doi: 10.1093/cid/ciaa1411. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1411/5908705
 Findings: Infant outcomes after maternal SARS-CoV-2 infection are not well-described. In a prospective U.S. registry of 263 infants born to mothers testing positive or negative for SARS-CoV-2, SARS-CoV-2 status was not associated with birth weight, difficulty breathing, apnea or upper or lower respiratory infection through 8 weeks of age.
- 53. Maternal, Perinatal and Neonatal Outcomes with COVID-19: A Multicenter Study of 242
 Pregnancies and Their 248 Infant Newborns during Their First Month of Life. Marín Gabriel
 MA, Reyne Vergeli M, Caserío Carbonero S, et al. Pediatr Infect Dis J. 2020 Sep 11. doi:
 10.1097/INF.000000000002902.
 https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=ovft&AN=0000
 6454-900000000-96042&PDF=y

Findings: Caesarean sections were performed on 63 (26%) women. The initial clinical symptoms were coughing (33%) and fever (29.7%). Mothers hospitalized due to COVID-19 pathology had a higher risk of ending their pregnancy via C-section. Newborns whose mothers had been admitted due to their COVID-19 infection had a higher risk of premature delivery. We admitted 115 (46.3%) newborn infants to the neonatal unit, of those, 87 (75.6%) were only admitted due to organizational circumstances. No infants died and no vertical or horizontal transmission was detected. Regarding type of feeding, 41.7% of the newborns received exclusive breast-feeding at discharge and 40.4% at 1 month. We did not detect COVID-19 transmission during delivery or throughout the first month of life in the newborns included in our study. Exclusive breast-feeding rates at discharge and at 1 month of age were lower than expected.

GUIDELINES & CONSENSUS STATEMENTS

<u>Critical Care Guidance for Tracheostomy Care during the COVID-19 Pandemic: A Global,</u>
<u>Multidisciplinary Approach.</u> Pandian V, Morris LL, Brodsky MB, et al. *Am J Crit Care*. 2020 Sep 15:e1-e12. doi: 10.4037/ajcc2020561.

<u>Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients</u> <u>with COVID-19</u>. UPDATE (9/15/20): Version 3.2.0 has been released and contains an additional recommendation on remdesivir.

COVID-19 Interim Guidance: Return to Sports. American Academy of Pediatrics.

<u>Update Alert 4: Risks and Impact of Angiotensin-Converting Enzyme Inhibitors or Angiotensin-Receptor Blockers on SARS-CoV-2 Infection in Adults.</u> Mackey K, Kansagara D, Vela K. *Ann Intern Med.* 2020 Sep 22. doi: 10.7326/L20-1177.

A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. PIMS-TS National Consensus Management Study Group. *Lancet Child Adolesc Health*. 2020 Sep 18:S2352-4642(20)30304-7. doi: 10.1016/S2352-4642(20)30304-7.

Comparison of published guidelines for management of coagulopathy and thrombosis in critically ill patients with COVID 19: implications for clinical practice and future investigations. Flaczyk A, Rosovsky RP, Reed CT, et al. *Crit Care*. 2020 Sep 16;24(1):559. doi: 10.1186/s13054-020-03273-y.

FDA / CDC / NIH / WHO Updates

CDC – <u>Updated guidance on spread of COVID-19 to include aerosols on Friday Sept. 18, then removed</u> on Monday Sept. 21.

CDC - Overview of Testing for SARS-CoV-2 (COVID-19). Change made on September 18, 2020, "Due to the significance of asymptomatic and pre-symptomatic transmission, this guidance further reinforces the need to test asymptomatic persons, including close contacts of a person with documented SARS-CoV-2 infection."

FDA – <u>EUA given to Roche Molecular Systems for the rapid version of its Cobas SARS-CoV-2 & Influenza A/B test that can deliver results within 20 minutes</u>

Commentary & Press Releases

Fear of Coronavirus Disease 2019-An Emerging Cardiac Risk.

From doctors as patients: a manifesto for tackling persisting symptoms of covid-19.

Lack of Antigen Test Reporting Leaves Country 'Blind to the Pandemic'

<u>Lilly announces proof of concept data for neutralizing antibody LY-CoV555 in the COVID-19</u> <u>outpatient setting</u>

<u>Rigel Announces NIH/NHLBI-Sponsored Trial of Fostamatinib in Hospitalized COVID-19 Patients in</u>
Collaboration with Inova

<u>Suboptimal US Response to COVID-19 despite Robust Capabilities and Resources.</u> *JAMA*. September 16, 2020. doi:10.1001/jama.2020.17395

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