

COVID-19 Resource Desk

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New Research

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

Basic Science / Virology / Pre-clinical

- 1. Favipiravir at high doses has potent antiviral activity in SARS-CoV-2-infected hamsters, whereas hydroxychloroquine lacks activity.** Kaptein SJF, Jacobs S, Langendries L, et al. *Proc Natl Acad Sci U S A*. 2020 Oct 9:202014441. doi: 10.1073/pnas.2014441117.
<https://www.pnas.org/content/early/2020/10/08/2014441117>
Findings: We established an infection model in Syrian hamsters to evaluate the efficacy of small molecules on both infection and transmission. Treatment of SARS-CoV-2-infected hamsters with a low dose of favipiravir or hydroxychloroquine with(out) azithromycin resulted in, respectively, a mild or no reduction in virus levels. However, high doses of favipiravir significantly reduced infectious virus titers in the lungs and markedly improved lung histopathology. Moreover, a high dose of favipiravir decreased virus transmission by direct contact, whereas hydroxychloroquine failed as prophylaxis. Pharmacokinetic modeling of hydroxychloroquine suggested that the total lung exposure to the drug did not cause the failure. Our data on hydroxychloroquine (together with previous reports in macaques and ferrets) thus provide no scientific basis for the use of this drug in COVID-19 patients. In contrast, the results with favipiravir demonstrate that an antiviral drug at nontoxic doses exhibits a marked protective effect against SARS-CoV-2 in a small animal model. Clinical studies are required to assess whether a similar antiviral effect is achievable in humans without toxic effects.
- 2. REGN-COV2 antibodies prevent and treat SARS-CoV-2 infection in rhesus macaques and hamsters.** Baum A, Ajithdoss D, Copin R, et al. *Science*. 2020 Oct 9:eabe2402. doi: 10.1126/science.abe2402.
<https://science.sciencemag.org/content/early/2020/10/08/science.abe2402>
Findings: We previously described REGN-COV2, a cocktail of two potent neutralizing antibodies (REGN10987+REGN10933) targeting non-overlapping epitopes on the SARS-CoV-2 spike protein. In this report, we evaluate the in vivo efficacy of this antibody cocktail in both rhesus macaques, which may model mild disease, and golden hamsters, which may model more severe disease. We demonstrate that REGN-COV-2 can greatly reduce virus load in lower and upper airways and decrease virus induced pathological sequelae when administered prophylactically

or therapeutically in rhesus macaques. Similarly, administration in hamsters limits weight loss and decreases lung titers and evidence of pneumonia in the lungs. Our results provide evidence of the therapeutic potential of this antibody cocktail.

Clinical Syndrome

3. **Microcirculatory, Endothelial and Inflammatory Responses in Critically Ill Patients with COVID-19 are Distinct from those Seen in Septic Shock: A Case Control Study.** Hutchings SD, Watchorn J, Trovato F, et al. *Shock*. 2020 Oct 5. doi: 10.1097/SHK.0000000000001672. [https://journals.lww.com/shockjournal/Abstract/9000/Microcirculatory, Endothelial and Inflammatory.97367.aspx](https://journals.lww.com/shockjournal/Abstract/9000/Microcirculatory,_Endothelial_and_Inflammatory.97367.aspx)
Findings: Critically ill patients with COVID-19 infection frequently exhibit a hyperinflammatory response and develop organ failures, however the underlying mechanisms are unclear. We investigated the microcirculatory, endothelial and inflammatory responses in critically ill COVID-19 patients and compared them to a group of patients with septic shock in a prospective observational case control study. 30 critically ill patients with COVID-19 were compared to 33 patients with septic shock. COVID-19 patients had significantly less vasoactive drug requirement and lower plasma lactate than those with septic shock. Microcirculatory flow was significantly worse in septic patients than those with COVID-19. IL-6 was higher in patients with septic shock than COVID-19. IL-6 levels in COVID 19 patients were not elevated compared to healthy controls except on the day of ICU admission. Syndecan-1 levels were not different between the 2 pathological groups. Compared to patients with undifferentiated septic shock an overt shock state with tissue hypoperfusion does not appear typical of COVID-19 infection. There was no evidence of significant sublingual microcirculatory impairment, widespread endothelial injury or marked inflammatory cytokine release in this group of critically ill COVID-19 patients.
4. **A Prospective Study of Neurologic Disorders in Hospitalized COVID-19 Patients in New York City.** Frontera JA, Sabaia S, Lalchan R, et al. *Neurology*. 2020 Oct 5:10.1212/WNL.0000000000010979. doi: 10.1212/WNL.0000000000010979. <https://n.neurology.org/content/neurology/early/2020/10/05/WNL.0000000000010979.full.pdf>
Findings: Of 4,491 COVID-19 patients hospitalized during the study timeframe, 13.5% developed a new neurologic disorder in a median of 2 days from COVID-19 symptom onset. The most common diagnoses were: toxic/metabolic encephalopathy (6.8%), seizure (1.6%), stroke (1.9%), and hypoxic/ischemic injury (1.4%). No patient had meningitis/encephalitis, or myelopathy/myelitis referable to SARS-CoV-2 infection and 18/18 CSF specimens were RT-PCR negative for SARS-CoV-2. Patients with neurologic disorders were more often older, male, white, hypertensive, diabetic, intubated, and had higher sequential organ failure assessment (SOFA) scores. Neurologic disorders were detected in 13.5% of COVID-19 patients and were associated with increased risk of in-hospital mortality and decreased likelihood of discharge home. Many observed neurologic disorders may be sequelae of severe systemic illness.

5. **Atypical clinical presentation of COVID-19 infection in residents of a long-term care facility.** Blain H, Rolland Y, Benetos A, et al. *Eur Geriatr Med.* 2020 Oct 6:1-4. doi: 10.1007/s41999-020-00352-9. <https://link.springer.com/article/10.1007/s41999-020-00352-9>
Findings: Thirty-eight of the 79 residents (48.1%) tested positive for SARS-CoV-2. Respiratory symptoms were preceded by diarrhea (26.3%), a fall (18.4%), fluctuating temperature with hypothermia (34.2%) and delirium in one resident. Respiratory symptoms, including cough and oxygen desaturation, appeared after those initial symptoms or as the first sign in 36.8% and 52.2%, respectively. At any time of the disease, fever was observed in 65.8%. Twelve deaths occurred among the COVID-19 residents. Among the 41 residents negative for SARS-CoV-2, symptoms included cough (21.9%), diarrhea (7.3%), fever (21.9%), hypothermia (9.7%), and transient hypoxemia (9.8%). The rapid dissemination of the COVID-19 infection may be explained by the delay in the diagnosis of the first cases due to atypical presentation.

6. **Neuroanatomical substrates of generalized brain dysfunction in COVID-19.** Newcombe VFJ, Spindler LRB, Das T, et al. *Intensive Care Med.* 2020 Oct 9:1-3. doi: 10.1007/s00134-020-06241-w. <https://link.springer.com/article/10.1007/s00134-020-06241-w>
Findings: We report MRI findings in six patients with severe COVID-19-related respiratory failure, imaged 19 days (range 16–26) post admission, using conventional MRI and diffusion tensor imaging. The scans were performed for clinical reasons while the patients were in the intensive care unit with data prospectively collected. Indications included: persistent unresponsiveness after washout of sedative agents; severe delirium; or generalized myoclonus. Three patients had small acute ischemic lesions in the frontal deep white matter and two of these also had subarachnoid, intraventricular, or small parenchymal hemorrhage. However, none of the patients had abnormalities on conventional MRI that explained their clinical presentation or indicated hypoxic-ischemic injury.

7. **Lung Histopathology in COVID-19 as Compared to SARS and H1N1 Influenza: A Systematic Review.** Hariri LP, North CM, Shih AR, et al. *Chest.* 2020 Oct 7:S0012-3692(20)34868-6. doi: 10.1016/j.chest.2020.09.259. [https://journal.chestnet.org/article/S0012-3692\(20\)34868-6/fulltext](https://journal.chestnet.org/article/S0012-3692(20)34868-6/fulltext)
Findings: In COVID-19, acute phase diffuse alveolar damage (DAD) was reported in 88% of patients, which was similar to the proportion of cases with DAD in both H1N1 (90%) and SARS (98%). Pulmonary microthrombi were reported in 57% of COVID-19 and 58% of SARS patients, as compared to 24% of H1N1 influenza patients. DAD, the histologic correlate of ARDS, is the predominant histopathologic pattern identified in lung pathology from patients with COVID-19, H1N1 influenza and SARS. Microthrombi were reported more frequently in both patients with COVID-19 and SARS as compared to H1N1 influenza. Future work is needed to validate this histopathologic finding and, if confirmed, elucidate the mechanistic underpinnings and characterize any associations with clinically important outcomes.

8. **Takotsubo Syndrome in Coronavirus Disease 2019.** Templin C, Manka R, Cammann VL, et al. *Am J Cardiol.* 2020 Oct 9:S0002-9149(20)31071-7. doi: 10.1016/j.amjcard.2020.10.005. [https://www.ajconline.org/article/S0002-9149\(20\)31071-7/fulltext](https://www.ajconline.org/article/S0002-9149(20)31071-7/fulltext)

Findings: Around one-fifth of patients with coronavirus disease 2019 (COVID-19) show evidence of acute myocardial injury. The severe inflammatory response that occurs in COVID-19 may work in concert with the exaggerated sympathetic stimulation of TTS to activate similar pathways, resulting in severe microcirculatory dysfunction, global/regional myocardial edema, and decompensated acute heart failure. We hypothesize the coronary microcirculatory disturbances resulting from the combination of COVID-19+TTS could trigger a sudden calcium influx, culminating in contraction band necrosis. Therefore, patients with a dual diagnosis of TTS and COVID are at increased risk of adverse events.

9. **COVID-19 in older adults: a series of 76 patients 85 years old and above with COVID-19.**

Vrillon A, Hourregue C, Azuar J, et al. *J Am Geriatr Soc.* 2020 Oct 12. doi: 10.1111/jgs.16894. <https://onlinelibrary.wiley.com/doi/10.1111/jgs.16894>

Findings: From March 14th to April 9th, 76 patients (median age: 90; women: 55.3%) were admitted for confirmed COVID-19. 64.5% of patients presented with 3 or more comorbidities. Most common symptoms were asthenia (76.3%), fever (75.0%), confusion and delirium (71.1%). Inaugural fall was reported in 25.0% of cases and digestive symptoms in 22.4%. COVID-19 was severe in 51.3% of cases, moderate in 32.9% and mild in 15.8%. Complications included acute respiratory syndrome (28.9%), cardiac decompensation (14.5%) and hypotensive shock (9.0%). Fatality at 21 days was 28.9%, after a median course of disease of 13 (8-17) days. Males were overrepresented in non-survivors (68.2%). In survivors, median length of stay was 12 (9-19.5) days. Independent predictive factors of death were CRP level at admission and lymphocytes count at nadir. Specific clinical features, multi-organ injury and high case fatality rate are observed in older adults with COVID-19.

Diagnosics & Screening

10. **The Role of Imaging in the Management of Suspected or Known COVID-19 Pneumonia: A Multidisciplinary Perspective.** Roshkovan L, Chatterjee N, Galperin-Aizenberg M, et al. *Ann Am Thorac Soc.* 2020 Oct 6. doi: 10.1513/AnnalsATS.202006-600CME.

<https://www.atsjournals.org/doi/pdf/10.1513/AnnalsATS.202006-600CME>

Findings: Imaging plays a central role in the management of patients with known or suspected COVID-19 pneumonia. COVID-19 pneumonia has a suggestive appearance on chest radiograph, chest ultrasound, and CT and the use of imaging is contingent on the clinical question being asked, prevalence of the virus in the patient population, patient risk factors and health care resources. The specific imaging aspects of COVID-19 pneumonia are only beginning to emerge, and our current understanding is rapidly evolving with increasing medical experience in this pandemic. CT reporting guidelines have been suggested to assist clinical decision-making though the accuracy and utility of these reporting criteria have yet to be established.

11. **Detection of SARS-CoV-2 RNA by multiplex RT-qPCR.** Kudo E, Israelow B, Vogels CBF, et al. *PLoS Biol.* 2020 Oct 7;18(10):e3000867. doi: 10.1371/journal.pbio.3000867.

<https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3000867>

Findings: The current quantitative reverse transcription PCR (RT-qPCR) assay recommended for SARS-CoV-2 testing in the United States requires analysis of 3 genomic targets per sample: 2

viral and 1 host. To simplify testing and reduce the volume of required reagents, we devised a multiplex RT-qPCR assay to detect SARS-CoV-2 in a single reaction. We used existing N1, N2, and RP primer and probe sets by the Centers for Disease Control and Prevention but substituted fluorophores to allow multiplexing of the assay. The cycle threshold (Ct) values of our multiplex RT-qPCR were comparable to those obtained by the single assay adapted for research purposes. Low copy numbers (≥ 500 copies/reaction) of SARS-CoV-2 RNA were consistently detected by the multiplex RT-qPCR. Our novel multiplex RT-qPCR improves upon current single diagnostics by saving reagents, costs, time, and labor.

- 12. Clinical evaluation of BD Veritor SARS-CoV-2 point-of-care test performance compared to PCR-based testing and versus the Sofia 2 SARS Antigen point-of-care test.** Young S, Taylor SN, Cammarata CL, et al. *J Clin Microbiol*. 2020 Oct 6;JCM.02338-20. doi: 10.1128/JCM.02338-20. <https://jcm.asm.org/content/jcm/early/2020/10/05/JCM.02338-20.full.pdf>
Findings: Veritor met FDA-EUA acceptance criteria for SARS-CoV-2 antigen testing for the 0-5 and 0-6 DSO ranges. Veritor and Sofia 2 showed a high degree of agreement for SARS-CoV-2 detection. The Veritor test allows for more rapid COVID-19 testing utilizing easy-to-collect nasal swabs but demonstrated less than 100% PPA compared to PCR.
- 13. Clinical impact of molecular point-of-care testing for suspected COVID-19 in hospital (COV-19POC): a prospective, interventional, non-randomised, controlled study.** Clark T, Brendish NJ, Poole S, et al. *Lancet Respir Med* 2020 Oct 8. DOI:[https://doi.org/10.1016/S2213-2600\(20\)30454-9](https://doi.org/10.1016/S2213-2600(20)30454-9) [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(20\)30454-9/fulltext](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(20)30454-9/fulltext)
Findings: 499 patients were recruited to the point-of-care testing group and tested by the QIAstat-Dx Respiratory SARS-CoV-2 Panel. 555 contemporaneously identified patients were included in the control group and tested by laboratory PCR. The two groups were similar with regard to the distribution of sex, age, and ethnicity. 197 (39%) patients in the point-of-care testing group and 155 (28%) in the control group tested positive for COVID-19. Median time to results was 1.7 h in the point-of-care testing group and 21.3 h in the control group (difference 19.6 h). Point-of-care testing is associated with large reductions in time to results and could lead to improvements in infection control measures and patient flow compared with centralised laboratory PCR testing.
- 14. Rapid, sensitive and specific SARS coronavirus-2 detection: a multi-center comparison between standard qRT-PCR and CRISPR based DETECTR.** Brandsma E, Verhagen HJMP, van de Laar TJW, et al. *J Infect Dis*. 2020 Oct 10;jiaa641. doi: 10.1093/infdis/jiaa641. <https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa641/5920647>
Findings: Here we compare DETECTR with qRT-PCR to diagnose COVID-19 on 378 patient samples. Patient sample dilution assays suggest a higher analytical sensitivity of DETECTR compared to qRT-PCR, however, this was not confirmed in this large patient cohort, where we report 95% reproducibility between the two tests. These data showed that both techniques are equally sensitive in detecting SARS-CoV-2 providing additional value of DETECTR to the currently used qRT-PCR platforms. For DETECTR, different gRNAs can be used simultaneously to obviate negative results due to mutations in N-gene. Lateral flow strips, suitable as a point of

care test, showed a 100% correlation to the high-throughput DETECTR assay. Importantly, DETECTR was 100% specific for SARS-CoV-2 relative to other human coronaviruses. As there is no need for specialized equipment, DETECTR could be rapidly implemented as a complementary technically independent approach to qRT-PCR thereby increasing the testing capacity of medical microbiological laboratories and relieving the existent PCR-platforms for routine non-SARS-CoV-2 diagnostic testing.

15. **Targeted Rapid Testing for SARS-CoV-2 in the Emergency Department is Associated with Large Reductions in Uninfected Patient Exposure Time.** Hinson JS, Rothman RE, Carroll K, et al. *J Hosp Infect.* 2020 Oct 7:S0195-6701(20)30460-6. doi: 10.1016/j.jhin.2020.09.035.

[https://www.journalofhospitalinfection.com/article/S0195-6701\(20\)30460-6/fulltext](https://www.journalofhospitalinfection.com/article/S0195-6701(20)30460-6/fulltext)

Findings: We performed a retrospective cohort analysis to measure the effect of targeted rapid molecular testing for SARS-CoV-2 on these outcomes. In comparison to standard-platform testing, rapid testing was associated with a 65.6% reduction (12.6 hours) in median time to removal from isolation cohort for patients with negative diagnostic results. This translated to an increase in COVID-19 treatment capacity of 3,028 bed hours and 7,500 less patient interactions that required consumption of personal protective equipment per week.

Epidemiology & Public Health

16. **Prevalence and outcome of COVID-19 infection in cancer patients: a national Veterans Affairs study.** Fillmore NR, La J, Szalat RE, et al. *J Natl Cancer Inst.* 2020 Oct 8:djaa159. doi: 10.1093/jnci/djaa159. <https://academic.oup.com/jnci/advance-article/doi/10.1093/jnci/djaa159/5919590>

Findings: Of 22,914 cancer patients tested for COVID-19, 1794 (7.8%) were positive. The prevalence of COVID-19 was similar across age. Higher prevalence was observed in African-American (AA) (15.0%) compared to White (5.5%) and in patients with hematologic malignancy compared to those with solid tumors (10.9% vs 7.8%). The COVID-19 attributable mortality was 10.9%. Higher attributable mortality rates were observed in older patients, those with higher Charlson comorbidity score, and in certain cancer types. Recent (<6 months) or past treatment did not influence attributable mortality. Importantly, AA patients had 3.5-fold higher COVID-19 attributable hospitalization, however had similar attributable mortality as White patients. Pre-existence of cancer affects both susceptibility to COVID-19 infection and eventual outcome. The overall COVID-19 attributable mortality in cancer patients is affected by age, comorbidity and specific cancer types, however, race or recent treatment including immunotherapy does not impact outcome.

17. **Case Series of Multisystem Inflammatory Syndrome in Adults Associated with SARS-CoV-2 Infection - United Kingdom and United States, March-August 2020.** Morris SB, Schwartz NG, Patel P, et al. *MMWR Morb Mortal Wkly Rep.* 2020 Oct 9;69(40):1450-1456. doi: 10.15585/mmwr.mm6940e1. <https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e1.htm>

Findings: During the course of the COVID-19 pandemic, reports of a new multisystem inflammatory syndrome in children (MIS-C) have been increasing in Europe and the United States. Since June 2020, several case reports have described a similar syndrome in adults; this

review describes in detail nine patients reported to CDC, seven from published case reports, and summarizes the findings in 11 patients described in three case series in peer-reviewed journals. These 27 patients had cardiovascular, gastrointestinal, dermatologic, and neurologic symptoms without severe respiratory illness and concurrently received positive test results for SARS-CoV-2, the virus that causes COVID-19, by PCR or antibody assays indicating recent infection. Reports of these patients highlight the recognition of an illness referred to here as multisystem inflammatory syndrome in adults (MIS-A), the heterogeneity of clinical signs and symptoms, and the role for antibody testing in identifying similar cases among adults. These patients might not have positive SARS-CoV-2 PCR or antigen test results, and antibody testing might be needed to confirm previous SARS-CoV-2 infection. Because of the temporal association between MIS-A and SARS-CoV-2 infections, interventions that prevent COVID-19 might prevent MIS-A. Further research is needed to understand the pathogenesis and long-term effects of this newly described condition.

18. Deep phenotyping of 34,128 adult patients hospitalised with COVID-19 in an international network study. Burn E, You SC, Sena AG, et al. *Nat Commun.* 2020 Oct 6;11(1):5009. doi:

10.1038/s41467-020-18849-z. <https://www.nature.com/articles/s41467-020-18849-z>

Findings: Here, we describe the characteristics of adults hospitalised with COVID-19 and compare them with influenza patients. We include 34,128 (US: 8362, South Korea: 7341, Spain: 18,425) COVID-19 patients, summarising between 4811 and 11,643 unique aggregate characteristics. COVID-19 patients have been majority male in the US and Spain, but predominantly female in South Korea. Age profiles vary across data sources. Compared to 84,585 individuals hospitalised with influenza in 2014-19, COVID-19 patients have more typically been male, younger, and with fewer comorbidities and lower medication use. While protecting groups vulnerable to influenza is likely a useful starting point in the response to COVID-19, strategies will likely need to be broadened to reflect the particular characteristics of individuals being hospitalised with COVID-19.

19. Influenza Vaccination to Reduce Cardiovascular Morbidity and Mortality in Patients With COVID-19: JACC State-of-the-Art Review. Behrouzi B, Araujo Campoverde MV, Liang K, et al. *J Am Coll Cardiol.* 2020 Oct 13;76(15):1777-1794. doi: 10.1016/j.jacc.2020.08.028.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7535809/>

Findings: The cardiac complications of COVID-19 are “approximately commensurate with SARS and influenza analogs”. There are rigorous epidemiological data linking influenza infection with subsequent cardiovascular complications and several ongoing investigations of the potential risk reduction derived from standard and innovative influenza vaccine strategies. Three large, ongoing influenza vaccine CVOTs have an opportunity to contribute further to our understanding of the underlying comorbidities in these patients that may be driving morbidity and mortality associated with COVID-19 infection. These cohorts may also be an opportunity to explore novel infection prevention therapies beyond influenza vaccination in patients who have already volunteered to participate in a respiratory virus vaccine cardiovascular outcome study. While developing new vaccines, we will also learn soon whether influenza vaccination is an effective, low-cost, widely available therapy that reduces cardiovascular risk, which may further help prevent fatal and nonfatal cardiovascular complications of COVID-19

20. **Excess Deaths from COVID-19 and Other Causes, March-July 2020.** Woolf SH, Chapman DA, Sabo RT, et al. *JAMA*. October 12, 2020. doi:10.1001/jama.2020.19545 <https://jamanetwork.com/journals/jama/fullarticle/2771761?resultClick=1>

Findings: Between March 1 and August 1, 2020, 1,336,561 deaths occurred in the US, a 20% increase over expected deaths. The 10 states with the highest per capita rate of excess deaths were New York, New Jersey, Massachusetts, Louisiana, Arizona, Mississippi, Maryland, Delaware, Rhode Island, and Michigan. COVID-19 was a documented cause of only 67% of these excess deaths. Some states had greater difficulty than others in containing community spread, causing protracted elevations in excess deaths that extended into the summer. US deaths attributed to some noninfectious causes increased during COVID-19 surges. Excess deaths attributed to causes other than COVID-19 could reflect deaths from unrecognized or undocumented infection with severe acute respiratory syndrome coronavirus 2 or deaths among uninfected patients resulting from disruptions produced by the pandemic.

*see also **COVID-19 and Excess All-Cause Mortality in the US and 18 Comparison Countries.** *JAMA*. October 12, 2020. doi:10.1001/jama.2020.20717

Compared with other countries, the US experienced high COVID-19–associated mortality and excess all-cause mortality into September 2020. After the first peak in early spring, US death rates from COVID-19 and from all causes remained higher than even countries with high COVID-19 mortality.

21. **The household secondary attack rate of SARS-CoV-2: A rapid review.** Fung HF, Martinez L, Alarid-Escudero F, et al. *Clin Infect Dis*. 2020 Oct 12:ciaa1558. doi: 10.1093/cid/ciaa1558. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1558/5921151>
- Findings: The overall pooled random-effects estimate of the household SAR was 17.1%. In study-level, random-effects meta-regressions stratified by testing frequency (1 test, 2 tests, >2 tests), SAR estimates were 9.2%, 17.5%, and 21.3%, respectively. Household SAR tended to be higher among older adult contacts and among contacts of symptomatic cases. These findings suggest that SAR reported using a single follow-up test may be underestimated and that testing household contacts of COVID-19 cases on multiple occasions may increase the yield for identifying secondary cases.

Laboratory Results

22. **Antibody dynamics to SARS-CoV-2 in asymptomatic COVID-19 infections.** Lei Q, Li Y, Hou HY, et al. *Allergy*. 2020 Oct 10. doi:10.1111/all.14622.

<https://onlinelibrary.wiley.com/doi/epdf/10.1111/all.14622>

Findings: A combination test of NAT and serological testing for IgM antibody with discovered 55.5% of the total of 63 asymptomatic infections, which significantly raises the detection sensitivity when compared with the NAT alone (19%). Serum proteome microarray analysis demonstrated that asymptomatics mainly produced IgM and IgG antibodies against S1 and N proteins out of 20 proteins of SARS-CoV-2. IgM responses, which evolved in asymptomatic individuals as early as the seventh day after exposure, peaked on days from 17d to 25d, and

then disappeared in two months, might be used as an early diagnostic biomarker. 11.8% (6/51) mild patients and 38.1% (24/63) asymptomatic individuals did not produce neutralizing antibody. Neutralizing antibody in asymptomatics gradually vanished in two months. Our findings might have important implications for the definition of asymptomatic COVID-19 infections, diagnosis, serological survey, public health and immunization strategies.

23. **Persistence of serum and saliva antibody responses to SARS-CoV-2 spike antigens in COVID-19 patients.** Isho B, Abe KT, Zuo M, et al. *Sci Immunol*. 2020 Oct 8;5(52):eabe5511. doi: 10.1126/sciimmunol.abe5511. <https://immunology.sciencemag.org/content/5/52/eabe5511>
Findings: While the antibody response to SARS-CoV-2 has been extensively studied in blood, relatively little is known about the antibody response in saliva and its relationship to systemic antibody levels. Here, we profiled by enzyme-linked immunosorbent assays (ELISAs) IgG, IgA and IgM responses to the SARS-CoV-2 spike protein (full length trimer) and its receptor-binding domain (RBD) in serum and saliva of acute and convalescent patients with laboratory-diagnosed COVID-19 ranging from 3-115 days post-symptom onset (PSO), compared to negative controls. Anti-SARS-CoV-2 antibody responses were readily detected in serum and saliva, with peak IgG levels attained by 16-30 days PSO. Longitudinal analysis revealed that anti-SARS-CoV-2 IgA and IgM antibodies rapidly decayed, while IgG antibodies remained relatively stable up to 105 days PSO in both biofluids. Lastly, IgG, IgM and to a lesser extent IgA responses to spike and RBD in the serum positively correlated with matched saliva samples. This study confirms that serum and saliva IgG antibodies to SARS-CoV-2 are maintained in the majority of COVID-19 patients for at least 3 months PSO. IgG responses in saliva may serve as a surrogate measure of systemic immunity to SARS-CoV-2 based on their correlation with serum IgG responses.
*see also: **Persistence and decay of human antibody responses to the receptor binding domain of SARS-CoV-2 spike protein in COVID-19 patients.** Iyer AS, Jones FK, Nodoushani A, et al. *Sci Immunol*. 2020 Oct 8;5(52):eabe0367. doi: 10.1126/sciimmunol.abe0367.

Prognosis

24. **Machine learning based early warning system enables accurate mortality risk prediction for COVID-19.** Gao Y, Cai GY, Fang W, et al. *Nat Commun*. 2020 Oct 6;11(1):5033. doi: 10.1038/s41467-020-18684-2. <https://www.nature.com/articles/s41467-020-18684-2>
Findings: Here, we present a mortality risk prediction model for COVID-19 (MRPMC) that uses patients' clinical data on admission to stratify patients by mortality risk, which enables prediction of physiological deterioration and death up to 20 days in advance. We validate MRPMC in an internal validation cohort and two external validation cohorts, where it achieves an AUC of 0.9621, and 0.9246, respectively. This model enables expeditious and accurate mortality risk stratification of patients with COVID-19, and potentially facilitates more responsive health systems that are conducive to high risk COVID-19 patients.
25. **Severity of respiratory failure at admission and in-hospital mortality in patients with COVID-19: a prospective observational multicentre study.** Santus P, Radovanovic D, Saderi L, et al.

BMJ Open. 2020 Oct 10;10(10):e043651. doi: 10.1136/bmjopen-2020-043651.

<https://bmjopen.bmj.com/content/10/10/e043651>

Findings: 412 patients were enrolled (280 males, 68%). Median age was 66 years with a PaO₂/FiO₂ at admission of 262 mm Hg. 50.2% had a cardiovascular disease. Prevalence of mild, moderate and severe hARF was 24.4%, 21.9% and 15.5%, respectively. In-hospital mortality proportionally increased with increasing impairment of gas exchange. The only independent risk factors for mortality were age ≥65 years, PaO₂/FiO₂ ratio ≤200 mm Hg and respiratory failure at admission. A moderate-to-severe impairment in PaO₂/FiO₂ was independently associated with a threefold increase in risk of in-hospital mortality. Severity of respiratory failure is useful to identify patients at higher risk of mortality.

26. **Obesity and the Risk of Intubation or Death in Patients with Coronavirus Disease 2019.** Frank RC, Mendez SR, Stevenson EK, et al. *Crit Care Med*. 2020 Nov;48(11):e1097-e1101. doi: 10.1097/CCM.0000000000004553.

<https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=ovft&AN=00003246-202011000-00038&PDF=y>

Findings: A total of 305 patients were included in this study. We stratified patients by body mass index category: < 25 kg/m (54 patients, 18%), ≥ 25 kg/m to < 30 kg/m (124 patients, 41%), ≥ 30 kg/m to < 35 kg/m (58 patients, 19%), and ≥ 35 kg/m (69 patients, 23%). In total, 128 patients (42%) had a primary endpoint (119 patients [39%] were intubated and nine died [3%] without intubation). Sixty-five patients (51%) with body mass index greater than or equal to 30 kg/m were intubated or died. Body mass index greater than or equal to 30 kg/m was associated with a 2.3-fold increased risk of intubation or death compared with individuals with body mass index less than 25 kg/m. Diabetes was also independently associated with risk of intubation or death. Fifty-six out of 127 patients (44%) with body mass index greater than or equal to 30 kg/m had diabetes, and the combination of both diabetes and body mass index greater than or equal to 30 kg/m was associated with a 4.5-fold increased risk of intubation or death compared with patients without diabetes and body mass index less than 25 kg/m.

Survivorship & Rehabilitation

27. **Follow-up of adults with non-critical COVID-19 two months after symptoms' onset.** Carvalho-Schneider C, Laurent E, Lemaigen A, et al. *Clin Microbiol Infect*. 2020 Oct 5:S1198-743X(20)30606-6. doi: 10.1016/j.cmi.2020.09.052.

[https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30606-6/fulltext#](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30606-6/fulltext#)

Findings: At D30, 68% (n=103/150) of patients presented at least one symptom and 66% (n=86/130) at D60, mainly anosmia/ageusia: (59% at symptom onset, 28% at D30 and 23% at D60). Dyspnea concerned 36.7% patients at D30 and 30% at D60. Half of the patients at D30 and 40% at D60 reported asthenia. Persistent symptoms at D60 were significantly associated with age 40 to 60 years old, hospital admission and abnormal auscultation at symptom onset. At D30, severe COVID-19 and/or dyspnea at symptom onset were additional factors associated with persistent symptoms. Up to 2 months after symptom onset, two thirds of adults with non-critical COVID-19 had complaints, mainly anosmia/ageusia, dyspnea or asthenia.

Therapeutics

28. **Remdesivir for the Treatment of Covid-19 — Final Report.** Beigel JH, et al. *NEJM* 2020 Oct 8. DOI: 10.1056/NEJMoa2007764 <https://www.nejm.org/doi/full/10.1056/NEJMoa2007764>
Findings: A total of 1062 patients underwent randomization (with 541 assigned to remdesivir and 521 to placebo). Those who received remdesivir had a median recovery time of 10 days, as compared with 15 days among those who received placebo. Patients who received remdesivir were found to be more likely than those who received placebo to have clinical improvement at day 15. The Kaplan–Meier estimates of mortality were 6.7% with remdesivir and 11.9% with placebo by day 15 and 11.4% with remdesivir and 15.2% with placebo by day 29. Serious adverse events were reported in 131 of the 532 patients who received remdesivir (24.6%) and in 163 of the 516 patients who received placebo (31.6%). Our data show that remdesivir was superior to placebo in shortening the time to recovery in adults who were hospitalized with Covid-19 and had evidence of lower respiratory tract infection.
29. **Effect of Hydroxychloroquine in Hospitalized Patients with Covid-19.** RECOVERY Collaborative Group, et al. *N Engl J Med.* 2020 Oct 8. doi: 10.1056/NEJMoa2022926. <https://www.nejm.org/doi/full/10.1056/NEJMoa2022926>
Findings: The enrollment of patients in the hydroxychloroquine group was closed on June 5, 2020, after an interim analysis determined that there was a lack of efficacy. Death within 28 days occurred in 421 patients (27.0%) in the hydroxychloroquine group and in 790 (25.0%) in the usual-care group. Consistent results were seen in all prespecified subgroups of patients. The results suggest that patients in the hydroxychloroquine group were less likely to be discharged from the hospital alive within 28 days than those in the usual-care group (59.6% vs. 62.9%). Among the patients who were not undergoing mechanical ventilation at baseline, those in the hydroxychloroquine group had a higher frequency of invasive mechanical ventilation or death (30.7% vs. 26.9%). There was a small numerical excess of cardiac deaths but no difference in the incidence of new major cardiac arrhythmia among the patients who received hydroxychloroquine. Among patients hospitalized with Covid-19, those who received hydroxychloroquine did not have a lower incidence of death at 28 days than those who received usual care.
30. **Fondaparinux Use in Patients with COVID-19: A Preliminary Multicenter Real-World Experience.** Russo V, Cardillo G, Viggiano GV, et al. *J Cardiovasc Pharmacol.* 2020 Oct;76(4):369-371. doi: 10.1097/FJC.0000000000000893. <https://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&AN=00005344-202010000-00001&LSLINK=80&D=ovft>
Findings: The aim of our study was to evaluate the clinical impact of venous thromboembolism prophylaxis with fondaparinux versus enoxaparin among 100 hospitalized COVID-19 patients. The incidence of pulmonary embolism, deep venous thrombosis, major bleeding (MB), clinically relevant non-MB, acute respiratory distress syndrome, and in-hospital mortality was compared between patients on fondaparinux versus enoxaparin therapy. The 2 groups were homogeneous for demographic, laboratory, and clinical characteristics. In a median follow-up of 28 days, no statistically significant difference in venous thromboembolism (14.5% vs. 5.3%),

MB and clinically relevant non-MB (3.2% vs. 5.3%), ARDS (17.7% vs. 15.8%), and in-hospital mortality (9.7% vs. 10.5%) has been shown between the enoxaparin group versus the fondaparinux group. Our preliminary results support the hypothesis of a safe and effective use of fondaparinux among patients with COVID-19 hospitalized in internal medicine units.

- 31. Awake prone positioning does not reduce the risk of intubation in COVID-19 treated with high-flow nasal oxygen therapy: a multicenter, adjusted cohort study.** Ferrando C, Mellado-Artigas R, Gea A, et al. *Crit Care*. 2020 Oct 6;24(1):597. doi: 10.1186/s13054-020-03314-6. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7537953/>
Findings: A total of 1076 patients with COVID-19 ARF were admitted, of which 199 patients received HFNO and were analyzed. Fifty-five (27.6%) were pronated during HFNO; 60 (41%) and 22 (40%) patients from the HFNO and HFNO + awake-PP groups were intubated. The use of awake-PP as an adjunctive therapy to HFNO did not reduce the risk of intubation. Patients treated with HFNO + awake-PP showed a trend for delay in intubation compared to HFNO alone, but awake-PP did not affect 28-day mortality. In patients with COVID-19 ARF treated with HFNO, the use of awake-PP did not reduce the need for intubation or affect mortality.
- 32. Effect of PEEP decremental on respiratory mechanics, gasses exchanges, pulmonary regional ventilation, and hemodynamics in patients with SARS-Cov-2-associated acute respiratory distress syndrome.** Bonny V, Janiak V, Spadaro S, et al. *Crit Care*. 2020 Oct 6;24(1):596. doi: 10.1186/s13054-020-03311-9. <https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-03311-9>
Findings: This series of SARS-Cov-2-related ARDS describe an individualized multimodal approach of lung mechanics, gasses exchanges, pulmonary regional ventilation, and hemodynamics at the early phase of the disease and suggest that low PEEP should be used as part of the ventilation strategy, rather than high PEEP.
- 33. Antecedent Administration of Angiotensin Converting Enzyme Inhibitors or Angiotensin II Receptor Antagonists and Survival after Hospitalization for SARS-CoV-2 (COVID-19).** Palazzuoli A, Mancone M, De Ferrari GM, et al. *J Am Heart Assoc*. 2020 Oct 7:e017364. doi: 10.1161/JAHA.120.017364. <https://www.ahajournals.org/doi/10.1161/JAHA.120.017364>
Findings: Among 781 acutely ill patients, 133 (17.0%) used an ARB and 171 (21.9%) used an ACEI. While neither sex nor smoking status differed by user groups, patients on ACEI/ARB tended to be older and more likely to have hypertension, diabetes mellitus, and congestive heart failure. The overall mortality rate was 15.1% (118/781) and increased with age. The crude odds ratios for death for ACEI users and ARB users were 0.98 and 1.13 respectively. After adjusting for age, hypertension, diabetes mellitus, and congestive heart failure, antecedent ACEI administration was associated with reduced mortality; a similar, but weaker trend was observed for ARB administration. In those aged ≥ 50 years hospitalized with COVID-19, antecedent use of ACEI was independently associated with reduced risk of inpatient death. Our findings suggest the protective role of renin-angiotensin-aldosterone system inhibition in patients with high cardiovascular risk affected by COVID-19.

34. **Convalescent plasma for patients with severe COVID-19: a matched cohort study.** Rogers R, Shehadeh F, Mylona EK, et al. *Clin Infect Dis*. 2020 Oct 10:ciaa1548. doi: 10.1093/cid/ciaa1548. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1548/5920703>
Findings: 64 patients who received CP a median of 7 days after symptom onset were compared to a matched control group of 177 patients. The incidence of in-hospital mortality was 12.5% and 15.8% in the CP and control groups, respectively ($p = 0.52$). There was no significant difference in the risk of in-hospital mortality between the two groups. The overall rate of hospital discharge was not significantly different between the two groups, although there was a significantly increased rate of hospital discharge among patients 65-years-old or greater who received CP. There was a greater than expected frequency of transfusion reactions in the CP group (2.8% reaction rate observed per unit transfused). We did not demonstrate a significant difference in risk of mortality or rate of hospital discharge between the CP and control groups. There was a signal for improved outcomes among the elderly, and further adequately powered randomized studies should target this subgroup when assessing the efficacy of CP treatment.
35. **Timing, Complications, and Safety of Tracheotomy in Critically Ill Patients With COVID-19.** Avilés-Jurado FX, Prieto-Alhambra D, González-Sánchez N, et al. *JAMA Otolaryngol Head Neck Surg*. 2020 Oct 8. doi: 10.1001/jamaoto.2020.3641. <https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2771317>
Findings: A total of 50 patients (mean age, 63.8 years; 33 [66%] male) participated in the study. All tracheotomies were performed at the bedside. The median time from intubation to tracheotomy was 9 days. A subthyroid approach was completed for 46 patients (92%), and the tracheal protocol was adequately achieved for 40 patients (80%). Adequate PPE was used, with no infection among surgeons identified 4 weeks after the last tracheotomy. Postoperative complications were rare, with minor bleeding (in 6 patients) being the most common complication. The successful weaning rate was higher in the early tracheotomy group than in the late tracheotomy group, but the difference was not statistically significant. There was less time of invasive mechanical ventilatory support with early tracheotomy compared with late tracheotomy (18 [5.4] vs 22.3 [5.7] days). The reduction of invasive ventilatory support was achieved at the expense of the pretracheotomy period. In this cohort study, with the use of a standardized protocol aimed at minimizing COVID-19 risks, bedside open tracheotomy was a safe procedure for patients and surgeons, with minimal complications. Timing of tracheotomy may be important in reducing time of invasive mechanical ventilation, with potential implications to intensive care unit availability during the COVID-19 pandemic.
36. **Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review.** Chai KL, Valk SJ, Piechotta V, et al. *Cochrane Database Syst Rev*. 2020 Oct 12;10:CD013600. doi: 10.1002/14651858.CD013600.pub3. <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013600.pub3/full>
AUTHORS' CONCLUSIONS: We are uncertain whether convalescent plasma is beneficial for people admitted to hospital with COVID-19. There was limited information regarding grade 3 and 4 AEs to determine the effect of convalescent plasma therapy on clinically relevant SAEs. In the absence of a control group, we are unable to assess the relative safety of convalescent plasma therapy. While major efforts to conduct research on COVID-19 are being made,

recruiting the anticipated number of participants into these studies is problematic. The early termination of the first two RCTs investigating convalescent plasma, and the lack of data from 20 studies that have completed or were due to complete at the time of this update illustrate these challenges. Well-designed studies should be prioritised. Moreover, studies should report outcomes in the same way, and should consider the importance of maintaining comparability in terms of co-interventions administered in all study arms. There are 138 ongoing studies evaluating convalescent plasma and hyperimmune immunoglobulin, of which 73 are RCTs (three already completed). This is the second living update of the review, and we will continue to update this review periodically. Future updates may show different results to those reported here.

37. **Association of Anticoagulation Dose and Survival in Hospitalized COVID-19 Patients: A Retrospective Propensity Score Weighted Analysis.** Ionescu F, Jaiyesimi I, Petrescu I, et al. *Eur J Haematol.* 2020 Oct 11. doi: 10.1111/ejh.13533.

<https://onlinelibrary.wiley.com/doi/10.1111/ejh.13533>

Findings: 3480 patients were included (mean age, 64.5 years; 51.5% female; 52.1% black and 40.6% white). 18.5% (n=642) required ICU stay. 60.9% received pAC (n=2121), 28.7% received ≥3 days of tAC (n=998), and 10.4% (n=361) received no AC. AC was associated with reduced risk of death at prophylactic and therapeutic doses compared to no AC. Major bleeding occurred more frequently in tAC patients (81 [8.1%]) compared to no AC (20 [5.5%]) or pAC (46 [2.2%]) subjects. Higher doses of AC were associated with lower mortality in hospitalized COVID-19 patients. Prospective evaluation of efficacy and risk of AC in COVID-19 is warranted.

Transmission / Infection Control

38. **Nosocomial SARS-CoV-2 transmission in postoperative infection and mortality: analysis of 14,798 procedures.** Elliott JA, Kenyon R, Kelliher G, et al. *Br J Surg.* 2020 Oct 8. doi: 10.1002/bjs.12053. <https://bjssjournals.onlinelibrary.wiley.com/doi/10.1002/bjs.12053>

Findings: This study used a national administrative database to estimate perioperative SARS-CoV-2 infection risk, and associated mortality, relative to nosocomial transmission rates. The impact of nosocomial transmission was greatest after major emergency surgery, whereas laparoscopic surgery may be protective owing to reduced duration of hospital stay. Procedure-specific risk estimates are provided to facilitate surgical decision-making and informed consent.

39. **Duration of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infectivity: When Is It Safe to Discontinue Isolation?** Rhee C, Kanjilal S, Baker M, Klompas M. *Clin Infect Dis.* 2020 Aug 25:ciaa1249. doi: 10.1093/cid/ciaa1249.

<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1249/5896916>

Findings: SARS-CoV-2 appears to be most contagious around the time of symptom onset, and infectivity rapidly decreases thereafter to near-zero after about 10 days in mild-moderately ill patients and 15 days in severely-critically ill and immunocompromised patients. The longest interval associated with replication-competent virus thus far is 20 days from symptom onset. This review summarizes evidence-to-date on the duration of infectivity of SARS-CoV-2, and how

this has informed evolving public health recommendations on when it is safe to discontinue isolation precautions.

40. **Risk of COVID-19 from hospital admission during the pandemic.** Nalleballe K, Siddamreddy S, Kovvuru S, et al. *Infect Control Hosp Epidemiol*. 2020 Oct 8:1-7. doi: 10.1017/ice.2020.1249. <https://tinyurl.com/y4qzmpy8>
Findings: We obtained the total number of COVID-19 positive patients in United States, from the CDC up to July 14 2020, among the total population of the United States from the United States Census Bureau. 101,533 patients were discharged from the hospitals with non-COVID-19 related illnesses from January 20, 2020 to June 30, 2020. Among them 44 (0.043%) patients tested positive for COVID-19 on RT-PCR within 14 days from discharge. The percentage of positive COVID-19 patients among total US population is 1.0353 % as of July 14 2020. The odds of contracting COVID-19 is 24.1 times higher in general population when compared to hospitalized patients. Overall, this result suggests low risk of COVID-19 from hospitalization.
41. **Extended use or re-use of single-use surgical masks and filtering facepiece respirators during COVID-19: A rapid systematic review.** Toomey E, Conway Y, Burton C, et al. *Infect Control Hosp Epidemiol*. 2020 Oct 8:1-25. doi: 10.1017/ice.2020.1243. <https://tinyurl.com/y2fqut3v>
Findings: Six guidance documents were identified. Levels of detail and consistency across documents varied. Four high-quality systematic reviews were included: three focused on reprocessing (decontamination) of N95 respirators, one on reprocessing of surgical masks. Vaporised hydrogen peroxide and ultraviolet germicidal irradiation were highlighted as the most promising reprocessing methods, but evidence on the relative efficacy and safety of different methods was limited. We found no well-established methods for reprocessing respirators at scale. There is limited evidence on the impact of extended use and re-use of surgical masks and respirators and gaps and inconsistencies exist in current guidance. Where extended use or re-use is being practiced, healthcare organisations should ensure that policies and systems are in place to ensure these practices are carried out safely and in line with available guidance.
42. **Characteristics Associated with Adults Remembering to Wash Hands in Multiple Situations Before and During the COVID-19 Pandemic — United States, October 2019 and June 2020.** Haston JC, Miller GF, Berendes D, et al. *MMWR Morb Mortal Wkly Rep* 2020;69:1443–1449. DOI: <http://dx.doi.org/10.15585/mmwr.mm6940a2>
<https://www.cdc.gov/mmwr/volumes/69/wr/mm6940a2.htm>
Findings: U.S. adult Internet survey respondents in June 2020 were more likely to remember to wash their hands after experiencing respiratory symptoms, before eating in a restaurant, and before eating at home than were October 2019 survey respondents. Despite improvements, <75% of survey respondents reported remembering to wash their hands in these situations in 2020. Public health efforts should promote frequent handwashing for all, with attention to tailoring messaging to men, young adults, and non-Hispanic White adults. Focus should be placed on encouraging handwashing at important times such as before eating and after experiencing respiratory symptoms.

43. **Safety and Efficacy of Bronchoscopy in Critically Ill Patients with COVID-19.** Chang SH, Jiang J, Kon ZN, et al. *Chest*. 2020 Oct 8:S0012-3692(20)34873-X. doi: 10.1016/j.chest.2020.09.263. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7543920/pdf/main.pdf>
Findings: This study demonstrates the safety and feasibility of performing bronchoscopy with intermittent apnea for patients with severe COVID-19. We noted a 33% rate of bronchoscopy in intubated patients, which is unusually high compared to non-COVID-19 ARDS. This increased need may be secondary to thick distal secretions associated with COVID-19 or bloody secretions due to the anticoagulation given the reported increased thrombotic risk. A bronchoscopy technique designed to decrease the risk of aerosolization of SARS-CoV-2 was adopted. The protocol for neuromuscular blockade to decrease coughing and the performance of bronchoscopy under apnea was designed to minimize healthcare provider exposure to COVID-19. Although this protocol differs from common practice, this procedure was tolerated well by patients. No healthcare provider involved in the bronchoscopies became positive for COVID-19.
44. **Classification of aerosol-generating procedures: a rapid systematic review.** Jackson T, Deibert D, Wyatt G, et al. *BMJ Open Respir Res*. 2020 Oct;7(1):e000730. doi: 10.1136/bmjresp-2020-000730. <https://bmjopenrespres.bmj.com/content/7/1/e000730>
Findings: In the context of covid-19, aerosol generating procedures have been highlighted as requiring a higher grade of personal protective equipment. We investigated how official guidance documents and academic publications have classified procedures in terms of whether or not they are aerosol-generating. We performed a rapid systematic review using preferred reporting items for systematic reviews and meta-analyses standards. Guidelines, policy documents and academic papers published in english or french offering guidance on aerosol-generating procedures were eligible. We systematically searched two medical databases (medline, cochrane central) and one public search engine (google) in march and april 2020. Data on how each procedure was classified by each source were extracted. We determined the level of agreement across different guidelines for each procedure group, in terms of its classification as aerosol generating, possibly aerosol-generating, or nonaerosol-generating. 128 documents met our inclusion criteria; they contained 1248 mentions of procedures that we categorised into 39 procedure groups. Procedures classified as aerosol-generating or possibly aerosol-generating by $\geq 90\%$ of documents included autopsy, surgery/postmortem procedures with high-speed devices, intubation and extubation procedures, bronchoscopy, sputum induction, manual ventilation, airway suctioning, cardiopulmonary resuscitation, tracheostomy and tracheostomy procedures, non-invasive ventilation, high-flow oxygen therapy, breaking closed ventilation systems, nebulised or aerosol therapy, and high frequency oscillatory ventilation. Disagreements existed between sources on some procedure groups, including oral and dental procedures, upper gastrointestinal endoscopy, thoracic surgery and procedures, and nasopharyngeal and oropharyngeal swabbing. There is sufficient evidence of agreement across different international guidelines to classify certain procedure groups as aerosol generating. However, some clinically relevant procedures received surprisingly little mention in our source documents. To reduce dissent on the remainder, we recommend that (a) clinicians define procedures more clearly and specifically, breaking them down into their constituent components where possible; (b) researchers undertake further studies of aerosolisation during

these procedures; and (c) guideline-making and policy-making bodies address a wider range of procedures.

Women and Children

45. **Outcomes of Neonates Born to Mothers with Severe Acute Respiratory Syndrome Coronavirus 2 Infection at a Large Medical Center in New York City.** Dumitriu D, Emeruwa UN, Hanft E, et al. *JAMA Pediatr.* 2020 Oct 12. doi: 10.1001/jamapediatrics.2020.4298. <https://jamanetwork.com/journals/jamapediatrics/fullarticle/2771636>
Findings: In total, 141 tests were obtained from 101 newborns (54 girls [53.5%]) on 0 to 25 days of life (median, DOL-1). Two newborns had indeterminate test results, indicative of low viral load; 1 newborn never underwent retesting but remained well on follow-up, and the other had negative results on retesting. Maternal severe/critical COVID-19 was associated with newborns born approximately 1 week earlier and at increased risk of requiring phototherapy compared with newborns of mothers with asymptomatic/mild COVID-19. Fifty-five newborns were followed up in a new COVID-19 Newborn Follow-up Clinic at DOL-3 to DOL-10 and remained well. Twenty of these newborns plus 3 newborns followed up elsewhere had 32 nonroutine encounters documented at DOL-3 to DOL-25, and none had evidence of SARS-CoV-2 infection, including 6 with negative retesting results. No clinical evidence of vertical transmission was identified in 101 newborns of mothers positive for or with suspected SARS-CoV-2 infection, despite most newborns rooming-in and direct breastfeeding practices.
46. **COVID-19 and first trimester spontaneous abortion: a case-control study of 225 pregnant patients.** Cosma S, Carosso AR, Cusato J, et al. *Am J Obstet Gynecol.* 2020 Oct 8:S0002-9378(20)31177-7. doi: 10.1016/j.ajog.2020.10.005. [https://www.ajog.org/article/S0002-9378\(20\)31177-7/pdf](https://www.ajog.org/article/S0002-9378(20)31177-7/pdf)
Findings: Twenty-three of the 225 women (10.2%) tested positive for COVID-19 infection. There was no difference in the cumulative incidence of COVID-19 between the cases (11/100, 11%) and the controls (12/125, 9.6%). Logistic regression analysis confirmed that COVID-19 was not an independent predictor of early pregnancy loss. COVID-19 related symptoms in the first trimester were fever, anosmia, ageusia, cough, arthralgia and diarrhea; no pneumonia or Hospital admission due to COVID-19-related symptoms were recorded. No difference in the incidence of symptoms was noted between the two groups. SARS-CoV-2 infection during the first trimester of pregnancy does not appear to predispose to early pregnancy loss; its cumulative incidence did not differ between women with spontaneous abortion and women with ongoing pregnancy. COVID-19 appears to have a favorable maternal course at the beginning of pregnancy, consistent with what has been observed during the second and the third trimester.
47. **Symptoms and Transmission of SARS-CoV-2 among Children-Utah and Wisconsin, March-May 2020.** Laws RL, Chancey RJ, Rabold EM, et al. *Pediatrics.* 2020 Oct 8:e2020027268. doi: 10.1542/peds.2020-027268. <https://pediatrics.aappublications.org/content/pediatrics/early/2020/10/06/peds.2020-027268.full.pdf>

Findings: Among 58 households, 188 contacts were enrolled (120 adults; 68 children). Secondary infection rates for adults (30%) and children (28%) were similar. Among households with potential for transmission from children, child-to-adult transmission may have occurred in 2/10 (20%), and child-to-child transmission may have occurred in 1/6 (17%). Pediatric case-patients most commonly reported headache (79%), sore throat (68%), and rhinorrhea (68%); symptoms had low PPVs except measured fever. Compared to symptomatic adults, children were less likely to report cough, loss of taste, and loss of smell, and more likely to report sore throat. Children and adults had similar secondary infection rates, but children generally had less frequent and severe symptoms. In two states early in the pandemic, we observed possible transmission from children in approximately one-fifth of households with potential to observe such transmission patterns.

48. **Acute Kidney Injury in Pediatric Inflammatory Multisystem Syndrome Temporally Associated with Severe Acute Respiratory Syndrome Coronavirus-2 Pandemic: Experience from PICUs Across United Kingdom.** Deep A, Upadhyay G, du Pré P, et al. *Crit Care Med.* 2020 Oct 12. doi: 10.1097/CCM.0000000000004662. https://journals.lww.com/ccmjournals/Abstract/9000/Acute_Kidney_Injury_in_Pediatric_Inflammatory.95467.aspx

Findings: Severe acute kidney injury was defined as stage 2/3 acute kidney injury. Over the study period, 116 patients with pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus-2 were admitted to 15 United Kingdom PICUs. Any-stage acute kidney injury occurred in 48 of 116 patients (41.4%) and severe acute kidney injury in 32 of 116 (27.6%) patients, which was mostly evident at admission (24/32, 75%). In univariable analysis, body mass index, hyperferritinemia, high C-reactive protein, Pediatric Index of Mortality 3 score, vasoactive medication, and invasive mechanical ventilation were associated with severe acute kidney injury. In multivariable logistic regression, hyperferritinemia was associated with severe acute kidney injury. Severe acute kidney injury was associated with longer PICU stay (median 5 days) and increased duration of invasive mechanical ventilation (median 4 days). Severe acute kidney injury occurred in just over a quarter of children admitted to United Kingdom PICUs with pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus-2. Hyperferritinemia was significantly associated with severe acute kidney injury. Severe acute kidney injury was associated with increased duration of stay and ventilation. Although short-term outcomes for acute kidney injury in pediatric inflammatory multisystem syndrome temporally associated with severe acute respiratory syndrome coronavirus-2 appear good, long-term outcomes are unknown.

49. **Clinical Presentation of Coronavirus Disease 2019 (COVID-19) in Pregnant and Recently Pregnant People.** Afshar Y, Gaw SL, Flaherman VJ, et al. *Obstet Gynecol.* 2020 Oct 7. doi: 10.1097/AOG.0000000000004178. https://journals.lww.com/greenjournal/Fulltext/9900/Clinical_Presentation_of_Coronavirus_Disease_2019.2.aspx

Findings: Of 991 participants enrolled from March 22, 2020, until July 10, 2020, 736 had symptoms of COVID-19 at the time of testing; 594 tested positive for SARS-CoV-2 infection and 142 tested negative in this symptomatic group. Mean age was 31.3 years, and 37% will

nulliparous. Ninety-five percent were outpatients. Participants who tested positive for SARS-CoV-2-infection were a geographically diverse cohort: 34% from the Northeast, 25% from the West, 21% from the South, and 18% from the Midwest. Thirty-one percent of study participants were Latina, and 9% were Black. The average gestational age at enrollment was 24.1 weeks, and 13% of participants were enrolled after pregnancy. The most prevalent first symptoms in the cohort of patients who tested positive for SARS-CoV-2 infection were cough (20%), sore throat (16%), body aches (12%), and fever (12%). Median time to symptom resolution was 37 days. One quarter (25%) of participants who tested positive for SARS-CoV-2 infection had persistent symptoms 8 or more weeks after symptom onset. COVID-19 has a prolonged and nonspecific disease course during pregnancy and in the 6 weeks after pregnancy.

50. **Outcomes of Critically Ill Pregnant Women with COVID-19 in the United States.** Easter SR, Gupta S, Brenner SK, Leaf DE. *Am J Respir Crit Care Med.* 2020 Oct 7. doi: 10.1164/rccm.202006-2182LE. <https://www.atsjournals.org/doi/pdf/10.1164/rccm.202006-2182LE>

Findings: Using data from a large, multicenter, geographically-diverse cohort of critically ill adults with laboratory-confirmed COVID-19 admitted to 67 hospitals across the United States, we report the clinical features of 32 pregnant and 64 non-pregnant women matched according to age and severity of illness. All pregnant women survived, and there were no fetal deaths, but pregnant women had high rates of preterm delivery and cesarean section.

51. **Compassionate Use of Remdesivir in Pregnant Women with Severe Covid-19.** Burwick RM, Yawetz S, Stephenson KE, et al. *Clin Infect Dis.* 2020 Oct 8:ciaa1466. doi: 10.1093/cid/ciaa1466. <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1466/5919737>

Findings: Nineteen of 86 women delivered before their first dose and were reclassified as immediate "postpartum". At baseline, 40% of pregnant women required invasive ventilation, in contrast to 95% of postpartum women. By Day 28 of follow-up, the level of oxygen requirement decreased in 96% and 89% of pregnant and postpartum women, respectively. Among pregnant women, 93% of those on mechanical ventilation were extubated, 93% recovered, and 90% were discharged. Among postpartum women, 89% were extubated, 89% recovered, and 84% were discharged. Remdesivir was well tolerated, with a low incidence of serious adverse events (16%). Most adverse events were related to pregnancy and underlying disease; most laboratory abnormalities were Grades 1 or 2. There was one maternal death attributed to underlying disease and no neonatal deaths. Among 86 pregnant and postpartum women with severe COVID-19 who received compassionate use remdesivir, recovery rates were high, with a low rate of serious adverse events.

GUIDELINES & CONSENSUS STATEMENTS

[Updated guidance on the management of COVID-19: from an American Thoracic Society/European Respiratory Society coordinated International Task Force \(29 July 2020\).](#) Bai C et al. *Eur Respir Rev.* 2020 Oct 5;29(157):200287. doi: 10.1183/16000617.0287-2020. Print 2020 Sep 30.

[IFCC interim guidelines on biochemical/hematological monitoring of COVID-19 patients.](#) Thompson S, Bohn MK, Mancini N, et al. *Clin Chem Lab Med*. 2020 Oct 7:/j/cclm.ahead-of-print/cclm-2020-1414/cclm-2020-1414.xml. doi: 10.1515/cclm-2020-1414.

[IFCC interim guidelines on serological testing of antibodies against SARS-CoV-2.](#) Taskforce on COVID-19, International Federation of Clinical Chemistry (IFCC), Milan, Italy. *Clin Chem Lab Med*. 2020 Oct 7:/j/cclm.ahead-of-print/cclm-2020-1413/cclm-2020-1413.xml. doi: 10.1515/cclm-2020-1413.

[IFCC interim guidelines on molecular testing of SARS-CoV-2 infection.](#) Bohn MK, Mancini N, Loh TP, et al. *Clin Chem Lab Med*. 2020 Oct 7:/j/cclm.ahead-of-print/cclm-2020-1412/cclm-2020-1412.xml. doi: 10.1515/cclm-2020-1412.

American Academy of Pediatrics - [COVID-19 Testing Guidance](#) - updated

American Academy of Pediatrics - [Guidance on the Use of Personal Protective Equipment \(PPE\) for Pediatric Care in Ambulatory Care Settings During the SARS-CoV-2 Pandemic](#) - updated

[Update Alert 2: Ventilation Techniques and Risk for Transmission of Coronavirus Disease, Including COVID-19.](#) Thomas R, Lotfi T, Morgano GP, Darzi A, Reinap M. *Ann Intern Med*. 2020 Oct 13. doi: 10.7326/L20-1211.

FDA / CDC / NIH / WHO Updates

FDA: [Recommendations on Providing Clear Instructions to Patients Who Self-Collect an Anterior Nares \(Nasal\) Sample in a Health Care Setting for SARS-CoV-2 Testing - Letter to Health Care Providers](#)

FDA: [Emergency Use Authorization for Vaccines to Prevent COVID-19](#)

NIH: [COVID-19 Treatment Guidelines: What's New in the Guidelines](#)

News / Press Releases

[Eli Lilly antibody trial is paused because of potential safety concerns.](#) *NY Times*, 10-13-2020.

Commentary

[Dying in a Leadership Vacuum.](#) The Editors, *N Engl J Med* 2020 Oct 8; 383:1479-1480 DOI: 10.1056/NEJMe2029812

[Long-term Health Consequences of COVID-19.](#) Del Rio C, Collins LF, Malani P. *JAMA*. 2020 Oct 5. doi: 10.1001/jama.2020.19719.

[Excess Deaths From COVID-19, Community Bereavement, and Restorative Justice for Communities of Color.](#) Cooper LA, Williams DR. *JAMA*. 2020 Oct 12. doi: 10.1001/jama.2020.19567.

[Mental Health Disorders Related to COVID-19-Related Deaths.](#) Simon NM, Saxe GN, Marmar CR.
JAMA. 2020 Oct 12. doi: 10.1001/jama.2020.19632.

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