Providence

COVID-19 Resource Desk

#3 | 5.6.2020 to 5.12.2020

Prepared by System Library Services

New Research

*note, **PREPRINTS** have not undergone formal peer review

Basic Science / Virology / Pre-clinical

1. **Shared Antigen-specific CD8+ T cell Responses against the SARS-COV-2 Spike Protein in HLA-A*02:01 COVID-19 Participants.** Chour W at Institute for Systems Biology, et al. MedRxiv. 2020 May 8 PREPRINT doi: https://doi.org/10.1101/2020.05.04.20085779 https://www.medrxiv.org/content/10.1101/2020.05.04.20085779v1.full.pdf
   Findings: We report here on antigens from the SARS-CoV-2 virus spike protein, that when presented by Class I MHC, can lead to cytotoxic CD8+ T cell anti-viral responses in COVID-19 patients. We present a method in which the SARS-CoV-2 spike protein is converted into a library of peptide antigen-Major Histocompatibility Complexes (pMHCs) as single chain trimers that contain the peptide antigen, the MHC HLA allele subunit, and the β-2 microglobulin subunit. This library is used to detect the evolution of virus-specific T cell populations in four COVID-19 study participants two of which share one HLA allele, and the other two a second HLA allele, at two time points over the initial course of infection. HLA-matched participants exhibit similar virus specific T cell populations, but very different time-trajectories of those populations. This strategy can be used to track those virus-specific T cell populations over the course of an infection, thus providing deep insight into the SARS-CoV-2 immune system trajectories observed in different COVID-19 patients.

2. **A strategic approach to COVID-19 vaccine R&D.** Corey L, Mascola JR, Fauci AS, Collins FS. Science. Published online 11 May 2020. doi: 10.1126/science.abc5312 https://science.sciencemag.org/content/early/2020/05/08/science.abc5312
   Findings: The full development pathway for an effective vaccine for SARS-CoV-2 will require that industry, government, and academia collaborate in unprecedented ways, each adding their individual strengths. We discuss one such collaborative program that has recently emerged: the ACTIV (Accelerating COVID-19 Therapeutic Interventions and Vaccines) public-private partnership. Spearheaded by the U.S. National Institutes of Health (NIH), this effort brings together the strengths of all sectors at this time of global urgency.

3. **Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals.** Ni L, Ye F, Cheng, M-L, et al. *Immunity* (2020), doi: https://doi.org/10.1016/j.immuni.2020.04.023 https://www.cell.com/action/showPdf?pii=S1074-7613%2820%2930181-3

Findings: We collected blood from COVID-19 patients who have recently become virus-free and detected SARS-CoV-2-specific humoral and cellular immunity in 8 newly discharged patients. Follow-up analysis on another cohort of 6 patients 2 weeks post discharge also revealed high titers of IgG antibodies. In all 14 patients tested, 13 displayed serum neutralizing activities in a pseudotype entry assay. Notably, there was a strong correlation between neutralization antibody titers and the numbers of virus-specific T cells. Our work provides a basis for further analysis of protective immunity to SARS-CoV-2, and understanding the pathogenesis of COVID-19, especially in the severe cases.

4. **Structural Basis for Potent Neutralization of Betacoronaviruses by Single-Domain Cameli Antibodies.** Wrapp D et al. *Cell* (2020), https://doi.org/10.1016/j.cell.2020.04.031
https://www.cell.com/cell/pdf/S0092-8674(20)30494-3.pdf
Findings: Coronaviruses make use of a large envelope protein called spike (S) to engage host cell receptors and catalyze membrane fusion. Because of the vital role that these S proteins play, they represent a vulnerable target for the development of therapeutics. Here, we describe the isolation of single-domain antibodies (VHHs) from a **llama** immunized with prefusion-stabilized coronavirus spikes. These VHHs neutralize MERS-CoV or SARS- CoV-1 S pseudotyped viruses, respectively. Crystal structures of these VHHs bound to their respective viral targets reveal two distinct epitopes, but both VHHs interfere with receptor binding. We also show cross-reactivity between the SARS-CoV-1 S-directed VHH and SARS-CoV-2 S and demonstrate that this cross-reactive VHH neutralizes SARS-CoV-2 S pseudotyped viruses as a bivalent human IgG Fc-fusion. These data provide a molecular basis for the neutralization of pathogenic betacoronaviruses by VHHs and suggest that these molecules may serve as useful therapeutics during coronavirus outbreaks.

5. **Spike mutation pipeline reveals the emergence of a more transmissible form of SARS-CoV-2.** Korber B, Fischer WM, Gnanakaran S April 30, 2020. bioRxiv PREPRINT doi:
https://doi.org/10.1101/2020.04.29.069054.
https://www.biorxiv.org/content/10.1101/2020.04.29.069054v1
Findings: We have developed an analysis pipeline to facilitate real-time mutation tracking in SARS-CoV-2, focusing initially on the Spike (S) protein because it mediates infection of human cells and is the target of most vaccine strategies and antibody-based therapeutics. To date we have identified fourteen mutations in Spike that are accumulating. The mutation Spike D614G is of urgent concern; it began spreading in Europe in early February, and when introduced to new regions it rapidly becomes the dominant form. Also, we present evidence of recombination between locally circulating strains, indicative of multiple strain infections. These findings have important implications for SARS-CoV-2 transmission, pathogenesis and immune interventions.
***Note, receiving much press re: mutated strain but several saying no evidence more contagious or deadly https://www.nytimes.com/2020/05/06/health/coronavirus-mutation-transmission.html**

Clinical Syndrome

6. **Gastrointestinal and Hepatic Manifestations of 2019 Novel Coronavirus Disease in a Large Cohort of Infected Patients from New York: Clinical Implications**. Hajifathalian K, Krisko T, Mehta A, et al. 2020 May 7. *Gastroenterology*. 2020;S0016-5085(20)30602-8. doi:10.1053/j.gastro.2020.05.010 https://www.gastrojournal.org/article/S0016-5085(20)30602-8/pdf
   Findings: 1059 patients diagnosed with COVID-19 with a mean age of 61(SD 18) years (58% male) were included in the study. At presentation, 22% of patients had diarrhea, 7% had abdominal pain, and 16% and 9% had nausea and vomiting, respectively. 33% of patients had at least one GI manifestation. At presentation, patients had a mean ALT of 50 (65), mean AST 60 (79) U/L, mean total bilirubin 0.7 (0.6) mg/dL, and mean alkaline phosphatase of 88 (74) U/L. 62% of the patients had biochemical evidence of liver injury with at least one of their liver enzymes elevated.

7. **Abdominal Imaging Findings in COVID-19: Preliminary Observations**. Bhayana R, Som A, Li MD, et al. 2020 May 11. *Radiology.* 2020;201908. doi:10.1148/radiol.2020201908 https://pubs.rsna.org/doi/10.1148/radiol.2020201908
   Findings: 412 patients (average age 57 years; range 18->90 years; 241 men, 171 women) were evaluated. 224 abdominal imaging studies were performed (radiographs, n=137; ultrasound, n=44; CT, n=42; MRI, n=1) in 134 patients (33%). Bowel abnormalities and cholestasis were common findings on abdominal imaging of inpatients with COVID-19. Patients who went to laparotomy often had ischemia, possibly due to small vessel thrombosis.

8. **High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study.** Helms J, Tacquard C, et al; *Intensive Care Med*. 2020 May 4. doi: 10.1007/s00134-020-06062-x.
   https://link.springer.com/article/10.1007/s00134-020-06062-x
   Findings: 150 COVID-19 patients were included (122 men, median age 63 [53; 71] years, SAPSII 49 [37; 64] points). Sixty-four clinically relevant thrombotic complications were diagnosed in 150 patients, mainly pulmonary embolisms (16.7%). 28/29 patients (96.6%) receiving continuous renal replacement therapy experienced circuit clotting. Three thrombotic occlusions (in 2 patients) of centrifugal pump occurred in 12 patients (8%) supported by ECMO. Most patients (> 95%) had elevated D-dimer and fibrinogen. No patient developed disseminated intravascular coagulation. Comparison with non-COVID-19 ARDS patients (n = 145) confirmed that COVID-19 ARDS patients (n = 77) developed significantly more thrombotic complications, mainly pulmonary embolisms (11.7 vs. 2.1%, $p < 0.008$). Despite anticoagulation, a high number of patients with ARDS secondary to COVID-19 developed life-threatening thrombotic complications. Higher anticoagulation targets than in usual critically ill patients should therefore probably be suggested.

9. **Acute Kidney Injury in COVID-19: Emerging Evidence of a Distinct Pathophysiology.** Batlle D, Soler MJ, Sparks MA, et al. *J Am Soc Nephrol.* 2020 May 4. pii: ASN.2020040419. doi:

10.1681/ASN.2020040419.
https://jasn.asnjournals.org/content/early/2020/05/04/ASN.2020040419
Findings: Despite the very limited information on kidney involvement in COVID-19, AKI appears to involve a complex process driven by virus-mediated injury, cytokine storm, AngII pathway activation, dysregulation of complement, hypercoagulation, and microangiopathy interacting with common and known risk factors for AKI. There is paucity of data regarding clinical and laboratory characteristics of AKI in patients with COVID-19.

10. **Clinical Characteristics of and Medical Interventions for COVID-19 in Hemodialysis Patients in Wuhan, China.** Xiong F, Tang H, Liu L, Tu C, et al. *J Am Soc Nephrol*. 2020 May 8. pii: ASN.2020030354. doi: 10.1681/ASN.2020030354.
https://jasn.asnjournals.org/content/early/2020/05/08/ASN.2020030354
Findings: Of 7154 patients undergoing hemodialysis, 154 had laboratory-confirmed COVID-19. The mean age of the 131 patients in our analysis was 63.2 years; 57.3% were men. Many had underlying comorbidities, with cardiovascular disease being the most common (68.7%). Only 51.9% of patients manifested fever; 21.4% of infected patients were asymptomatic. The most common finding on chest computed tomography (CT) was ground-grass or patchy opacity (82.1%). After initiating comprehensive interventions-including entrance screening of body temperature and symptoms, universal chest CT and blood tests, and other measures-new patients presenting with COVID-19 peaked at 10 per day on January 30, decreasing to 4 per day on February 11. No new cases occurred between February 26 and March 10, 2020. We found that patients receiving maintenance hemodialysis were susceptible to COVID-19 and that hemodialysis centers were high-risk settings during the epidemic. Increasing prevention efforts, instituting universal screening, and isolating patients with COVID-19 and directing them to designated hemodialysis centers were effective in preventing the spread of COVID-19 in hemodialysis centers.

11. **Abnormal pulmonary function in COVID-19 patients at time of hospital discharge.** Mo X, Jian W, Su Z, et al. *Eur Respir J.* 2020 May 7:2001217. doi: 10.1183/13993003.01217-2020.
https://erj.ersjournals.com/content/erj/early/2020/05/04/13993003.01217-2020.full.pdf
Findings: On the 11th of March 2020, WHO declared the Coronavirus Disease 2019 (COVID-19) as a pandemic. As of 22 April, more than 2.4 million cases have been confirmed worldwide [1]. In light of the widely documented lung injuries related with COVID-19 [2–3], concerns are raised regarding the assessment of the lung injury for discharged patients. A recent report portrayed that discharged patients with COVID-19 pneumonia are still having residual abnormalities in chest CT scans, with ground-glass opacity as the most common pattern.

12. **Lupus Anticoagulant and Abnormal Coagulation Tests in Patients with Covid-19.** Bowles L, Platton S, Yartey N, et al. *N Engl J Med*. 2020 May 5. doi: 10.1056/NEJMc2013656.
https://www.nejm.org/doi/full/10.1056/NEJMc2013656
Findings: Blood specimens obtained from 216 patients who were positive for SARS-CoV-2 were received for coagulation screening, and 44 (20%) were found to have a prolonged aPTT. The specimens from 9 patients were excluded, and those from 35 patients were investigated further.

Diagnostics & Screening

13. **Using the diagnostic model based on routine laboratory tests to distinguish patients infected with SARS-CoV-2 from those infected with influenza virus.** Luo Y, Yuan X, Xue Y, et al. *Int J Infect Dis*. 2020 May 1:S1201-9712(20)30295-2. doi:10.1016/j.ijid.2020.04.078. https://www.ijidonline.com/article/S1201-9712(20)30295-2/pdf
Findings: Some routine laboratory results had statistical difference between NCPP and IP. A diagnostic model based on combination of routine laboratory results provides an adjunct approach in the differential diagnosis between NCPP and IP.

14. **T cell subset counts in peripheral blood can be used as discriminatory biomarkers for diagnosis and severity prediction of COVID-19.** Jiang M, Guo Y, Luo Q, et al. *J Infect Dis*. 2020 May 7. pii: jiaa252. doi: 10.1093/infdis/jiaa252. https://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa252/5831863
Findings: This study evaluated the significance of lymphocyte subsets detection in peripheral blood in the diagnosis and prognosis of coronavirus disease 2019. Our results revealed that CD3+T, CD4+T, CD8+T cells and NK cells were significantly decreased in COVID-19 patients. COVID-19 patients had a relatively slight decrease in CD4+T cells but a severe decrease of CD8+T cells. The significantly elevated CD4/CD8 ratio was observed in COVID-19 patients. T cell subset counts were related to the severity and prognosis of COVID-19. The counts of CD8+T and CD4+T cells can be used as diagnostic markers of COVID-19 and predictors of disease severity.

15. **Comparison of SARS-CoV-2 Detection from Nasopharyngeal Swab Samples by the Roche cobas® 6800 SARS-CoV-2 Test and a Laboratory-Developed Real-Time RT-PCR test.** Pujadas E, Ibeh N, Hernandez MM, et al. *J Med Virol*. 2020 May 8. doi: 10.1002/jmv.25988. https://onlinelibrary.wiley.com/doi/epdf/10.1002/jmv.25988
Findings: The urgent need to implement and rapidly expand testing for SARS-CoV-2 infection has led to development of multiple assays. How these tests perform relative to one another is poorly understood. We evaluated the concordance between the Roche Diagnostics cobas® 6800 SARS-CoV-2 Test and a laboratory-developed Real-Time RT-PCR test (LDT) based on a modified CDC protocol, for the detection of SARS-CoV-2 in samples submitted to the Clinical Laboratories of the Mount Sinai Health System. 1006 Nasopharyngeal swabs in universal transport medium from persons under investigation were tested for SARS-CoV-2 as part of routine clinical care using the cobas SARS-CoV2 test with subsequent evaluation by the LDT. Cycle threshold values were analyzed and interpreted as either positive, negative, inconclusive, or invalid. Statistical analysis was performed using GraphPad Prism 8. The cobas SARS-CoV2 test reported 706 positives and 300 negatives. The LDT reported 640 positives, 323 negatives, 34 inconclusive, and 9 invalids. When excluding inconclusive and invalid results, the overall percent agreement between the two platforms was 95.8%. An overall discordance rate of 4.2% between the two systems may reflect differences in primer sequences, assay limit of detection, or other factors, highlighting the importance of comparing the performance of different testing platforms.

Epidemiology & Public Health

16. **Public Health Response to the Initiation and Spread of Pandemic COVID-19 in the United States, February 24-April 21, 2020.** Schuchat A; CDC COVID-19 Response Team. *MMWR Morb Mortal Wkly Rep*. 2020 May 8;69(18):551-556. doi:10.15585/mmwr.mm6918e2. https://www.cdc.gov/mmwr/volumes/69/wr/mm6918e2.htm
Findings: From January 21 through February 23, 2020, a total of 14 cases of coronavirus disease 2019 (COVID-19) were diagnosed in six U.S. states, including 12 cases in travelers arriving from China and two in household contacts of persons with confirmed infections. An additional 39 cases were identified in persons repatriated from affected areas outside the US. Starting in late February, reports of cases with no recent travel to affected areas or links to known cases signaled the initiation of pandemic spread in the US. By mid-March, transmission of SARS-CoV-2 had accelerated, with rapidly increasing case counts indicating established transmission in the US. Public health responses included intensive efforts to detect cases and trace contacts, and implementation of multiple community mitigation strategies. Because most of the population remains susceptible to infection, recognition of factors associated with amplified spread during the early acceleration period will help inform future decisions as locations in the US scale back some components of mitigation and strengthen systems to detect a potential transmission resurgence. U.S. circulation of SARS-CoV-2 continues, and sustained efforts will be needed to prevent future spread within the US.

17. **Estimating the Infection Fatality Rate among Symptomatic COVID-19 Cases in the United States.** Basu A. *Health Aff*. 2020 May 7:101377hlthaff202000455. doi:10.1377/hlthaff.2020.00455.
https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2020.00455
Findings: Knowing the infection fatality rate (IFR) of SARS-CoV and SARS-CoV-2 infections is essential for the fight against the COVID-19 pandemic. Using data through April 20, 2020, we fit a statistical model to COVID-19 case fatality rates over time at the US county level to estimate the COVID-19 IFR among symptomatic cases (IFR-S) as time goes to infinity. The IFR-S in the US was estimated to be 1.3% (95% central credible interval: 0.6% to 2.1%). County-specific rates varied from 0.5% to 3.6%. The overall IFR for COVID-19 should be lower when we account for cases that remain and recover without symptoms. When used with other estimating approaches, our model and our estimates can help disease and policy modelers to obtain more accurate predictions for the epidemiology of the disease and the impact of alternative policy levers to contain this pandemic. Substantial variation across patient demographics likely exists and should be the focus of future studies.

18. **COVID-19 Testing, Epidemic Features, Hospital Outcomes, and Household Prevalence, New York State-March 2020.** Rosenberg ES, Dufort EM, Blog DS, et al. *Clin Infect Dis*. 2020 May 8:ciaa549. doi: 10.1093/cid/ciaa549.
https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa549/5831986
Findings: During March In NY state, outside of New York City, a total of 47,326 persons tested positive for SARS-CoV-2, out of 141,495 tests (33% test-positive), with the highest number of cases located in the metropolitan region counties. Among 229 initial cases diagnosed through

March 12, by March 30 13% were hospitalized and 2% died. Testing conducted among 498 members of these case's households found prevalent infection among 57%; excluding first-reported cases 38%. In these homes, we found a significant age gradient in prevalence, from 23% among those <5 years to 68% among those ≥65 years (p<.0001).

19. **Modeling shield immunity to reduce COVID-19 epidemic spread.** Weitz JS, Beckett SJ, Coenen AR, et al. *Nat Med.* 2020 May 7. doi: 10.1038/s41591-020-0895-3. https://www.nature.com/articles/s41591-020-0895-3
Findings: The COVID-19 pandemic has precipitated a global crisis, with more than 1,430,000 confirmed cases and more than 85,000 confirmed deaths globally as of 9 April 2020. We have developed and analyzed an epidemiological intervention model that leverages serological tests to identify and deploy recovered individuals as focal points for sustaining safer interactions via interaction substitution, developing what we term 'shield immunity' at the population scale. The objective of a shield immunity strategy is to help to sustain the interactions necessary for the functioning of essential goods and services while reducing the probability of transmission. Our shield immunity approach could substantively reduce the length and reduce the overall burden of the current outbreak, and can work synergistically with social distancing. The present model highlights the value of serological testing as part of intervention strategies, in addition to its well-recognized roles in estimating prevalence and in the potential development of plasma-based therapies.

20. **Changes in SARS-CoV-2 Positivity Rate in Outpatients in Seattle and Washington State, March 1-April 16, 2020.** Randhawa AK, Fisher LH, Greninger AL, et al. *JAMA*. 2020 May 8. doi:10.1001/jama.2020.8097. https://jamanetwork.com/journals/jama/fullarticle/2766035
Findings: SARS-CoV-2 infections in patients seen in Washington outpatient clinics and Seattle ED settings peaked in late March and have been declining. This trajectory is aligned with local physical distancing guidelines enacted on March 16, 2020 and the “Stay Home, Stay Healthy” order announced by Governor Inslee on March 23, 2020.

21. **Preliminary Estimate of Excess Mortality During the COVID-19 Outbreak — New York City, March 11–May 2, 2020.** *MMWR Morb Mortal Wkly Rep*. 11 May 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6919e5
Findings: During March 11–May 2, 2020, a total of 32,107 deaths were reported; of these deaths, 24,172 were found to be in excess of the seasonal expected baseline. Included in the 24,172 deaths were 13,831 (57%) laboratory-confirmed COVID-19–associated deaths and 5,048 (21%) probable COVID-19–associated deaths, leaving 5,293 (22%) excess deaths that were not identified as either laboratory-confirmed or probable COVID-19–associated deaths.

Healthcare Delivery/Health Care Workers

22. **Occurrence, prevention, and management of the psychological effects of emerging virus outbreaks on healthcare workers: rapid review and meta-analysis.** Kisely S, Warren N, McMahon L, et al. *BMJ* 2020; 369 :m1642.https://www.bmj.com/content/369/bmj.m1642

Findings: Staff in contact with affected patients had greater levels of both acute or post-traumatic stress and psychological distress. These findings were the same as in the other studies not included in the meta-analysis. Risk factors for psychological distress included being younger, being more junior, being the parents of dependent children, or having an infected family member. Longer quarantine, lack of practical support, and stigma also contributed. Clear communication, access to adequate personal protection, adequate rest, and both practical and psychological support were associated with reduced morbidity.

23. **Characteristics of Doctors' Fatality due to COVID-19 in Western Europe and Asia-Pacific countries**. Yoshida I, Tanimoto T, Schiever N, Patelli F, Kami M. *QJM*. 2020 May 6:hcaa159. doi: 10.1093/qjmed/hcaa159.
https://academic.oup.com/qjmed/advance-article/doi/10.1093/qjmed/hcaa159/5831301
Findings: Under the COVID-19 pandemic, the deaths of healthcare professionals have been increasingly reported worldwide. We performed a cross-sectional, observational study using news reports on the websites among selected countries as of April, 2020. We found 120 dead medical doctors due to COVID-19 in Western Europe and Asia-Pacific countries; 67 in Italy (47 in the North), 34 in China (22 in Hubei), 6 in France, 4 in the UK, the US, and Spain, and 1 in South Korea, respectively. Among them, 90% were men, and specialties were reported as general practitioners for 30% and as physicians for 11.6%. The overall proportions of dead medical doctors amounted to 1.9 per 10,000 confirmed cases and 30.2 per 10,000 dead cases, respectively. Proactive measures are warranted to protect doctors especially who often encounters with COVID-19 patients.

24. **Strategies for daily operating room management of ambulatory surgery centers following resolution of the acute phase of the COVID-19 pandemic.** Dexter F, Elhakim M, Loftus RW, et al. *J Clin Anesth*. 2020 Apr 29;64:109854. doi: 10.1016/j.jclinane.2020.109854.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7188624/
Findings: We performed a narrative review to explore the economics of daily operating room management decisions for ambulatory surgery centers following resolution of the acute phase of the COVID-19 pandemic.

25. **Hospital capacity and operations in the coronavirus disease 2019 (COVID-19) pandemic—planning for the nth patient.** Cavallo J, Donoho D, Forman H. *JAMA Health Forum*. 2020;1(3):e200345. May 6, 2020 doi:10.1001/jamahealthforum.2020.0345
https://jamanetwork.com/channels/health-forum/fullarticle/2765800?resultClick=1
Findings: We illustrate how “flattening the curve” has created time for Los Angeles County to improve hospital capabilities that are vital to success against COVID-19.

Therapeutics

26. **Association of Treatment with Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State**. Rosenberg ES, Dufort EM, Udo T, et al. 2020 May 11. *JAMA.* 2020;10.1001/jama.2020.8630. doi:10.1001/jama.2020.863
https://jamanetwork.com/journals/jama/fullarticle/2766117

Findings: Among patients hospitalized in metropolitan New York with COVID-19, treatment with hydroxychloroquine, azithromycin, or both, compared with neither treatment, was not significantly associated with differences in in-hospital mortality. However, the interpretation of these findings may be limited by the observational design.

27. **The Society for Immunotherapy of Cancer perspective on regulation of interleukin-6 signaling in COVID-19-related systemic inflammatory response**. Arnaldez FI, O'Day SJ, Drake CG, Fox, BA, Fu, B, Urba, W et al. *Journal for ImmunoTherapy of Cancer* 2020, May 7;8:e000930. doi: 10.1136/jitc-2020-000930 https://jitc.bmj.com/content/8/1/e000930
Findings: One hallmark feature of the profound inflammatory state seen in patients with COVID-19 who succumb to pneumonia and hypoxia is marked elevation of serum cytokines, especially interferon gamma, tumor necrosis factor alpha, interleukin 17 (IL-17), interleukin 8 (IL-8) and interleukin 6 (IL-6). Initial experience from the outbreaks in Italy, China and the USA has anecdotally demonstrated improved outcomes for critically ill patients with COVID-19 with the administration of cytokine-modulatory therapies, especially anti-IL-6 agents. Although ongoing trials are investigating anti-IL-6 therapies, access to these therapies is a concern, especially as the numbers of cases worldwide continue to climb. An immunology-informed approach may help identify alternative agents to modulate the pathological inflammation seen in patients with COVID-19. Drawing on extensive experience administering these and other immune-modulating therapies, the Society for Immunotherapy of Cancer offers this perspective on potential alternatives to anti-IL-6 that may also warrant consideration for management of the systemic inflammatory response and pulmonary compromise that can be seen in patients with severe COVID-19.

28. **Association of Treatment Dose Anticoagulation with In-Hospital Survival among Hospitalized Patients with COVID-19.** Paranjpe I, Fuster V, Lala A, et al. *J Am Coll Cardiol.* 2020 May 06. DOI:10.1016/j.jacc.2020.05.001
http://www.onlinejacc.org/content/accj/early/2020/05/05/j.jacc.2020.05.001.full.pdf
Findings: We assessed association between administration of in-hospital systemic anticoagulation (AC) and survival in a large cohort of hospitalized patients with COVID-19. Although limited by its observational nature, our findings suggest that systemic AC may be associated with improved outcomes among patients hospitalized with COVID-19. The potential benefits of systemic AC, however, need to be weighed against the risk of bleeding and therefore should be individualized.

29. **Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy.** Toniati P, Piva S, Cattalini M, et al. *Autoimmun Rev*. 2020 May 3:102568. doi: 10.1016/j.autrev.2020.102568.
https://www.sciencedirect.com/science/article/abs/pii/S1568997220301300
Findings: A prospective series of 100 consecutive patients with confirmed COVID-19 pneumonia and ARDS requiring ventilatory support was analyzed to determine whether intravenous administration of tocilizumab (TCZ), a monoclonal antibody that targets the interleukin 6 receptor, was associated with improved outcome. Tocilizumab was administered at a dosage of

8 mg/kg by two consecutive intravenous infusions 12 h apart. A third infusion was optional based on clinical response. Out of 100 treated patients (88 M, 12 F; median age: 62 years), 43 received TCZ in the intensive care unit (ICU), while 57 in the general ward as no ICU beds were available. Of these 57 patients, 37 (65%) improved and suspended noninvasive ventilation (NIV) (median BCRSS: 1 [IQR 0-2]), 7 (12%) patients remained stable in NIV, and 13 (23%) patients worsened (10 died, 3 were admitted to ICU). Of the 43 patients treated in ICU, 32 (74%) improved (17 of them were taken off the ventilator and were discharged to the ward), 1 (2%) remained stable (BCRSS: 5) and 10 (24%) died (all of them had BCRSS≥7 before TCZ). Overall at 10 days, the respiratory condition was improved or stabilized in 77 (77%) patients, of whom 61 showed a significant clearing of diffuse bilateral opacities on chest x-ray and 15 were discharged from the hospital. Respiratory condition worsened in 23 (23%) patients, of whom 20 (20%) died. In conclusion, our series showed that COVID-19 pneumonia with ARDS was characterized by HIS. The response to TCZ was rapid, sustained, and associated with significant clinical improvement.

30. **Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial.** Hung I F-N et al. *Lancet.* 2020 May 8. doi: https://doi.org/10.1016/S0140-6736(20)31042-4 https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31042-4/fulltext
Findings: Between Feb 10 and March 20, 2020, 127 patients were recruited; 86 were randomly assigned to the combination group and 41 were assigned to the control group. The median number of days from symptom onset to start of study treatment was 5 days (IQR 3–7). The combination group had a significantly shorter median time from start of study treatment to negative nasopharyngeal swab (7 days [IQR 5–11]) than the control group (12 days [8–15]; hazard ratio 4·37 [95% CI 1·86–10·24], p=0·0010). Adverse events included self-limited nausea and diarrhoea with no difference between the two groups. One patient in the control group discontinued lopinavir–ritonavir because of biochemical hepatitis. No patients died during the study. Early triple antiviral therapy was safe and superior to lopinavir–ritonavir alone in alleviating symptoms and shortening the duration of viral shedding and hospital stay in patients with mild to moderate COVID-19. Future clinical study of a double antiviral therapy with interferon beta-1b as a backbone is warranted.

31. **COVID-19 and ECMO: the interplay between coagulation and inflammation-a narrative review.** Kowalewski M, Fina D, Słomka A, et al. *Crit Care*. 2020 May 8;24(1):205. doi: 10.1186/s13054-020-02925-3. https://ccforum.biomedcentral.com/articles/10.1186/s13054-020-02925-3
Findings: Infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has presently become a rapidly spreading and devastating global pandemic. Veno-venous extracorporeal membrane oxygenation (V-V ECMO) may serve as life-saving rescue therapy for refractory respiratory failure in the setting of acute respiratory compromise such as that induced by SARS-CoV-2. The present review summarizes the evidence on ECMO management of severe ARDS in light of recent COVID-19 pandemic, at the same time focusing on differences and similarities between SARS-CoV-2 and ECMO in terms of hematological and inflammatory interplay when these two settings merge.

32. **Interleukin-1 blockade with high-dose anakinra in patients with COVID-19, acute respiratory distress syndrome, and hyperinflammation: a retrospective cohort study.** Cavalli G et al. *Lancet.* 2020 May 7. doi: https://doi.org/10.1016/S2665-9913(20)30127-2
https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(20)30127-2/fulltext
Findings: In this retrospective cohort study of patients with COVID-19 and ARDS managed with non-invasive ventilation outside of the ICU, treatment with high-dose anakinra was safe and associated with clinical improvement in 72% of patients. Confirmation of efficacy will require controlled trials.

Prognosis

33. **Acute Physiology and Chronic Health Evaluation II Score as a Predictor of Hospital Mortality in Patients of Coronavirus Disease 2019.** Zou X, Li S, Fang M, et al. *Crit Care Med*. 2020 May 1. doi: 10.1097/CCM.0000000000004411.
https://journals.lww.com/ccmjournal/Abstract/9000/Acute_Physiology_and_Chronic_Health_Evaluation_II.95659.aspx
Findings: Acute Physiology and Chronic Health Evaluation II score was an effective clinical tool to predict hospital mortality in patients with coronavirus disease 2019 compared with Sequential Organ Failure Assessment score and CURB65 score. Acute Physiology and Chronic Health Evaluation II score greater than or equal to 17 serves as an early warning indicator of death and may provide guidance to make further clinical decisions.

34. **Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis.** Zhao Q, Meng M, Kumar R, et al. *Int J Infect Dis*. 2020 May 3. pii: S1201-9712(20)30301-5. doi:10.1016/j.ijid.2020.04.086.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7196544/pdf/main.pdf
Findings: Overall 13 case-series with a total of 2282 cases were included in the study. The pooled analysis showed that lymphocyte count was significantly lower in severe COVID-19 patients (MD -0.31×109/L; 95%CI: -0.42 to -0.19×109/L). The presence of lymphopenia was associated with nearly threefold increased risk of severe COVID-19. Lymphopenia is a prominent part of severe COVID-19 and a lymphocyte count of less than 1.5×109/L may be useful in predicting the severity clinical outcomes.

35. **Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes.** Zhu L et al. *Cell Metab.* 2020 May 1:S1550-4131(20)30238-2. doi: 10.1016/j.cmet.2020.04.021.
https://www.cell.com/cell-metabolism/pdfExtended/S1550-4131(20)30238-2
Findings: Type 2 diabetes is a major comorbidity of COVID-19, however the impact of blood glucose control on the degree of required medical interventions and on mortality in patients with COVID-19 and T2D remains uncertain. We performed a retrospective, multi-centered study of 7,337 cases of COVID-19 in Hubei Province, China, among which 952 had pre-existing T2D. We found that subjects with T2D required more medical interventions and had a significantly higher mortality (7.8% versus 2.7%; adjusted hazard ratio [HR], 1.49) and multiple organ injury

than the non-diabetic individuals. Further, we found that well-controlled BG (glycemic variability within 3.9 to 10.0 mmol/L) was associated with markedly lower mortality compared to individuals with poorly controlled BG (upper limit of glycemic variability exceeding 10.0 mmol/L) (adjusted HR, 0.14) during hospitalization. These findings provide clinical evidence correlating improved glycemic control with better outcomes in patients with COVID-19 and pre-existing T2D.

Transmission / Infection Control

36. **Can N95 Respirators Be Reused after Disinfection? How Many Times?** Liao L, Xiao W, Zhao M, et al. *ACS Nano*. 2020 May 5. doi: 10.1021/acsnano.0c03597.
https://pubs.acs.org/doi/10.1021/acsnano.0c03597
Findings: We investigated multiple commonly used disinfection schemes on media with particle filtration efficiency of 95%. Heating was recently found to inactivate the virus in solution within 5 min at 70 °C and is among the most scalable, user-friendly methods for viral disinfection. We found that heat (≤85 °C) under various humidities (≤100% relative humidity, RH) was the most promising, nondestructive method for the preservation of filtration properties in meltblown fabrics as well as N95-grade respirators. At 85 °C, 30% RH, we were able to perform 50 cycles of heat treatment without significant changes in the filtration efficiency. At low humidity or dry conditions, temperatures up to 100 °C were not found to alter the filtration efficiency significantly within 20 cycles of treatment. Ultraviolet (UV) irradiation was a secondary choice, which was able to withstand 10 cycles of treatment and showed small degradation by 20 cycles. However, UV can potentially impact the material strength and subsequent sealing of respirators. Finally, treatments involving liquids and vapors require caution, as steam, alcohol, and household bleach all may lead to degradation of the filtration efficiency, leaving the user vulnerable to the viral aerosols.

37. **Epidemiology of and Risk Factors for Coronavirus Infection in Health Care Workers: A Living Rapid Review.** Chou R, Dana T, Buckley DI, Selph S, Fu R, Totten AM. *Ann Intern Med.* 2020 May 5. doi: 10.7326/M20-1632.
https://www.acpjournals.org/aim/fullarticle/2765801/epidemiology-risk-factors-coronavirus-infection-health-care-workers-living-rapid
Findings: 64 studies met inclusion criteria; 43 studies addressed burden of HCW infections (15 on SARS-CoV-2), and 34 studies addressed risk factors (3 on SARS-CoV-2). Health care workers accounted for a significant proportion of coronavirus infections and may experience particularly high infection incidence after unprotected exposures. Illness severity was lower than in non-HCWs. Depression, anxiety, and psychological distress were common in HCWs during the coronavirus disease 2019 outbreak. The strongest evidence on risk factors was on PPE use and decreased infection risk. The association was most consistent for masks but was also observed for gloves, gowns, eye protection, and handwashing; evidence suggested a dose-response relationship. No study evaluated PPE reuse. Certain exposures (such as involvement in intubations, direct patient contact, or contact with bodily secretions) were associated with increased infection risk. Infection control training was associated with decreased risk.

38. **Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019.** Li D, Jin M, Bao P, Zhao W, Zhang S. *JAMA Netw Open*. 2020 May 1;3(5):e208292. doi: 10.1001/jamanetworkopen.2020.8292.
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765654
Findings: In this cohort study, we found that SARS-CoV-2 can be present in the semen of patients with COVID-19, and SARS-CoV-2 may still be detected in the semen of recovering patients. If it could be proved that SARS-CoV-2 can be transmitted sexually in future studies, sexual transmission might be a critical part of the prevention of transmission.

39. **Clinical evidence based review and recommendations of aerosol generating medical procedures in otolaryngology - head and neck surgery during the COVID-19 pandemic.** Thamboo A, Lea J, Sommer DD, Sowerby L, et al. *J Otolaryngol Head Neck Surg*. 2020 May 6;49(1):28. doi: 10.1186/s40463-020-00425-6.
https://journalotohns.biomedcentral.com/articles/10.1186/s40463-020-00425-6
Findings: Direct evidence indicates that CO2 laser ablation, the use of high-speed rotating devices, electrocautery and endotracheal suctioning are AGMPs. Indirect evidence indicates that tracheostomy should be considered as potential AGMPs. Nasal endoscopy and nasal packing/epistaxis management can result in droplet transmission, but it is unknown if these procedures also carry the risk of airborne transmission. During the COVID-19 pandemic, special care should be taken when CO2 lasers, electrocautery and high-speed rotating devices are used in potentially infected tissue. Tracheal procedures like tracheostomy and endotracheal suctioning can also result in airborne transmission via small virus containing aerosols.

40. **Prolonged Persistence of SARS-CoV-2 RNA in Body Fluids.** Sun J, Xiao J, Sun R, et al. *Emerg Infect Dis*. 2020 May 8;26(8). doi: 10.3201/eid2608.201097.
https://wwwnc.cdc.gov/eid/article/26/8/20-1097_article
Findings: We prospectively assessed 49 coronavirus disease cases in Guangdong, China, to estimate the frequency and duration of detectable severe acute respiratory syndrome coronavirus 2 RNA in human body fluids. The prolonged persistence of virus RNA in various body fluids may guide the clinical diagnosis and prevention of onward virus transmission.

41. **SARS-CoV-2: air/aerosols and surfaces in laboratory and clinical settings.** Zhang DX. *J Hosp Infect*. 2020 May 6. pii: S0195-6701(20)30232-2. doi:10.1016/j.jhin.2020.05.001.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7204655/pdf/main.pdf
Abstract: Combined with previous reports implicating other coronaviruses in super-spreading events and nosocomial outbreaks3, researchers are now investigating air/aerosol and fomite transmission as potential transmission routes of SARS-CoV-2. Since SARS-CoV-2 is novel, our understanding of its transmission characteristics remains limited. In very close relation to this context, there are four recent studies representative of current investigation of SARS-CoV-2 in air/aerosols and on surfaces in laboratory and clinical settings[4], [5], [6], [7].

42. **Symptomatic Infection is associated with Prolonged Duration of Viral Shedding in Mild Coronavirus Disease 2019: A Retrospective Study of 110 Children in Wuhan.** Lu Y, Li Y, Deng W, Liu M, He Y, Huang L, Lv M, Li J, Du H. *Pediatr Infect Dis J*. 2020 May 5. doi:

10.1097/INF.0000000000002729.
http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&AN=00006454-202005000-00001&LSLINK=80&D=ovft
Findings: Prolonged duration of viral shedding in children with COVID-19 was associated with symptomatic infection, fever, pneumonia and lymphocyte count =2.0 × 10/L. Monitoring of symptoms could help to know the viral shedding in children with COVID-19.

Women & Children

43. **Clinical course of severe and critical COVID-19 in hospitalized pregnancies: a US cohort study**. Pierce-Williams RAM, Burd J, Felder L, et al. May 8. *Am J Obstet Gynecol MFM*. 2020;100134. doi:10.1016/j.ajogmf.2020.100134
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7205698/pdf/main.pdf
Findings: This is a cohort study of pregnant women with severe or critical COVID-19 infection hospitalized at 12 US institutions between March 5, 2020 and April 20, 2020. Of 64 pregnant women hospitalized with COVID-19, 44 (69%) had severe and 20 (31%) critical disease. In hospitalized pregnant women with severe or critical COVID-19 infection, admission typically occurred about 7 days after symptom onset, and the duration of hospitalization was 6 days (6 severe versus 12 critical). Critically ill women had a high rate of ARDS, and there was one case of cardiac arrest, but there were no cases of cardiomyopathy, or maternal mortality. Hospitalization for severe or critical COVID-19 infection resulted in delivery during the course of infection in 50% of this cohort, usually in the third trimester. There were no perinatal deaths in this cohort.

44. **Characteristics and Outcomes of Children with Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units.** Lara S. Shekerdemian, Nabihah R. Mahmood, Katie K. Wolfe; et al *JAMA Pediatr*. May 11, 2020. doi:10.1001/jamapediatrics.2020.1948
https://jamanetwork.com/journals/jamapediatrics/fullarticle/2766037
Findings: In this cross-sectional study of 46 North American PICUs, between March 14 and April 3, 2020, 48 children were admitted to 14 PICUs in the US and none in Canada. A total of 40 children (83%) had preexisting underlying medical conditions, 35 (73%) presented with respiratory symptoms, and 18 (38%) required invasive ventilation, and the hospital mortality rate was 4.2%.

45. **Hyperinflammatory shock in children during COVID-19 pandemic.** Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. *Lancet*. May 6, 2020. doi:https://doi.org/10.1016/S0140-6736(20)31094-1
https://www.thelancet.com/lancet/article/s0140-6736(20)31094-1
Findings: During a period of 10 days in mid-April 2020, we noted an unprecedented cluster of eight children with hyperinflammatory shock, showing features similar to atypical Kawasaki disease, Kawasaki disease shock syndrome, or toxic shock syndrome (typical number is one or two children per week). This case cluster formed the basis of a national alert.

46. **Care of critically ill pregnant patients with COVID-19: a case series.** Hirshberg A, Kern-Goldberger AR, Levine LD, et al. *Am J Obstet Gynecol*. 2020 May 1:S0002-9378(20)30515-9. doi: 10.1016/j.ajog.2020.04.029.
https://www.ajog.org/article/S0002-9378(20)30515-9/pdf

GUIDELINES & CONSENSUS STATEMENTS

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https://onlinelibrary.wiley.com/doi/abs/10.1111/jgs.16537?af=R

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FDA / CDC / NIH/ WHO Updates

CDC Interim Guidance: Outpatient and Ambulatory Care Settings: Responding to Community Transmission of COVID-19 in the United States https://www.cdc.gov/coronavirus/2019-ncov/hcp/ambulatory-care-settings.html

FDA Authorizes First Diagnostic Test Using At-Home Collection of Saliva Specimens
https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-diagnostic-test-using-home-collection-saliva

WHO Scientific Brief: COVID-19 and the use of angiotensin-converting enzyme inhibitors and receptor blockers
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Commentary

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