Providence

COVID-19 Resource Desk

#62| 6.27.21 to 7.3.21

Prepared by System Library Services Retraction Watch

New Research

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

COVID-19 related publications by Providence caregivers – see Digital Commons

Basic Science / Virology / Pre-clinical

1. **SARS-CoV-2 immune evasion by the B.1.427/B.1.429 variant of concern.** McCallum M et al. *Science*. 2021 Jul 1:eabi7994. doi: 10.1126/science.abi7994.
https://science.sciencemag.org/content/early/2021/06/30/science.abi7994
A novel variant of concern (VOC) named CAL.20C (B.1.427/B.1.429), originally detected in California, carries spike glycoprotein mutations S13I in the signal peptide, W152C in the N-terminal domain (NTD), and L452R in the receptor-binding domain (RBD). Plasma from individuals vaccinated with a Wuhan-1 isolate-based mRNA vaccine or convalescent individuals exhibited neutralizing titers, which were reduced 2-3.5 fold against the B.1.427/B.1.429 variant relative to wildtype pseudoviruses. The L452R mutation reduced neutralizing activity of 14 out of 34 RBD-specific monoclonal antibodies (mAbs). The S13I and W152C mutations resulted in total loss of neutralization for 10 out of 10 NTD-specific mAbs since the NTD antigenic supersite was remodeled by a shift of the signal peptide cleavage site and formation of a new disulphide bond, as revealed by mass spectrometry and structural studies.

Diagnostics & Screening

2. **Study of Thoracic CT in COVID-19: The STOIC Project.** Revel MP et al. *Radiology*. 2021 Jun 29:210384. doi: 10.1148/radiol.2021210384.
https://pubs.rsna.org/doi/10.1148/radiol.2021210384
Results Of 10,930 subjects screened for eligibility, 10,735 were included and 6,448 (60.0%) had a positive RT-PCR result. With RT-PCR as reference, the sensitivity and specificity and CT were 80.2% and 79.7%, respectively with strong agreement between junior and senior radiologists. Of all the variables analysed, the extent of pneumonia on CT was the best predictor of severe outcome at one month. Using pre-defined criteria, CT reading is not influenced by reader's experience and helps predict the outcome at one month.

Epidemiology & Public Health

3. **COVID-19-related state-wise racial and ethnic disparities across the USA: an observational study based on publicly available data from The COVID Tracking Project.** Jordan JE, et al. **[Providence author]** *BMJ Open*. 2021 Jun 21;11(6):e048006. doi: 10.1136/bmjopen-2020-048006. https://bmjopen.bmj.com/content/bmjopen/11/6/e048006.full.pdf
   Publicly available data from The COVID Tracking Project at The Atlantic were accessed between 9 September 2020 and 14 September 2020. The Hispanic population had a median of 158% higher COVID-19 infection relative to their % population proportion. This was followed by AA, with 50% higher COVID-19 infection relative to their % population proportion. The AA population had the most disproportionate mortality, with a median of 46% higher mortality than the % population proportion. Disproportionate impact of COVID-19 was also seen in AI/AN and Asian populations, with 100% excess infections than the % population proportion seen in nine states for AI/AN and seven states for Asian populations. There was no disproportionate impact in the white population in any state.

4. **Comparison of COVID-19 Vaccine Approvals at the US Food and Drug Administration, European Medicines Agency, and Health Canada.** Lythgoe MP, Middleton P. *JAMA Netw Open*. 2021 Jun 1;4(6):e2114531. doi: 10.1001/jamanetworkopen.2021.14531. https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2781352
   Between 2010 and 2020, the FDA approved 21 new vaccines for use, with a median review time from submission to approval of 12 months. By permitting EUA for COVID-19 vaccines, the median review time was 21 days during the COVID-19 pandemic. Regulators have adopted new pathways and frameworks that allow for rapid vaccine authorization in specific circumstances and have acknowledged the need for more data regarding safety and efficacy to permit full approval. Medicine regulators are engaging with vaccine developers earlier; for example, HC has developed fast-track approval processes specifically for COVID-19 vaccines, which begins the review process earlier and allows evidence to be reviewed as it becomes available. Furthermore, increasing global regulatory harmonization is enabling the robust and timely approval of COVID-19 vaccines. With the potential challenges that new variants of SARS-CoV-2 may bring, the COVID-19 vaccine armamentarium will likely need further additions and requires prompt regulatory approval to ensure that we can meet the continuing challenges brought by the global pandemic.

5. **Hospital Capacities and Shortages of Healthcare Resources among U.S. Hospitals During COVID-19 Pandemic, National Healthcare Safety Network, March 27-July 14, 2020.** Wu H et al. *Infect Control Hosp Epidemiol.* 2021 Jun 24:1-12. doi: 10.1017/ice.2021.280. https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/hospital-capacities-and-shortages-of-healthcare-resources-among-us-hospitals-during-covid19-pandemic-national-healthcare-safety-network-march-27july-14-2020/D1259271CF109B72A3BB878D7249617F
   During March 27-July 14, 2020, the CDC's National Healthcare Safety Network extended its surveillance to hospital capacities responding to COVID-19 pandemic. The data showed wide

variations across hospitals in case burden, bed occupancies, ventilator usage, and healthcare personnel and supply status. These data were used to inform emergency responses.

Prognosis

6. **Factors associated with mortality in patients with COVID-19 admitted to intensive care: a systematic review and meta-analysis.** Taylor EH, et al. *Anaesthesia*. 2021 Jun 29. doi: 10.1111/anae.15532. https://associationofanaesthetists-publications.onlinelibrary.wiley.com/doi/10.1111/anae.15532
   A higher sequential organ failure assessment score and acute physiology and chronic health evaluation-2 score; a lower PaO2 :FI O2 and the need for mechanical ventilation at admission were associated with mortality. Increasing age, pre-existing comorbidities, severity of illness based on validated scoring systems, and the host response to the disease were associated with mortality; while male sex and increasing BMI were not. These factors have prognostic relevance for patients admitted to intensive care with COVID-19.

7. **SARS-CoV-2 viremia is associated with distinct proteomic pathways and predicts COVID-19 outcomes.** Li Y et al. *J Clin Invest.* 2021 Jul 1;131(13):148635. doi: 10.1172/JCI148635. https://www.jci.org/articles/view/148635
   This study included 300 participants with nucleic acid test-confirmed COVID-19. Plasma SARS-CoV-2 viremia levels at the time of presentation predicted adverse disease outcomes. Proteomic analyses revealed prominent proteomic pathways associated with SARS-CoV-2 viremia, including upregulation of SARS-CoV-2 entry factors (ACE2, CTSL, FURIN), heightened markers of tissue damage to the lungs, gastrointestinal tract, and endothelium/vasculature, and alterations in coagulation Pathways. CONCLUSION These results highlight the cascade of vascular and tissue damage associated with SARS-CoV-2 plasma viremia that underlies its ability to predict COVID-19 disease outcomes.

Survivorship & Rehabilitation

8. **Long-term Outcomes Following Severe COVID-19 Infection: A Multicenter Cohort Study of Family Member Outcomes.** McPeake J et al. *Ann Am Thorac Soc.* 2021 Jun 30. doi: 10.1513/AnnalsATS.202104-481RL.
   https://www.atsjournals.org/doi/abs/10.1513/AnnalsATS.202104-481RL
   Consistent with previous research, family members of critical care survivors in this cohort experienced high levels of anxiety and depression following discharge. Carer strain was higher in this cohort compared to previously reported cohorts. Although the psychosocial burden of COVID-19 family members may appear similar to other family member cohorts following critical care, the symptom trajectory of this unique cohort remains poorly characterised. Previous research has shown that family members' psychosocial problems often improve over time. However, the COVID-19 family cohort is distinctive; not only did family members have less access while the patients were in hospital, but the usual support mechanisms, primarily other family and friends, have also been unavailable or inaccessible due to public health lockdowns and social restrictions.

Therapeutics

9. **Effect of prone versus supine position in COVID-19 patients: A systematic review and meta-analysis.** Chua EX, et al. *J Clin Anesth*. 2021 Jun 22;74:110406. doi: 10.1016/j.jclinane.2021.110406. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8216875/
   Our meta-analysis demonstrated that prone position improved PaO_2/FiO_2 ratio with better SpO_2 than supine position in COVID-19 patients. Given the limited number of studies with small sample size and substantial heterogeneity of measured outcomes, further studies are warranted to standardize the regime of prone position to improve the certainty of evidence.

10. **Ivermectin for the treatment of COVID-19: A systematic review and meta-analysis of randomized controlled trials.** Roman YM, et al. *Clin Infect Dis.* 2021 Jun 28:ciab591. doi: 10.1093/cid/ciab591. https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab591/6310839
    In comparison to SOC or placebo, IVM did not reduce all-cause mortality, length of stay or viral clearance in RCTs in COVID-19 patients with mostly mild disease. IVM did not have an effect on AEs or severe AEs. IVM is not a viable option to treat COVID-19 patients.

Transmission / Infection Control

11. **Efficacy of Portable Air Cleaners and Masking for Reducing Indoor Exposure to Simulated Exhaled SARS-CoV-2 Aerosols — United States, 2021.** Lindsley WG, et al. *MMWR Morb Mortal Wkly Rep*. ePub: 2 July 2021. DOI: http://dx.doi.org/10.15585/mmwr.mm7027e1
    A simulated infected meeting participant who was exhaling aerosols was placed in a room with two simulated uninfected participants and a simulated uninfected speaker. Using two HEPA air cleaners close to the aerosol source reduced the aerosol exposure of the uninfected participants and speaker by up to 65%. A combination of HEPA air cleaners and universal masking reduced exposure by up to 90%. Portable HEPA air cleaners can reduce exposure to simulated SARS-CoV-2 aerosols in indoor environments, especially when combined with universal masking.

Vaccines / Immunology

12. **B and T cell immune responses elicited by the Comirnaty® COVID-19 vaccine in nursing home residents.** Torres I, et al. *Clin Microbiol Infect*. 2021 Jun 23:S1198-743X(21)00332-3. doi: 10.1016/j.cmi.2021.06.013. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00332-3/fulltext
    The Comirnaty® COVID-19 vaccine elicits robust SARS-CoV-2-S antibody responses in nursing home residents. Nevertheless, the rate and frequency of detectable SARS-CoV-2 IFN-γ T-cell responses after vaccination was lower in nursing home residents compared to controls.

13. **Vaccine effectiveness of the first dose of ChAdOx1 nCoV-19 and BNT162b2 against SARS-CoV-2 infection in residents of long-term care facilities in England (VIVALDI): a prospective cohort**

study. Shrotri M, et al. *Lancet Infect Dis*. 2021 Jun 23:S1473-3099(21)00289-9. doi: 10.1016/S1473-3099(21)00289-9.
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00289-9/fulltext
Single-dose vaccination with BNT162b2 and ChAdOx1 vaccines provides substantial protection against infection in older adults from 4-7 weeks after vaccination and might reduce SARS-CoV-2 transmission. However, the risk of infection is not eliminated, highlighting the ongoing need for non-pharmaceutical interventions to prevent transmission in long-term care facilities.

14. **Effectiveness of BNT162b2 and ChAdOx1 nCoV-19 COVID-19 vaccination at preventing hospitalisations in people aged at least 80 years: a test-negative, case-control study.** Hyams C et al. *Lancet Infect Dis.* 2021 Jun 23:S1473-3099(21)00330-3. doi: 10.1016/S1473-3099(21)00330-3. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00330-3/fulltext
One dose of either BNT162b2 or ChAdOx1 nCoV-19 resulted in substantial risk reductions of COVID-19-related hospitalisation in people aged at least 80 years.

15. **High seroconversion rate but low antibody titers after two injections of BNT162b2 (Pfizer-BioNTech) vaccine in patients treated by chemotherapy for solid cancers.** Palich R, et al. *Ann Oncol.* 2021 Jun 22:S0923-7534(21)02075-5. doi: 10.1016/j.annonc.2021.06.018.
https://www.annalsofoncology.org/article/S0923-7534(21)02075-5/fulltext
An mRNA vaccine boost led to a high seroconversion rate, reinforcing the need not to delay the second dose. However, anti-spike antibody titers were 3-10 times lower in patients with SCs than in healthy controls, raising concerns about impaired humoral immunity, especially in patients treated by chemotherapy. At the same time, the seroconversion data are rather reassuring among patients on anti-HER2, anti PD-1/PD-L1, antiangiogenic treatment or hormone therapy without associated chemotherapy.

16. **SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses.** Turner JS et al. *Nature*. 2021 Jun 28. doi: 10.1038/s41586-021-03738-2.
https://www.nature.com/articles/s41586-021-03738-2
Our studies demonstrate that SARS-CoV-2 mRNA-based vaccination of humans induces a persistent GC B cell response, enabling the generation of robust humoral immunity.

17. **Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial.** Borobia AM et al. *Lancet*. 2021 Jun 25:S0140-6736(21)01420-3. doi: 10.1016/S0140-6736(21)01420-3.
https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01420-3/fulltext
BNT162b2 given as a second dose in individuals prime vaccinated with ChAdOx1-S induced a robust immune response, with an acceptable and manageable reactogenicity profile.

18. **Adverse events after first COVID-19 vaccination in patients with autoimmune diseases.** Boekel L et al. *Lancet Rheumatol.* 2021 Jun 18. doi: 10.1016/S2665-9913(21)00181-8.
https://www.thelancet.com/journals/lanrhe/article/PIIS2665-9913(21)00181-8/fulltext

Analysis of the results of our questionnaire demonstrate that adverse events of COVID-19 vaccinations in patients with autoimmune diseases are comparable with controls, independent of the type of vaccine. The observed adverse events consisted of expected transient local or systemic reactions that were mostly self-limiting. The frequency of participants who reported adverse events was lower than that reported in clinical trials, but similar to a nationwide observational study on adverse events of COVID-19 vaccinations in the general population done in the UK. Our data are consistent with previous studies that reported higher frequencies of adverse events in women and younger people. We did not observe any serious adverse events, but the number of participants included in our study was too low to draw conclusions about rare serious events.

19. **Myocarditis Occurring After Immunization with mRNA-Based COVID-19 Vaccines.** Shay DK, Shimabukuro TT, DeStefano F. *JAMA Cardiol.* 2021 Jun 29. doi: 10.1001/jamacardio.2021.2821. https://jamanetwork.com/journals/jamacardiology/fullarticle/2781600
Two reports in the current issue of JAMA Cardiology describe cases of acute myocarditis that occurred among persons who received the BNT162b2-mRNA (Pfizer-BioNTech) or mRNA-1273 (Moderna) messenger RNA (mRNA)–based COVID-19 vaccines authorized for use in the US.1,2 During the clinical evaluations of these patients, alternative etiologies for myocarditis were not detected.

    See also: Patients With Acute Myocarditis Following mRNA COVID-19 Vaccination. Kim HW et al. *JAMA Cardiol.* 2021 Jun 29. doi: 10.1001/jamacardio.2021.2828.
    Myocarditis Following Immunization With mRNA COVID-19 Vaccines in Members of the US Military. Montgomery J et al. *JAMA Cardiol*. 2021 Jun 29. doi: 10.1001/jamacardio.2021.2833.

20. **COVID-19 mRNA vaccine induced antibody responses against three SARS-CoV-2 variants.** Jalkanen P et al. *Nat Commun.* 2021 Jun 28;12(1):3991. doi: 10.1038/s41467-021-24285-4. https://www.nature.com/articles/s41467-021-24285-4
Vaccinees' neutralization titres exceeded those of recovered non-hospitalized COVID-19 patients. Our work provides evidence that the second dose of the BNT162b2 vaccine induces cross-neutralization of at least some of the circulating SARS-CoV-2 variants.

21. **Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2.** Collier DA et al. *Nature*. 2021 Jun 30. doi: 10.1038/s41586-021-03739-1. https://www.nature.com/articles/s41586-021-03739-1
Although two-dose mRNA vaccination provides excellent protection against SARS-CoV-2, data are scarce on vaccine efficacy against variants of concern (VOC) in individuals above 80 years of age. We conclude that the elderly are a high risk population that warrant specific measures to boost vaccine responses, particularly where variants of concern are circulating.

22. **Prevention and Attenuation of Covid-19 with the BNT162b2 and mRNA-1273 Vaccines.** Thompson MG et al. *N Engl J Med.* 2021 Jun 30. doi: 10.1056/NEJMoa2107058. https://www.nejm.org/doi/10.1056/NEJMoa2107058

Authorized mRNA vaccines were highly effective among working-age adults in preventing SARS-CoV-2 infection when administered in real-world conditions, and the vaccines attenuated the viral RNA load, risk of febrile symptoms, and duration of illness among those who had breakthrough infection despite vaccination. (Funded by the National Center for Immunization and Respiratory Diseases and the Centers for Disease Control and Prevention.).

23. **Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine.** Heath PT et al. *N Engl J Med*. 2021 Jun 30. doi: 10.1056/NEJMoa2107659. https://www.nejm.org/doi/full/10.1056/NEJMoa2107659 = A two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection and showed high efficacy against the B.1.1.7 variant.

24. **Brief Report: Humoral and cellular immune responses to SARS-CoV-2 infection and vaccination in B cell depleted autoimmune patients.** Simon D et al. *Arthritis Rheumatol*. 2021 Jul 1. doi: 10.1002/art.41914. https://onlinelibrary.wiley.com/doi/pdf/10.1002/art.41914 These data show that B cell depletion completely blocks humoral but not T cell SARS-CoV-2 vaccination response. Furthermore, limited humoral immune responses are found in B cell depleted patients after SARS-CoV-2 infection.

Women & Children

25. **Risk of Pregnancy Loss Prior to 20 weeks Gestation with COVID-19.** Jacoby VL, et al. *Am J Obstet Gynecol.* 2021 Jun 24:S0002-9378(21)00747-X. doi: 10.1016/j.ajog.2021.06.080. https://www.ajog.org/article/S0002-9378(21)00747-X/fulltext
In this nationwide study of pregnant people in the U.S., the risk of pregnancy loss at <20 weeks gestation was about 6%, both for participants with COVID-19 (N=94) and COVID-19 negative controls (N=15). This data compares favorably to the 10% rate of miscarriage among clinically recognized first trimester pregnancies prior to the pandemic.6 To our knowledge, this is the largest analyses of COVID-19 in the first trimester in a U.S. longitudinal cohort. With this sample size, the upper bound of the confidence interval for pregnancy loss of 13.4% is reassuring because it is not significantly higher than the expected miscarriage rate without viral infection. These results can guide counseling for people infected with SARS-CoV-2 early in pregnancy.

26. **Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study.** Papageorghiou AT et al. *Am J Obstet Gynecol.* 2021 Jun 26:S0002-9378(21)00561-5. doi: 10.1016/j.ajog.2021.05.014. https://www.ajog.org/article/S0002-9378(21)00561-5/fulltext
COVID-19 during pregnancy is strongly associated with preeclampsia, especially among nulliparous women. This association is independent of any risk factors and preexisting conditions. COVID-19 severity does not seem to be a factor in this association. Both conditions are associated independently of and in an additive fashion with preterm birth, severe perinatal morbidity and mortality, and adverse maternal outcomes. Women with preeclampsia should be considered a particularly vulnerable group with regard to the risks posed by COVID-19.

27. **SARS-CoV-2 among Infants <90 Days of Age Admitted for Serious Bacterial Infection Evaluation.** Paret M, et al. *Pediatrics.* 2021 Jun 30:e2020044685. doi: 10.1542/peds.2020-044685. https://pediatrics.aappublications.org/content/early/2021/06/29/peds.2020-044685 SARS-CoV-2 was common among young infants hospitalized for SBI evaluation during periods of high, but not low, community SARS-CoV-2 circulation in New York City, although most infants did not require intensive care admission.

28. **AZD1222-induced neutralising antibody activity against SARS-CoV-2 Delta VOC.** Wall EC et al. *Lancet*. 2021 Jun 28:S0140-6736(21)01462-8. doi: 10.1016/S0140-6736(21)01462-8. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01462-8/fulltext Our data reinforce the need to recognise the increased protection offered by a second vaccine dose as COVID-19 cases associated with the B.1.617.2 variant increase. They also suggest that further booster immunisations might be needed, especially for more susceptible groups that have received vaccines that induce lower than average NAbTs. As with mRNA vaccines, it might be feasible to prioritise the use of the AZD1222 vaccine, in light of severely restricted supply, for people with a confirmed history of COVID-19. Overall, our findings highlight the urgent need for expanded serological monitoring of NAbTs within sub-populations.

GUIDELINES & CONSENSUS STATEMENTS

Nutritional management of individuals with obesity and COVID-19: ESPEN expert statements and practical guidance. endorsed by the ESPEN Council. *Clin Nutr.* 2021 May 11:S0261-5614(21)00248-X. doi: 10.1016/j.clnu.2021.05.006.

FDA / CDC / NIH / WHO Updates

FDA Revokes Emergency Use Authorizations for Certain Respirators and Decontamination Systems as Access to N95s Increases Nationwide, 6-30-21

Commentary & News

Temporal Associations Between Immunization With the COVID-19 mRNA Vaccines and Myocarditis: The Vaccine Safety Surveillance System Is Working. Navar AM, et al. *JAMA Cardiol*. 2021 Jun 29. doi: 10.1001/jamacardio.2021.2853.

Covid-19: Pfizer vaccine could provide lasting immunity, small study suggests. Mahase E. *BMJ.* 2021 Jul 1;374:n1675. doi: 10.1136/bmj.n1675.

Sharing Technology and Vaccine Doses to Address Global Vaccine Inequity and End the COVID-19 Pandemic. Kavanagh MM, et al. *JAMA.* 2021 Jul 1. doi: 10.1001/jama.2021.10823.

Ethical Considerations of Offering Benefits to COVID-19 Vaccine Recipients. Persad G, Emanuel EJ. *JAMA*. 2021 Jul 1. doi: 10.1001/jama.2021.11045.

How long does covid-19 immunity last? Baraniuk C. *BMJ*. 2021 Jun 30;373:n1605. doi: 10.1136/bmj.n1605.

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