

COVID-19 Resource Desk

#51 | 4.10.21 to 4.16.21

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Retraction Watch

New Research

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

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

Basic Science / Virology / Pre-clinical

 Antibody evasion by the P.1 strain of SARS-CoV-2. Dejnirattisai W et al. *Cell.* 2021 Mar 30:S0092-8674(21)00428-1. doi: 10.1016/j.cell.2021.03.055. https://www.sciencedirect.com/science/article/pii/S0092867421004281

Current vaccines elicit neutralizing antibody responses to the virus spike derived from early isolates. However, new strains have emerged with multiple mutations, including P.1 from Brazil, B.1.351 from South Africa, and B.1.1.7 from the UK (12, 10, and 9 changes in the spike, respectively). We show that, surprisingly, P.1 is significantly less resistant to naturally acquired or vaccine-induced antibody responses than B.1.351, suggesting that changes outside the receptor-binding domain (RBD) impact neutralization. Monoclonal antibody (mAb) 222 neutralizes all three variants despite interacting with two of the ACE2-binding site mutations. We explain this through structural analysis and use the 222 light chain to largely restore neutralization potency to a major class of public antibodies.

Clinical Syndrome

2. Comorbid illnesses are associated with altered adaptive immune responses to SARS-CoV-2. Choi Robert Y, et al. [Providence author]. JCI Insight. 2021 Mar 22;6(6):146242. doi: 10.1172/jci.insight.146242. <u>https://insight.jci.org/articles/view/146242</u> Comorbid medical illnesses are associated with more severe COVID-19, hospitalization, and death. However, the role of the immune system has not been determined. We found a functionally diverse and coordinated response between T cells and antibodies targeting SARS-CoV-2, which is reduced in the presence of comorbid illnesses that are known risk factors for severe COVID-19.

Diagnostics & Screening

3. Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. Tsang NNY, et al. *Lancet Infect Dis.* 2021 Apr 12:S1473-3099(21)00146-8. doi: 10.1016/S1473-3099(21)00146-8. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00146-8/fulltext Compared with the gold standard of nasopharyngeal swabs, pooled nasal and throat swabs offered the best diagnostic performance of the alternative sampling approaches for diagnosis of SARS-CoV-2 infection in ambulatory care. Saliva and nasal swabs gave comparable and very good diagnostic performance and are clinically acceptable alternative specimen collection methods. Throat swabs gave a much lower sensitivity and positive predictive value and should not be recommended. Self-collection for pooled nasal and throat swabs and nasal swabs was not associated with any significant impairment of diagnostic accuracy. Our results also provide a useful reference framework for the proper interpretation of SARS-CoV-2 testing results using different clinical specimens.

Epidemiology & Public Health

4. Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study. Graham MS et al. *Lancet Public Health* 2021 Apr 12. doi: https://doi.org/10.1016/S2468-2667(21)00055-4

The lack of change in symptoms identified in this study indicates that existing testing and surveillance infrastructure do not need to change specifically for the B.1.1.7 variant. In addition, given that there was no apparent increase in the reinfection rate, vaccines are likely to remain effective against the B.1.1.7 variant.

- 5. Evolving changes in mortality of 13,301 critically ill adult patients with COVID-19 over 8 months. Kurtz P, et al. Intensive Care Med. 2021 Apr 14. doi: 10.1007/s00134-021-06388-0. https://link.springer.com/article/10.1007/s00134-021-06388-0 Among 13,301 confirmed-COVID-19 patients, 60-day in-hospital mortality was 13%. Across four time periods identified, younger patients were progressively more common, non-invasive respiratory support was increasingly used, and the 60-day in-hospital mortality decreased in the last two periods. We found that younger age, absence of frailty and the use of non-invasive respiratory support as first support strategy were independently associated with improved survival.
- Trends in Racial and Ethnic Disparities in COVID-19 Hospitalizations, by Region United States, March-December 2020. Romano SD, et al. MMWR Morb Mortal Wkly Rep. 2021 Apr 16;70(15):560-565. doi:10.15585/mmwr.mm7015e2.

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https://www.cdc.gov/mmwr/volumes/70/wr/mm7015e2.htm
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Within each of the four U.S. Census regions, the cumulative age-adjusted COVID-19 proportionate hospitalization ratios (aPHR) was highest for Hispanic or Latino patients. Racial and ethnic disparities in COVID-19 hospitalization were largest during May-July 2020; the peak monthly aPHR among Hispanic or Latino patients was >9.0 in the West and Midwest, >6.0 in the South, and >3.0 in the Northeast. The aPHRs declined for most racial and ethnic groups during July-November 2020 but increased for some racial and ethnic groups in some regions during December. Disparities in COVID-19 hospitalization by race/ethnicity varied by region and became less pronounced over the course of the pandemic, as COVID-19 hospitalizations increased among non-Hispanic White persons.

- 7. COVID-19 Stats: COVID-19* and Influenza(†) Discharge Diagnoses as a Percentage of Emergency Department (ED) Visits,(§) by Year United States, June 2018-March 2021. MMWR Morb Mortal Wkly Rep. 2021 Apr 16;70(15):573. doi: 10.15585/mmwr.mm7015a7. https://www.cdc.gov/mmwr/volumes/70/wr/mm7015a7.htm?s_cid=mm7015a7_x
 In late June 2020, the percentage of ED visits for COVID-19 increased and reached a peak of 2.8% of all ED visits in early July before declining through August. This decline was followed by a larger and more prolonged increase beginning in September 2020 that reached a peak (7.2%) in early January 2021. Influenza activity generally begins in October with increased activity throughout the winter months. By the beginning of February 2018, the percentage of ED visits for influenza reached 3.1%, and by the beginning of February 2019, reached 5.0%. During June 2020–March 2021, ED visits for influenza accounted for less than 0.1% of all visits.
- 8. Notes from the Field: Update on Excess Deaths Associated with the COVID-19 Pandemic -United States, January 26, 2020-February 27, 2021. Rossen LM, et al. *MMWR Morb Mortal Wkly Rep.* 2021 Apr 16;70(15):570-571. doi: 10.15585/mmwr.mm7015a4. <u>https://www.cdc.gov/mmwr/volumes/70/wr/mm7015a4.htm</u> Since April 2020, CDC's National Center for Health Statistics (NCHS) has published weekly data on excess deaths associated with the COVID-19 pandemic. A previous report identified nearly 300,000 excess deaths during January 26–October 3, 2020, with two thirds directly associated with COVID-19. Using more recent data from the National Vital Statistics System (NVSS), CDC estimated that 545,600–660,200 excess deaths occurred in the United States during January 26, 2020–February 27, 2021.
- 9. Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil. Faria NR et al. Science. 2021 Apr 14:eabh2644. doi: 10.1126/science.abh2644. https://science.sciencemag.org/content/early/2021/04/13/science.abh2644 Cases of SARS-CoV-2 infection in Manaus, Brazil, resurged in late 2020, despite previously high levels of infection. Genome sequencing of viruses sampled revealed the emergence and circulation of a novel SARS-CoV-2 variant of concern. Lineage P.1, acquired 17 mutations, including a trio in the spike protein (K417T, E484K and N501Y) associated with increased binding to the human ACE2 receptor. Molecular clock analysis shows that P.1 emergence occurred around mid-November 2020 and was preceded by a period of faster molecular evolution. We estimate that P.1 may be 1.7-2.4-fold more transmissible, and that previous (non-P.1) infection provides 54-79% of the protection against infection with P.1 that it provides against non-P.1 lineages.

Healthcare Delivery & Healthcare Workers

10. Hospital-Acquired Infections among Adult Patients Admitted for COVID-19. Smith L, et al. Infect Control Hosp Epidemiol. 2021 Apr 13:1-15. doi: 10.1017/ice.2021.148. https://www.cambridge.org/core/journals/infection-control-and-hospitalepidemiology/article/hospitalacquired-infections-among-adult-patients-admitted-forcovid19/F665C6D4B8969375ED03DB11AD3D8077 In a multicenter cohort of 963 adults hospitalized due to COVID-19, 5% had a proven HAI and 21% had a proven/probable or possible HAI. Risk factors for proven/probable HAIs included intensive care unit admission, dexamethasone use, severe COVID-19, heart failure and antibiotic exposure upon admission.

- 11. Hospital-acquired infections in critically-ill COVID-19 patients. Grasselli G et al. Chest. 2021 Apr 12:S0012-3692(21)00679-6. doi: 10.1016/j.chest.2021.04.002. <u>https://journal.chestnet.org/article/S0012-3692(21)00679-6/fulltext</u> Critically-ill COVID-19 patients are at high risk for HAIs, especially VAPs and BSIs due to MDR organisms. HAIs prolong mechanical ventilation and hospitalization, and HAIs complicated by septic-shock almost doubled mortality.
- 12. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative healthcare workers in England: a large, multicentre, prospective cohort study (SIREN). SIREN Study Group. Lancet. 2021 Apr 9:S0140-6736(21)00675-9. doi: 10.1016/S0140-6736(21)00675-9. <u>https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00675-9/fulltext</u> A previous history of SARS-CoV-2 infection was associated with an 84% lower risk of infection, with median protective effect observed 7 months following primary infection. This time period is the minimum probable effect because seroconversions were not included. This study shows that previous infection with SARS-CoV-2 induces effective immunity to future infections in most individuals.
- 13. Health Care Acquired COVID-19 is Less Symptomatic than Community Acquired Disease Among Healthcare Workers. Fletcher JJ, et al. *Infect Control Hosp Epidemiol*. 2021 Apr 15:1-28. doi: 10.1017/ice.2021.167. <u>https://www.cambridge.org/core/journals/infection-control-and-hospital-epidemiology/article/health-care-acquired-covid19-is-less-symptomatic-than-community-acquired-disease-among-healthcare-workers/C56D1FE11C49A83C6D357D58533BBC70</u>

Health care acquired COVID-19 increases the probability of asymptomatic or mild COVID-19 disease compared to community acquired disease. This suggests infection prevention strategies (including masks and eye protection) may be mitigating inoculum and supports the variolation theory in COVID-19.

Prognosis

 Renin-Angiotensin system inhibitors effect before and during hospitalization in COVID-19 outcomes: final analysis of the international HOPE COVID-19 (Health Outcome Predictive Evaluation for COVID-19) Registry. Núñez-Gil IJ et al. Am Heart J. 2021 Apr 9:S0002-8703(21)00089-2. doi: 10.1016/j.ahj.2021.04.001.

https://www.clinicalkey.com/#!/content/journal/1-s2.0-S0002870321000892

RASi historic use, at admission, is not related to an adjusted worse prognosis in hospitalized COVID-19 patients, although it points out a high-risk population. In this setting, the in-hospital prescription of RASi is associated with improved survival and fewer short-term complications.

15. Postoperative In-Hospital Morbidity and Mortality of Patients with COVID-19 Infection Compared with Patients Without COVID-19 Infection. Haffner MR, et al. JAMA Netw Open.

2021 Apr 1;4(4):e215697. doi: 10.1001/jamanetworkopen.2021.5697.

https://jamanetwork.com/journals/jamanetworkopen/article-abstract/2778455 These findings suggest that COVID-19 infection positivity was an independent risk factor for increased perioperative mortality but not complications. Specifically, the overall mortality rate in the cohort with COVID-19 (14.8%) was more than double that in the cohort without COVID-19 (7.1%). To our knowledge, this study represents the largest comparative cohort study between surgical patients testing positive for COVID-19 and those testing negative for the virus, and it is the first to compare outcomes among different hospital settings.

 Physical inactivity is associated with a higher risk for severe COVID-19 outcomes: a study in 48 440 adult patients. Sallis R, et al. *Br J Sports Med*. 2021 Apr 13:bjsports-2021-104080. doi: 10.1136/bjsports-2021-104080.

https://bjsm.bmj.com/content/bjsports/early/2021/04/07/bjsports-2021-104080.full.pdf Patients with COVID-19 who were consistently inactive had a greater risk of hospitalisation, admission to the ICU and death than patients who were consistently meeting physical activity guidelines and patients who were doing some physical activity. Consistently meeting physical activity guidelines was strongly associated with a reduced risk for severe COVID-19 outcomes among infected adults.

Survivorship & Rehabilitation

17. Integrative respiratory follow-up of severe COVID-19 reveals common functional and lung imaging sequelae. Froidure A, et al. *Respir Med.* 2021 Apr 4;181:106383. doi: 10.1016/j.rmed.2021.106383.

https://www.sciencedirect.com/science/article/pii/S0954611121000895

Although most hospitalized COVID-19 patients recover, a substantial proportion complains from persisting dyspnea and fatigue. Impairment of DLCO and signs suggestive of fibrosis are common but are not strictly related to long-lasting symptoms.

- 18. Lung ultrasonography for long-term follow-up of COVID-19 survivors compared to chest CT scan. Giovannetti G, et al. *Respir Med*. 2021 Mar 31;181:106384. doi: 10.1016/j.rmed.2021.106384. <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8010331/</u>LUS has an outstanding discrimination ability compared to CT in identifying an ILD of at least mild grade in the post COVID-19 follow-up. LUS should be considered as the first-line tool in follow-up programs, while chest CT could be performed based on LUS findings.
- 19. 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records. Taquet M, et al. Lancet Psychiatry. 2021 Apr 1:S2215-0366(21)00084-5. doi: 10.1016/S2215-0366(21)00084-5. https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(21)00084-5/fulltext Our study provides evidence for substantial neurological and psychiatric morbidity in the 6 months after COVID-19 infection. Risks were greatest in, but not limited to, patients who had

severe COVID-19. This information could help in service planning and identification of research priorities. Complementary study designs, including prospective cohorts, are needed to corroborate and explain these findings.

Therapeutics

- 20. Methylprednisolone or dexamethasone, which one is superior corticosteroid in the treatment of hospitalized COVID-19 patients: a triple-blinded randomized controlled trial. Ranjbar K, et al. *BMC Infect Dis.* 2021 Apr 10;21(1):337. doi: 10.1186/s12879-021-06045-3. https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06045-3. https://bmcinfectdis.biomedcentral.com/a
- 21. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial. Ramakrishnan S et al. Lancet Respir Med. 2021 Apr 9:S2213-2600(21)00160-0. doi: 10.1016/S2213-2600(21)00160-0. https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00160-0/fulltext Early administration of inhaled budesonide reduced the likelihood of needing urgent medical care and reduced time to recovery after early COVID-19.
- 22. A randomized, double-blind, placebo-controlled phase 1 trial of inhaled and intranasal niclosamide: A broad spectrum antiviral candidate for treatment of COVID-19. Backer V, et al. Lancet Reg Health Eur. 2021 Apr 6:100084. doi: 10.1016/j.lanepe.2021.100084. https://www.thelancet.com/journals/lanepe/article/PIIS2666-7762(21)00061-2/fulltext UNI91104, a promising candidate for inhalation and intranasal therapy against COVID-19 and other viral respiratory tract infections is well-tolerated in healthy volunteers and warrants further testing in patient trials.
- 23. Emergency Airway Management in Patients with COVID-19: A Prospective International Multicenter Cohort Study. Wong DJN et al. *Anesthesiology*. 2021 Apr 13. doi: 10.1097/ALN.00000000003791. <u>https://pubs.asahq.org/anesthesiology/article-lookup/doi/10.1097/ALN.000000000003791</u>

Although successful first-attempt intubation was noted in 89.7% of intubations, 0.5% required four or more attempts, an emergency surgical airway was required in 0.2%, and a composite variable of failed intubation occurred in 0.8%. Successful first attempts were more likely with rapid sequence intubations, when operators used powered air-purifying respirators, and with increasing operator experience. Intubations performed in low- and middle-income countries were nearly half as likely to be successful on first attempt than in high-income countries.

24. Different Anticoagulant Regimens, Mortality, and Bleeding in Hospitalized Patients with COVID-19: A Systematic Review and an Updated Meta-Analysis. Parisi R, et al. Semin Thromb Hemost. 2021 Apr 13. doi: 10.1055/s-0041-1726034. <u>https://www.thieme-</u> connect.com/products/ejournals/abstract/10.1055/s-0041-1726034 Meta-analysis on 25,719 hospitalized COVID-19 patients showed that anticoagulant use was associated with 50% reduced in-hospital mortality risk. Both anticoagulant regimens (therapeutic and prophylactic) reduced in-hospital all-cause mortality, compared with no anticoagulation. Particularly in ICU patients, the anticoagulant therapeutic regimen was associated with a reduced in-hospital mortality risk compared with the prophylactic one. However, the former was also associated with a higher risk of bleeding. Anticoagulant use, mainly heparin, reduced all-cause mortality in COVID-19 patients during hospitalization. Due to the higher risk of bleeding at therapeutic doses, the use of prophylactic dosages of anticoagulant is probably to be preferred in noncritically ill COVID-19 patients.

Transmission / Infection Control

25. Fitted Filtration Efficiency of Double Masking During the COVID-19 Pandemic. Sickbert-Bennett EE, et al. JAMA Intern Med. April 16, 2021. doi:10.1001/jamainternmed.2021.2033 <u>https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2778913?resultClick=1</u> Results of this quality improvement study demonstrated that wearing a medical procedure mask underneath a cloth mask provided the best improvement to FFE of all the combinations evaluated. The improvement in the FFE of procedure masks when doubled or when worn underneath reusable cloth face coverings is consistent with minimizing leaks between the mask and facial skin, including the bridge of the nose.

26. Viral sequencing reveals US healthcare personnel rarely become infected with SARS-CoV-2 through patient contact. Braun KM, et al. *Clin Infect Dis.* 2021 Apr 15:ciab281. doi: 10.1093/cid/ciab281. <u>https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciab281/6226897</u>

We found no evidence for healthcare-associated transmission in the majority of HCP infections evaluated here. Though we cannot rule out the possibility of cryptic healthcare-associated transmission, it appears that HCP most commonly becomes infected with SARS-CoV-2 via community exposure. This emphasizes the ongoing importance of mask-wearing, physical distancing, robust testing programs, and rapid distribution of vaccines.

27. Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study. Frampton D et al. Lancet Infect Dis 2021 Apr 12. doi: <u>https://doi.org/10.1016/S1473-3099(21)00170-5</u> Emerging evidence exists of increased transmissibility of B.1.1.7, and we found increased virus load by proxy for B.1.1.7 in our data. We did not identify an association of the variant with severe disease in this hospitalised cohort.

Vaccines / Immunology

28. Do Corticosteroid Injections for the Treatment of Pain Influence the Efficacy of Adenovirus Vector-Based COVID-19 Vaccines? Spine Intervention Society's Patient Safety Committee. Pain Med. 2021 Apr 11:pnab130. doi: 10.1093/pm/pnab130. https://academic.oup.com/painmedicine/advance-article/doi/10.1093/pm/pnab063/6144926 There is currently no direct evidence to suggest that a corticosteroid injection before or after the administration of an adenovirus vector-based COVID-19 vaccine decreases the efficacy of the vaccine. However, based on the known timeline of hypothalamic-pituitary-adrenal (HPA) axis suppression following epidural and intraarticular corticosteroid injections, and the timeline of the reported peak efficacy of the Janssen and AstraZeneca vaccines, physicians should consider timing an elective corticosteroid injection such that it is administered no less than two weeks prior to and no less than two weeks following a COVID-19 adenovirus vector-based vaccine dose, whenever possible.

29. COVID-19 vaccine safety questions and answers for healthcare providers (CONSIDER).

Kochhar S, et al. *Vaccine*. 2021 Mar 22:S0264-410X(21)00364-9. doi: 10.1016/j.vaccine.2021.03.060.

https://www.sciencedirect.com/science/article/pii/S0264410X21003649

Vaccine hesitancy is being fueled by concerns regarding the COVID-19 pandemic response of vaccine manufacturers, regulatory agencies and their governments. As for all new vaccines, there is the possibility that rare serious adverse reactions will not be identified in clinical trials and only found once a larger number of people are vaccinated. Additionally, when vaccinating a large number of people, some of them will have adverse health outcomes shortly after vaccination by chance alone. Short, clear, evidence-based answers to COVID-19 vaccine safety questions are needed to inform and increase scientific literacy among the various stakeholders.

30. Evidence for increased breakthrough rates of SARS-CoV-2 variants of concern in BNT162b2 mRNA vaccinated individuals. Kustin T et al. *medRxiv PREPRINT*. 2021.04.06.21254882; doi: <u>https://doi.org/10.1101/2021.04.06.21254882</u>

We performed a case-control study that examined whether BNT162b2 vaccinees with documented SARS-CoV-2 infection were more likely to become infected with B.1.1.7 or B.1.351 compared with unvaccinated individuals. Vaccinees infected at least a week after the second dose were disproportionally infected with B.1.351 (odds ratio of 8:1). Those infected between two weeks after the first dose and one week after the second dose, were disproportionally infected by B.1.1.7 (odds ratio of 26:10), suggesting reduced vaccine effectiveness against both VOCs under different dosage/timing conditions. Nevertheless, the B.1.351 incidence in Israel to-date remains low and vaccine effectiveness remains high against B.1.1.7, among those fully vaccinated. These results overall suggest that vaccine breakthrough infection is more frequent with both VOCs, yet a combination of mass-vaccination with two doses coupled with non-pharmaceutical interventions control and contain their spread.

31. A Deferred-Vaccination Design to Assess Durability of COVID-19 Vaccine Effect After the Placebo Group Is Vaccinated. Follmann D et al. Ann Intern Med. 2021 Apr 13. doi: 10.7326/M20-8149. <u>https://www.acpjournals.org/doi/10.7326/M20-8149</u> High efficacies reported for multiple vaccine candidates add complexity and uncertainty to the environment surrounding access to the vaccine for trial participants who were assigned to receive placebo. Continued blinded follow-up in the original study groups is optimal to assess vaccine efficacy over time and is endorsed by the U.S. FDA in their guidance pertaining to COVID-19 vaccine development. Deferred vaccination allows placebo recipients timely access to

the vaccine when it would no longer be proper to maintain participants on placebo. We demonstrate that critical information regarding durability of the vaccine effect can be obtained even after the placebo group participants receive the vaccine.

32. Herpes zoster following BNT162b2 mRNA Covid-19 vaccination in patients with autoimmune inflammatory rheumatic diseases: a case series. Furer V, et al. *Rheumatology (Oxford)*. 2021 Apr 12:keab345. doi: 10.1093/rheumatology/keab345.

https://academic.oup.com/rheumatology/advancearticle/doi/10.1093/rheumatology/keab345/6225015

Six female patients aged 49 ± 11 years with stable AIIRD developed HZ within a short time after the first vaccine dose in 5 cases and after the second vaccine dose in one case. In the majority of cases, HZ infection was mild, except a case of HZ ophthalmicus, without corneal involvement, in RA patient treated with tofacitinib. There were no cases of disseminated HZ disease or postherpetic neuralgia. All but one patient received antiviral treatment with a resolution of HZrelated symptoms up to 6 weeks. Five patients completed the second vaccine dose without other adverse effects.

- 33. Cerebral venous sinus thrombosis associated with thrombocytopenia post-vaccination for COVID-19. Castelli GP, et al. *Crit Care*. 2021 Apr 12;25(1):137. doi: 10.1186/s13054-021-03572-y. https://ccforum.biomedcentral.com/articles/10.1186/s13054-021-03572-y We report about a previously healthy 50-year-old Caucasian man admitted to the city hospital of Mantua on March 15, 2021, with severe headache during the previous four days, slight deviation of the right buccal rim, loss of strength in the right lower limb, unstable walking and slight visual impairment. On March 4, 2021, he had received the first dose of the anti-COVID-19 AstraZeneca vaccine with no immediate adverse reaction.
- 34. SARS-CoV-2 Antibody Response in Persons with Past Natural Infection. Anichini G, et al. *N Engl J Med*. 2021 Apr 14. doi: 10.1056/NEJMc2103825.

https://www.nejm.org/doi/full/10.1056/NEJMc2103825

These findings provide evidence that after the administration of a single dose of vaccine, the humoral response against SARS-CoV-2 in persons with a history of SARS-CoV-2 infection is greater than the response in previously uninfected participants who have received a second dose.

35. Sera neutralizing activities against SARS-CoV-2 and multiple variants six month after hospitalization for COVID-19. French COVID cohort study group. *Clin Infect Dis.* 2021 Apr 14:ciab308. doi: 10.1093/cid/ciab308. <u>https://academic.oup.com/cid/advance-</u> article/doi/10.1093/cid/ciab308/6225251?rss=1

Our results indicate a sustained humoral response against the ancestral strain and the D614G, B.1.1.7 and P.1 variants for at least 6 months in patients previously hospitalized for COVID-19. A weaker protection was however observed for the B.1.351 variant.

36. Asymptomatic COVID-19 cases among older patients despite BNT162b2 vaccination: a case series in a geriatric rehabilitation ward during an outbreak. Donadio C, et al. *J Infect*. 2021 Apr

11:S0163-4453(21)00167-5. doi: 10.1016/j.jinf.2021.04.004. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8038862/

The findings suggest that asymptomatic SARS-CoV-2 infection may be frequent in vaccinated frail older patients, and that the main effect of vaccination in this population might be a decrease of the severity of the disease rather than completely avoiding it. That has implications when designing measures for limiting the spread of SARS-CoV-2.

- 37. Spike Antibody Levels of Nursing Home Residents with or without Prior COVID-19 3 Weeks After a Single BNT162b2 Vaccine Dose. Blain H, et al. JAMA. 2021 Apr 15. doi: 10.1001/jama.2021.6042. <u>https://jamanetwork.com/journals/jama/fullarticle/2778926</u> This preliminary study suggests that a single dose of BNT162b2 vaccine may be sufficient to obtain a high level of S-protein IgG antibody in nursing home residents previously diagnosed with COVID-19 based on RT-PCR results. Measuring S-protein IgG antibody levels just before the second vaccine dose could be useful in determining whether a second dose is required in individuals whose infection history is unknown. This could limit possible adverse effects related to reactogenicity in previously infected patients and spare precious vaccine doses.
- 38. SARS-CoV-2 seropositivity and subsequent infection risk in healthy young adults: a prospective cohort study. Letizia AG et al. *Lancet Respir Med.*

DOI:https://doi.org/10.1016/S2213-2600(21)00158-2

https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(21)00158-2/fulltext Seropositive young adults had about one-fifth the risk of subsequent infection compared with seronegative individuals. Although antibodies induced by initial infection are largely protective, they do not guarantee effective SARS-CoV-2 neutralisation activity or immunity against subsequent infection. These findings might be relevant for optimisation of mass vaccination strategies.

39. Thrombotic Thrombocytopenia after Ad26.COV2.S Vaccination — Response from the Manufacturer. Sadoff J, et al. NEJM 2021 Apr 16. DOI: 10.1056/NEJMc2106075 https://www.nejm.org/doi/full/10.1056/NEJMc2106075?query=main_nav_lg Among the more than 75,000 participants in the clinical trial program for our Janssen Ad26.COV2.S vaccine (of which approximately 50,000 received active vaccine), a single case of CVST with thrombocytopenia occurred in a vaccine recipient. We paused our program to review this case from our first phase 3 study; after consultation with external clinical experts, no clear causality was established, and the data and safety monitoring board agreed that we could restart the study. The vaccine recipient was subsequently found to have had antibodies against platelet factor 4 (PF4) at the time of the event. As part of our postauthorization pharmacovigilance program, Janssen ongoing safety surveillance received reports of six cases of CVST with thrombocytopenia occurring 7 to 14 days after vaccination. These cases were reported among more than 7.2 million persons who had been vaccinated with Ad26.COV2.S globally as of April 14, 2021. Thus, the reporting rate is less than 1 in 1,000,000 vaccinations, though it is possible that the cases are underreported. 40. Pathologic Antibodies to Platelet Factor 4 after ChAdOx1 nCoV-19 Vaccination. Scully M, et al. *NEJM* 2021 Apr 16. DOI: 10.1056/NEJMoa2105385

https://www.nejm.org/doi/full/10.1056/NEJMoa2105385?query=main_nav_lg In the absence of previous prothrombotic medical conditions, 22 patients presented with acute thrombocytopenia and thrombosis, primarily cerebral venous thrombosis, and 1 patient presented with isolated thrombocytopenia and a hemorrhagic phenotype. A pathogenic PF4dependent syndrome, unrelated to the use of heparin therapy, can occur after the administration of the ChAdOx1 nCoV-19 vaccine. Rapid identification of this rare syndrome is important because of the therapeutic implications.

Women & Children

41. Preliminary Evidence on Long Covid in children. Buonsenso D, et al. Acta Paediatr. 2021 Apr 9. doi: 10.1111/apa.15870. https://onlinelibrary.wiley.com/doi/10.1111/apa.15870 More than half of the children assessed during the survey reported at least one symptom. In particular, 42.6% presented at least one symptom >60 days after infection. Symptoms like fatigue, muscle and joint pain, headache, insomnia, respiratory problems and palpitations were particularly frequent. An unexpected finding is that also children with an asymptomatic or paucy-symptomatic COVID-19 developed chronic, persisting symptoms, although followed-up for a relatively short time after the diagnosis.

42. Infectivity of severe acute respiratory syndrome coronavirus 2 in children compared with adults. Bullard J, et al. *CMAJ*. 2021 Apr 9:cmaj.210263. doi: 10.1503/cmaj.210263. https://www.cmaj.ca/content/early/2021/04/09/cmaj.210263 Compared with adults, children with nasopharyngeal swabs that tested positive for SARS-CoV-2 were less likely to grow virus in culture, and had higher cycle thresholds and lower viral concentrations, suggesting that children are not the main drivers of SARS-CoV-2 transmission.

43. SARS-CoV-2-Specific Antibodies in Breast Milk after COVID-19 Vaccination of Breastfeeding Women. Perl SH, et al. JAMA. 2021 Apr 12. doi: 10.1001/jama.2021.5782. https://jamanetwork.com/journals/jama/fullarticle/2778766

This study found robust secretion of SARS-CoV-2 specific IgA and IgG antibodies in breast milk for 6 weeks after vaccination. IgA secretion was evident as early as 2 weeks after vaccination followed by a spike in IgG after 4 weeks (a week after the second vaccine). A few other studies have shown similar findings in women infected with COVID-19.5 Antibodies found in breast milk of these women showed strong neutralizing effects, suggesting a potential protective effect against infection in the infant.

 44. Neonatal SARS-CoV-2 Infections in Breastfeeding Mothers. Shlomai NO, et al. *Pediatrics*. 2021 Apr 13:e2020010918. doi: 10.1542/peds.2020-010918. https://pediatrics.aappublications.org/content/early/2021/04/09/peds.2020-010918 No viral infection was identified in neonates born to and separated from their SARS-CoV-2-positive mothers at birth and subsequently fed unpasteurized breast milk. All infants breastfed at home remained SARS-CoV-2 negative. These findings may provide insights regarding the redundancy of postpartum mother-newborn separation in SARS-CoV-2-positive women and, assuming precautions are adhered to support the safety of breast milk.

GUIDELINES & CONSENSUS STATEMENTS

Discharge Practices for COVID-19 Patients: Rapid Review of Published Guidance and Synthesis of Documents and Practices at 22 US Academic Medical Centers. HOMERuN collaborative working group. J Gen Intern Med. 2021 Apr 9:1-7. doi: 10.1007/s11606-021-06711-x.

FDA / CDC / NIH / WHO Updates

Joint CDC and FDA Statement on Johnson & Johnson COVID-19 Vaccine, 4-13-2021

NIH – COVID-19 Treatment Guidelines update - <u>The COVID-19 Treatment Guidelines Panel's Statement</u> on the Emergency Use Authorization of Anti-SARS-CoV-2 Monoclonal Antibodies for the Treatment of <u>COVID-19</u>

FDA Recommends Transition from Use of Decontaminated Disposable Respirators - Letter to Health Care Personnel and Facilities

CDC Health Alert Network - <u>Cases of Cerebral Venous Sinus Thrombosis with Thrombocytopenia after</u> <u>Receipt of the Johnson & Johnson COVID-19 Vaccine</u>

Commentary & News Releases

Risk of rare blood clotting higher for COVID-19 than for vaccines

The story behind COVID-19 vaccines. Fauci AS. Science. 2021 Apr 9;372(6538):109. doi: 10.1126/science.abi8397.

Pfizer and BioNTech Request Regulatory Agencies Expand Emergency Use of Their COVID-19 Vaccine to Adolescents

Regeneron: <u>PHASE 3 PREVENTION TRIAL SHOWED 81% REDUCED RISK OF SYMPTOMATIC SARS-COV-2</u> INFECTIONS WITH SUBCUTANEOUS ADMINISTRATION OF REGEN-COV™ (CASIRIVIMAB WITH IMDEVIMAB)

"In an ocean of ashes, islands of order": WHO's SARS-CoV-2 origin report. Lancet Infect Dis. 2021 Apr 9:S1473-3099(21)00213-9. doi: 10.1016/S1473-3099(21)00213-9.

<u>Covid-19: EU investigates four reports of blood clots after Janssen vaccine.</u> *BMJ.* 2021 Apr 13;373:n961. doi: 10.1136/bmj.n961.

<u>Beyond COVID-19-will self-sampling and testing become the norm?</u> *Lancet Infect Dis.* 2021 Apr 12:S1473-3099(21)00197-3. doi: 10.1016/S1473-3099(21)00197-3.

Thrombosis after covid-19 vaccination. BMJ. 2021 Apr 14;373:n958. doi: 10.1136/bmj.n958.

<u>Covid-19 has redefined airborne transmission.</u> *BMJ.* 2021 Apr 14;373:n913. doi: 10.1136/bmj.n913. *See also*: <u>Ten scientific reasons in support of airborne transmission of SARS-CoV-2.</u>

<u>SARS-CoV-2 Vaccine–Induced Immune Thrombotic Thrombocytopenia.</u> *NEJM* 2021 Apr 16. DOI: 10.1056/NEJMe2106315

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