New Research

*note, PREPRINTS have not undergone formal peer review

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

Clinical Syndrome

   
   Our early analyses suggest a significantly reduced odds of hospitalisation among individuals with SGTF versus non-SGTF infections diagnosed during the same time period. SGTF-infected individuals had a significantly reduced odds of severe disease compared with individuals infected earlier with the delta variant. Some of this reduced severity is probably a result of previous immunity.

Healthcare Delivery & Healthcare Workers

   
   Although disease severity appears lower with the Omicron variant, the high volume of hospitalizations can strain local health care systems and the average daily number of deaths remains substantial. This underscores the importance of national emergency preparedness, specifically, hospital surge capacity and the ability to adequately staff local health care systems. In addition, being up to date on vaccinations and following other recommended prevention strategies are critical to preventing infections, severe illness, or death from COVID-19.

   
   The pulse oximeter provides regular non-invasive measurements of blood oxygenation and is used in a wide range of clinical settings. The light wave transmission that this technology uses is modified by skin pigmentation and thus may vary by skin colour. A recent study of paired measures of oxygen saturation from pulse oximetry and arterial blood gas reported differing
outputs in patients with black skin compared to patients with white skin that has the potential to adversely impact on patient care.

Prognosis


Patients with elevated both NPs and troponin levels had higher risk of death compared with those with normal levels of both (hazard ratio 2.94; 95% confidence interval 1.31 to 6.64; p = 0.009), and this remained significant after adjustment for age, gender, oxygen saturation, HF history, and chronic kidney disease. Interestingly, NPs provided risk stratification also in patients with normal troponin values (hazard ratio 2.86; 95% confidence interval 1.21 to 6.72; p = 0.016 with high NPs levels). These data show the combined prognostic role of troponin and NPs in COVID-19 patients. NPs value may be helpful in identifying patients with a worse prognosis among those with normal troponin values. Further, NPs' cut-point used for diagnosis of acute HF has a predictive role in patients with COVID-19.


In this single-center case series of 102 consecutive patients who underwent a lung transplant between January 21, 2020, and September 30, 2021, survival was 100% in the 30 patients who had COVID-19-associated ARDS as of November 15, 2021.

Survivorship & Rehabilitation


We executed a deep multi-omic, longitudinal investigation of 309 COVID-19 patients from initial diagnosis to convalescence (2-3 months later), integrated with clinical data, and patient-reported symptoms. We resolved four PASC-anticipating risk factors at the time of initial COVID-19 diagnosis: type 2 diabetes, SARS-CoV-2 RNAemia, Epstein-Barr virus viremia, and
specific autoantibodies. In patients with gastrointestinal PASC, SARS-CoV-2-specific and CMV-specific CD8+ T cells exhibited unique dynamics during recovery from COVID-19. Analysis of symptom-associated immunological signatures revealed coordinated immunity polarization into four endotypes exhibiting divergent acute severity and PASC. We find that immunological associations between PASC factors diminish over time leading to distinct convalescent immune states. Detectability of most PASC factors at COVID-19 diagnosis emphasizes the importance of early disease measurements for understanding emergent chronic conditions and suggests PASC treatment strategies.


The persistence of COVID-19-related olfactory and gustatory dysfunctions up to 12 months after the disease onset in a noteworthy proportion (approximately 3 out of 10) of patients with paucisymptomatic-to-mild clinical presentation deserves further investigations due to its possible pathophysiological implications and impact on the quality of life.


In this exploratory study of patients in 11 Dutch hospitals who survived 1 year following ICU treatment for COVID-19, physical, mental, or cognitive symptoms were frequently reported.


PASC may be extraordinarily common 1 year after COVID-19, and these symptoms are sufficiently severe to impact the daily exercise tolerance of patients. PASC symptoms are broadly distributed, are not limited to one specific patient group, and appear to be unrelated to age. These data have implications for vaccine hesitant individuals, policy makers, and physicians managing the emerging longer-term yet unknown impact of the COVID-19 pandemic.


Frailty and disability were more frequent 90 days after hospital discharge compared with baseline in COVID-19 patients admitted to the ICU. Our results show that most COVID-19 critical care survivors transition to poorer health status, highlighting the importance of long-term medical follow-up for this population.
Among patients with acute hypoxemic respiratory failure due to COVID-19, an initial strategy of CPAP significantly reduced the risk of tracheal intubation or mortality compared with conventional oxygen therapy, but there was no significant difference between an initial strategy of HFNO compared with conventional oxygen therapy. The study may have been underpowered for the comparison of HFNO vs conventional oxygen therapy, and early study termination and crossover among the groups should be considered when interpreting the findings.

https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2788377
In this meta-analysis of 8 randomized clinical trials enrolling 2341 participants, individual patient data were monitored in real time and analyzed using a robust bayesian framework and advanced statistical modeling. No association of convalescent plasma with clinical outcomes was found.

The omicron variant was found to have at least 33 mutations (29 amino acid substitutions, 1 insertion of three amino acids, and 3 small deletions) in its spike (S) protein, as compared with early SARS-CoV-2 strains identified in Wuhan, China. Notably, 15 of the 29 substitutions were in the receptor-binding domain of the S protein, which is the primary target for monoclonal antibody–based therapy. This finding suggests that the monoclonal antibodies that have been approved by the Food and Drug Administration may be less effective against the omicron variant.

14. High-Dose Convalescent Plasma for Treatment of Severe COVID-19. De Santis GC et al. Emerg Infect Dis. 2022 Jan 26;28(3). doi: 10.3201/eid2803.212299. To assess whether high-dose coronavirus disease (COVID-19) convalescent plasma (CCP) transfusion may benefit patients with severe COVID-19, we conducted a multicenter randomized trial in Brazil. Patients with severe COVID-19 who were within 10 days of initial symptom onset were eligible. Patients in the CCP group received 3 daily doses of CCP (600 mL/d) in addition to standard treatment; control patients received standard treatment only. Primary outcomes were death rates at days 30 and 60 of study randomization. Secondary outcomes were ventilator-free days and hospital-free days. We enrolled 107 patients: 36 CCP and 71 control. At day 30, death rates were 22% for CCP and 25% for the control group; at day 60, rates were 31% for CCP and 35% for control. Needs for invasive mechanical ventilation and durations of hospital stay were similar between
groups. We conclude that high-dose CCP transfused within 10 days of symptom onset provided no benefit for patients with severe COVID-19.

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciac014/6515763
Remdesivir/dexamethasone treatment is associated with significant reduction in mortality, length of hospitalization, and faster SARS-CoV-2 clearance, compared to dexamethasone alone.

Vaccines / Immunology

16. Three exposures to the spike protein of SARS-CoV-2 by either infection or vaccination elicit superior neutralizing immunity to all variants of concern. Paul R. Wratil PR, et al. Nature Medicine (2022) https://doi.org/10.1038/s41591-022-01715-4
https://www.nature.com/articles/s41591-022-01715-4
We conclude that an infection-plus-vaccination-induced hybrid immunity or a triple immunization can induce high-quality antibodies with superior neutralization capacity against VoCs, including omicron.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00055-1/fulltext
Two doses of SCB-2019 vaccine plus CpG and alum provides notable protection against the entire severity spectrum of COVID-19 caused by circulating SAR-CoV-2 viruses, including the predominating delta variant.

https://doi.org/10.1016/j.amjcard.2021.12.007
Our study found that the incidence of myocarditis was 0.000011 (95% confidence interval 0.000005 to 0.000025) in subjects vaccinated with the mRNA COVID-19 vaccine, which implies an average of 11 cases of myocarditis per 1 million subjects vaccinated with the mRNA COVID-19 vaccine. This very low incidence not only indicates the rarity of myocarditis but also suggests a risk of myocarditis after mRNA vaccination.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00090-3/fulltext
The most recent SARS-CoV-2 variant of concern to emerge has been named omicron. Its immune evasion potential was predicted by genomic data and has been preliminarily confirmed by observations of an increased incidence of reinfections and breakthrough infections. This has
triggered calls to intensify vaccination programmes including provision of vaccine booster
doses.

Among individuals seeking testing for COVID-like illness in the US in December 2021, receipt of 3 doses of mRNA COVID-19 vaccine (compared with unvaccinated and with receipt of 2 doses) was less likely among cases with symptomatic SARS-CoV-2 infection compared with test-negative controls. These findings suggest that receipt of 3 doses of mRNA vaccine, relative to being unvaccinated and to receipt of 2 doses, was associated with protection against both the Omicron and Delta variants, although the higher odds ratios for Omicron suggest less protection for Omicron than for Delta.

Before the emergence of the Delta and Omicron variants, persons with recent infection had strong protection against symptomatic reinfections for 7 months compared with unvaccinated, previously uninfected individuals. Protection in immunocompromised persons, racial and ethnic subgroups, and asymptomatic index case patients is unclear. The durability of protection in the setting of the Delta and Omicron variants is unknown.

In this study, individuals with prior SARS-CoV-1 infection and 1 dose of ChAdOx1 had higher anti–SARS-CoV-2-spike RBD antibody levels than those without infection and either 1 or 2 doses of ChAdOx1, despite being older and having a longer interval between vaccination and antibody level measurement. The presence of antinucleocapsid antibodies in participants with previous SARS-CoV-1 infection is consistent with previous reports of cross-reactivity to SARS-CoV-2–nucleocapsid in individuals with prior SARS-CoV-1 infection, even if evaluated 18 years after the infection.

Based on passive surveillance reporting in the US, the risk of myocarditis after receiving mRNA-based COVID-19 vaccines was increased across multiple age and sex strata and was highest after the second vaccination dose in adolescent males and young men. This risk should be considered in the context of the benefits of COVID-19 vaccination.
[https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00094-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00094-0/fulltext)  
Antibody concentrations were low at 6 months after previous immunisation with two doses of CoronaVac. However, all four vaccines administered as a third dose induced a significant increase in binding and neutralising antibodies, which could improve protection against infection. Heterologous boosting resulted in more robust immune responses than homologous boosting and might enhance protection.

Results showed that after the primary two-dose series of the mRNA-1273 vaccine, neutralization titers against the omicron variant were 35.0 times lower than those against the D614G variant. These lower titers could lead to an increased risk of severe breakthrough infection. However, a booster dose of mRNA-1273 vaccine was associated with neutralization titers against the omicron variant that were 20.0 times higher than those assessed after the second dose of vaccine, and these titers may substantially reduce the risk of breakthrough infection. The decline in neutralization of the omicron variant 6 months after the booster injection was similar to the decline in neutralization titers against the D614G variant 7 months after the second dose.

The mRNA-1273–induced protection against infection appeared to wane month by month after the second dose. Meanwhile, protection against hospitalization and death appeared to be robust, with no evidence of waning for several months after the second dose.

Of the 458 participants who were enrolled in the trial, 154 received mRNA-1273, 150 received Ad26.COV2.S, and 153 received BNT162b2 as booster vaccines. Homologous boosters increased neutralizing antibody titers by a factor of 4 to 20, whereas heterologous boosters increased titers by a factor of 6 to 73. Homologous and heterologous booster vaccines had an acceptable safety profile and were immunogenic in adults who had completed a primary Covid-19 vaccine regimen at least 12 weeks earlier.

We analyzed the capacity of sera derived from 24 individuals before and after heterologous ChAdOx1 nCoV-19 BNT162b2 prime-boost vaccination to neutralize genuine OC43, NL63 and 229E hCoVs, as well as viral pseudoparticles carrying the SARS-CoV-1, SARS-CoV-2, MERS-CoV, hCoV-OC43, -NL63 and -229E spike proteins. Genuine hCoVs or spike containing pseudovirions were incubated with different concentrations of sera and neutralization efficiencies were determined by measuring viral RNA yields, intracellular viral nucleocapsid expression, or reporter gene expression in Huh-7 cells. Heterologous COVID-19 vaccination may confer some cross-protection against endemic seasonal coronaviruses.


Among 1,875 adults without immunocompromising conditions (including 1,065 [57%] unvaccinated, 679 [36%] 2-dose recipients, and 131 [7%] 3-dose [booster] recipients), VE against COVID-19 hospitalization was higher among those who received a booster dose (97%; 95% CI = 95%-99%) compared with that among 2-dose recipients (82%; 95% CI = 77%-86%) (p <0.001). Among 1,077 adults with immunocompromising conditions (including 324 [30%] unvaccinated, 572 [53%] 2-dose recipients, and 181 [17%] 3-dose recipients), VE was higher among those who received a third dose to complete a primary series (88%; 95% CI = 81%-93%) compared with 2-dose recipients (69%; 95% CI = 57%-78%) (p <0.001). Administration of a third COVID-19 mRNA vaccine dose as part of a primary series among immunocompromised adults, or as a booster dose among immunocompetent adults, provides improved protection against COVID-19-associated hospitalization.


A single mRNA or ChAdOx1 vaccine dose gave important protection against SARS-CoV-2, including early variants-of-concern. ChAdOx1 VE was lower against infection but one dose of either vaccine reduced the hospitalization risk by >85% to at least 8 weeks post-vaccination. Findings inform program options, including longer dosing intervals.

Women & Children


Between March 5, 2020, and July 4, 2021, 73 666 pregnant people delivered, 18 335 of whom had at least one SARS-CoV-2 test during pregnancy before Feb 14, 2021. SARS-CoV-2 infection indicated an increased risk of preterm delivery (p<0.05) and stillbirth (p<0.05), accounted for
primarily by first and second trimester SARS-CoV-2 infections. Gestational age at SARS-CoV-2 infection was correlated with gestational age at delivery (p<0·01) and had the greatest impact on predicting gestational age at delivery. The people in this study had mild or moderate SARS-CoV-2 infections and acute COVID-19 severity was not correlated with gestational age at delivery (p=0·31). These results suggest that pregnant people would benefit from increased monitoring and enhanced prenatal care after first or second trimester SARS-CoV-2 infection, regardless of acute COVID-19 severity.


Our local experience at Rady Children’s Hospital San Diego, the tertiary care center for children in San Diego, California, and surrounding counties, was that the incidence of new-onset T1D during the COVID-19 global pandemic in 2020 and 2021 appeared to have increased compared with previous years. We performed a 6-year retrospective review of the medical record to evaluate whether the perceived increased incidence was significant and whether or not more children had diabetic ketoacidosis (DKA) at presentation or required pediatric intensive care unit (PICU) admission (at our institution for altered mental status or severe acidosis only) as a measure of the severity of illness at diabetes onset.


Pregnancy is a risk factor for severe COVID-19 and meet EUA criteria for mAb treatment. Monoclonal antibodies are well tolerated, effective, may benefit the fetus, and should be considered in pregnancy. This study supports the favorable safety and tolerability profile reported in earlier studies. Although two oral antivirals are now available, one is not indicated in pregnancy and the other is affected by limited supplies.


Administration of COVID-19 mRNA vaccines was not associated with an adverse effect on stimulation or early pregnancy outcomes after IVF. Our findings contribute to the growing body of evidence regarding the safety of COVID-19 vaccination in women who are trying to conceive.

This study compared the neutralization susceptibility of serum specimens collected from 49 individuals of <18 years old, including 34 adolescent BNT162b2 (Pfizer-BioNTech) vaccine recipients, and 15 recovered COVID-19 patients aged between 2 and 17. We demonstrated that only 38.2% of BNT162b2 vaccine recipients and 26.7% of recovered COVID-19 patients had their serum neutralization titer at or above the detection threshold in our live virus microneutralization assay. Furthermore, the neutralizing antibody titer against Omicron variant was substantially lower than those against the ancestral virus or the Beta variant. Our results suggest that vaccine recipients and COVID-19 patients in the pediatric age group will likely be more susceptible to vaccine breakthrough infections or reinfections due to Omicron variant.

GUIDELINES & CONSENSUS STATEMENTS


PRACTICE POINT 1: Do not use SARS-CoV-2 antibody tests for the diagnosis of SARS-CoV-2 infection.

PRACTICE POINT 2: Do not use SARS-CoV-2 antibody tests to predict the degree or duration of natural immunity conferred by antibodies against reinfection, including natural immunity against different variants.

RETIREMENT FROM LIVING STATUS: Although natural immunity remains a topic of scientific interest, this topic is being retired from living status given the availability of effective vaccines for SARS-CoV-2 and widespread recommendations for and prevalence of their use. Currently, vaccination is the best clinical recommendation for preventing infection, reinfection, and serious illness from SARS-CoV-2 and its variants.

FDA / CDC / NIH / WHO Updates


CDC - Interim Guidelines for COVID-19 Antibody Testing.

FDA - Coronavirus (COVID-19) Update: FDA Limits Use of Certain Monoclonal Antibodies to Treat COVID-19 Due to the Omicron Variant.

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