New Research

*note, PREPRINTS have not undergone formal peer review

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

Clinical Syndrome


   We enrolled a cohort of 23 patients who were diagnosed and managed as having SARS-CoV-2-associated skin eruptions (including 21 pandemic chilblains [PC]) during the first wave of the pandemic in Connecticut. Antibody responses were determined through endpoint titration enzyme-linked immunosorbent assay and serum epitope repertoire analysis. T cell responses to SARS-CoV-2 were assessed by T cell receptor sequencing and in vitro SARS-CoV-2 antigen-specific peptide stimulation assays. Immunohistochemical and PCR studies of PC biopsies and tissue microarrays for evidence of SARS-CoV-2 were performed. Among patients diagnosed and managed as "covid toes" during the pandemic, we find a percentage of prior SARS-CoV-2 infection (9.5%) that approximates background seroprevalence (8.5%) at the time. Immunohistochemistry studies suggest that SARS-CoV-2 staining in PC biopsies may not be from SARS-CoV-2. Our results do not support SARS-CoV-2 as the causative agent of pandemic chilblains; however, our study does not exclude the possibility of SARS-CoV-2 seronegative abortive infections.


   Two-thirds of patients with COVID-19 showed electrocardiographic abnormalities. Our serial assessment suggests that myocardial injury is common in mechanically ventilated patients with COVID-19 and is associated with outcome.


   The incidence of adverse clinical outcomes remains high among COVID-19 patients with clinical diagnosis only. Patients with COVID-19 entering the hospital are at elevated risk of adverse outcomes.

Our systematic review provides a profile of clinical features and outcomes of patients with a prior COVID-19 infection diagnosis who subsequently developed IE. Due to the ongoing COVID-19 pandemic, it is essential that clinicians appreciate the possibility of IE as a unique complication of COVID-19 infection.

5. **Contribution of the elevated thrombosis risk of males to the excess male mortality observed in COVID-19: an observational study.** Cohen KR, et al. *BMJ Open.* 2022 Feb 25;12(2):e051624. doi: 10.1136/bmjopen-2021-051624. [https://bmjopen.bmj.com/content/12/2/e051624](https://bmjopen.bmj.com/content/12/2/e051624)

Our findings suggest the higher COVID-19 mortality rate in males may be significantly accounted for by the elevated risk of thrombosis among males. Understanding the mechanisms that underlie increased male thrombotic risk may allow for the advancement of effective anticoagulation strategies that reduce COVID-19 mortality in males.

**Epidemiology & Public Health**


COVID-19-related discrimination is common, and it appears that the pandemic has exacerbated preexisting resentment against racial/ethnic minorities and marginalized communities. Efforts are needed to minimize and discredit racially driven language and discrimination around COVID-19 and future epidemics.


Strict adherence to public mask use and fully vaccinated status are associated with improved COVID-19-related outcomes and can mitigate the spread, morbidity, and mortality of COVID-19. Anesthesiologists and intensivists should adhere to evidence-based guidelines in their approach and management of patients to help mitigate spread.


We analyzed first-dose coronavirus disease vaccination coverage among US children 5-11 years of age during November-December 2021. Pediatric vaccination coverage varied widely by jurisdiction, age
group, and race/ethnicity, and lagged behind vaccination coverage for adolescents aged 12-15 years during the first 2 months of vaccine rollout.

**Healthcare Delivery & Healthcare Workers**


For patients with severe ARDS, receipt of ECMO may improve survival. During the COVID-19 pandemic, the number of patients with COVID-19 referred for ECMO has exceeded the capacity of specialized centers to provide ECMO. The outcomes of patients with COVID-19 who are eligible to receive ECMO, but do not because of limited health system capacity, have not been reported.


Non-specific respiratory symptoms overlap with COVID-19. Prompt diagnosis of COVID-19 in hospital employees is crucial to prevent nosocomial transmission. Rapid molecular SARS-CoV-2 testing was performed for 115 symptomatic employees. The case positivity rate was 2.6%. Employees with negative tests returned to work after 80 +/- 28 minutes.


Burnout syndrome was common in all multiprofessional ICU team members prior to and increased substantially during the pandemic, independent of whether one treated coronavirus disease 2019 patients. Nurses had the highest prevalence of burnout during coronavirus disease 2019 and had the highest increase in burnout from the prepandemic baseline. Female clinicians were significantly more impacted by burnout than males. Different susceptibility to burnout syndrome may require profession-specific interventions as well as work system improvements.


In this cohort study, COVID-19-dedicated hospitals had multiple benefits, including providing high-volume repetitive treatment and isolating patients with the infection. This experience suggests
improved in-hospital mortality for patients treated at dedicated hospitals owing to improved processes of care and supports the use of establishing cohorts for future pandemics.

**Prognosis**


Multiple biomarkers prognostic for clinical outcomes were confirmed in COVACTA. Ferritin was identified as a predictive biomarker for the effects of tocilizumab in the COVACTA patient population; high ferritin levels were associated with better clinical outcomes for tocilizumab compared with placebo at day 28.

**Survivorship & Rehabilitation**


Our findings highlight the importance of considering sleep and circadian health after hospital discharge. Within this context, IMV during the ICU stay could aid in predicting an increased fragmentation of the rest-activity rhythm at the 3-month follow-up. Furthermore, compromised mental health could be a marker for sleep disruption at the post-COVID period.


Long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome from coronavirus disease 2019 are promising. Extracorporeal membrane oxygenation therapy may confer morbidity benefits in patients with coronavirus disease and remains a valuable modality with excellent functional outcomes and preserved quality of life for survivors.

**Therapeutics**


This study did not establish the efficacy of sarilumab in hospitalized patients with severe/critical COVID-19. Post-hoc analyses were consistent with other studies that found a benefit of sarilumab in patients receiving corticosteroids.

In hospitalized patients with COVID-19 pneumonia receiving low-flow oxygen and dexamethasone, the addition of remdesivir was not associated with shorter hospitalization or lower in-hospital mortality but may have reduced the combined outcome of death and transfer to the intensive care unit.


Hydroxychloroquine probably increases the risk of diarrhoea and nausea and/or vomiting and may increase the risk of cardiac toxicity and cognitive dysfunction/delirium. Lopinavir/ritonavir may increase the risk of diarrhoea and nausea and/or vomiting. Remdesivir may have no important effect on risk of acute kidney injury or cognitive dysfunction/delirium. These findings provide important information to support the development of evidence-based management strategies for patients with COVID-19.


Further trials with larger numbers are warranted to evaluate efficacy of nitazoxanide therapy in preventing progression to severe illness in patients at high risk of severe illness and reducing TSR in patients with mild illness.

**Transmission / Infection Control**


Our results show that major risk factors for airborne SARS-CoV-2 include short physical distance, high patient viral load and poor room ventilation. AGPs, as traditionally defined, seem to be of secondary importance.

Coupled with preventive measures such as personal protective equipment use and physical distancing, serial testing of HCP and patients could help detect and prevent transmission within healthcare facilities during outbreaks and when nosocomial transmission is suspected.


Intensive care unit patients infected with SARS-CoV-2 can shed high titres of virus both in the upper and lower respiratory tract and tend to be prolonged shedders. This information is important for decision making around cohorting patients, de-escalation of PPE, and undertaking potential aerosol generating procedures.


Our study demonstrated probable hamster-to-human transmission of SARS-CoV-2. As pet trading is common around the world, this can represent a route of international spread of this pandemic virus.

**Vaccines / Immunology**


Vaccination remains highly effective against hospitalisation, but vaccine effectiveness declined after 200 days, particularly for older patients or those with specific comorbidities. Additional protection (eg, a booster vaccination) might be warranted for everyone, but especially for these populations. In addition to promoting general vaccine uptake, clinicians and policy makers should consider prioritising booster vaccinations in those most at risk of severe COVID-19.


Fully vaccinated patients hospitalised with COVID-19 in Norway have a shorter LoS and lower risk of ICU admission than unvaccinated patients. These findings can support patient management and ongoing capacity planning in hospitals.


Interim results of this ongoing longitudinal study show that among frail, older people, previous SARS-CoV-2 infection and the type of mRNA vaccine influenced antibody responses when used with a 16-week interval between doses. In these cohorts of frail, older individuals with a similar age and comorbidity distribution, we found that serological responses were similar and clinically equivalent between the discovery and confirmatory cohorts. Homologous and heterologous use of mRNA vaccines was not associated with significant differences in antibody responses 4 weeks following the second dose, supporting their interchangeability.


Here, we showed that humoral immunity components, including anti-S + N, anti-RBD IgG, and neutralizing antibodies (NAbs), gradually waned and decreased the neutralizing capacity against emerging Omicron variants at 3 and 6 months after two inactivated COVID-19 vaccinations. We evaluated two boosting strategies with either a third dose of inactivated vaccine (homologous, I-I-I) or a recombinant subunit vaccine (heterologous, I-I-S). Both strategies induced the production of high levels of NAbs with a broad neutralizing capacity and longer retention. Interestingly, I-I-S induced 3.5-fold to 6.8-fold higher NAb titres than I-I-I, with a broader neutralizing capacity against six variants of concern, including Omicron. Further immunological analysis revealed that the two immunization strategies differ considerably, not only in the magnitude of total NAbs produced, but also in the composite pattern of NAbs and the population of virus-specific CD4+ T cells produced. Additionally, in some cases, heterologous boosted immunity induced the production of more effective epitopes than natural infection. The level of I-I-S-induced NAbs decreased to 48% and 18% at 1 and 3 months after booster vaccination, respectively. Overall, our data provide important evidence for vaccination strategies based on available vaccines and may help guide future global vaccination plans.

28. **Implications of COVID-19 Vaccination on Hospital Encounters and Outcomes.** Case BC, et al. *Am J Cardiol.* 2022 Feb 26:S0002-9149(22)00089-3. doi: 10.1016/j.amjcard.2022.01.029. [https://bmjopen.bmj.com/content/12/2/e055137](https://bmjopen.bmj.com/content/12/2/e055137)

Our analysis suggests that there is no significant association of COVID-19 vaccination with the rate of hospital encounters for cardiac disease, including acute coronary syndrome, pericarditis, myocarditis, congestive heart failure, and conduction abnormality. Further, administration of the vaccine resulted in a significant decrease in hospital encounters for SARS-CoV-2 infections and associated complications.

Our case series provide insight into the characteristics of individuals in whom Graves' disease was triggered by the SARS-CoV-2 vaccination. Clinicians need to be vigilant of precipitation or exacerbation of autoimmune thyroid disorders in predisposed individuals after exposure to the SARS-CoV-2 vaccination. Further epidemiological and mechanistic studies are required to elucidate the possible associations between the SARS-CoV-2 vaccines and the development of thyroid autoimmunity.


During this period, receipt of 3,418 Pfizer-BioNTech booster doses were reported to v-safe for adolescents. Reactions were reported to v-safe with equal or slightly higher frequency after receipt of a booster dose than after dose 2, were primarily mild to moderate in severity, and were most frequently reported the day after vaccination. VAERS received 914 reports of adverse events after Pfizer-BioNTech booster dose vaccination of adolescents; 837 (91.6%) were nonserious and 77 (8.4%) were serious. Health care providers, parents, and adolescents should be advised that local and systemic reactions are expected among adolescents after homologous Pfizer-BioNTech booster vaccination, and that serious adverse events are rare.

Women & Children


Here, we describe a small number of individuals with MIS-C who had received one or more doses of a COVID-19 vaccine before illness onset; the contribution of vaccination to these illnesses is unknown. Our findings suggest that MIS-C after COVID-19 vaccination is rare. Continued reporting of potential cases and surveillance for MIS-C illnesses after COVID-19 vaccination is warranted.


Cases of myocarditis following the second dose of messenger RNA (mRNA) vaccine are accruing worldwide, especially in younger male adults and adolescents. In weighing the risk of myocarditis against the benefit of preventing severe COVID-19, Norway, the UK, and Taiwan have suspended the second dose of mRNA vaccine for adolescents. Similarly, adolescents (aged 12-17 years) in Hong Kong have been recommended to receive 1 dose of BNT162b2 instead of 2 doses 21 days apart since September 15, 2021.

33. Effectiveness of COVID-19 Pfizer-BioNTech BNT162b2 mRNA Vaccination in Preventing COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Nonimmunocompromised Children and Adolescents Aged 5-17 Years
Among children aged 5-11 years, VE against laboratory-confirmed COVID-19-associated ED and UC encounters 14-67 days after dose 2 (the longest interval after dose 2 in this age group) was 46%. Among adolescents aged 12-15 and 16-17 years, VE 14-149 days after dose 2 was 83% and 76%, respectively; VE ≥150 days after dose 2 was 38% and 46%, respectively. Among adolescents aged 16-17 years, VE increased to 86% ≥7 days after dose 3 (booster dose). VE against COVID-19-associated ED and UC encounters was substantially lower during the Omicron predominant period than the B.1.617.2 (Delta) predominant period among adolescents aged 12-17 years, with no significant protection ≥150 days after dose 2 during Omicron predominance. However, in adolescents aged 16-17 years, VE during the Omicron predominant period increased to 81% ≥7 days after a third booster dose. During the full study period, including pre-Delta, Delta, and Omicron predominant periods, VE against laboratory-confirmed COVID-19-associated hospitalization among children aged 5-11 years was 74% 14-67 days after dose 2, with wide CIs that included zero. Among adolescents aged 12-15 and 16-17 years, VE 14-149 days after dose 2 was 92% and 94%, respectively; VE ≥150 days after dose 2 was 73% and 88%, respectively. All eligible children and adolescents should remain up to date with recommended COVID-19 vaccinations, including a booster dose for those aged 12-17 years.

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**GUIDELINES & CONSENSUS STATEMENTS**


Update to living WHO guideline on drugs for covid-19. BMJ. 2022 Mar 2;376:o534. doi: 10.1136/bmj.o534.


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**FDA / CDC / NIH / WHO Updates**

NIH: The COVID-19 Treatment Guidelines Panel’s Statement on the Role of Bebtelovimab for the Treatment of High-Risk, Nonhospitalized Patients With Mild to Moderate COVID-19

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