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

Basic Science / Virology / Pre-clinical


   We show probenecid potently blocks SARS-CoV-2 replication in mammalian cells and virus replication in a hamster model. Furthermore, we demonstrate that plasma concentrations up to 50-fold higher than the protein binding adjusted IC90 value are achievable for 24 h following a single oral dose. These data support the potential clinical utility of probenecid to control SARS-CoV-2 infection in humans.

Clinical Syndrome


   Of 221 patients with MIS-A, the median age was 21 years, and 70% were men. 36% were non-Hispanic Black individuals, and 58% had no underlying comorbidity. Most patients with MIS-A presented with fever, hypotension, cardiac dysfunction, shortness of breath, and/or diarrhea. The median number of organ systems involved was 5. Median hospital stay was 8 days; 57% were admitted to the intensive care unit; 47% required respiratory support, and 7% died. These findings suggest that MIS-A is a serious hyperinflammatory condition that presents approximately 4 weeks after onset of acute COVID-19 with extrapulmonary multiorgan dysfunction.

Epidemiology & Public Health

3. **Daily testing for contacts of individuals with SARS-CoV-2 infection and attendance and SARS-CoV-2 transmission in English secondary schools and colleges: an open-label, cluster-randomised trial.** Young BC et al. *Lancet.* 2021 Sep 14:S0140-6736(21)01908-5. doi:
Daily contact testing of school-based contacts was non-inferior to self-isolation for control of COVID-19 transmission, with similar rates of symptomatic infections among students and staff with both approaches. Infection rates in school-based contacts were low, with very few school contacts testing positive. Daily contact testing should be considered for implementation as a safe alternative to home isolation following school-based exposures.


After an initial decline from April through June 2020 (from 22.2% to 11.9%), adjusted in-hospital mortality in COVID-19 inpatients peaked twice and was significantly higher than June 2020 for subsequent months except in July and October 2020. Adjusted mortality trends differed across age groups between November 2020 and February 2021.


Beyond excess deaths alone, the COVID-19 pandemic imposed a greater life expectancy burden on persons aged 25 to 64 years, including those with average or above-average life expectancies, and a disproportionate burden on Black and Hispanic communities.


Without the national vaccination campaign, Israel probably would have had triple the number of hospitalisations and deaths compared with what actually occurred during its largest wave of the pandemic to date, and the health-care system might have become overwhelmed. Indirect effects and long-term benefits of the programme, which could be substantial, were not included in these estimates and warrant future research.


In the crude analysis, the odds of a school-associated COVID-19 outbreak in schools with no mask requirement were 3.7 times higher than those in schools with an early mask requirement. After adjusting for potential described confounders, the odds of a school-associated COVID-19 outbreak in schools without a mask requirement were 3.5 times higher than those in schools with an early mask requirement.

Healthcare Delivery & Healthcare Workers


There were 592 responses to the phase one survey, conducted prior to publication of trial data. At this time physicians were most willing to treat with macrolide antibiotics (50.5%), followed by antimalaria agents (36.1%), corticosteroids (24.5%), antiretroviral agents (22.6%), and angiotensin inhibitors (4.4%). Greater evidence skepticism, greater need for closure, and greater risk tolerance were associated with an increased willingness to treat; while greater need for cognition and greater research engagement were associated with decreased willingness to treat. In phase two, most physicians updated their beliefs after publication of trial data about antimalarial agents and corticosteroids. Physicians with greater evidence skepticism more likely to persist in their beliefs.

Survivorship & Rehabilitation


The median time from the onset of infection to neurological symptoms was 16 days. Patients with SARS-CoV-2 infection shared uniform neurological features, similar to those previously described in other post-viral GBS patients. The frequency (22%) of a preceding SARS-CoV-2 infection in our study population was higher than estimates of the contemporaneous background prevalence of SARS-CoV-2, which may be a result of recruitment bias during the pandemic, but could also indicate that GBS may rarely follow a recent SARS-CoV-2 infection. Consistent with previous studies, we found no increase in patient recruitment during the pandemic for our ongoing International GBS Outcome Study compared to previous years, making a strong relationship of GBS with SARS-CoV-2 unlikely. A case-control study is required to determine if there is a causative link or not.

Therapeutics


Early initiation (< 24 h of HFNC use) of APP in acute hypoxemic respiratory failure secondary to COVID-19 improves 28-day survival. Trial registration ClinicalTrials.gov NCT04325906.

A total of 8 studies comprising of 13,573 adult patients with COVID-19, including 4191 in the BAM (administered alone) and 9382 in the control group arm, were included in this meta-analysis. The meta-analysis showed the overall mortality was lower in the BAM group compared to control group. Moreover, BAM treatment were associated with lower risk of hospitalization and developing severe COVID-19 disease. Pooled analysis of adjusted results revealed that BAM group had a lower risk of mortality and hospitalization compared with control group. In conclusion, our meta-analysis provides evidence that BAM is effective in the treatment of COVID-19 patients. There is an urgent need for well-designed randomized trials to determine the effectiveness and safety of BAM in severe COVID-19.


No clinical benefit was observed from the use of remdesivir in patients who were admitted to hospital for COVID-19, were symptomatic for more than 7 days, and required oxygen support.


Data show that treatment of hospitalized COVID19 patients with CCP did not significantly improve patient hospitalization length of stay or inpatient mortality.

**Transmission / Infection Control**


The ARs among travellers varied by seat distance from the index case and joint travel time, but the variation was not significant between the types of aircraft. The overall risk of SARS-CoV-2 transmission during domestic travel on planes was relatively low. These findings can improve our understanding of COVID-19 spread during travel and inform response efforts in the pandemic.

**Vaccines / Immunology**

The BNT162 vaccine is highly effective in preventing new SARS-CoV-2 cases. Among ≥80 year old individuals, high effectiveness develops more slowly. In breakthrough cases, vaccination reduces complications and death.


The inactivated COVID-19 vaccine BBIBP-CorV is safe and well tolerated at all tested dose levels in participants aged 3-17 years. BBIBP-CorV also elicited robust humoral responses against SARS-CoV-2 infection after two doses. Our findings support the use of a 4 μg dose and two-shot regimen BBIBP-CorV in phase 3 trials in the population younger than 18 years to further ascertain its safety and protection efficacy against COVID-19.


Boosting could be appropriate for some individuals in whom the primary vaccination, defined here as the original one-dose or two-dose series of each vaccine, might not have induced adequate protection—eg, recipients of vaccines with low efficacy or those who are immunocompromised (although people who did not respond robustly to the primary vaccination might also not respond well to a booster). It is not known whether such immunocompromised individuals would receive more benefit from an additional dose of the same vaccine or of a different vaccine that might complement the primary immune response.


Among adults with ED/UC encounters for COVID-19–like illness (18,231; median patient age = 43 years), laboratory-confirmed SARS-CoV-2 infections were identified among 28.9% of unvaccinated and 7.0% of fully vaccinated patients. VE against COVID-19 ED/UC encounters was 82%. VE was highest among Moderna vaccine recipients (92%), followed by Pfizer-BioNTech vaccine recipients (77%), and was lowest (65%) for Janssen vaccine recipients.


During February 1–August 6, 2021, vaccine effectiveness among U.S. veterans hospitalized at five Veterans Affairs Medical Centers was 87%. mRNA COVID-19 vaccines remain highly
effective, including during periods of widespread circulation of the SARS-CoV-2 B.1.617.2 (Delta) variant. Vaccine effectiveness in preventing COVID-19–related hospitalization was 80% among adults aged ≥65 years compared with 95% among adults aged 18–64 years. To protect against COVID-19–related hospitalization, all eligible persons should receive COVID-19 vaccination.


As the trial is currently ongoing, this exploratory interim analysis includes preliminary descriptive results only of four booster groups (n = 20 per group). Immediately before the booster dose, neutralizing antibodies against wild-type D614G virus had waned relative to peak titers against wild-type D614G measured 1 month after the primary series, and neutralization titers against B.1.351 (Beta), P.1 (Gamma) and B.1.617.2 (Delta) VOCs were either low or undetectable. Both the mRNA-1273 booster and variant-modified boosters were safe and well-tolerated. All boosters, including mRNA-1273, numerically increased neutralization titers against the wild-type D614G virus compared to peak titers against wild-type D614G measured 1 month after the primary series; significant increases were observed for mRNA-1273 and mRNA-1273.211. In addition, all boosters increased neutralization titers against key VOCs and VOIs, including B.1.351, P.1. and B.1.617.2, that were statistically equivalent to peak titers measured after the primary vaccine series against wild-type D614G virus, with superior titers against some VOIs. This trial is ongoing.

21. **Risk prediction of covid-19 related death and hospital admission in adults after covid-19 vaccination: national prospective cohort study.** Hippisley-Cox J et al. BMJ. 2021 Sep 17;374:n2244. doi: 10.1136/bmj.n2244. [https://www.bmj.com/content/374/bmj.n2244](https://www.bmj.com/content/374/bmj.n2244)

Of 6,952,440 vaccinated patients in the derivation cohort, 74.1% had two vaccine doses. Of 2031 covid-19 deaths and 1929 covid-19 hospital admissions, 81 deaths (4.0%) and 71 admissions (3.7%) occurred 14 days or more after the second vaccine dose. Incidence of covid-19 mortality increased with age and deprivation, male sex, and Indian and Pakistani ethnic origin. Cause specific hazard ratios were highest for patients with Down's syndrome (12.7-fold increase), kidney transplantation (8.1-fold), sickle cell disease (7.7-fold), care home residency (4.1-fold), chemotherapy (4.3-fold), HIV/AIDS (3.3-fold), liver cirrhosis (3.0-fold), neurological conditions (2.6-fold), recent bone marrow transplantation or a solid organ transplantation ever (2.5-fold), dementia (2.2-fold), and Parkinson's disease (2.2-fold). This population based risk algorithm performed well showing high levels of discrimination for identifying those patients at highest risk of covid-19 related death and hospital admission after vaccination.


From April to October 2020 we screened 44,698 HCW of which 2,811 were seropositive at least once. The seroprevalence increased from 4.0% to 7.4% during the period and was significantly
higher than in non-HCW. Frontline HCW had a significantly increased risk of seropositivity compared to non-frontline HCW. The seroprevalence was 1.42- to 2.25-fold higher in HCW from dedicated COVID-19 wards. HCW remained at increased risk of infection with SARS-CoV-2 during the six months period. Seropositivity against SARS-CoV-2 persisted for at least six months in the vast majority of HCW and was associated with a significantly lower risk of reinfection.


The mRNA-1273 vaccine continued to be efficacious in preventing Covid-19 illness and severe disease at more than 5 months, with an acceptable safety profile, and protection against asymptomatic infection was observed.


The BNT162b2 and mRNA-1273 vaccines were highly effective under real-world conditions in preventing symptomatic Covid-19 in health care personnel, including those at risk for severe Covid-19 and those in racial and ethnic groups that have been disproportionately affected by the pandemic.


Ad5-vectored COVID-19 vaccine with a single dose was safe and induced robust immune responses in children and adolescents aged 6-17 years. A prime-boost regimen needs further exploration for Ad5-vectored COVID-19 vaccine.


Our data demonstrated that individuals that had SARS-CoV-2 infection prior to vaccination and younger aged individuals had significantly higher levels of antibodies after primary immunization with a SARS-CoV-2 mRNA vaccine and had significantly longer antibody half-life measured at 7 months after vaccination. The rate of antibody decay observed here are consistent with reports of other vaccine platforms and convalescent individuals after infection. In this study, individuals had recent infection within 60 days prior to the administration of vaccine. It will be critical to determine if individuals with SARS-CoV-2 infection beyond 60 days before vaccination also have higher antibody responses that are maintained longer.
Continued use of the Pfizer-BioNTech COVID-19 vaccine, now fully approved by the FDA in persons aged ≥16 years, is recommended based on increased certainty that its benefits (prevention of asymptomatic infection, COVID-19, and associated hospitalization and death) outweigh vaccine-associated risks.

Women & Children

There is increased morbidity seen in pregnancy with COVID-19 during the recent surge associated with the Delta variant, particularly in an underserved pregnant population where vaccine acceptance is low. Overall rates of severe or critical illness in this cohort are consistent with previously published data from our institution. However, recent trends demonstrate that along with increasing case volume, the proportion requiring hospitalization is rising. Potential pathophysiologic mechanisms for increased severity of illness with B.1.617.2 in pregnancy are unclear. Our results highlight the urgency of prevention measures including COVID-19 vaccination during pregnancy.

The impact of COVID-19 on the menstrual cycle is largely unknown. People who reported changes in their menstrual cycle after SARS-CoV-2 infection reported more COVID-19 symptoms as compared to those who did not; however, identification of other differences between these groups were limited in this study due to the small sample size and inability to adjust for potential confounding factors. Additionally, information on COVID-19 symptoms were assessed every six weeks for SARS89 CoV-2 positive participants which may lead to misclassification. The duration of menstrual cycle changes indicates the need to further investigate the role of PASC on reproductive health.

In a motivated population covered by a National Health Insurance Plan, we found a 40.2% rate of vaccination for the Covid-19 vaccine during the third trimester of pregnancy which was not
associated with adverse maternal outcomes and decreased the risk for neonatal adverse outcomes.

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

**CDC** - [Statement on ACIP Booster Recommendations](#) CDC issued its first recommendations for who should receive booster doses of the Pfizer-BioNTech Covid-19 vaccine, in a departure from ACIP opted to recommend boosters for those at risk of coronavirus exposure due to their jobs. 9-24-21

**FDA** - [Authorizes Booster Dose of Pfizer-BioNTech COVID-19 Vaccine for Certain Populations](#) for adults 65 years and older and those who are at high risk of severe Covid-19, whether because of their health or their job. 9-22-21


**Commentary / Press Releases**

**PFIZER AND BIONTECH ANNOUNCE POSITIVE TOPLINE RESULTS FROM PIVOTAL TRIAL OF COVID-19 VACCINE IN CHILDREN 5 TO 11 YEARS**, Sept 20, 2021


**C.D.C. Chief Overrules Agency Panel and Recommends Pfizer-BioNTech Boosters for Workers at Risk**, *NY Times*, 9-24-21

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