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Clinical Syndrome


Patients with COVID-19 breakthrough infections had a significantly higher proportion of CT scans without pneumonia compared to unvaccinated patients. Vaccinated patients with breakthrough infections had lower likelihood of requiring supplemental oxygen or ICU admission.


The prevalence of bacterial co-infections was significantly lower in patients with community-acquired SARS-CoV-2 positive pneumonia as compared to influenza and RSV positive pneumonia.

3. **Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge.** Killingley B, Mann A, Kalinova M et al. 01 February 2022, *PREPRINT* (Version 1) available at Research Square [https://doi.org/10.21203/rs.3.rs-1121993/v1](https://doi.org/10.21203/rs.3.rs-1121993/v1)

To establish a novel SARS-CoV-2 human challenge model, 36 volunteers aged 18-29 years without evidence of previous infection or vaccination were inoculated with 10 TCID50 of a wild-type virus (SARS-CoV-2/human/GBR/484861/2020) intranasally. Eighteen (~53%) became infected, with viral load (VL) rising steeply and peaking at ~5 days post-inoculation. Virus was first detected in the throat but rose to significantly higher levels in the nose, peaking at ~8.87 log10 copies/ml (median, 95% CI [8.41,9.53]). Viable virus was recoverable from the nose up to ~10 days post-inoculation, on average. There were no serious adverse events. Mild-to-moderate symptoms were reported by 16 (89%) infected individuals, beginning 2-4 days post-inoculation. Anosmia/dysosmia developed more gradually in 12 (67%) participants. No quantitative correlation was noted between VL and symptoms, with high VLs even in...
asymptomatic infection, followed by the development of serum spike-specific and neutralising antibodies. However, lateral flow results were strongly associated with viable virus and modelling showed that twice-weekly rapid tests could diagnose infection before 70-80% of viable virus had been generated. Thus, in this first SARS-CoV-2 human challenge study, no serious safety signals were detected and the detailed characteristics of early infection and their public health implications were shown.

**Diagnostics & Screening**


FebriDx improved the triage of patients with suspected COVID-19 and reduced the time that SARS-CoV-2 PCR-negative patients spent in high-risk areas alongside positive patients.

**Epidemiology & Public Health**


COVID-19 deaths are rare in fully vaccinated persons, occurring most commonly in those with risk factors for severe disease, including older age and underlying health conditions. All eligible persons should be fully vaccinated against COVID-19 and follow other prevention measures to mitigate exposure risk.


Compared to non-Latino White members, members of other race/ethnic groups had higher positivity rates that were only minimally reduced after controlling for medical and neighborhood conditions and self-reported social risk factors. These findings suggest that traditional infection transmission factors such as essential work roles and household size that have disproportionate representation among communities of color may be important contributors to SARS-COV-2 infection among insured adults.

The Los Angeles County (LAC) Department of Public Health (LACDPH) used COVID-19 surveillance and California Immunization Registry 2 (CAIR2) data to describe age-adjusted 14-day cumulative incidence and hospitalization rates during November 7, 2021-January 8, 2022, by COVID-19 vaccination status and variant predominance. For the 14-day period ending December 11, 2021, the last week of Delta predominance, the incidence and hospitalization rates among unvaccinated persons were 12.3 and 83.0 times, respectively, those of fully vaccinated persons with a booster and 3.8 and 12.9 times, respectively, those of fully vaccinated persons without a booster. These rate ratios were lower during Omicron predominance (week ending January 8, 2022), with unvaccinated persons having infection and hospitalization rates 3.6 and 23.0 times, respectively, those of fully vaccinated persons with a booster and 2.0 and 5.3 times, respectively, those of fully vaccinated persons without a booster. In addition, during the entire analytic period, admission to intensive care units (ICUs), intubation for mechanical ventilation, and death were more likely to occur among unvaccinated persons than among fully vaccinated persons without or with a booster. Incidence and hospitalization rates were consistently highest for unvaccinated persons and lowest for fully vaccinated persons with a booster. Being up to date with COVID-19 vaccination is critical to protecting against SARS-CoV-2 infection and associated hospitalization.


During August 29-October 30, 2021, data from the National Immunization Survey Adult COVID Module (NIS-ACM) were analyzed to assess COVID-19 vaccination coverage and confidence in COVID-19 vaccines among LGBT adults aged ≥18 years. By sexual orientation, gay or lesbian adults reported higher vaccination coverage overall (85.4%) than did heterosexual adults (76.3%). By race/ethnicity, adult gay or lesbian non-Hispanic White men (94.1%) and women (88.5%), and Hispanic men (82.5%) reported higher vaccination coverage than that reported by non-Hispanic White heterosexual men (74.2%) and women (78.6%). Among non-Hispanic Black adults, vaccination coverage was lower among gay or lesbian women (57.9%) and bisexual women (62.1%) than among heterosexual women (75.6%). Vaccination coverage was lowest among non-Hispanic Black LGBT persons across all categories of sexual orientation and gender identity. Among gay or lesbian adults and bisexual adults, vaccination coverage was lower among women (80.5% and 74.2%, respectively) than among men (88.9% and 81.7%, respectively). By gender identity, similar percentages of adults who identified as transgender or nonbinary and those who did not identify as transgender or nonbinary were vaccinated. Gay or lesbian adults and bisexual adults were more confident than were heterosexual adults in COVID-19 vaccine safety and protection; transgender or nonbinary adults were more confident in COVID-19 vaccine protection, but not safety, than were adults who did not identify as transgender or nonbinary. To prevent serious illness and death, it is important that all persons in the United States, including those in the LGBT community, stay up to date with recommended COVID-19 vaccinations.

Several studies reported that the severe acute respiratory syndrome coronavirus-2 antibody levels change over 6 months in participants receiving the vaccination. For the enrolled 272 healthcare workers (HCWs), blood samplings were performed at 2, 16, and 24 weeks after the second vaccination dose. In the 267 non-infected HCWs, the neutralizing antibodies decreased by 23.9%, and the anti-spike/receptor binding domain antibody decreased by 53.8% at 24 weeks. We observed no significant difference in antibody reduction between the sexes; however, in younger individuals, there was higher antibody formation and lower reduction rates of the neutralizing antibody. In 3 HCWs with breakthrough infections, the antibody levels were relatively low just before the coronavirus disease 2019 infection. In conclusion, as antibody titers decrease over time after the second vaccination dose and HCWs with low antibody titers tend to have a high probability of breakthrough infection, an additional dose should be considered after several months.


Infections occurring after vaccination with the BNT162b2 vaccine are mostly asymptomatic and are not associated with the serum titre of anti-S1 antibodies. We did not find a predominance of specific viral variants, with several lineages represented.

### Prognosis


Patients with a disability who were admitted to hospital with COVID-19 had longer stays and elevated readmission risk than those without disabilities. Disability-related needs should be addressed to support these patients in hospital and after discharge.


Elevated inflammatory biomarkers and SOFA score at ICU admission were detected as significant predictors of ICU mortality in this cohort, while initiation of invasive mechanical ventilation is the most relevant interventional mortality risk factor in critically ill COVID-19 patients.
Therapeutics

   [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00101-5/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00101-5/fulltext)
   When administered with standard of care including remdesivir, SARS-CoV-2 hIVIG did not demonstrate efficacy among patients hospitalised with COVID-19 without end-organ failure. The safety of hIVIG might vary by the presence of endogenous neutralising antibodies at entry.

   Overall, we did not find evidence for an important beneficial effect of IL-1 blocking agents. The evidence is uncertain or very uncertain for several outcomes. Sixteen trials of anakinra and canakinumab with no results are currently registered, of which four are completed, and four terminated. The findings of this review are updated on the COVID-NMA platform (covid-nma.com).

   Although select antivirals have exhibited efficacy to improve clinical outcomes in COVID-19 patients, none demonstrated efficacy in reducing mortality. Larger RCTs are needed to conclusively establish efficacy.

   [https://academic.oup.com/jac/article/77/2/303/6430403](https://academic.oup.com/jac/article/77/2/303/6430403)
   The results presented in this systematic review do not support the use of azithromycin in the management of COVID-19. Future research on treatment for patients with COVID-19 may need to focus on other drugs.

Transmission / Infection Control

   [https://www.nature.com/articles/s41467-022-28199-7](https://www.nature.com/articles/s41467-022-28199-7)
   Here, we investigate differences in RT-qPCR Ct values across Qatar’s national cohorts of primary infections, reinfections, BNT162b2 (Pfizer-BioNTech) breakthrough infections, and mRNA-1273 (Moderna) breakthrough infections. Our matched-cohort analyses of the randomly diagnosed infections show higher mean Ct value in all cohorts of breakthrough infections compared to the cohort of primary infections in unvaccinated individuals. The Ct value is 1.3 (95% CI: 0.9-1.8) cycles higher for BNT162b2 breakthrough infections, 3.2 (95% CI: 1.9-4.5) cycles higher for
mRNA-1273 breakthrough infections, and 4.0 (95% CI: 3.5-4.5) cycles higher for reinfections in unvaccinated individuals. Since Ct value correlates inversely with SARS-CoV-2 infectiousness, these differences imply that vaccine breakthrough infections and reinfections are less infectious than primary infections in unvaccinated individuals. Public health benefits of vaccination may have been underestimated, as COVID-19 vaccines not only protect against acquisition of infection, but also appear to protect against transmission of infection.


The risk of SARS-CoV-2 infection was considerable among close contacts of infected persons. The higher risk associated with household contacts, immigrants, older index cases, close contacts with lower income level and comorbidities should be considered to address preventive interventions.

**Vaccines / Immunology**


Two injections of CoV2 preS dTM-AS03 showed acceptable safety and reactogenicity, and robust immunogenicity in adults who were SARS-CoV-2 naive and non-naive. These results supported progression to phase 3 evaluation of the 10 μg antigen dose for primary vaccination and a 5 μg antigen dose for booster vaccination.


Omicron partially evades vaccine-induced immunity, but a third vaccine dose increases omicron nAb responses in the general population. Comparable data in patients with cancer are lacking, leaving patients and cancer physicians without the means to calibrate infection risk while maintaining necessary cancer treatments. We used live-virus micro-neutralisation assays to evaluate response to omicron following three doses of COVID-19 vaccine in participants of the CAPTURE study (NCT03226886), a prospective, longitudinal cohort of patients with cancer.

21. **Three exposures to the spike protein of SARS-CoV-2 by either infection or vaccination elicit superior neutralizing immunity to all variants of concern.** Wratil PR et al. *Nat Med.* 2022 Jan 28. doi: 10.1038/s41591-022-01715-4. [https://www.nature.com/articles/s41591-022-01715-4](https://www.nature.com/articles/s41591-022-01715-4)

Infection-neutralizing antibody responses after SARS-CoV-2 infection or COVID-19 vaccination are an essential component of antiviral immunity. Antibody-mediated protection is challenged...
by the emergence of SARS-CoV-2 variants of concern (VoCs) with immune escape properties, such as omicron (B.1.1.529) that is rapidly spreading worldwide. Here, we report neutralizing antibody dynamics in a longitudinal cohort of COVID-19 convalescent and infection-naive individuals vaccinated with mRNA BNT162b2 by quantifying anti-SARS-CoV-2-spike antibodies and determining their avidity and neutralization capacity in serum. Using live-virus neutralization assays, we show that a superior infection-neutralizing capacity against all VoCs, including omicron, developed after either two vaccinations in convalescents or after a third vaccination or breakthrough infection of twice-vaccinated, naive individuals. These three consecutive spike antigen exposures resulted in an increasing neutralization capacity per anti-spike antibody unit and were paralleled by stepwise increases in antibody avidity. 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.

22. **Protection by 4th dose of BNT162b2 against Omicron in Israel.** Bar-On YM, et al. *MedRxiv PREPRINT* 2022.02.01.22270232; doi: [https://doi.org/10.1101/2022.02.01.22270232](https://doi.org/10.1101/2022.02.01.22270232)
The rate of confirmed infection was lower in people 12 or more days after their fourth dose than among those who received only three doses and those 3 to 7 days after vaccination by factors of 2.0 (95% confidence interval [CI], 2.0 to 2.1) and 1.9 (95% CI, 1.8 to 2.0), respectively. The rate of severe illness was lower by factors of 4.3 (95% CI, 2.4 to 7.6) and 4.0 (95% CI, 2.2 to 7.5). Rates of confirmed Covid-19 and severe illness were lower following a fourth dose compared to only three doses.

No safety concerns or immune interference were observed for concomitant administration of QIV-HD with mRNA-1273 booster in adults aged 65 years and older, supporting co-administration recommendations.

[https://jamanetwork.com/journals/jama/fullarticle/2788894](https://jamanetwork.com/journals/jama/fullarticle/2788894)
As of December 28, 2021, approximately 27% of the US population was unvaccinated against SARS-CoV-2,1 yet the prevalence of natural immunity remains unknown. Blood donor studies may have selection bias and lack clinical information.2 Previous COVID-19 infection is a possible surrogate for natural immunity, but 1 study suggested that 36% of COVID-recovered individuals are serologic nonresponders.3 Even among individuals who develop antibodies, durability of this response beyond 6 months remains unknown. We characterized natural immunity and long-term durability among unvaccinated individuals using anti–spike antibodies, the first line of defense against SARS-CoV-2.

The highly mutated SARS-CoV-2 Omicron (B.1.1.529) variant has been shown to evade a substantial fraction of neutralizing antibody responses elicited by current vaccines that encode the WA1/2020 Spike1. Cellular immune responses, particularly CD8+ T cell responses, likely contribute to protection against severe SARS-CoV-2 disease2-6. Here we show that cellular immunity induced by current SARS-CoV-2 vaccines is highly conserved to the SARS-CoV-2 Omicron Spike. Individuals who received Ad26.COV2.S or BNT162b2 vaccines demonstrated durable Spike-specific CD8+ and CD4+ T cell responses, which showed extensive cross-reactivity against both the Delta and Omicron variants, including in central and effector memory cellular subpopulations. Median Omicron Spike-specific CD8+ T cell responses were 82-84% of WA1/2020 Spike-specific CD8+ T cell responses. These data provide immunologic context for the observation that current vaccines still show robust protection against severe disease with the SARS-CoV-2 Omicron variant despite the substantially reduced neutralizing antibody responses7,8.


The SARS-CoV-2 Omicron variant has multiple Spike (S) protein mutations that contribute to escape from antibody neutralization and reduce vaccine protection from infection. The extent to which other components of the adaptive response such as T cells may still target Omicron and contribute to protection from severe outcomes is unknown. We assessed the ability of T cells to react with Omicron spike in participants who were vaccinated with Ad26.CoV2.S, BNT162b2, or unvaccinated convalescent COVID-19 patients (n=70). We found that 70-80% of the CD4+ and CD8+ T cell response to spike was maintained across study groups. Moreover, the magnitude of Omicron cross-reactive T cells was similar to Beta and Delta variants, despite Omicron harboring considerably more mutations. In Omicron-infected hospitalized patients (n=19), there were comparable T cell responses to ancestral spike, nucleocapsid and membrane proteins to those patients hospitalized in previous waves dominated by the ancestral, Beta or Delta variants (n=49). Thus, despite Omicron's extensive mutations and reduced susceptibility to neutralizing antibodies, the majority of T cell responses, induced by vaccination or infection, cross-recognize the variant. It remains to be determined whether well-preserved T cell immunity to Omicron contributes to protection from severe COVID-19, and is linked to early clinical observations from South Africa and elsewhere.

Women & Children

COVID-19 vaccine hesitancy was frequent among pregnant and postpartum individuals. Those who may face barriers to accessing healthcare services were more likely to report vaccine hesitancy. These results can inform interventions to increase COVID-19 vaccine uptake in pregnancy.


Children and adolescents exhibit a broad range of clinical outcomes from SARS-CoV-2 infection, with the majority having minimal to mild symptoms. Additionally, some succumb to a severe hyperinflammatory post-infectious complication called multisystem inflammatory syndrome in children (MIS-C), predominantly affecting previously healthy individuals. Studies characterizing the immunological differences associated with these clinical outcomes have identified pathways important for host immunity to SARS-CoV-2 and innate modulators of disease severity. In this Review, we delineate the immunological mechanisms underlying the spectrum of pediatric immune response to SARS-CoV-2 infection in comparison with that of adults.

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**GUIDELINES & CONSENSUS STATEMENTS**


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


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