Humoral Responses to SARS-CoV-2 mRNA Vaccines: Role of Past Infection

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Background

The severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) pandemic of 2019-2021 has led to millions of excess deaths across the globe. Amongst public health efforts to control disease and limit spread, the rapid production and testing of vaccines has remained central. In the United States, two novel mRNA-based vaccines (BNT162b2/Pfizer-BioNTech and mRNA-1273/Moderna) against SARS-CoV-2 have received emergency use authorization (EUA) for use in a two-dose schedule for all individuals, including those with previous SARS-CoV-2 infection. Understanding of the antibody response to vaccination after previous infection may help to more equitably distribute immunizations to those who most need protection—particularly as distribution challenges and limited vaccine supply impede vaccine delivery, and the emergence of variant SARS-CoV-2 strains threatens to spark new outbreaks.

Objectives

- Evaluate anti-spike IgG antibody responses prior to and following each dose of mRNA vaccination, and at 31-60 days and 61-90 days after completion of the 2-dose series vaccination with mRNA-based vaccines in a population offered early immunization (healthcare workers & first responders)
- Determine timing and peak antibody response in previously infected (PI) and not previously infected (NPI) participants
- Explore differences in humoral responses between vaccine types

Methods

Health services workers at the University of California, Los Angeles (UCLA) and first responders in the Los Angeles County Fire Department (LACoFD) were enrolled in a longitudinal cohort study assessing rates of SARS-CoV-2 infection in high-risk individuals. Nasal swab and blood samples at regular intervals to determine presence of SARS-CoV-2 infection. SARS-CoV-2 vaccines were offered to participants by their employers, per state guidelines and vaccine availability. Participants had blood drawn between 7 days after the first vaccine dose and just prior to the second dose (up to 20 days after the first dose of BNT162b2 and up to 27 days after the first dose of mRNA-1273). Blood was also collected 7-28 days, 31-60 days and 61-90 days after completion of the two-dose series. Not all participants provided blood samples at every time point.

Results

All PI individuals had anti-S IgG prior to vaccination. All immunocompetent individuals developed high anti-S IgG titers after 2 doses of vaccine. Two immunocompromised individuals did not develop anti-S IgG above the limit of detection of the assay. Peak antibody titers were higher and antibody titer decay rate was slower for PI individuals ($p < 0.0001$, $p = 0.0375$). Peak antibody titers were significantly associated with age, but not sex, of the individuals, with younger individuals achieving higher anti-Spike IgG levels. 70% of PIs had titers >3950 AU/mL after a single dose of vaccine. Among NPI individuals, peak antibody titers were higher for those who received mRNA-1273 vaccination than for BNT-162b2 at 3 out of 4 time points. The rate of antibody decay was noted to be significantly faster in NPI participants versus PI participants, at 0.16 versus 0.12 ln-units/week; p=0.0375. The BNT162b2 group displayed a more rapid antibody decay following the 2nd vaccine dose when compared to the mRNA-1273 group (0.16 versus 0.13 Ln-units/week, p=0.0212).

Figure 1: Longitudinal Immune Response to Anti-Spike IgG Following Each Vaccination Dose and up to 90 days Post-Vaccination

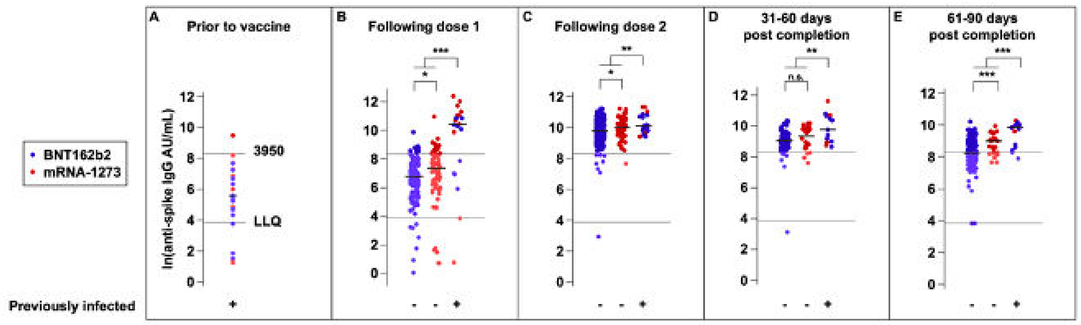


Figure 2: Post-vaccination Anti-Spike IgG Antibody Levels by Age

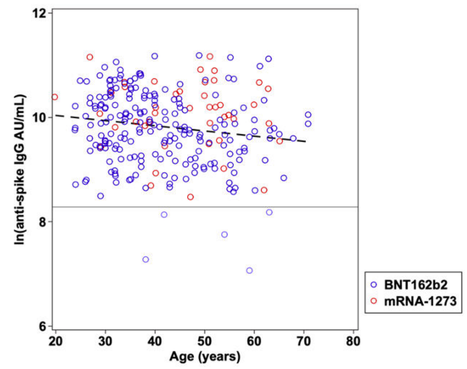
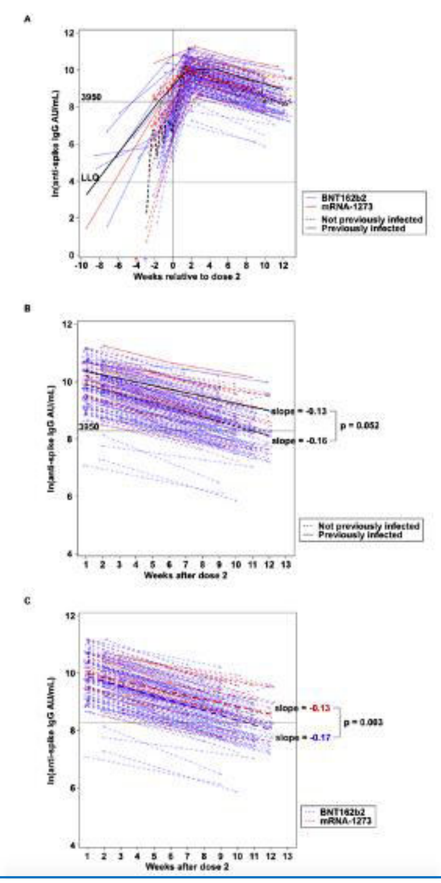


Figure 3: Anti-Spike IgG Antibody Dynamics and Decay up to 90 days Post-Vaccination



Conclusions

- All immunocompetent individuals responded to vaccination, regardless of the type of vaccination (mRNA-1273 or BNT162b2).
- PI individuals had a rapid and more robust response to initial vaccination than did NPI individuals.
- However, there was a subset of PI individuals that did not produce a high-titer antibody response after a single vaccine dose
- PI individuals had higher mean antibody titers and slower rate of antibody decay than did NPI individuals
- NPI individuals who received mRNA-1273 had higher median antibody titers and slower rates of antibody decay than NPI who received BNT162b2
- Younger individuals, regardless of infection history and vaccine type received, had higher median anti-S IgG levels after vaccination than did older individuals.
- Immunocompromised individuals may have a poor response even after 2 doses of mRNA-based vaccine

Next Steps/Policy Implications

- Administration of a single dose of vaccine to those with previous infection may help to achieve herd immunity faster by preserving limited doses of vaccine for those with little or no immunity; however, as a significant portion of people with previous infection do not produce high IgG titers after the first vaccine dose, some discrimination between responders and non-responders may be necessary
- This study suggests differences in median peak antibody titer and antibody decay rate between those who receive mRNA-1273 and those who receive BNT162b2, which could affect recommendations for timing and need for booster vaccine doses
- Further studies should assess duration of antibody response in immunocompromised and immunocompetent individuals to determine the need for mRNA-based re-vaccination schedules. Lastly, further evaluations assessing the coordinated immunological responses to mRNA-based vaccinations (such as memory B-cell and T-cell responses) are also needed.

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