

Letter to the Editor: Waning Vaccine Immunity and the Need for a Third (Booster) Vaccine to Prevent Breakthrough Infections against COVID-19

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Letter to the Editor

The COVID-19 pandemic caused by transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), admission to intensive care units and death continues to be a global public health crisis. During infection, viral replication and mutations in the spike protein occur. [1] Vaccine effectiveness with the SARS-CoV-2 mRNA vaccines, BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) have demonstrated efficacy rates of 95% and 94.1% during clinical trials. [2] Polack et al. (2021) reported that there was 95% efficacy against COVID-19 seven days after the first dose and 60 days after the second dose. [3] However, four months after the second dose with the BNT162b2 vaccine, vaccine effectiveness waned down to 84% in their global, randomized, placebo controlled, phase 1-2-3 pivotal trial where two 30ug doses were administered 21 days from each other. [4] Vaccine effectiveness was also observed to wane in other observational cohort studies that received mRNA vaccines against the Delta variant that is twice as infectious as the Alpha variant. [3,5,6] Lastly, a 6-month prospective longitudinal study revealed that six months after the second dose of the BNT162b2 vaccine, the humoral response decreased especially among men and individuals 65 years and older and those with immunosuppression. [5]

What remains unclear is how long are individuals effectively protected from the coronavirus after being fully vaccinated or from natural immunity. Although reports of vaccine breakthrough COVID-19 infections are being reported in greater frequency globally, they are generally clinically milder due to lower viral loads that have resulted in fewer hospital admissions and deaths. [7]

As breakthrough cases are expected as no vaccine is 100% effective, there is intense policy discussion if a third vaccination (booster dose) in individuals completely vaccinated is needed to prevent reinfection. [3,5,6,8] Further, there is controversy regarding the science of immunity and the ethical basis if a booster dose is warranted. It is the authors opinion that a third dose could be an important treatment strategy to protect individuals against new variants of SARS-CoV-2 and the burden of disease. This is an important public health policy decision as the winter months approach and there will be less social distancing and the use of face coverings.

Immunologic studies have demonstrated that SARS-CoV-2 vaccination does provide protection from future reinfection. The BNT162b2 vaccine provides high IgG and neutralizing antibody titers 7 to 14 days after administration of the second dose. [5] However, in several Phase 3 clinical trials significant waning of the humoral response (IgG and neutralizing antibodies) that provide protection from reinfection was observed. [5,9,10] As the humoral response decreases over time, IgG and neutralizing antibodies decrease, vaccine elicited immunity wanes, and increased immune evasion by the virus all result in breakthrough infection in individuals previously infected with the coronavirus or are fully vaccinated. [11]

In a study by Zollner and colleagues, [12] 14 patients with prior to moderate COVID-19 infection who received two doses of the Pfizer vaccine (BioNTech/Pfizer BNT162b2) received a third dose that resulted in a factor greater than twenty in the Spike specific neutralizing antibodies after the first dose and factor of six increase after the second dose compared to individuals that were not vaccinated. An increased neutralization titer may lead to increased protection against COVID-19 infection and severe illness resulting in ICU admissions. [9] Falsey et. al.

⁸ administered a third 30ug BNT1622b dose between 7 to 9 months after the two standard series doses in two different cohort groups (11 subjects 18 to 55 years and 12 subjects 65 to 85 years). Eliakim-Raz et. al. [13] evaluated anti spike (anti-S) Ig G antibody titers before and after a third dose of the BNT162b2 vaccine in a cohort aged 60 years and older. They observed an increase in the humoral response, as IgG antibody titers increased 10-19 days after vaccination. Both studies suggest that a third dose may prolong protection against coronavirus disease without major adverse side effects.

COVID-19 infections will continue to circulate in the community and the emergence of new lethal variants due to mutations should not be underestimated. Studies mentioned in this editorial have shown that the humoral response and vaccines do protect the public from COVID-19 infection. However, as the number of individuals become fully vaccinated, breakthrough cases will occur. This is especially likely to occur among individuals with severe comorbidities. To continue to protect the public, a booster vaccine should be available to control the COVID-19 pandemic.

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