

## Dynamics of Humoral Immunity Post COVID Vaccination – A Case Report

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### ABSTRACT

*In order to evaluate when antibody to the SARS-CoV-2 spike protein and neutralizing antibody to spike protein occurs subsequent to vaccination, we tested a 67-year-old healthy male subject at day 0, 6, 10, 14, 21, 35, and 56 who received the two-dose Pfizer BioNTech COVID-19 vaccine at day 0 and 21. IgG antibody avidity to spike protein was first detected at day 14, and neutralizing antibody activity was first detected at day 21. Both IgG and neutralizing antibody to spike protein peaked at day 35 and decreased modestly at day 56. This case report is consistent with the Pfizer BioNTech Phase III clinical trial showing protection is established early post vaccination and continues to increase with the second dose boost.*

### Keywords

COVID-19 vaccine, Humoral immunity, Neutralizing antibody.

### Introduction

The Pfizer BioNTech SARS-CoV-2 messenger RNA vaccine for full-length spike protein given 3 weeks apart has been shown to have 95% efficacy in preventing symptomatic COVID-19 disease two weeks after the second dose is given [1]. In order to evaluate when antibody to the SARS-CoV-2 spike protein and neutralizing antibody to spike protein occurs subsequent to vaccination, we tested a 67-year-old healthy male subject (body mass index 22.5) at day 0 (prior to vaccination), 6, 10, 14, 21 (prior to second vaccination dose), 35, and 56. Patient had no history of COVID-19 infection or exposure to COVID infection, and had tested negative several times for COVID-19 by PCR on nasal swab specimens and negative several times for antibody to COVID-19 three to eight months before vaccination for eligibility to participate in several activities and events.

Plasma was tested for IgG antibody to spike protein using the DiaSorin assay (LIAISON® SARS-CoV-2 S1/S2 IgG) and the Roche assay for detection of IgG and IgM antibodies to nucleocapsid protein (Elecsys<sup>®</sup> Anti-SARS-CoV-2) [2]. The signal cutoff for a positive result in the DiaSorin assay was  $\geq 15.0$  AU/mL.

The cutoff index for a positive result in the Roche assay was  $\geq 1.0$ . Samples of one ml of plasma in EDTA were aliquoted and frozen at  $-10^{\circ}\text{C}$  within one hour of specimen collection. Prior studies have shown that these assays become positive at the earliest at 5-7 days after COVID-19 RT-PCR positivity and are nearly 100% positive by 3 weeks [2,3]. In terms of specificity, 139 existing plasma samples collected from individuals prior to December 2019 (i.e. pre-COVID-19) were run on both the DiaSorin and Roche assays, and 139 of 139 (100%) were antibody negative by the Roche assay and 138 of 139 (99.3%) were antibody negative by the DiaSorin assay [2].

Neutralizing antibody titers in plasma samples were determined using vesicular stomatitis virus (VSV) pseudovirions in which the native VSV glycoprotein, G, was replaced with SARS-CoV-2 glycoprotein (ie, spike antigen). These pseudovirions express luciferase from the VSV genome. Pseudovirions were incubated with serial dilutions of patient plasma for one hour at  $37^{\circ}\text{C}$  prior to addition to Vero E6 cells. Expression of a virus-driven reporter gene was assessed 24 hours following infection to identify dilutions of plasma that impaired virus infection. Plasma samples were deemed to be neutralizing antibody negative if virus infection was not reduced at least 2-fold at a 1:40 dilution of plasma.

|        | Roche Nucleocapsid Ab Cutoff Index | DiaSorin Spike protein Ab Signal AU/mL | Neutralizing Ab titer |
|--------|------------------------------------|--|-----------------------|
| Day 0  | <0.1                               | <3.8                                   | NEGATIVE              |
| Day 6  | <0.1                               | <3.8                                   | NEGATIVE              |
| Day 10 | <0.1                               | <3.8                                   | NEGATIVE              |
| Day 14 | <0.1                               | 19                                     | NEGATIVE              |
| Day 21 | <0.1                               | 49                                     | 236                   |
| Day 35 | <0.1                               | 284                                    | 4210                  |
| Day 56 | <0.1                               | 215                                    | 1965                  |

**Table 1:** Timing of antibody development after vaccination with Pfizer BioNTech COVID-19 vaccine at day 0 and day 21.

Cutoff index for Roche antibody to nucleocapsid:  $\geq 1.0$ .

Cutoff signal for DiaSorin antibody to spike protein:  $\geq 15.0$  AU/mL.

Cutoff for Neutralizing Antibody titer – Negative if virus infection not reduced at least 2-fold at a 1:40 dilution.

Table 1 shows that antibody to spike protein using the DiaSorin assay was not detected until day 14 and peaked two weeks after the second dose (day 35) and remained high but modestly lower at 3 weeks (day 56) post second dose. Antibody to nucleocapsid protein by the Roche assay was negative at each timepoint. A titer of neutralizing antibody to spike protein was first detected at day 21 and peaked at day 35 reaching a peak of 4210 and then declining to a titer of 1965 at day 56.

IgG antibody binding to spike protein was first detected at day 14, and neutralizing antibody activity was first detected at day 21. As expected, no antibody activity was detected in the Roche assay for antibody to nucleocapsid protein. These data are consistent with the data from the Pfizer BioNTech phase III trial, which showed protection from disease starting at day 12 after receiving the first dose, and even greater protection at two weeks after the second dose [1]. The fact that the neutralizing antibody titer is detected at day 21 post first dose suggests that protection is established early post vaccination and continues to increase with the second dose boost.

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### References

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