Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Effect of the third dose of BNT162b2 COVID-19 mRNA vaccine on anti-SARS-CoV-2 antibody levels in healthcare workers

Hidenori Tanaka a, Junji Mukai b, Kenichi Kushibiki c, Sayuri Mizushima d, Kyoko Maeda d, Yuko Fujimoto d, Ryugo Sawada e,f, Manabu Oda f, Hiroshi Okuda b, Mayumi Yamaki g, Shin Hashiguchi h, Ichiro Kawai h, Izumi Kawaguchi i, Noriyuki Masuda a,h,i, Haruhiko Matsushita a

⇑ Corresponding author at: Department of Respiratory Medicine, Izumi City General Hospital, 4-5-1 Wakecho, Izumi, Osaka 594-0073, Japan.

E-mail address: noriyuki.masuda@tokushukai.jp (N. Masuda).

Article Info

Article history:
Received 20 September 2022
Received in revised form 26 October 2022
Accepted 20 November 2022
Available online 24 November 2022

Keywords:
BNT162b2 vaccine
SARS-CoV-2 spike protein
Booster vaccination
Healthcare workers

Abstract

Purpose: Administration of three doses of Pfizer-BioNTech BNT162b2 COVID-19 mRNA vaccine was completed in Japan in the spring of 2022. This study aimed to evaluate the antibody responses, and kinetics of three doses of vaccine in healthcare workers (HCWs).

Patients and methods: We conducted a longitudinal cohort study with HCWs, who had no history of COVID-19 or serologic evidence of SARS-CoV-2 infection, from a single hospital. Immunoglobulin G (IgG) titers of anti-SARS-CoV-2 spike protein (SP) and nucleocapsid protein (NP) titers were measured using an automated chemiluminescent enzyme immunoassay system.

Results: A total of 636 HCWs participated in the study. The anti-SP IgG titers decreased slowly after the second dose of the BNT162b2 vaccine in all participants, and robust antibody response was observed after the third dose of the vaccine. The peak anti-SP IgG titer after the third dose was approximately 4.1-fold higher than that after the first and second doses, and the rate of decrease in the anti-SP IgG titer after the third dose was significantly more gradual, than that after the second dose. After the second dose of vaccine, the antibody response was weaker in older participants than in younger participants, and in males than in females respectively, whereas the response to the third dose of vaccine did not differ significantly by sex or age. Adverse events following immunization were generally mild to moderate.

Conclusion: The third dose of the BNT162b2 vaccine induced a significant and sustained increase in anti-SP IgG titers, and was generally safe and well-tolerated.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first emerged in Wuhan, China, towards the end of 2019 and spread worldwide, [1] resulting in the coronavirus disease 2019 (COVID-19) pandemic. COVID-19 is still a threat to health systems worldwide and the global economy.

The introduction of vaccines against SARS-CoV-2 altered the course of the pandemic. However, vaccination reduces but does not altogether prevent the spread of SARS-CoV-2 infection. The BNT162b2 COVID-19 mRNA vaccine (Pfizer, New York, USA and
BioNTech, Mainz, Germany) contains a nucleoside-modified RNA, encoding the full-length of the SARS-CoV-2 spike protein (SP). The vaccine, administered in two doses 21 days apart, generally has mild side-effects, and has been shown to have 95 % efficacy in preventing COVID-19 between seven days to two months after the second dose, [2] but the efficacy decreases to 84 %, four to six months after the second dose. [3].

As the COVID-19 pandemic continues into its third year, many countries have begun to recommend the administration of a third (booster) dose of vaccine to further reduce the spread of the pandemic. Waning immunity, and viral diversification have led the Japanese government to recommend an additional dose of the vaccine at least six months after the second dose. Although some previous studies have evaluated the antibody response after the third dose of vaccine, the duration of follow-up has generally been less than three months. [4–10] A longer follow-up period is needed to assess antibody kinetics in individuals after the third dose of BNT162b2 vaccine.

Healthcare workers (HCWs) are at high risk of SARS-CoV-2 infection due to direct exposure to infected patients. Thus, shortly after the vaccine was approved by the Japanese Ministry of Health, Labour, and Welfare, HCWs were prioritized for vaccination. Therefore, HCWs in Japan could be followed up for a relatively longer period than that reported in previous studies.

We carried out a study to compare anti-SP antibody titers after the administration of the second and third doses of the BNT162b2 vaccine respectively, in HCWs.

2. Material and methods

2.1. Study population

We conducted a longitudinal study of HCWs at Izumi City General Hospital, a secondary medical center in Izumi City in Osaka, Japan, which has 307 beds, and 635 HCWs. We analyzed data of HCWs who had received a third dose of the BNT162b2 vaccine, which was administered between December 2021 and January 2022. The first and second doses of the vaccine had been administered between March and June 2021.

HCWs who were positive for SARS-CoV-2 PCR test, and SARS-CoV-2 anti-SP and anti-nucleocapsid protein (NP) serology tests, prior to vaccination, or had a history of COVID-19 were excluded from the study. Participants with detectable SARS-CoV-2 NP antibodies or a history of COVID-19 during the follow-up period were also excluded.

Serum specimens were obtained before the first dose; during the baseline period (days 4–17 after the second vaccination); and every fourth week thereafter: during days 18–42 (period 1); days 43–70 (period 2); days 71–98 (period 3); days 99–126 (period 4); days 127–154 (period 5); and days 155–175 (period 6). The follow-up period ended six months after the third dose of the vaccine.

We investigated factors associated with SARS-CoV-2 antibody titers before, and three and six months after the second dose of vaccine, and before and approximately 1–2 and 5–6 months after the third dose of vaccine and compared the change in SARS-CoV-2 antibody titers before and after the third dose of vaccine.

2.2. Data collection

Background information was collected from the participants’ medical records and using a web-based questionnaire. The web-based questionnaire was used to assess the incidence of adverse events following immunization (AEFs).

2.3. Measurement of antibodies

We measured the SARS-CoV-2 anti-SP and anti-NP immunoglobulin G (IgG) index values using an automated chemiluminescent enzyme immunoassay (CLEIA) system, AIA-CL 1200 (Tosoh, Tokyo, Japan) and commercial CLEIA reagents (AIA-CL SARS-CoV-2 SP-IgG antibody detection reagent; Tosoh, Tokyo, Japan)[11,12] The threshold index value was set to 1, based on previous validations.[11] This threshold value has been shown to have high sensitivity and specificity.

2.4. Statistical analysis

A linear mixed model was used to investigate longitudinal antibody responses. In this model, the dependent variable was the logarithmically transformed values of the antibody titers, and the explanatory variables were the number of days from the day of the third vaccine dose (baseline) to the day of antibody titer measurement in each participant and whether antibody titers were measured before or after, the third dose (dummy variable: 0 or 1). Based on the results of the analyses using the mixed-effects model, two regression lines were generated for antibody titers before and after receiving the third dose of vaccine to evaluate the rate of increase in antibody titers after the third dose of vaccine.

In the post-hoc analysis, the data were divided into two groups: before and after the third dose of vaccine, and analyses were performed using the mixed-effects model for each sex and age group. The rate of increase in the antibody titer after the third dose of vaccine was also evaluated in the same manner, stratified by sex and age. In the analysis by age, participants were divided into four age groups: <30 years, 30–39 years, 40–49 years, and ≥50 years.

Differences in the incidence of adverse events after each vaccine dose were analyzed using the Cochrane Q test, based on responses obtained from web-based questionnaires.

Statistical analyses were carried out using IBM SPSS Statistics version 28.0 (Armonk, NY, USA).

2.5. Ethical approval

All study procedures were performed in accordance with the principles of the Declaration of Helsinki. The Tokushukai Group Ethics Committee approved the study protocol (approval no. TGE01750-070). The ethics committee waived the requirement for informed consent from participants because most of the blood samples were leftover blood during the annual check-up, prescribed by Article 66, Japanese Industrial Safety and Health Act, and it was a service for participants who would like to know their antibody titer values. So, we checked the disagreement in optout.

3. Results

3.1. Participant characteristics

The COVID-19 vaccination rate was 75.8 % among the participants in our study. In contrast, the overall vaccine coverage rate for all Japanese population is 65.8 % (as of October 2020,2022; reported in press release by Prime Minister of Japan and his Cabinet [https://www.kantei.go.jp/jp/headline/kansensho/vaccine.html]). A total of 635 participants were recruited and followed up, of whom 435 (68.5 %) were female. Their ages ranged from 19 to 81 years, and 112 (17.6 %) were aged ≥50 years (Table 1).

Because our hospital re-employs retired police officers and emeritus professors as advisors, the maximum age reached in our study was 81 years. The participants included 98 (15.4 %) physicians, 297
Participant characteristics (N = 635).

| Characteristic                  | Value         |
|---------------------------------|---------------|
| Sex, n (%)                      |               |
| Male                            | 200 (31.5)    |
| Female                          | 435 (68.5)    |
| Age                             |               |
| Mean ± SD                       | 37.6 ± 12.4   |
| Median (IQR)                    | 36 (27–46)    |
| Age group, years, n (%)         |               |
| <30                             | 231 (36.3)    |
| 30–31                           | 135 (21.2)    |
| 40–49                           | 158 (24.8)    |
| ≥50                             | 112 (17.6)    |
| Job type, n (%)                 |               |
| Physician                       | 98 (15.4)     |
| Nurse or nurse aid              | 297 (46.8)    |
| Paramedical worker              | 122 (19.2)    |
| Administrative or logistic worker | 119 (18.6) |
| Interval between the 1st and 2nd dose (days) | 21.2 ± 1.4 |
| Median (IQR)                    | 21 (21–21)    |
| Interval between the 2nd and 3rd dose (days) | 240.1 ± 17.0 |
| Mean ± SD                       | 246 (232–252) |
| Median (IQR)                    |               |

Abbreviations: IQR, interquartile range; SD, standard deviation.

(46.8 %) nurses and nurse aids, 122 (19.2 %) paramedical workers, and 118 (18.6 %) administrative or logistic workers. The median interval between the first and second doses of the vaccine was 21 days, and the interquartile range (IQR) was 21–21 days. The median interval between the second and third doses of the vaccine was 246 days, and the IQR was 232–252 days.

3.2. Antibody response

All participants had SP IgG titers below the cutoff value of 1.0 before the first vaccine dose and were seropositive for anti-SP IgG prior to the third dose of vaccine. The median SP IgG titer before the third dose was 3.3.

3.3. Comparison of antibody titers after the second and third doses of the vaccine

Changes in antibody titers before and after the third dose of vaccine, as well as the regression lines generated from the analyses using the mixed-effects model, are shown in Fig. 1. The anti-SP IgG titers were expected to reach their peak on day seven after the third dose (125.4). [8,9]

The comparison of the antibody titer before the third dose of vaccine (t = 0) with that on day seven after the third dose of vaccine (t = 7) revealed a marked increase in the anti-SP IgG titer after the third dose of vaccine, representing a 38.0-fold (125.4/3.3) increase in median values of antibody titers from the pre-third dose levels. In addition, the slope (β) of the antibody decline indicated that antibody titers decreased more gradually after the third dose than after the first and second doses (interaction: p < 0.001).

Factors associated with a weaker antibody response after the second dose included older age and male sex (Figs. 2 and 3). We compared the antibody response to vaccination according to sex. The anti-SP IgG titers after the second dose were higher in females than in males (Fig. 2), but there was no significant difference according to sex after the third dose of the vaccine. Compared to the period after the second vaccine dose, the antibody responses were estimated to be 3.8-fold and 5.3-fold greater after the third dose in females and males, respectively. The responses to the third dose of the vaccine did not differ significantly by sex. Post-hoc analysis by sex showed that there was a significant difference before the third dose of vaccine (p < 0.001), but there was no significant difference after the third dose of vaccine (p = 0.098).

Similarly, we assessed whether antibody responses to vaccination varied by age. Fig. 3 shows the changes in antibody titers over time according to age group. Although the antibody titers were higher in the younger age groups before the third dose, the anti-SP IgG titers in the older participants increased to almost the same level after the third inoculum. The antibody levels increased 3.2-fold in participants aged younger than 30 years, 3.8-fold in those aged 30–39 years, 4.9-fold in those aged 40–49 years, and 6.3-fold in those aged 50 years and older, after the second dose. Thus, the antibody response after the second dose of vaccine was inversely correlated with age, whereas the response to the third dose of vaccine did not differ significantly by age.

Post-hoc analysis by age group showed that when participants aged < 30 years were used as the reference group, there was significant difference between all groups before the third dose of vaccine. However, after the third dose of vaccine, there was significant difference with those aged 40–49 years and aged 50 years and older (p < 0.041, p < 0.007, respectively), but no significant difference with those aged 30–39 years (p = 0.606).

Table 2 shows the AEFIs reported by 538 of 635 participants who completed the web-based questionnaire. Ninety-eight participants did not complete the questionnaire. The severity of AEFIs was generally reported to be mild to moderate after the first, second, and third doses of the BNT162b2 vaccine. The most common AEFI was pain at the injection site (77.0 %, 79.0 %, and 74.5 % after doses one, two, and three, respectively), fatigue (50.2 %, 61.5 %, and 59.3 % after doses one, two, and three, respectively), and myalgia/joint pain (47.6 %, 53.2 %, and 49.6 % after doses one, two, and three, respectively). The most frequent total number of events was reported after the second BNT162b2 dose. Reported AEFIs were less frequent after the third dose of the vaccine than after the first and second doses of the vaccine. However, adenopathy was reported more frequently following the third dose of the vaccine than following the first and second doses.

4. Discussion

The purpose of this study was to analyze the quantitative SARS-CoV-2 anti-SP IgG antibody levels over a span of six months after completing the established BNT126b2 vaccine regimen and 21–28 days following the third dose of BNT162b2 vaccine, administered six months after the second dose, although serological screening has shown very low sensitivity compared to that of nasopharyngeal swab test in identifying infected health workers. [13] The antibody titers were lower after three months, compared to 21–28 days, for the second dose. In addition, in the samples collected 1–7 days after the third dose of the vaccine, the antibody titers were lower than those reported 21–28 days after the second dose of the vaccine. Comparisons with antibody titers over the following months (6, 9, or 12) after the second dose is necessary to analyze the evolution, and duration of the immune response in any population. This large cohort included HCWs with a female predominance. HCWs are an important group in the population who are at high risk and have high exposure to COVID-19 but are also typically young and healthy. Our study demonstrated that all participants who received three homologous BNT162b2 doses, and were negative for anti-SARS-CoV-2 NP throughout the trial showed a rapid (38.0-fold) increase in anti-SARS-CoV-2 SP antibodies compared to before the administration of the third dose (Fig. 1). These findings are consistent with previous studies highlighting that BNT162b2 administration as the third dose boosted IgG glycoprotein median titers by a factor of 46.6,[7] 57.9,[4] 33, [14] or 30,[9].
The interval between vaccine doses may affect the resulting antibody response. Compared to the recommendation from the US Centers for Disease Control and Prevention to administer the third vaccine dose six months after the second dose,[15] we had a relatively longer median interval of 246 days between the second and third dose, similar to the mean interval of 214 days reported by Lau et al.[9].

One of the novel findings from this study is that the slope ($b$) of the antibody decline indicates that antibody titers fade more slowly with time after the third, rather than after the second dose (interaction: $P < 0.001$) (Fig. 1). This is consistent with the findings of Lau et al.,[9] who reported that neutralizing antibodies after the third dose show a longer half-life compared to post-second dose (58 vs 48 days). Circulating IgG- and IgA-secreting plasmablasts that target the SARS-CoV-2 spike protein peaked one week after the second immunization, from the memory B cells already generated after the first vaccine dose. SARS-CoV-2 mRNA-based vaccines induce a persistent germinal center B cell response in humans.
which enables the generation of robust humoral immunity.[16] Based on these results, Kim et al. [17] speculated that these results may be related to the slower rate of decay in antibodies over time.

Another strength of our study is that our mixed model has shown interesting results in terms of patient sex and age. The response to the second BNT162b2 COVID-19 vaccine was sex-dependent, but the significant difference in immune response between males and females disappeared after the third dose (Fig. 2). These results have recently been confirmed.[18,19] In contrast, Cucunawangsih et al. [20] found, using the SARS-CoV-2 mRNA (mRNA-1273, Moderna) vaccine as the third (booster) dose, that age was negatively associated with the anti-S antibodies level after the third dose, not prior to it. Bensouna et al. [21] reported that patients with a greater increase in anti-S1 antibody levels after the third dose had lower antibody levels after the second dose of the BNT162b2 vaccine. Our results show that the antibody response after the first and second vaccine doses was inversely proportional to age in accordance with previous investigations; [20,22–24]: young adults mounted a significantly higher antibody response than elderly participants (Fig. 3). However, consistent with the report by Broseta et al. [25], the antibody response to the third dose was different in that a significant inverse relationship was not detected between age and antibody levels (Fig. 3).

The third dose of the BNT162b2 vaccine reportedly substantially increases antibody levels in elderly persons with low antibody levels after the second dose. In contrast, there was little increase in antibody levels after the third dose in younger participants with high anti-SARS-CoV-2 SP levels.

Another concern with the application of the third dose was the relative lack of information on the development of possible AEFI. In

| Table 2 |
| --- |
| **Adverse events following immunization after each dose of BNT162b2 COVID-19 mRNA vaccine administration (N = 538).** |
| **Any local injection site reaction** | 1st dose | 2nd dose | 3rd dose | P-value |
| Injection site induration | 40 (7.4) | 38 (7.1) | 47 (8.7) | 0.123 |
| Injection site pain | 414 (77) | 425 (79) | 401 (74.5) | 0.009 |
| Injection site swelling | 240 (44.6) | 224 (41.6) | 208 (38.7) | 0.004 |
| Itching | 79 (14.7) | 78 (14.5) | 77 (14.3) | 0.983 |
| Redness | 127 (23.6) | 116 (21.6) | 100 (18.6) | <0.001 |
| **Any systemic reaction** | 1st dose | 2nd dose | 3rd dose | P-value |
| Anaphylaxis | 2 (0.4) | 1 (0.2) | 2 (0.4) | 0.368 |
| Chills | 104 (19.3) | 144 (26.8) | 123 (22.9) | <0.001 |
| Diarrhea | 17 (3.2) | 9 (1.7) | 12 (2.2) | 0.097 |
| Fatigue | 270 (50.2) | 331 (61.5) | 319 (59.3) | <0.001 |
| Feeling hot | 222 (41.3) | 245 (45.5) | 234 (43.5) | 0.046 |
| Fever (≥38 °C) | 111 (20.6) | 171 (31.8) | 150 (27.9) | <0.001 |
| Headache | 138 (25.7) | 170 (31.6) | 160 (29.7) | 0.002 |
| Lymphadenopathy | 19 (3.5) | 28 (5.2) | 78 (14.5) | <0.001 |
| Myalgia/joint pain | 256 (47.6) | 286 (51.2) | 267 (49.6) | 0.010 |
| Nausea/vomiting | 31 (5.8) | 25 (4.6) | 23 (4.3) | 0.307 |
| Rash | 4 (0.7) | 4 (0.7) | 5 (0.9) | 0.368 |

P values were calculated using Cochran’s Q test.

![Graph](image_url)
accordance with other reports on AEFI after the third dose, [26–30] the most frequent AEFI observed after the third dose included pain at the injection site, fatigue, and myalgia/joint pain, with no associated severe complications such as hospitalization or emergency room visits (Table 2). Our study also found that the AEFI associated with the third dose were minimal. Only adenopathy increased in frequency (3.3, 5.2, and 14.5%, respectively). Tolerance to the first, second, and third dose was good. Adverse events did not appear to be more common or severe after the third vaccine dose.

5. Conclusion

The third dose of the BNT162b2 vaccine increases the quantitative anti-SP IgG titer, with no severe short-term AEFI observed in this study.

6. Ethics approval and informed consent

All study procedures were performed in accordance with the principles of the Declaration of Helsinki. The Tokushukai Group Ethics Committee approved the study protocol (approval no. TGE01750-070).

7. Consent for publication

All authors gave final approval of the version to be published.

8. Data availability

Data reported in this manuscript are available within the article.

9. Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

10. Authors’ contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

Data availability

No data was used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We would like to thank Editage (www.editage.com) for English language editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2022.11.049.

References

[1] Zhu Na, Zhang D, Wang W, Li X, Yang Bo, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020;382(8):727–33.
[2] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020;383(27):2603–15.
[3] Thomas SJ, Moreira ED, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine through 6 Months. N Engl J Med 2021;385(19):1761–73.
[4] Elaiakim-Raz N, Leitbovis-Weisman Y, Stemmer A, Ness A, Awwad M, Ghaustor N, et al. Antibody Titers Before and After a Third Dose of the SARS-CoV-2 BNT162b2 Vaccine in Adults Aged ≥60 Years. JAMA 2021;326(21):2203.
[5] Romero-Ibarguenoitia ME, Rivera-Salainai D, Hernandez-Ruiz YG, Armendariz-Vazquez AG, Gonzalez-Castor A, Barco-Flores IA, et al. Effect of the third dose of BNT162b2 vaccine on quantitative SARS-CoV-2 spike 1–2 IgG antibody titers in healthcare personnel. PLoS One 2022;17(3):e0263942.
[6] Blain H, Tsaiolln E, Gannon L, Pisoni A, Miot S, Rolland Y, et al. Antibody response after one and two jabs of the BNT162b2 vaccine in nursing home residents: The CONSort-19 study. Allergy 2022;77(1):271–81.
[7] Keskin AU, Bolukcu S, Ciragil P, Topkaya AE. SARS-CoV-2 specific antibody responses after third CoronaVac or BNT162b2 vaccine following two-dose CoronaVac vaccine regimen. J Med Virol 2022;94:39–41. https://doi.org/10.1002/jmv.27350, PMID 34536028.
[8] Bensouna I, Caudwell V, Kubsh S, Acquaviva S, Pardon A, Vittoz N, et al. SARS-CoV-2 Antibody Response After a Third Dose of the BNT162b2 Vaccine in Patients Receiving Maintenance Hemodialysis or Peritoneal Dialysis. Am J Kidney Dis 2022;79(2).
[9] Lau CS, Phua SK, Liang YL, Oh MLH, Aw TC. SARS-CoV-2 Spike and Neutralizing Antibody Kinetics 90 Days after Three Doses of BNT162b2 mRNA COVID-19 Vaccine in Singapore. Vaccines 2022;10(2):331.
[10] Saltoğlu N, Dinç HO, Balkan II, Can G, Ozboy D, Beytur AN, et al. Heterologous booster COVID-19 vaccination elicited potent immune responses in HCWs. Diagn Microbiol Infect Dis 2022;104(2):115758.
[11] Kubo S, Ohata N, Miyakawa K, Jeremiah SS, Yamaoka Y, Murohashi K, et al. Development of an Automated Chemiluminescence Assay System for Quantitative Measurement of Multiple Anti-SARS-CoV-2 Antibodies. Front Microbiol 2020;11.. https://doi.org/10.3389/fmicb.2020.628281, PMID 3351970628281.
[12] Kato H, Miyakawa K, Ohata N, Go H, Yamaoka Y, Yajima S, et al. Antibody titers against the Alpha, Beta, Gamma, and Delta variants of SARS-CoV-2 induced by BNT162b2 vaccination measured using automated chemiluminescent enzyme immunoassay. J Infect Chemother 2022;28(2):273–8.
[13] Vimercati I, Stefanzii P, De Maria L, Caputi A, Cavone D, Quarato M, et al. Large-scale IgM and IgG SARS-CoV-2 serological screening among healthcare workers with a low infection prevalence based on nasopharyngeal swab tests in an Italian university hospital: Perspectives for public health. Environ Res 2021;195:110793.
[14] Gilboa M, Mandelboim M, Indenbaum V, Lustig Y, Cohen C, Rahav G, et al. Early Immunogenicity and Safety of the Third Dose of BNT162b2 Messenger RNA Coronavirus Disease 2019 Vaccine Among Adults Older Than 60 Years: Real-World Experience. J Infect Dis 2022;223(5):785–92.
[15] Wald A. Booster Vaccination to Reduce SARS-CoV-2 Transmission and Infection. JAMA 2022;327:327–8. https://doi.org/10.1001/jama.2021.32727, PMID 35066265.
[16] Turner JS, O’Halloran JA, Kalaidina E, Kim W, Schmitz AJ, Zhou QJ, et al. SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses. Nature 2021;596(7870):109–13.
[17] Kim HJ, Yun HJ, Kim J, Kym S, Choi Q. Antibody response to second dose of the BNT162b2 mRNA vaccine in the first 12 weeks in South Korea: A prospective longitudinal study. Vaccine 2022;40:437–43. https://doi.org/10.1016/j.vaccine.2021.12.017, PMID 34959206.
[18] Jalkanen P, Kolehmainen P, Häkkinen HK, Huttunen M, Tähtinen PA, Lundberg R, et al. Antibody response after one and two jabs of the BNT162b2 vaccine in patients receiving maintenance hemodialysis or peritoneal dialysis. Nat Commun 2021;12(1). https://doi.org/10.1038/s41467-021-24285-4, PMID 34183681.
[19] Lustig Y, Sapir E, Regev-Yochay G, Cohen C, Fluss R, Olmer L, et al. BNT162b2 COVID-19 vaccine and correlates of humoral immune responses and dynamics: a prospective, single-centre, longitudinal study in healthcare workers. Lancet Respir Med 2021;9(9):999–1009.
[20] Cucunawangsih C, Wijaya RS, Lugito NPH, Suriapranata I. Antibody response after three-dose inactivated SARS-CoV-2 vaccine. Int J Infect Dis 2022;118:116–8. https://doi.org/10.1016/j.ijid.2022.02.016, PMID 35192955.
[21] Bensouna I, Caudwell V, Kubsh S, Acquaviva S, Pardon A, Vittoz N, et al. SARS-CoV-2 Antibody Response After a Third Dose of the BNT162b2 Vaccine in...
Patients Receiving Maintenance Hemodialysis or Peritoneal Dialysis. Am J Kidney Dis 2022;79(2):185.

[22] Müller L, André M, Moskorz W, Dresler I, Walotka L, Grothmann R, et al. Age-dependent Immune Response to the Biontech/Pfizer BNT162b2 Coronavirus Disease 2019 Vaccination. Clin Infect Dis 2021;73(11):2065–72.

[23] Terpos E, Trougakos IP, Apostolakou F, Charitaki L, Skirrou AD, Mavrianou N, et al. Age-dependent and gender-dependent antibody responses against SARS-CoV-2 in health workers and octogenarians after vaccination with the BNT162b2 mRNA vaccine. Am J Hematol 2021;96:E257–9. https://doi.org/10.1002/ajh.26185. PMID 33837984.

[24] Favresse J, Bayart J-L, Mullier F, Eisen M, Eucher C, Van Eeckhoudt S, et al. Antibody titres decline 3-month post-vaccination with BNT162b2. Emerg Microbes Infect 2021;10(1):1495–8.

[25] Broseta JJ, Rodriguez-Espinosa D, Cuadrado E, Rodriguez N, Bedini JL, Maduell F. Humoral Response after Three Doses of mRNA-1273 or BNT162b2 SARS-CoV-2 Vaccines in Hemodialysis Patients. Vaccines (Basel) 2022:10. https://doi.org/10.3390/vaccines10040522.

[26] Peled Y, Ram E, Lavee J, Segev A, Matezki S, Wieder-Finesod A, et al. Third dose of the BNT162b2 vaccine in heart transplant recipients: Immunogenicity and clinical experience. J Heart Lung Transplant 2022;41(2):148–57.

[27] Mofaz M, Yecheksel M, Guan G, Brandeau ML, Patalon T, Gazit S, et al. Self-Reported and Physiologic Reactions to Third BNT162b2 mRNA COVID-19 (Booster) Vaccine Dose. Emerg Infect Dis 2022;28(7):1375–83.

[28] Tawinprai K, Siripongboonsiri T, Pornharukhareon T, Wittayasak K, Thonpirak N, Soonklang K, et al. Reactogenicity, immunogenicity, and humoral immune response dynamics after the third dose of heterologous COVID-19 vaccines in participants fully vaccinated with inactivated vaccine. Expert Rev Vaccines. 2022;1:1–9. doi: 10.1080/14760584.2022.2099380, PMID 35792752.

[29] Shinkai M, Sonoyama T, Kamitani A, Shibata RY, Seki NM, Omoto S, et al. Immunogenicity and safety of booster dose of S-268019-b or BNT162b2 in Japanese participants: An interim report of phase 2/3, randomized, observer-blinded, noninferiority study. Vaccine 2022;40(32):4328–33.

[30] Menni C, May A, Polidori L, Louca P, Wolf J, Capdevila J, et al. COVID-19 vaccine waning and effectiveness and side-effects of boosters: a prospective community study from the ZOE COVID Study. Lancet Infect Dis 2022;22(7):1002–10.