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.

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Letter to the Editor

Comparative effects of mRNA vaccine booster and natural Omicron infection on the neutralizing antibody response

Dear Editor,

A recent report found that booster vaccination could significantly increase the neutralizing responses to all the variant of concern, including Omicron [1]. Other studies questioned whether a booster dose of vaccine is more effective than two doses in preventing symptomatic SARS-CoV-2 in pre-Omicron populations [2]. New waves of infection can occur in populations whose immunity is due to a prior infection and/or vaccination [3], while other studies indicate that Omicron overcomes the immunity provided by vaccination and/or infection with an earlier variant [4]. Public health policies can benefit from knowledge of the immune responses elicited by vaccination and natural infection.

We analyzed the neutralizing antibody responses of 115 individuals matched for age and sex: 23 were unvaccinated and had been infected with Omicron, 23 had been vaccinated with two doses and had never been infected, 23 had been infected with Omicron after two doses of vaccine, 23 had received a mRNA vaccine booster (third dose) and had no infection, 23 had been infected with Omicron after a mRNA vaccine boost. Infections were detected using a nucleic-acid amplification method (Aptima^{TM}, Hologic, USA) [5] and SARS-CoV-2 RNA was sequenced using single-molecule real-time sequencing (Pacific Biosciences, USA) [6]. Serological samples were taken from those vaccinated without infection one month after the last dose of vaccine and from infected subjects 3 to 6 weeks after infection. Neutralizing antibody titers were assessed by end-point dilution using Vero cells (ATCC, CCL-81^{TM}) and a clinical SARS-CoV-2 Omicron BA.1 strain (EPI_ISL_10316329). This study was approved by the French Research Ethics Committee Est-III (COVID BioToul, ID-RCB 2020-A01292-37, ClinicalTrials.gov Identifier: NCT04385108).

The median age of the 115 subjects (80 men, 69.6%) was 39 years (range: 21–61). The frequencies of symptomatic infections were: unvaccinated: 82.6%, 2-dose vaccinated: 87% and 3-dose vaccinated: 82.6% ($p > 0.05$, Cochran *Q*-test). No individual in any of the groups had required hospitalization for their SARS-CoV-2 Omicron infection. Two-dose vaccinates uninfected subjects had the lowest neutralizing antibody titers (median 2, IQR 0–3, blue box Fig. 1); they were significantly lower than those of the unvaccinated Omicron-infected subjects (median 8, IQR 4–24, red box Fig. 1, $p < 0.01$ Wilcoxon signed rank test). The neutralizing antibody titers of the 3-dose-vaccinated uninfected subjects (median 16, IQR 8–16, green box Fig. 1) and the unvaccinated Omicron-infected subjects ($p = 0.11$, Wilcoxon signed rank test) were not different, as were the titres of the 3 dose-vaccinated infected (median 64, IQR 64–128, grey box Fig. 1) and 2-dose vaccinated infected subjects (median 64, IQR 32–128, orange box Fig. 1, $p = 0.79$, Wilcoxon signed rank test). The neutralizing antibody titers of the 2-dose-vaccinated uninfected subjects who became Omicron-infected were significantly higher than those who were given a booster dose (median 16, IQR 8–16, green box Fig. 1, $p < 0.01$, Wilcoxon signed rank test).

These data indicate that a SARS-CoV-2 Omicron infection elicits a stronger immune response against Omicron than a full (2 dose) course of vaccination. The booster dose increased the neutralizing antibody response of the 2-dose-vaccinated subjects but it remained below the level conferred by an Omicron infection.

Our findings could, despite the small sample size, help optimize future vaccination strategies.

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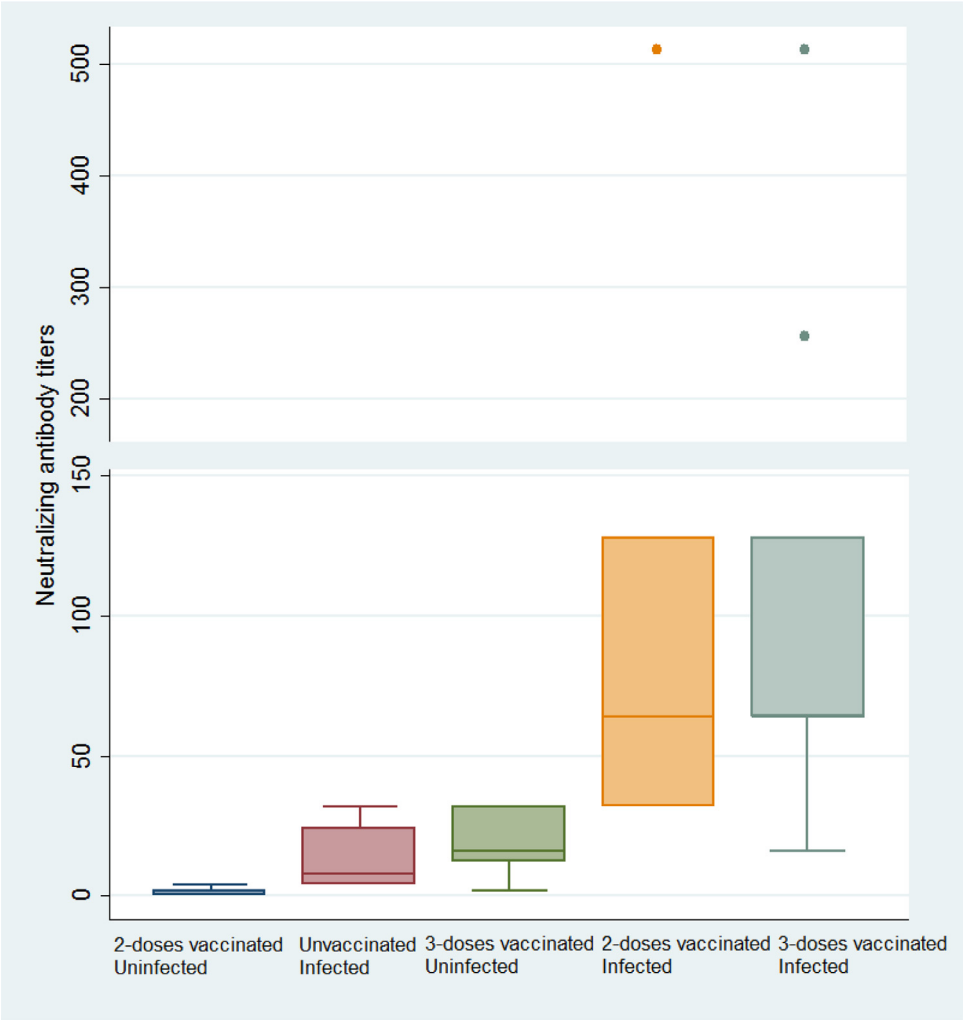

Fig. 1. Neutralizing antibody titers: influence of infection status and vaccination schedule.

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Declaration of Competing Interest

Authors declare that they have no conflict of interest.

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References

[1]. Yang Y, Gong X, Yang L, Li J, Zhang J, Wei L, et al. Regular and booster vaccination with inactivated vaccines enhance the neutralizing activity against Omicron variant both in the breakthrough infections and vaccinees. *J Infect* 2022;**84**(4):579–613. doi:10.1016/j.jinf.2022.01.004.

[2]. Butt AA, Talisa VB, Yan P, Shaikh OS, Omer SB, Mayr FB. Vaccine effectiveness of three vs. two doses of SARS-CoV-2 mRNA vaccines in a high risk national population. *Clin Infect Dis* 2022:ciac178. doi:10.1093/cid/ciac178.

[3]. Pulliam JRC, van Schalkwyk C, Govender N, von Gottberg A, Cohen C, Groome MJ, et al. Increased risk of SARS-CoV-2 reinfection associated with emergence of Omicron in South Africa. *Science* 2022:4947. doi:10.1126/science.abn4947.

[4]. Kuhlmann C, Mayer CK, Claassen M, Maponga T, Burgers WA, Keeton R, et al. Breakthrough infections with SARS-CoV-2 omicron despite mRNA vaccine booster dose. *Lancet* 2022;**399**(10325):625–6. doi:10.1016/S0140-6736(22)00090-3.

[5]. Tremeaux P, Lhomme S, Abravanel F, Raymond S, Mengelle C, Mansuy JM, et al. Evaluation of the Aptima transcription-mediated amplification assay (Hologic(R)) for detecting SARS-CoV-2 in clinical specimens. *J Clin Virol* 2020;**129**:104541.

[6]. Lhomme S, Latour J, Jeanne N, Trémeaux P, Ranger N, Migueres M, et al. Prediction of SARS-CoV-2 variant lineages using the S1-encoding region sequence obtained by PacBio single-molecule real-time sequencing. *Viruses* 2021;**13**(12):2544. doi:10.3390/v13122544.

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