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.

Low neutralisation of the omicron BA.2 sublineage in boosted individuals who had breakthrough infections

The omicron variant of SARS-CoV-2 comprises several sublineages (BA.1, BA.1·1, BA.2, and BA.3, etc) with an increasing prevalence of the sublineage BA.2.[1] Although the receipt of a third (booster) dose of an mRNA-based SARS-CoV-2 vaccine is associated with improved protection against the omicron variant, many breakthrough infections occurred during the initial omicron surge,[2,3] and it is unknown whether a breakthrough infection with BA.1 in an individual who had received a booster vaccine would provide protection from infection from another sublineage.

To address this question, we compared surrogate neutralisation against BA.1, BA.2, and BA.3 omicron sublineages, in addition to the vaccine strain, in plasma from individuals who were boosted (N=36) or had a breakthrough infection during the BA.1 surge after boosting (N=18). All participants were enrolled according to protocols approved by the Johns Hopkins University institutional review board and provided written informed consent. From boosted uninfected participants, a total of 28 samples were taken 1–3 weeks post-boost and 16 samples were taken 1–3 months post-boost; and from individuals with a breakthrough infection, 18 samples were taken 1–3 weeks post-infection and 14 samples were taken 4–7 weeks post-infection. The samples were tested for surrogate neutralisation.

Median surrogate neutralisation was highest in the 4–7 weeks post-breakthrough subgroup across all four variants tested, followed by the uninfected group at 1–3 weeks post-boost. Surrogate neutralisation decreased between the 1–3 weeks and 1–3 months groups in the boosted uninfected cohort, but increased between the 1–3 weeks and 4–7 weeks groups in the breakthrough cohort across all variants (appendix). The only statistically significant difference in surrogate neutralisation between the individual pairs of subgroups after correcting for multiple comparisons was within the boosted cohort between the 1–3 weeks and 1–3 months timepoints for the vaccine strain (p=0·03; appendix). The median percent inhibition was less than 20% (a level previously associated with the neutralisation of the live virus)[4] for all variants in the boosted cohort at 4–7 weeks, whereas the median neutralisation was more than 20% against all three sublineages (BA.1, BA.2, and BA.3) at the 4–7 week timepoint in the breakthrough cohort, which suggests some, albeit low, cross-neutralisation of other omicron subvariants after a breakthrough infection with BA.1.

Our study is limited as a small observational cohort with heterogeneous sample collection times, with samples collected post-exposure. However, our findings are important because BA.2 is now the dominant variant circulating in the USA, and the data suggest that previous BA.1 infections might not provide sufficient neutralising antibodies in addition to vaccination to prevent a high number of cases of BA.2 infections.

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*Andrew H Karaba, Trevor S Johnston, Tihitina Y Aytenfisu, Bezawit A Woldemeskel, Caroline C Garliss, Andrea L Cox, *Joel N Blankson*
jblanks@jhmi.edu

Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA

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See Online for appendix