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Comparable neutralisation evasion of SARS-CoV-2 omicron subvariants BA.1, BA.2, and BA.3

The SARS-CoV-2 omicron (B.1.1.529) variant has rapidly become globally dominant, displacing the previously dominant delta (B1.617.2) variant. The viral spike (S) protein is the key target of the neutralising antibody response, and the omicron variant harbours more than 35 mutations in the S protein, which allow highly efficient evasion from neutralising antibodies.[1] In keeping with these findings, the omicron variant efficiently spreads in populations with a high percentage of convalescent or vaccinated individuals.[2,3]

The three main subvariants of the omicron variant are BA.1, BA.2, and BA.3. Initial data suggest that BA.2 might have a growth advantage over BA.1,[4] posing a rapidly increasing threat to health systems. The omicron subvariants display remarkable differences regarding S protein mutations, particularly with respect to the N-terminal domain and the receptor-binding domain (appendix pp 2–3), which are known to harbour key epitopes of neutralising antibodies.[5,6] Here, we compared BA.1, BA.2, and BA.3 for sensitivity to neutralisation by antibodies induced by infection and vaccination, using pseudoviruses as a model system, which adequately mirrors SARS-CoV-2 neutralisation by antibodies.[7]

We analysed particles harbouring the S protein of B.1—which is identical to the wildtype strain apart from the D614G mutation—and S proteins of BA.1, BA.2, and BA.3. We first examined neutralisation by antibodies from convalescent patients, who were infected during the first (February to May, 2020) and second (December, 2020, to February, 2021) waves of COVID-19 in Germany (appendix pp 2–3, 4–6). Neutralisation of particles bearing the B.1 S protein ($B.1_{pp}$) was robust, whereas neutralisation of $BA.1_{pp}$ and $BA.3_{pp}$ was at least 32-times less than $B.1_{pp}$ (BA.1 p=0·0020; BA.3 p=0·0020). Neutralisation of $BA.2_{pp}$ was also diminished, but the reduction was less pronounced than that measured for the other omicron subvariants (9·2-times less than $B.1_{pp}$; p=0·0020).

Analysis of neutralisation by antibodies induced by double vaccination with BNT162b2 (BNT) yielded similar results as neutralisation with antibodies from convalescent patients (appendix pp 2–3). Particles harbouring the S proteins of BA.1 and BA.3 showed 17-times lower neutralisation than $B.1_{pp}$ (BA.1 p=0·0020; BA.3 p=0·0020), whereas neutralisation of $BA.2_{pp}$ was 9-times reduced (p=0·0020). Triple BNT vaccination induced a more potent antibody response, and only modest evasion of neutralisation was seen for particles bearing omicron S proteins (BA.1 2·5-times, p=0·0039; BA.2 1·9-times, p=0·012; BA.3 2·4-times, p=0·0039; appendix pp 2–3). Finally, neutralisation by antibodies induced in fully vaccinated (three vaccine doses) individuals with breakthrough infection during the fourth wave in Germany (October, 2021, to January, 2022, dominated by the delta variant) was most potent and neutralisation of particles bearing omicron S protein was 9–12-times less efficient than $B.1_{pp}$ (BA.1 p=0·0020; BA.2 p=0·0039; BA.3 p=0·0039; appendix pp 2–3). However, no significant differences were observed between $BA.1_{pp}$, $BA.2_{pp}$, and $BA.3_{pp}$ (appendix pp 2–3).

Our results show that all presently circulating omicron subvariants evade neutralisation by vaccine-induced antibodies with comparably high efficiency, suggesting that increased antibody evasion is not the reason for the current expansion of BA.2 in several countries.[4,8] Since currently available vaccines provided robust protection against early omicron isolates circulating in South Africa from Nov 15 to Dec 7, 2021,[3] which was likely to be BA.1, our results suggest that this protection should extend to all omicron subvariants.

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A SARS-CoV-2 omicron (B.1.1.529) variant outbreak in a primary school in Geneva, Switzerland

The role of primary-school children in community circulation of SARS-CoV-2 remains unclear,[1] and this is particularly true for the highly transmissible omicron (B.1.1.529) variant, which has a high potential for immune escape, increasing the likelihood to infect or reinfect vaccinated family members.[2]

We investigated a SARS-CoV-2 outbreak in a primary school in Geneva, Switzerland, as part of a longitudinal, prospective, school class-based surveillance study (SEROCoV-Schools).[3] Detailed methods are in the appendix (pp 1–2). Briefly, children (aged 3–7 years), teachers, and school staff from four classes in the primary school (classes A–D) were invited to participate in the surveillance study. When a participant tested positive, we prospectively investigated the transmission of SARS-CoV-2 in the school and in the household.

The first case (class C) of SARS-CoV-2 infection with the omicron variant was notified to our team on Jan 11, 2022, which was the day after the start of the school term after the winter vacation, referred to as day 0. Children and staff members were tested for SARS-CoV-2 infection via RT-PCR on oropharyngeal swabs twice by our team, on day 3 and day 7, regardless of symptoms (appendix p 3). Additional tests were done on a few participants who developed symptoms after day 7. Within 3 days of identification of the first case, we identified cases in all four classes being investigated. Cumulative infection incidence was four (33%) of 12 children in class A (which increased to five [42%] of 12 if including a probable case, as defined in the appendix [p 1]), two (15%) of 13 in class B, nine (56%) of 16 in class C, and 11 (61%) of 18 in class D. At the time of the study, only two children were vaccinated against COVID-19 with one dose; both tested positive for SARS-CoV-2 infection. Because this outbreak investigation is part of a surveillance study that began on Oct 5, 2021, we were able to determine that 19 (29%) of 66 children (four to six children in each class) had anti-spike SARS-CoV-2 IgG antibodies (unrelated to vaccination) or PCR-confirmed infection, or both, before the beginning of the omicron outbreak in January, 2022. Among those, 17 were tested during the outbreak and five (29%) of 17 were infected. Among the children without indication of previous infection or vaccination who were tested, 20 (50%) of 40 were infected.

Five (50%) of ten teachers and one (20%) of five non-teaching staff members at the school tested positive during the omicron outbreak. Two (13%) of 15 staff members were not vaccinated against COVID-19, and both tested positive.

We also investigated the introduction of SARS-CoV-2 infections in 24 households of children who tested positive. 52 household members were tested once or twice within the week after their child or sibling tested positive (appendix p 3). Infections with the SARS-CoV-2 omicron variant were found in 15 (63%) of 24 households and 25 (48%) of 52 investigated household members (which increased to 27 [50%] of 54 if including probably cases), a household cumulative infection incidence that was similar to the findings of another report from South Korea.[4] 42 (91%) of 46 parents included were vaccinated, of whom 32 (76%) had received a booster. After excluding those who tested positive just before the outbreak and those who were not tested, the cumulative incidence of infection among those who had received a booster vaccination was 13 (43%) of 30, among those who had received one or two doses of vaccine was two (33%) of six, and among those who were unvaccinated was two (67%) of three, supporting the idea that this variant is highly transmissible even among fully vaccinated people.[5]

Most infections were symptomatic, with 25 (81%) of 31 children and siblings and 19 (86%) of 22 adults (parents, teachers, and non-teaching staff members combined) reporting symptoms. Four (100%) of four adults who were unvaccinated, three (75%) of four adults who were vaccinated

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