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quantify acquisition of mutations over the time course of infection. We will also stratify the number of mutations observed by vaccination status to test Ko's compelling hypothesis, although our modest sample size will likely limit our power to detect vaccine-induced selective pressure, which requires larger, national datasets.

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Anti-SARS-CoV-2 antibodies in healthy donor plasma pools and IVIG products—an update

In a previous Correspondence,¹ we demonstrated the appearance of antibodies to SARS-CoV-2 in pooled donor plasma and intravenous immunoglobulin (IVIG) products from these pools over the period of May–December, 2020. In this update, we describe increasing levels of anti-SARS-CoV-2 antibodies in pooled plasma and IVIG products up to September, 2021, and neutralising activity of these antibodies against wild-type virus and variants of concern (VOC).

Since May, 2020, we have measured SARS-CoV-2 antibodies (by ELISA²) in healthy donor plasma pools collected in Spain, Germany, Czech Republic, Slovakia, and the USA, and the products made from this plasma.¹ Plasma and products from Hungary and Italy have been included since May, 2021. Concentrated immunoglobulins have been, and are currently being, investigated as a potential treatment for COVID-19 (NCT04480424).³ Anti-SARS-CoV-2 antibody levels in these products could have bearing on their effectiveness. These plasma pools also reflect the antibody contributions of over 1000 donors and are an indirect measure of the epidemiology of COVID-19 at that time.

We previously showed early appearance of anti-SARS-CoV-2 antibodies in Spain and the USA and later appearance in central European countries.¹ Subsequent data show that anti-SARS-CoV-2 antibodies dramatically increased (ten to 50 times) in all plasma pools and IVIG products, regardless of geographic origin (appendix pp 1–3). The highest titres and the greatest increases in titres of anti-SARS-CoV-2 antibodies were seen in the regions

where antibodies first appeared (Spain and the USA). The titres of anti-SARS-CoV-2 antibodies in the final products showed similar changes over time as those seen in pooled plasma (appendix p 3). All products showed upwards trends in their titres except those from Slovakia.

Neutralisation studies were conducted with wild-type SARS-CoV-2 virus and pseudoviruses representing the native strain and several VOC. These studies showed neutralisation potency of several batches of IVIG (Gamunex-C and Flebogamma DIF) from plasma of different origins (appendix p 4). Importantly, IVIG products (from the USA and Germany) showed neutralisation activity against pseudoviruses representing the wild-type virus and alpha (B.1.1.7), beta (B.1.351), gamma (P.1), and delta (B.1.617.2) VOC (appendix p 4).

This follow-up provides even stronger evidence that anti-SARS-CoV-2 antibodies in pooled plasma and IVIG products mirror exposure in the general population. IVIG products are indicated for immunodeficient patients and for other prophylactic or therapeutic approaches. Continued monitoring of these antibodies and assessment of their functionality (eg, neutralisation capacity, effectiveness against VOC) is recommended.

CR, J-MD, and RG are full-time employees of Grifols, a manufacturer of IVIG products and other blood plasma derivatives.

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See Online for appendix