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.

Testing for responses to the wrong SARS-CoV-2 antigen?

Two commercial antibody tests (Abbott SARS-CoV-2 IgG, Abbott Diagnostics, Abbott Park, IL, USA; and Roche Elecsys Anti-SARS-CoV-2, Roche Diagnostics, Basel, Switzerland), both targeting antibodies to nucleoprotein (anti-NP), constitute the cornerstone of the UK Government's response to the COVID-19 pandemic. The test manufactured by Abbott, which is widely used in Europe and the USA, claims a specificity and sensitivity of greater than 99% at 14 days or more after symptoms started and has been validated by Public Health England.[1]

We received 2204 serum samples from staff and patients previously screened for anti-NP on the Abbott platform as part of the routine diagnostic service by the UK National Health Service. These samples, principally selected in the Abbott binding ratio range of 0·25–2·5, were further tested using an in-house double binding antigen ELISA (Imperial Hybrid DABA; Imperial College London, London, UK), which detects total antibodies to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) receptor binding domain (RBD). This assay has a specificity of 100% (95% CI 99·6–100), defined by testing 825 serum samples that predated the COVID-19 pandemic, and a sensitivity of 98·9% (96·8–99·8) when evaluating 276 serum samples from individuals with RT-PCR-confirmed SARS-CoV-2 infection.

Among 511 samples with Abbott binding ratios of 0·25 to less than 1·4, 294 (58%) had detectable anti-RBD antibodies (ranging from 34% for binding ratios 0·25–0·5 to 94% for binding ratios 1·25–1·4; appendix). Discordant samples were classified into five groups based on their Imperial Hybrid DABA binding ratio. Eight serum samples from each group were randomly selected and assayed by a second in-house assay, an S1 G and M capture ELISA, to verify the anti-RBD findings. Anti-S1 antibodies were detected in 28 (88%) of 32 samples that were reactive for anti-RBD but unreactive for anti-NP. The four serum samples not confirmed by the S1 capture ELISA had low binding ratios in the Imperial Hybrid DABA, the S1 non-reactivity being consistent with the lower sensitivity of the capture assay compared with the Imperial Hybrid DABA. Eight serum samples selected at random from 76 reactive only in the Abbott assay were unreactive for antibody to S1.

There are two possible explanations for these findings: either the Abbott assay results constitute false-positive reactions;[2] or these patients did not mount a detectable humoral response to S1, as can happen with asymptomatic or mild infection.[3,4]

The UK Government's decision to facilitate use of Abbott' assay was intemperate. Anti-NP is insensitive in the field: why was this insensitivity not recognised by those who validated its use in the UK? Moreover, Abbott's assay does not indicate accurately the presence of neutralising and potentially protective antibodies in the convalescent individual. Those who might still deign to use this assay as the sole marker of past infection would be wise to consider confirmatory algorithms to better inform individuals investigated for anti-NP.

RST, MOM, and CR declare an interest in the Imperial Hybrid DABA (patent file IRN.FID4816059). PR and MK declare no competing interests.
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*Carolina Rosadas, Paul Randell, Maryam Khan, Myra O McClure, *Richard S Tedder*
r.tedder@imperial.ac.uk

Department of Infectious Disease, Imperial College London, London, UK (CR, MK, MOM, RST); Jefferiss Research Trust Laboratories, Wright-Fleming Institute, Faculty of Medicine, Imperial College London, London W2 1PG, UK (RST); and Department of Infection and Immunity, Imperial College Healthcare NHS Trust, Charing Cross Hospital, London, UK (PR)

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See **Online** for appendix

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