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## Serological assays for delayed SARS-CoV-2 case identification

In their Article, published in *The Lancet Respiratory Medicine* in July, 2020, on point-of-care serological assays for delayed severe acute respiratory coronavirus 2 (SARS-CoV-2) case identification among health-care workers in the UK, Pallett and colleagues<sup>1</sup> evaluated two lateral flow serological assays.

The authors included sera positive for IgM or IgG antibodies against some infectious conditions in the assay specificity studies; however, they have not assessed the potential for assay cross-reactivity with autoantibodies present in the sera of patients with autoimmune disease.<sup>2</sup> Cross-reaction of SARS-CoV antigen with autoantibodies in autoimmune diseases was previously reported.<sup>3</sup> Immunodeficiency can lead to false negative serology results; therefore, the measurements of total immunoglobulins (such as total IgG) should be considered, along with any patient history of immunodeficiency.<sup>3</sup> Along with serum samples, evaluation using whole blood samples on the lateral flow serological assays should be done because a whole blood sample is likely to be the primary sample type at point-of-care.

Immune responses might differ with age (hence the proportion of patients who develop IgG antibodies

and their IgG persistence could differ with age), an investigation of age differences in the development of SARS-CoV-2 IgG antibodies in the study cohort might be worthwhile.<sup>4</sup>

It is unclear if repeat serum samples per study participant were used in the study; this information is useful to determine how many participants who were serologically positive for SARS-CoV-2 contributed to the evaluation of sensitivity.<sup>4</sup>

To improve the positive predictive value in SARS-CoV-2 testing, an orthogonal testing algorithm that directs a second test to individuals who initially test positive can be considered.<sup>5</sup> Effective orthogonal algorithms are generally based on testing a patient sample with two tests, each with unique assay design characteristics, such as antigens or assay formats.<sup>5</sup>

I declare no competing interests.

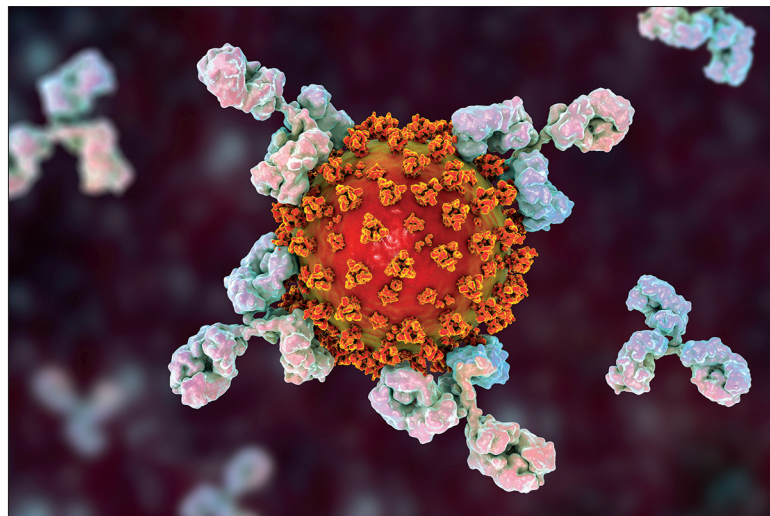
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