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Data used to assess risk of donor derived SARS-CoV-2 infection remain undefined, although case reports are emerging. In Australia, overall organ transplantation activity observed a reduction, with kidney transplantation rates down 27% compared with in 2019.⁹ Internationally, the reduction of overall organ transplantation rates was more than 50% in France, Spain and the United States by April 2020.¹⁰ A proven donor-to-recipient transmission of SARS-CoV-2 in a lung transplant recipient, despite negative clinical and laboratory screening of the donor, highlights the importance of additional test methods for screening.¹¹

Changes in the biochemical properties of blood following death are known to adversely affect the outcomes of serological tests. Inhibitory factors observed in cadaveric specimens include an increase in free haemoglobin, potentially compromising the sensitivity and specificity of an immunoassay.^{2,5} Furthermore, the performance of the Architect SARS-CoV-2 IgG assay has yet to be officially established for the use of cadaveric specimens or other specimens besides human serum or plasma by Abbott. Accurate detection of infectious markers in donors, especially cadavers, provides assurance that the presence of SARS-CoV-2 is effectively assessed and may assist the cohesive decision for tissue and SOT.

The current study demonstrated no significant difference between testing of sera from living and cadaveric individuals for the examined parameters for SARS-CoV-2 IgG. Furthermore, the storage study support claims established for cadaveric specimens, where it showed no significant shift of up to 72 h at 20–24°C and up to 144 h at 2–8°C. This indicates testing of human serum and plasma specimens collected up to 24 h post-mortem with the Abbott Architect SARS-CoV-2 IgG assay is acceptable.

The consistency between the test and control specimens for detection of past infection with SARS-CoV-2 using specific antibody detection, reflects assay capability for use in donor screening. Furthermore, detection of COVID-19 antibodies in conjunction with SARS-CoV-2 RT-PCR may alleviate the hesitancy surrounding donor derived infections. This could contribute to reducing the burden of COVID-19 on declining transplantation rates and increase the availability of potentially lifesaving organs.¹²

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Analysis of SARS-CoV-2 real-time PCR test CT values across a population may afford useful information to assist public health efforts and add refinement to epidemiological models



To the Editor,

Initial public health measures were effective at reducing transmission of SARS-CoV-2 in Australia. In New South Wales in late December 2021, relaxation of these measures coupled with a seasonal change in people movement and the emergence of the Omicron strain (B.1.1.529) led to a surge in community transmission. During the peak period in January, demand for polymerase chain reaction (PCR) testing exceeded capacity, and the true community prevalence of infection was unknown and likely underestimated. A decline in case

Table 1 Percentage of SARS-CoV-2 real-time PCR test CT values <30 or ≥30 divided by testing platform used and week tested

Week starting	Rapid - BD Max		Rapid - Liat		Batch - Cobas		Batch - GeneSig		Batch - Seegene	
	<30	≥30	<30	≥30	<30	≥30	<30	≥30	<30	≥30
29/11/2021	0%	100%	50%	50%					81%	19%
6/12/2021	100%	0%	80%	20%	77%	23%			74%	26%
13/12/2021	75%	25%	94%	6%					82%	18%
20/12/2021	98%	2%	94%	6%	79%	21%			85%	15%
27/12/2021	95%	5%	93%	7%	82%	18%			88%	12%
3/01/2022	93%	7%	89%	11%	80%	20%	88%	12%	84%	16%
10/01/2022	91%	9%	85%	15%	59%	41%	84%	16%	74%	26%
17/01/2022	69%	31%	70%	30%	42%	58%	62%	38%	73%	27%
24/01/2022	46%	54%	60%	40%	36%	64%	66%	34%	72%	28%
31/01/2022	50%	50%	45%	55%	44%	56%	68%	32%	68%	32%
7/02/2022	56%	44%	61%	39%	34%	66%			68%	32%
14/02/2022	83%	17%	52%	48%	52%	48%	70%	30%	72%	28%
21/02/2022	67%	33%	63%	37%	65%	35%	61%	39%	73%	27%
28/02/2022	100%	0%	71%	29%	65%	35%	85%	15%	71%	29%
7/03/2022	50%	50%	67%	33%	64%	36%	68%	32%	78%	22%
14/03/2022	70%	30%	72%	28%	61%	39%	71%	29%	78%	22%
21/03/2022	50%	50%	70%	30%	47%	53%	42%	58%	77%	23%

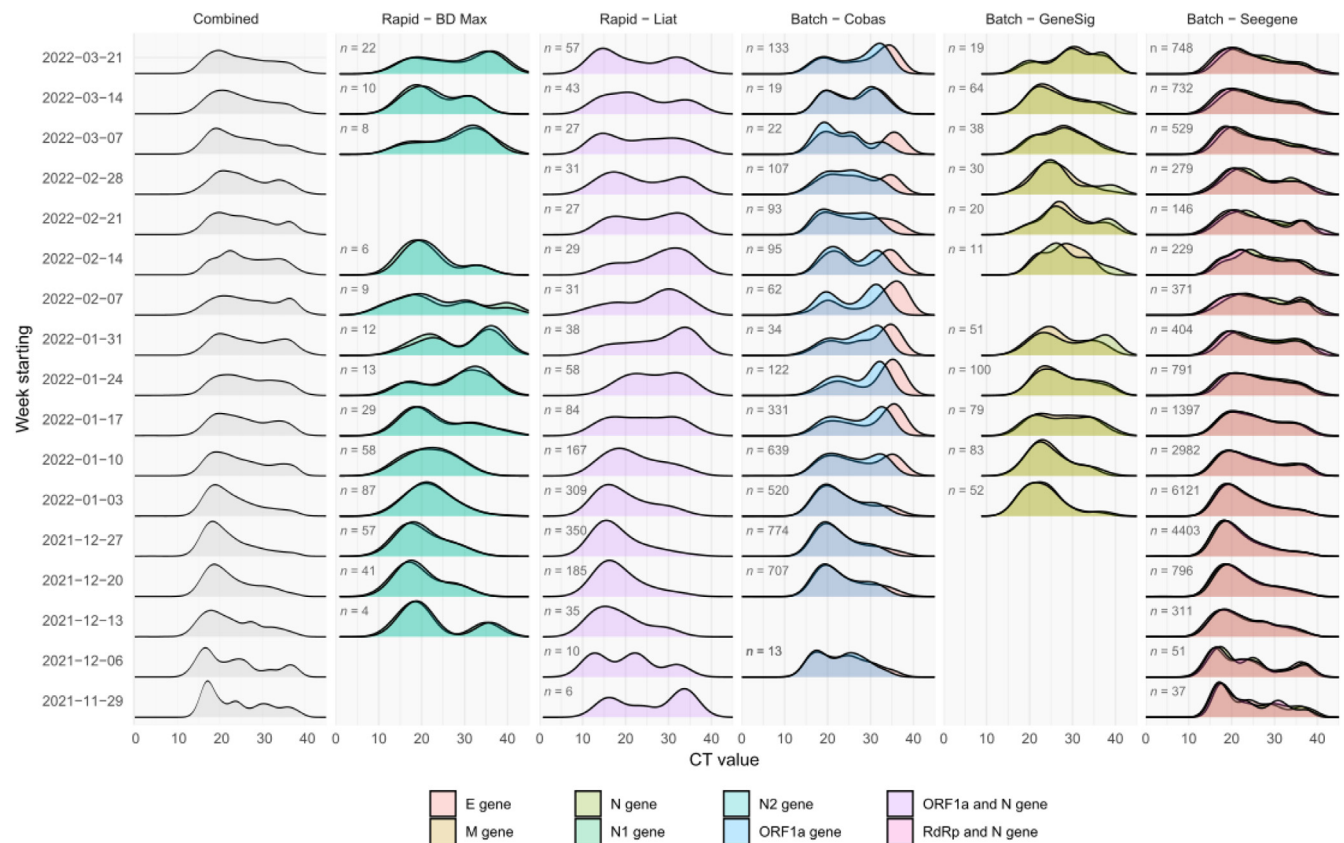
BD Max, BD, USA; Liat, Roche Diagnostics, Switzerland; Cobas, Roche Diagnostics, Switzerland; GeneSig, Primerdesign, UK; Seegene, Korea.

numbers was observed throughout February before case numbers increased again in March partially due to the emergence of the Omicron BA.2 sub-variant.

In the weeks following the presumed initial peak of infections an increased rate of positive tests with high cycle threshold (CT values) was observed. High CT values can be

obtained very early in infection or later in infection and have been correlated to reduced infectivity.¹ Detection of non-infectious viral remnants can lead to high CT value positive PCR tests for several weeks after the initial infection.² There is no reliable laboratory method to distinguish between high CT value results obtained early in infection with those reflecting past or historical infection. Given the expected large pool of undiagnosed infections due to capacity limitations during the preceding peak, and the markedly discrepant timeframes that high CT value tests are observed early in infection compared to the post infection period, the observed increased rate of high CT value results in the post peak period likely reflect previously undiagnosed historical infection. Early in the observed time period high CT value tests were repeated from the original sample on a different testing platform and invariably confirmed, suggesting that these were true results and not due to laboratory contamination (results excluded to prevent duplication). This practise was discontinued due to economic and efficiency considerations. Additionally, many patients with high CT value results were re-swabbed with reproducible findings on repeat testing supporting that this is a true finding. Difficulty in interpreting these high CT value results potentially led to flawed infection control and isolation decisions and overestimates of disease prevalence at that time.

Data obtained during this time period from multiple testing platforms at the St George and Prince of Wales Hospitals, encompassing an array of testing indications, from urgent to routine, and servicing several hospitals and community clinics in the Eastern and South Eastern Suburbs of Sydney are shown below. Data are not shown for testing platforms

**Fig. 1** Distribution of SARS-CoV-2 CT values by instrument and week of testing.

with less than four positive samples in that week. They show shifts in the proportion of higher CT value tests, defined here as CT value >30, changing with community prevalence (Table 1). An increased proportion of high CT value tests were seen as case numbers declined, and the opposite was observed as numbers increased again in March. Graphical representation of the data, generated using R with *ggridges* package,³ shows the changing distribution of CT values and in some instances the emergence of a bimodal curve reflecting probable distinct cohorts of past and acute infection (Fig. 1).

Although these tests are primarily designed to be qualitative and not quantitative, the use of CT values to assist with distinguishing acute from historical infection is widely accepted. Individual CT values obtained from different testing platforms may not be directly comparable, but large scale population data should smooth errors allowing valid interpretation of overall trends. These data suggest that analysis of CT values across a population may afford useful information that may be of assistance to public health efforts and add refinement to epidemiological models to predict community transmission. Further study should be considered.

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Severe autoimmune haemolytic anaemia following SARS-CoV-2 vaccination in patients with treatment naïve B-cell neoplasms: a case series



To the Editor,

A concerted global health initiative has led to the development of multiple effective vaccinations to help combat the SARS-CoV-2 (COVID-19) pandemic. While the safety of

these vaccines has been demonstrated in large, randomised studies, the incidence of rare complications, particularly in specific health subgroups such as haematological malignancies, is important to establish.

Autoimmune haemolytic anaemia (AIHA), a condition typified by antibody-mediated destruction of erythrocytes, has been reported in the setting of COVID-19.^{1–3} B-cell neoplasms are also a known driver of AIHA. We report four patients with a pre-existing or new concurrent diagnosis of B-cell neoplasms, who were diagnosed with first presentation severe AIHA following COVID-19 vaccination at our tertiary centres. We highlight that patients with B-cell malignancies may be an at-risk group for this rare immune complication following COVID-19 vaccination, and discuss management strategies.

Case 1 was a 76-year-old male with a history of untreated chronic lymphocytic leukaemia (CLL) RAI stage-0, presenting with malaise, lethargy and abdominal pain 4 days following his first dose of the ChAdOx1nCoV-19 vaccine. His baseline bloods, prior to vaccination, demonstrated a haemoglobin 133 g/L, white cell count (WCC) 60×10^9 , lymphocyte count 32×10^9 and bilirubin of 7 mcmol/L (0–20). On presentation his haemoglobin had fallen to 59 g/L (Table 1), with spherocytosis on blood film, and a reticulocytosis of 11.6%. A marked lymphocytosis was observed, with WCC 239×10^9 /L and a lymphocyte count 220×10^9 /L. SARS-CoV-2 polymerase chain reaction (PCR) was negative. There was biochemical evidence of haemolysis with bilirubin of 97 mcmol/L, haptoglobin <0.01 g/L (0.36–1.95) and lactate dehydrogenase (LDH) 835 U/L (120–250). Direct antiglobulin testing (DAT) was positive for C3d and negative for IgG, in contrast to his previously negative DAT in 2014. He was diagnosed with AIHA and commenced on prednisolone 1 mg/kg, warmed supportive red blood cell (RBC) transfusions to account for potential cold AIHA, and a single infusion of intravenous immunoglobulin (IVIg, 1 g/kg). CLL therapy was considered given the patient's progressive lymphocytosis and aggressive AIHA, however after 4 days his haemoglobin stabilised without transfusion. Prednisolone was slowly weaned, and one month post-admission, his WCC and lymphocyte count had returned to their pre-vaccination baseline. He received the BNT162b2 vaccine (Pfizer) for subsequent doses, with a mild relapse of haemolysis following the second, but not third dose, which responded to prednisolone. However, 6 months later he had an 'unprovoked' relapse of AIHA which responded to prednisolone and IVIg.

Case 2 was a 49-year-old male presenting 4 days following his second dose of the BNT162b2 COVID-19 vaccine with worsening exertional dyspnoea and central chest discomfort on a background of stable CLL. This was preceded with dark coloured urine, which in retrospect he had also noticed following the first vaccine. His baseline bloods included a haemoglobin 156 g/L, WCC 13.7×10^9 , and lymphocyte count 10.0×10^9 . His presenting investigations demonstrated a haemoglobin of 39 g/L, WCC 35.7×10^9 /L with lymphocytosis of 27.8×10^9 /L, and reticulocytes were 25.1% (Table 1). SARS-CoV-2 PCR was negative. A blood film showed moderate polychromasia, frequent spherocytes and presence of nucleated RBCs (8/100 WCC). A haemolysis screen demonstrated a raised bilirubin of 87 mcmol/L, haptoglobin of <0.01 g/L, and raised LDH of 953 U/L, with DAT positive for IgG and C3d (no prior DAT for comparison). The patient was commenced on prednisolone 1 mg/kg and supportive RBC transfusions. By day 5, his haemoglobin