Seroreactivity with COVID-19 antibody testing in CCP donors presenting without a SARS-CoV-2 diagnostic test

On March 24, 2020, the US Food and Drug Administration announced an investigational initiative to transfuse convalescent plasma (CCP) from patients recovered from coronavirus disease 2019 (COVID-19) to treat patients suffering from severe COVID-19.[1] Initial eligibility criteria required donors to have evidence of past severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection as determined by a positive molecular diagnostic test of upper respiratory sample (ie, nasopharyngeal [NP] swab), blood positive for SARS-CoV-2 RNA, or a positive serologic test.[1] Minimum antibody titers or evidence of neutralizing antibodies were reported if testing was able to be performed but was not required with sample storage for future testing.[2] Donors also needed to be at least 14 days from resolution of clinical symptoms and had to meet allogeneic blood donor criteria per the Code of Federal Regulations.[2]

The American Red Cross (ARC) mobilized CCP collection efforts at the end of March 2020. Serologic testing for antibodies to the SARS-CoV-2 spike glycoprotein using a semiquantitative enzyme-linked immunosorbent assay (VITROS Anti-SARS-CoV-2 Total Test; Ortho Clinical Diagnostics, Raritan, New Jersey) was instituted for CCP donors on 27 April 2020.[3] After implementation, only units from donors with a signal-to-cutoff (S/CO) ratio of 1.0 or greater (reactive per package insert) were labeled as CCP units.[3]

The ARC had an evolutionary approach to donor qualification. At first, an initially positive NP swab (or a physician's attestation) with date of symptom resolution were required. Donors 14 to 28 days from symptom resolution required a follow-up negative NP swab. Following serologic testing implementation, the ARC transitioned to qualifying donors without requiring diagnostic test proof, allowing donors to self-report previous diagnostic testing positivity. All donors needed to have had a symptomatic COVID-19 infection and be at least 14 days from symptom resolution.

Between 27 March and 14 May, 67 810 potential CCP donors registered via the ARC Web site; 38 085 (56%) acknowledged either an existing diagnostic COVID-19 polymerase chain reaction (PCR) or serologic test. The remainder did not have a diagnostic test (i.e., PCR or serologic) reporting presumptive clinical COVID-19 diagnosis only. Ortho Diagnostics VITROS Anti-SARS-CoV-2 results were available for 325 CCPs at the time of analysis: 77 donors with only a clinical COVID-19 diagnosis with the majority more than 28 days from symptom resolution, 62 donors with diagnostic testing and 14 to 28 days from symptom resolution, and 186 with diagnostic testing and more than 28 days from symptom resolution. A total of 36.4% of donors without diagnostic testing had a reactive VITROS test, with an overall median S/CO of 0.11 (Table 1). Among the donors with diagnostic testing, the early recovery group had 82.3% reactivity (overall median S/CO, 26.2). Those further in recovery had 91.9% (overall median S/CO, 129.5). Statistically, by χ^2 analysis, the percentage of donors with reactivity was significantly different among the three groups ($P < .0001$), and Kruskal-Wallis tests demonstrated statistical significance in S/CO values among the groups ($P < .0001$).

TABLE 1 Donor Testing Information

	CCP donation date range	% > 28 days from symptom resolution	% with reactive VITROS	Median S/CO (IQR)
Donors without diagnostic testing (N = 77)	4 May 2020 to 25 May 25, 2020	97.4	36.4	0.11 (32.05)
Donors with diagnostic testing and 14-28 days symptom resolution (N = 62)	8 April 2020 to 19 April 2020	0	82.3	26.20 (58.09)
Donors with diagnostic testing and > 28 days symptom resolution (N = 186)	9 April 2020 to 19 May 2020	100	91.9	129.50 (210.80)
P		<.0001	<.0001	<.0001

CCP, convalescent plasma; IQR, interquartile range; S/CO, signal-to-cutoff.

Our seroreactivity evaluation in CCP donors presenting with and without a diagnostic COVID-19 PCR test highlights the importance of testing to enrich for donors with SARS-CoV-2 antibodies. There were a few notable limitations to our study, including screening with only one testing platform examining a single immune response target to SARS-CoV-2 infection. This was a small study with a limited number of donors. The three groups were in different states of recovery but in this cohort, lack of diagnostic testing had the most pronounced effect on seroreactivity. Finally, this represents the experience of a single, large blood collector. Due to limitations of collection capacity, it is important to ensure the CCP population is likely to be COVID-19 antibody enriched. This information may be of value to other CCP collectors recruiting CCP donors and building inventory.

KEYWORDS
CCP, convalescent plasma, COVID-19, donor, SARS-CoV-2

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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Potentially clinically significant anti-Di^b identified by monocyte monolayer assay before transfusion

To the Editor

Antibodies directed to the high-prevalence Diego-b (Di^b) blood group antigen are very rare because the frequency of individuals who are Di(b–) is less than 0.01% in most populations.[1] Cases where the clinical significance of anti-Di^b has been determined are also sparse but there are reports of clinical significance in causing hemolytic disease of fetus and newborn[2] and a few reports of clinical significance after blood transfusion of Di(b+) blood.[3,4] Thus, additional evidence of potential for clinical significance of anti-Di^b is helpful. Herein, we report a patient where a monocyte monolayer assay (MMA) was used to decide whether the patient should donate autologous blood for future use. Patient was a male, 17 years old, admitted to our hospital with a diagnosis of systemic vasculitis. The patient had no history of transfusion and routine group and screen testing were performed. The patient's ABO group and D type was determined to be B+ and the direct antiglobulin test (DAT) was negative by standard serologic methods. The screening cells, by standard MTS-Gel testing, were negative. The patient was successfully transfused with 1 unit of B+ RBCs with no adverse transfusion events noted. Six months posttransfusion, the patient was readmitted to the hospital, and a standard group and screen test was performed. The patient was confirmed to be B+, DAT negative. However, the antibody screen was now strongly positive, 3+, with all screening and panel cells, autocontrol negative, by standard MTS-Gel testing.