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Rapid antibody testing for SARS-CoV-2 vaccine response in pediatric healthcare workers

Theodore W. Heyming[a,b,*], Diane Nugent[c], Aprille Tongol[d], Chloe Knudsen-Robbins[e], Janet Hoang[c], John Schomberg[d], Kellie Bacon[d], Bryan Lara[d], Terence Sanger[d,f]

[a] Department of Emergency Medicine, Children's Hospital of Orange County, Orange, California, USA
[b] Department of Emergency Medicine, University of California, Irvine, California, USA
[c] Department of Hematology, Children's Hospital of Orange County, Orange, California, USA
[d] Research Institute, Children's Hospital of Orange County, Orange, California, USA
[e] University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA
[f] Department of Electrical Engineering and Computer Science, University of California, Irvine, California, USA

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ABSTRACT

Background: The durability of the immune response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination remains unknown. The objective of this study was to evaluate a rapid SARS-CoV-2 IgM/IgG antibody detection kit as a qualitative screen for the humoral response to vaccination.

Methods: Study participants (n = 125) included pediatric healthcare workers (HCWs) who had received two doses of BNT162b2 or mRNA-1273. Participants were tested on study entry (March 12, 2021 to April 9, 2021). The mean number of days post second dose was 22 (range 17–36). Participants were tested for IgM/IgG antibodies to the SARS-CoV-2 spike protein with the RightSign COVID-19 IgG/IgM Rapid Test Cassette. ELISA/competitive inhibition ELISA (CI-ELISA) were subsequently run to assess for the neutralization effect and SARS-CoV-2 anti-nucleocapsid IgM/IgG antibodies.

Results: Overall, 98.4% of participants were IgG-positive and 0.8% were IgM-positive on rapid RightSign testing. Of those with IgG-positive results, 100% were anti-spike protein IgG-positive on CI-ELISA; none of those who tested IgG-negative via the rapid test were IgG-positive on CI-ELISA. All HCWs who tested RightSign positive demonstrated neutralizing capability on CI-ELISA. Overall, 1.6% demonstrated anti-nucleocapsid IgM antibodies and 5.6% demonstrated anti-nucleocapsid IgG antibodies.

Conclusions: The strong agreement between the rapid RightSign IgG results and confirmatory CI-ELISA testing suggests that this test may be used to assess for positive, and neutralizing, antibody responses to SARS-CoV-2 mRNA vaccination.

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic and the responses enacted to limit its devastation have profoundly impacted almost all aspects of society. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccinations have the potential to not only reduce the morbidity and mortality associated with COVID-19, but also to precipitate a return to 'normal' life. In phase 2/3 trials, two doses of mRNA-1273 demonstrated 94% efficacy in preventing COVID-19, and BNT162b2 has been shown to be 95% effective in preventing COVID-19; both vaccines induce antibodies to the SARS-CoV-2 spike protein (Baden et al., 2021; Polack, 2021). However, the antibody response to vaccines can be highly variable, and it is unknown how or whether the antibody response profile to SARS-CoV-2 vaccines will change over time, and if these changes will be clinically significant (Zimmermann and Curtis, 2019). To date, several studies have examined the SARS-CoV-2 mRNA vaccine immune response in relatively small cohorts (Sahin et al., 2020; Wang et al., 2021; Widge et al., 2021). These studies have all relied on ELISA, and in many cases on flow cytometry as well, which is

* Corresponding author: Theodore Heyming, Children's Hospital of Orange County, 1201 W La Veta Ave, Orange, CA 92868, USA. Tel: +1 714 509 9113. Fax: +1 714 509 9102
E-mail address: theyming@choc.org (T.W. Heyming).

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likely not sustainable or practical for fast, inexpensive, and large-scale testing.

The primary objective of this study was to evaluate the use of a rapid and relatively inexpensive SARS-CoV-2 IgM/IgG antibody detection kit, RightSign COVID-19 IgG/IgM Rapid Test Cassette, as a qualitative screening tool for determining the humoral immune response to SARS-CoV-2 vaccination by comparison to a competitive inhibition ELISA. Neutralizing antibodies, formed as a result of vaccination or natural infection, are key measures of protection, and while direct measurement of SARS-CoV-2 neutralizing antibodies is complicated due to biosafety laboratory restrictions, surrogate neutralization tests have been shown to be acceptable alternatives (Addetia et al., 2020; Favresse et al., 2021; Huang et al., 2020; Tan et al., 2020; Valcourt et al., 2021). The secondary objective of this study was to evaluate, through ELISA testing, the seroprevalence of SARS-CoV-2 anti-nucleocapsid antibodies in a pediatric healthcare worker (HCW) population to assess for historical coronavirus infection. A cohort of pediatric HCWs was chosen, as they are exposed to a variety of respiratory viruses more common in the pediatric population, including coronaviruses circulating prior to SARS-CoV-2.

2. Methods

2.1. Study design

Pediatric HCWs involved in direct patient contact care or working in close proximity to patient-care areas at this institution were invited to participate in the study during the period from March 12 through April 9, 2021. The study participants ($n = 125$) were $\geq$18 years of age and included physicians, physician assistants, nurse practitioners, nurses, aides, medical technicians, and additional clinical staff. All HCWs who participated in the study had received two doses of either BNT162b2 or mRNA-1273 vaccine, with receipt of the second dose 17–36 days prior to study enrollment. Any individual who had previously tested positive for SARS-CoV-2 via a reverse transcriptase PCR (RT-PCR) or any other antigen or antibody diagnostic test was excluded from the study. The average prevalence of positive COVID-19 testing for our county over a 14-day period during the study was 0.0034% (Orange County Health Care Agency, 2021). During the study, the county cumulative total number of cases was 250 431 since tracking began, representing 7.9% of the total county population. During the study period, the alpha, epsilon, and gamma variants made up more than 73% of COVID-19 cases in California, and the delta variant accounted for $<$2.1% of cases (California Department of Public Health, 2021). The study was approved by the Institutional Review Board and signed informed consent was obtained from all study participants.

2.2. Serological testing

Blood samples were obtained on the day of consent. All samples were tested with the Hangzhou Biotest Biotech RightSign COVID-19 IgG/IgM Rapid Test Cassette, which was issued an Emergency Use Authorization by the US Food and Drug Administration on June 4, 2020 (U.S. Food & Drug Administration F 2021) IgG analysis performed by the manufacturer showed that the RightSign kit has a 93.3% sensitivity to anti-spike IgG for 30 samples tested and a 100% specificity to anti-spike IgG for 80 samples tested. All fingerstick sampling and antibody testing related to the study were performed by trained personnel according to the manufacturer's instructions. Consensus between two blinded research team members was needed to declare a positive result; this methodology was used to ensure accuracy and assess ease of use. All serum/plasma samples were stored at 4°C prior to analysis.

2.3. ELISA

The SARS-CoV-2 Surrogate Virus Neutralization ELISA (GenScript, Piscataway, NJ, USA), a competitive inhibition assay, was used to detect neutralizing IgG antibodies targeting the viral spike (S) protein receptor binding domain. This assay utilizes the purified receptor binding domain (RBD) from the SARS CoV-2 spike (S) protein to test plasma for the presence of patient antibodies that would block binding of specific viral binding spike protein (spike RBD) to its host receptor, ACE2. Using a horseradish peroxidase-conjugated recombinant SARS-CoV-2 RBD binding fragment and an ELISA plate coated with its target protein (the human ACE2 receptor protein, hACE2), test plasma is measured for its ability to block this protein–protein interaction between the HRP-linked RBD (HRP-RBD) and hACE2, thus inhibiting binding of a viral protein used for cell entry and propagation. This assay has been shown to be effective in detecting neutralizing antibodies when compared to a plaque reduction neutralization test, and has shown a significant correlation with specific known positive samples (95% confidence interval 87–100%) and specific negative samples (95% confidence interval 95.8–100%) (Tan et al., 2020). Each assay that is run requires titering of positive and negative controls provided in the kit, to determine the actual optical density (OD) level that sets the limits to call a plasma positive or negative for antibody directed against the SARS-Co-V2 RBD. The cutoff of 30% inhibition was determined to confirm the presence of anti-SARS-CoV-2 antibodies based on the studies performed by Tan et al. using the World Health Organization guidelines, and in comparison to parallel assays (Tan et al., 2020).

SARS-CoV2- IgG and IgM antibodies specific to the SARS-CoV-2 nucleocapsid protein were detected with ELISA kits (Epitope Diagnostics Inc., San Diego, CA, USA), which were run according to the manufacturer's instructions. Samples were tested in duplicate. Positive and negative cutoff values for IgG and IgM were determined according to the package insert for each assay. Values greater than the cutoff were considered positive. Manufacturing specifications/inserts for RightSign and all ELISAs may be found in the **Supplementary Material**.

2.4. Statistical methods

To measure the concordance between RightSign IgG screening and CI-ELISA-based screening, McNemar's Chi-square test of concordance was utilized to identify any significant levels of discord. To supplement these results with a measurement of the strength of agreement between tests, Cohen's Kappa was used to measure the strength of agreement. In the event of perfect concordance between screening methods, McNemar's Chi-square would produce a not applicable (NA) value. This NA occurs as a result of 0 values in both the false-positive and false-negative quadrants of a 2×2 table.

3. Results

All study participants ($n = 125$) had received two doses of either BNT162b2 or mRNA-1273 vaccine; 113 had received BNT162b2 and 12 had received mRNA-1273. At the time of enrollment in the study, the range of days post second vaccine was 17–36, and the average was 22.1 (Table 1). Participant demographics are described in **Supplementary Material** Table S1.

There was 100% agreement between study team members regarding the reading of rapid antibody test results. Of the total 125 participants, 123 (98.4%) tested positive for IgG to the spike protein RBD on the RightSign rapid antibody test, and one patient (0.8%) tested IgM-positive. Of those with positive RightSign IgG results, 100% were IgG-positive on confirmatory anti-spike IgG CI-

Table 1
Results of serological testing

Patient number	RightSign rapid AB test	CI-ELISA		SARS-CoV-2 nucleocapsid ELISA		Vaccine type	Days since second vaccine dose
		IgG (+/−)	% inhibition	IgG (+/−)	IgM (+/−)		
1	IgG+/IgM−	Positive	94.58%	Negative	Negative	BNT162b2	21
2	IgG+/IgM−	Positive	83.93%	Negative	Negative	BNT162b2	18
3	IgG+/IgM−	Positive	59.75%	Negative	Negative	BNT162b2	20
4	IgG+/IgM−	Positive	79.50%	Negative	Negative	BNT162b2	21
5	IgG+/IgM−	Positive	97.18%	Negative	Negative	BNT162b2	20
6	IgG+/IgM−	Positive	50.98%	Negative	Positive	BNT162b2	20
7	IgG+/IgM−	Positive	98.11%	Negative	Negative	BNT162b2	25
8	IgG+/IgM−	Positive	96.42%	Negative	Negative	BNT162b2	24
9	IgG+/IgM−	Positive	89.94%	Positive	Negative	BNT162b2	20
10	IgG+/IgM−	Positive	90.27%	Negative	Negative	BNT162b2	21
11	Negative[a]	Negative	10.27%	Negative	Negative	BNT162b2	21
12	IgG+/IgM−	Positive	94.26%	Negative	Negative	BNT162b2	19
13	IgG+/IgM−	Positive	94.97%	Negative	Negative	BNT162b2	19
14	IgG+/IgM−	Positive	96.43%	Negative	Negative	BNT162b2	20
15	IgG+/IgM−	Positive	97.06%	Negative	Negative	BNT162b2	25
16	IgG+/IgM−	Positive	83.76%	Negative	Negative	BNT162b2	19
17	IgG+/IgM−	Positive	96.94%	Negative	Negative	BNT162b2	20
18	IgG+/IgM−	Positive	94.76%	Negative	Negative	BNT162b2	23
19	IgG+/IgM+	Positive	86.70%	Negative	Negative	BNT162b2	18
20	IgG+/IgM−	Positive	96.82%	Negative	Negative	BNT162b2	19
21	IgG+/IgM−	Positive	85.20%	Negative	Negative	BNT162b2	21
22	IgG+/IgM−	Positive	94.88%	Negative	Negative	BNT162b2	22
23	IgG+/IgM−	Positive	92.79%	Negative	Negative	BNT162b2	21
24	IgG+/IgM−	Positive	85.38%	Negative	Negative	BNT162b2	19
25	IgG+/IgM−	Positive	96.68%	Negative	Negative	BNT162b2	19
26	IgG+/IgM−	Positive	91.08%	Negative	Negative	BNT162b2	19
27	IgG+/IgM−	Positive	94.37%	Negative	Negative	BNT162b2	20
28	IgG+/IgM−	Positive	93.51%	Negative	Negative	BNT162b2	20
29	IgG+/IgM−	Positive	87.17%	Negative	Negative	BNT162b2	19
30	IgG+/IgM−	Positive	95.88%	Negative	Negative	BNT162b2	17
31	IgG+/IgM−	Positive	95.42%	Negative	Negative	BNT162b2	22
32	IgG+/IgM−	Positive	88.67%	Negative	Negative	BNT162b2	22
33	IgG+/IgM−	Positive	91.54%	Negative	Negative	BNT162b2	21
34	IgG+/IgM−	Positive	91.04%	Negative	Negative	BNT162b2	20
35	IgG+/IgM−	Positive	94.82%	Negative	Negative	BNT162b2	23
36	IgG+/IgM−	Positive	90.61%	Negative	Negative	BNT162b2	20
37	IgG+/IgM−	Positive	94.79%	Negative	Negative	BNT162b2	21
38	IgG+/IgM−	Positive	95.80%	Positive	Negative	BNT162b2	20
39	IgG+/IgM−	Positive	92.23%	Negative	Negative	BNT162b2	21
40	IgG+/IgM−	Positive	96.36%	Negative	Negative	BNT162b2	21
41	IgG+/IgM−	Positive	97.03%	Negative	Negative	BNT162b2	20
42	IgG+/IgM−	Positive	96.88%	Negative	Negative	BNT162b2	33
43	IgG+/IgM−	Positive	94.60%	Negative	Negative	BNT162b2	20
44	IgG+/IgM−	Positive	91.46%	Negative	Negative	BNT162b2	23
45	IgG+/IgM−	Positive	85.78%	Negative	Negative	BNT162b2	25
46	IgG+/IgM−	Positive	94.11%	Positive	Negative	BNT162b2	21
47	IgG+/IgM−	Positive	96.05%	Negative	Negative	BNT162b2	20
48	IgG+/IgM−	Positive	83.93%	Negative	Negative	BNT162b2	19
49	IgG+/IgM−	Positive	96.01%	Negative	Negative	BNT162b2	19
50	IgG+/IgM−	Positive	97.22%	Negative	Negative	BNT162b2	20
51	IgG+/IgM−	Positive	97.35%	Negative	Negative	mRNA-1273	29
52	Negative [Au?3]	Negative	15.98%	Negative	Negative	BNT162b2	22
53	IgG+/IgM−	Positive	96.20%	Negative	Negative	BNT162b2	21
54	IgG+/IgM−	Positive	96.97%	Negative	Negative	BNT162b2	29
55	IgG+/IgM−	Positive	95.69%	Negative	Negative	BNT162b2	21
56	IgG+/IgM−	Positive	96.53%	Positive	Negative	BNT162b2	21
57	IgG+/IgM−	Positive	87.79%	Negative	Negative	BNT162b2	17
58	IgG+/IgM−	Positive	95.77%	Negative	Negative	BNT162b2	27
59	IgG+/IgM−	Positive	95.16%	Negative	Negative	BNT162b2	22
60	IgG+/IgM−	Positive	96.39%	Negative	Negative	BNT162b2	21
61	IgG+/IgM−	Positive	95.35%	Negative	Negative	BNT162b2	27
62	IgG+/IgM−	Positive	93.43%	Negative	Negative	BNT162b2	21
63	IgG+/IgM−	Positive	97.71%	Negative	Negative	mRNA-1273	33
64	IgG+/IgM−	Positive	89.29%	Negative	Negative	BNT162b2	20
65	IgG+/IgM−	Positive	96.43%	Negative	Negative	BNT162b2	24
66	IgG+/IgM−	Positive	92.16%	Negative	Negative	BNT162b2	21
67	IgG+/IgM−	Positive	94.10%	Negative	Negative	BNT162b2	20
68	IgG+/IgM−	Positive	97.08%	Negative	Negative	BNT162b2	22
69	IgG+/IgM−	Positive	95.96%	Negative	Negative	BNT162b2	22
70	IgG+/IgM−	Positive	40.59%	Negative	Negative	BNT162b2	22
71	IgG+/IgM−	Positive	86.50%	Negative	Negative	BNT162b2	22
72	IgG+/IgM−	Positive	73.04%	Negative	Negative	BNT162b2	17

(*continued on next page*)

Table 1 (*continued*)

Patient number	RightSign rapid AB test	CI-ELISA		SARS-CoV-2 nucleocapsid ELISA		Vaccine type	Days since second vaccine dose
		IgG (+/−)	% inhibition	IgG (+/−)	IgM (+/−)		
73	IgG+/IgM−	Positive	94.86%	Negative	Negative	BNT162b2	21
74	IgG+/IgM−	Positive	93.49%	Negative	Negative	BNT162b2	24
75	IgG+/IgM−	Positive	95.78%	Negative	Negative	BNT162b2	21
76	IgG+/IgM−	Positive	96.12%	Negative	Negative	BNT162b2	21
77	IgG+/IgM−	Positive	94.48%	Negative	Negative	BNT162b2	21
78	IgG+/IgM−	Positive	90.93%	Negative	Negative	BNT162b2	21
79	IgG+/IgM−	Positive	95.91%	Negative	Negative	BNT162b2	22
80	IgG+/IgM−	Positive	93.32%	Negative	Negative	BNT162b2	21
81	IgG+/IgM−	Positive	95.89%	Negative	Negative	BNT162b2	26
82	IgG+/IgM−	Positive	60.69%	Negative	Negative	BNT162b2	21
83	IgG+/IgM−	Positive	92.93%	Negative	Negative	BNT162b2	22
84	IgG+/IgM−	Positive	97.59%	Negative	Negative	BNT162b2	23
85	IgG+/IgM−	Positive	96.13%	Negative	Negative	mRNA-1273	35
86	IgG+/IgM−	Positive	88.87%	Negative	Negative	BNT162b2	21
87	IgG+/IgM−	Positive	87.29%	Negative	Negative	BNT162b2	21
88	IgG+/IgM−	Positive	92.83%	Negative	Negative	BNT162b2	21
89	IgG+/IgM−	Positive	85.97%	Negative	Negative	BNT162b2	21
90	IgG+/IgM−	Positive	97.81%	Negative	Negative	BNT162b2	36
91	IgG+/IgM−	Positive	97.06%	Negative	Negative	mRNA-1273	26
92	IgG+/IgM−	Positive	95.33%	Negative	Negative	BNT162b2	21
93	IgG+/IgM−	Positive	95.74%	Negative	Negative	BNT162b2	21
94	IgG+/IgM−	Positive	97.31%	Negative	Negative	mRNA-1273	26
95	IgG+/IgM−	Positive	93.17%	Negative	Negative	BNT162b2	21
96	IgG+/IgM−	Positive	93.15%	Negative	Negative	BNT162b2	22
97	IgG+/IgM−	Positive	96.99%	Positive	Negative	BNT162b2	22
98	IgG+/IgM−	Positive	85.88%	Negative	Negative	BNT162b2	20
99	IgG+/IgM−	Positive	94.14%	Negative	Positive	BNT162b2	33
100	IgG+/IgM−	Positive	84.92%	Negative	Negative	BNT162b2	21
101	IgG+/IgM−	Positive	94.95%	Negative	Negative	BNT162b2	20
102	IgG+/IgM−	Positive	96.15%	Negative	Negative	BNT162b2	21
103	IgG+/IgM−	Positive	93.35%	Negative	Negative	BNT162b2	18
104	IgG+/IgM−	Positive	97.38%	Negative	Negative	mRNA-1273	28
105	IgG+/IgM−	Positive	96.15%	Negative	Negative	BNT162b2	20
106	IgG+/IgM−	Positive	93.84%	Negative	Negative	BNT162b2	24
107	IgG+/IgM−	Positive	96.79%	Positive	Negative	mRNA-1273	28
108	IgG+/IgM−	Positive	91.57%	Negative	Negative	BNT162b2	22
109	IgG+/IgM−	Positive	97.59%	Negative	Negative	mRNA-1273	22
110	IgG+/IgM−	Positive	96.43%	Negative	Negative	BNT162b2	21
111	IgG+/IgM−	Positive	94.98%	Negative	Negative	BNT162b2	24
112	IgG+/IgM−	Positive	94.17%	Negative	Negative	mRNA-1273	28
113	IgG+/IgM−	Positive	97.18%	Negative	Negative	mRNA-1273	24
114	IgG+/IgM−	Positive	95.56%	Negative	Negative	BNT162b2	21
115	IgG+/IgM−	Positive	93.26%	Negative	Negative	BNT162b2	22
116	IgG+/IgM−	Positive	92.98%	Negative	Negative	BNT162b2	20
117	IgG+/IgM−	Positive	94.69%	Negative	Negative	BNT162b2	22
118	IgG+/IgM−	Positive	92.68%	Negative	Negative	BNT162b2	20
119	IgG+/IgM−	Positive	81.48%	Positive	Negative	BNT162b2	22
120	IgG+/IgM−	Positive	93.02%	Negative	Negative	BNT162b2	22
121	IgG+/IgM−	Positive	95.22%	Negative	Negative	BNT162b2	21
122	IgG+/IgM−	Positive	94.04%	Negative	Negative	BNT162b2	18
123	IgG+/IgM−	Positive	97.32%	Negative	Negative	mRNA-1273	29
124	IgG+/IgM−	Positive	96.55%	Negative	Negative	BNT162b2	20
125	IgG+/IgM−	Positive	97.00%	Negative	Negative	mRNA-1273	29

AB, antibody; CI-ELISA, competitive inhibition ELISA; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
[a] Immunocompromised participant.

ELISA testing. No participant who tested IgG-negative via RightSign was positive on anti-spike IgG CI-ELISA testing. Table 1 shows the IgG/IgM RightSign results and the anti-spike IgG CI-ELISA results. All those testing IgG-positive via the RightSign test kit demonstrated antibody neutralizing capability, including 117 patients (93.6%) who demonstrated greater than 80% inhibition. The ELISA results for IgM and IgG to the nucleocapsid were as follows: two patients (1.6%) had anti-nucleocapsid IgM antibodies and seven patients (5.6%) had anti-nucleocapsid IgG antibodies (Table 1). Cohen's Kappa demonstrated excellent agreement between RightSign IgG results and confirmatory CI-ELISA results (Cohen's Kappa = 1.00). McNemar's Chi-square showed perfect agreement between RightSign and CI-ELISA.

4. Discussion

In this study, we sought to evaluate the use of a rapid qualitative antibody test to screen for a vaccine-mediated SARS-CoV-2 antibody response. It was found that IgG RightSign results correlated directly with confirmatory CI-ELISA testing. Positive IgG serology, 98.4%, was consistent with previous studies investigating the immunogenicity of both vaccines involved in this study. In phase 1 trials of mRNA-1273, Jackson et al. demonstrated IgG titers and a positive neutralization response in all participants (Jackson et al., 2020). Walsh et al. showed in phase 1 trials that, after a second dose of BNT162b2, even older adults demonstrated neutralizing geometric mean titers that were simi-

lar or greater to those found in SARS-CoV-2 convalescent serum (Walsh et al., 2020).

In many countries, HCWs were among the first to be vaccinated, and several larger studies have explored the vaccine-mediated antibody responses in this population. Abu Jabal et al. investigated the antibody response to one dose of BNT162b2 at 21 days post-vaccination in 514 HCWs, and found that 92% had anti-spike IgG antibodies (Jabal et al., 2020) Angyal et al. examined the T-cell and antibody response in 237 HCWs after one and two vaccine doses of BNT162b2, and demonstrated a robust immune response to vaccination; 99% mounted higher anti-spike IgG antibody responses than previously infected unvaccinated individuals (Angyal et al., 2021). However, it appears that there have been no studies examining the SARS-CoV-2 mRNA vaccine-mediated immune response in pediatric HCWs. This population is relatively unique in that, similar to schoolteachers, they are likely to be more frequently exposed to coronaviruses than the general population. This is of particular interest, as Ng et al. demonstrated that samples taken from 21 of 48 children in the age range 1–16 years, with no history of SARS-CoV-2 infection (samples were taken from 2011 to 2018), had detectable levels of IgG antibodies that reacted with the SARS-CoV-2 spike protein, as compared to one of 43 young adults (age range 17–25 years) (Ng et al., 2020).

However, very few participants in this study showed evidence of SARS-CoV-2 anti-nucleocapsid IgM or IgG. There were nine individuals with positive serology for SARS-CoV-2 anti-nucleocapsid antibodies, seven IgG-positive and two IgM-positive, none were IgG-positive/IgM-positive. Given the conserved nature of the nucleocapsid, IgG-positive results may represent historical infection with other coronaviruses or SARS-CoV-2 (despite attempts to exclude individuals with a positive history of COVID-19). It is more difficult to interpret the IgM-positive results, as both participants testing positive for anti-nucleocapsid IgM were negative for anti-spike IgM antibodies on rapid RightSign testing. Although the overall nucleocapsid results correlate with previous work done at this institution using the Abbott Architect IgG anti-nucleocapsid assay prior to vaccination, it is somewhat surprising, as both the spike protein and the nucleocapsid protein appear to be somewhat conserved (Der et al., 2020; Huang et al., 2021). The clinical implications of this finding, especially regarding historical coronavirus infection leading to the potential for an amplified vaccine response in the pediatric HCW population, remain unclear.

A limitation of this study was that pediatric HCWs were not compared to non-pediatric HCWs, which prevented comparison to a population potentially less frequently exposed to coronaviruses. As the percent inhibition was calculated rather than geometric mean titers or geometric mean concentrations, it was also not possible to directly contrast these results to those of previous studies. In addition, the generalizability of the results may be limited due to the small percentage of participants who received the mRNA-1273 vaccine. Future research may also include investigating how the vaccine-mediated immune response changes over time.

In summary, the strong agreement between the RightSign IgG results and confirmatory CI-ELISA testing suggests that this point-of-care test can be used to screen for positive, and neutralizing, antibody responses at 17–36 days post-SARS-CoV-2 mRNA vaccination. This may allow for rapid and relatively inexpensive documentation and monitoring of the individual immune response, including evaluating the need for booster vaccination, as well as aiding in large-scale immune surveillance.

	Author queries
	[Note: The text has undergone minor rephrasing throughout.]
[Au?1]	Abbreviations must be given in full at first use. Please provide abbreviation ACE2 in full. (Angiotensin-converting enzyme 2?)
[Au?2]	"Each assay that is run requires titering of positive and negative controls..." Should this be "the titration"?
[Au?3]	Table 1: Should footnote 'a' also be included here?

Ethical approval

Informed consent was obtained for experimentation on human subjects. This study was approved by the Institutional Review Board.

Conflict of interest

All authors have no conflicts of interest to disclose.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2021.09.065.

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