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.

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Seroconversion after coronavirus disease 2019 vaccination in patients with immune deficiency

Safety and efficacy are 2 major drivers for any vaccination strategy and have come to the forefront in the setting of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination. Patients with underlying primary or secondary immunodeficiencies have variable response to vaccination, but inactivated or nonviable vaccines are generally considered safe in patients with immune deficiency.[1] The efficacy of inactivated vaccines is variable in patients with humoral immune deficiencies, in which many can mount a protective T-cell–dependent antibody response to protein-conjugated vaccines, except for patients with congenital agammaglobulinemia, such as X-linked agammaglobulinemia (XLA), who may lack the ability to mount any antibody response.

The immune response to SARS-CoV-2 infection itself has revealed the interplay between the humoral and cellular adaptative immune systems. Measured response to SARS-CoV-2 infection has revealed a prominent CD4+ T-cell response, which in turn helps induce antibodies against the spike and nucleocapsid proteins of SARS-CoV-2.[2] Similarly, immune response to the messenger RNA (mRNA) COVID-19 vaccines has been found to induce a T-cell and neutralizing antibody response.[3] This presence of anti-nucleocapsid and anti-spike antibodies has been found to be significantly effective in prevention of subsequent reinfection and severe COVID-19 disease.[4,5]

There is currently limited data on the efficacy of SARS-CoV-2 vaccination in patients with immune deficiency. We report our early experience from 11 patients with immune deficiency from our institution evaluating vaccine responses to mRNA SARS-CoV-2 vaccines.

Retrospective chart review was performed as part of an institutional review board–approved study. There were 11 patients with underlying immune deficiency who received an mRNA COVID-19 vaccine, from either Pfizer-BioNTech or Moderna (Table 1) and tolerated it well. Patients were between the ages of 25 and 75 years, of whom 6 of 11 (54.5%) were of male sex. Most patients (6/11) had common variable immunodeficiency, 1 XLA, 1 Wiskott-Aldrich syndrome, 1 DiGeorge syndrome, and 2 hypogammaglobulinemia (isolated low immunoglobulin G levels). In addition, most (8/11) were on supplemental immunoglobulin therapy with intravenous immunoglobulin every 3 to 4 weeks, 1 received subcutaneous immunoglobulin, and 3 were not on any immunoglobulin replacement. Only 2 patients (patient numbers 4 and 11) were receiving additional immunomodulators for associated conditions. Patient number 4 was receiving hydroxychloroquine 200 mg daily for urticarial vasculitis and budesonide 9 mg for enteropathy. Patient number 11 was receiving mycophenolate 750 mg twice daily and belimumab intravenously monthly for diagnosis of systemic lupus erythematous, Sjogren's syndrome, and interstitial nephritis.

Lymphocyte subsets, including CD3+, CD4+, and CD8+ T-cells, CD19+ B-cells, and CD16/56+ natural killer cells, for all patients with common variable immunodeficiency were within normal limits at baseline, except for patient number 5 who had natural killer cell levels below the reference range at 59 cells/mcL (reference, 101-678 cells/mcL). Patient number 7 had no CD19+ B-cells, consistent with his known diagnosis of XLA. The only other patient with abnormal lymphocyte subset levels was patient number 11 who had low CD3+ (537 cells/mcL; reference, 550-2202 cells/mcL), low CD4+ (332 cells/mcL; reference, 365-1437 cells/mcL), low CD19+ (17 cells/mcL; reference, 45-409 cells/mcL), and low CD16/56+ (53 cells/mcL; reference, 59-513 cells/mcL), but normal CD8+ (210 cells/mcL; reference, 80-846 cells/mcL).

The time between completion of the 2 dose COVID-19 vaccine series and assessment of titers ranged from 2 to 10.5 weeks. All but 1 patient (patient number 7 with XLA) had a positive antibody response to the SARS-CoV-2 spike glycoprotein. Of the patients with a positive titer, most (8/10) were measured at greater than 250 U/mL. The lowest positive titer level, 7.8 U/mL, was found in patient number 11 who was receiving immune suppression with mycophenolate 750 mg twice daily and belimumab. Antibody response to the SARS-CoV-2 nucleocapsid was obtained for 8 of 11 patients, all of which were negative, as expected after vaccination and not natural infection.

The safety and efficacy of COVID-19 vaccination in patients with immune deficiency are largely unknown because these subjects were not included in the initial vaccine trials. Although positive anti–SARS-CoV-2 antibodies have been detected in supplemental immunoglobulin therapies,[6] it is unclear if this can provide sufficient protection against COVID-19 at this time. Furthermore, although the precise titer level of SARS-CoV-2 antibodies that should be obtained to be considered "protected" is unknown, it has been projected that immunoglobulin lots could contain similar concentrations of SARS-CoV-2–neutralizing antibodies as the convalescent plasma used in COVID-19 treatment by July 2021.[7] Despite this possibility, the risk of severe COVID-19 illness and related complications indicates that measures that improve and hasten protection from COVID-19 are needed. Our early report of 11 cases presented here reveal that vaccination with an mRNA COVID-19 vaccine is safe and can result in high-level antibody titers in patients with immune deficiency (with the exception of XLA), similar to those reported in health care workers after vaccination.[8] Of note, patient number 11, who was on moderate immune suppression with mycophenolate and belimumab, had the lowest recorded titer at 7.8 U/mL, though still above the threshold of seroconversion (>0.8 U/mL). Transplant patients receiving antimetabolite maintenance therapy have also been found to be less likely to develop antibody response to the first COVID-19 vaccine.[9] Patient number 11 may reveal that patients on maintenance immune suppression mount less robust responses to vaccination. Aside from developing high titer antibodies, cellular response to vaccination is an important aspect of vaccine effectiveness. It has been found that patients with XLA can mount normal dendritic and T-cell responses to

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Table 1
Characteristics and Vaccine Responses of Patients With Immune Deficiency

Patient number	Diagnosis	Demographics	Supplemental immunoglobulin	Immune suppression	Duration between second vaccine dose and serology	SARS-CoV-2 spike Ab (ref, <0.80 U/mL)	SARS-CoV-2 nucleocapsid Ab
1	CVID	M, 69 y	IVIG 40 g every 3 wk	None	2 wk	Positive, >250 U/mL	Negative
2	CVID	F, 59 y	IVIG 35 g every 4 wk	None	4 wk	Positive, >250 U/mL	Negative
3	CVID	F, 67 y	IVIG 30 g every 4 wk	None	4 wk	Positive, >250 U/mL	NA
4	CVID	F, 35 y	IVIG 25 g every 4 wk	Hydroxychloroquine, budesonide	7 wk	Positive, 229 U/mL	Negative
5	CVID	F, 39 y	SCIG 10 g weekly	None	4 wk	Positive, 1553 U/mL	NA
6	CVID	M, 73 y	IVIG 40 g every 3 wk	None	6-8 wk	Positive, >250 U/mL	Negative
7	XLA	M, 44 y	IVIG 30 g every 3 wk	None	6 wk	Negative, <0.40 U/mL	Negative
8	WAS	M, 49 y	IVIG 40 g every 4 wk	None	10.5 wk	Positive, >250 U/mL	Negative
9	DiGeorge syndrome	F, 25 y	None	None	3 wk	Positive, >250 U/mL	NA
10	Hypogammaglobinemia	M, 75 y	None	None	3 wk	Positive, >250 U/mL	Negative
11	Secondary immune deficiency	M, 72 y	None	Mycophenolate, belimumab	2 wk	Positive, 7.8 U/mL	Negative

Abbreviations: Ab, antibody; CVID, common variable immunodeficiency; F, female; IVIG, intravenous immunoglobulin; M, male; NA, not attained; ref, reference; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SCIG, subcutaneous immunoglobulin; WAS, Wiskott-Aldrich syndrome; XLA, X-linked agammaglobulinemia.

influenza vaccination.[10] Therefore, COVID-19 vaccination should be encouraged even in those unlikely to mount significant antibody response.

With natural COVID-19 infection, most patients will develop both anti-spike and anti-nucleocapsid antibodies, but after COVID-19 vaccination only anti-spike antibodies will be produced.[8] The measurement of both antibodies simultaneously can help distinguish between response to natural infection (positive to both antibodies) vs response to vaccination (positive anti-spike antibody and negative anti-nucleocapsid antibody). By measuring both the SARS-CoV-2 spike antibody and the nucleocapsid antibody in most patients reported here, this illustrates response to the vaccine rather than antibodies from immunoglobulin replacement which would be expected to contain both anti-spike and anti-nucleocapsid antibodies at this time owing to only recent initiation of large-scale COVID-19 vaccination. Although larger scale studies are needed, our data support the safety and effectiveness of mRNA COVID-19 vaccination in patients with immune deficiency and should encourage improved vaccine uptake in patients with humoral immunodeficiency.

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Exposure to species of Vespidae in the urbanized areas of New Orleans, Louisiana

The venom of social Hymenoptera is an important trigger for anaphylactic events. Currently available extracts for testing patients with venom allergy were standardized before recent changes in urbanization and introduction of invasive species. Failure to test for all relevant species may be one reason that these tests are unable to identify the cause of wasp venom allergies in some patients.[1] In addition, cross-reactivity between species in the Vespidae (genera *Vespa, Vespula, Dolichovespula, Polistes, Mischocyttarus*) may cause positive test results in patients for whom the primary sensitization was not one of the species tested.[2]

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