

# Allergists Can Safely Evaluate and Revaccinate Individuals With Immediate Allergic Reactions to mRNA COVID-19 Vaccines

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The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is responsible for 45 million infections and 722 000 fatalities in the United States through mid-October 2021 [1]. Despite 3 vaccines that are highly effective in preventing severe coronavirus disease 2019 (COVID-19) outcomes, only 57% of the eligible US population has received at least 1 vaccine dose [2]. While these vaccines are considered safe, there have been concerns regarding allergic reactions, in particular to the Moderna and Pfizer-BioNTech mRNA COVID-19 vaccines. Initial published reports suggested that allergic reactions may occur at ~2.5 (Moderna) and ~11 events (Pfizer-BioNTech) per million vaccinations, rates that exceed historical estimates for vaccine-associated anaphylaxis of 1.3 events per million [3, 4]. Polyethylene

glycol (PEG) in the vaccine is a suspected trigger excipient, though no evidence exists substantiating PEG as an allergen, responsible for these reactions through an IgE-mediated mechanism [5]. Yet, the mRNA vaccines are currently contraindicated in individuals with a history of allergy to PEG or prior severe immediate allergic reactions to mRNA vaccines, have a precaution for individuals with a history of severe allergic reactions to unrelated vaccines/parenteral medications, and are recommended to be withheld in individuals with positive skin tests to PEG. It is unclear how many persons have not completed a complete vaccination series due to these recommendations, nor it is clear how such measures have contributed to vaccine hesitancy. These recommendations deviate from prior vaccine allergy practice statements, which recommend graded dosing administration under allergist supervision in these situations, not withholding the vaccine [5].

So, what can we do for our patients seeking vaccination after an allergic reaction to their first dose? Allergy specialist evaluation, where/when available, can help. Tuong et al. report on 15 patients referred for evaluation after immediate allergic reactions to their first dose of mRNA vaccine, including 1 patient with anaphylaxis requiring epinephrine [6]. Eleven of the patients underwent skin testing to the vaccine excipients and the vaccine, and all underwent a multistep

desensitization irrespective of skin test findings [5]. Among these patients, 13/15 safely received their second dose via a multistep desensitization, including the patient with anaphylaxis to the first dose. Six experienced mild/self-limiting symptoms, 3 of whom received antihistamine treatment for uneventful resolution. Additionally, while 2 patients had a reaction judged by study investigators as severe enough to require epinephrine, occurring on their final step of the desensitization, both were promptly treated and the reactions resolved. Neither of these patients had a severe reaction with their first dose, though 1 had positive intradermal skin testing to the Moderna vaccine (but not to vaccine excipients). Investigators found no overall association between skin test results and vaccination outcome among these patients.

This study has multiple patient implications. First, it demonstrates that with allergist supervision, re-vaccination of individuals with a history of first-dose reactions to the COVID mRNA vaccines can be safely performed. Allergy specialists are well equipped to manage a spectrum of allergic reactions to a vaccine. While revaccination was associated with 6 mild and 2 severe reactions, these were promptly treated, and the patients (who recovered) are now fully vaccinated and can enjoy the benefits of this immunity. A recent meta-analysis noted that the rate of anaphylaxis to mRNA COVID-19 vaccines is 7.91 events per million doses—a

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very rare occurrence, but not an entirely absent one [5]. Allergists routinely manage both mild and severe reactions to common agents such as allergen immunotherapy in the office. All allergists are trained to manage the spectrum of allergic reactions, from mild hives to severe anaphylaxis. There is no reason allergists cannot also manage less frequent events such as a vaccine reaction, including immediate severe reactions, especially when the benefit is increased vaccine efficacy and immunogenicity. While graded or multistep dosing may eventually prove unnecessary, at the moment, it is a reasonable alternative to vaccine deferral if this is the step in a bidirectional process of shared decision-making. Second, the results of this report imply that contraindicating a second dose for persons with a first-dose allergic reaction may be unnecessary, and at the very least the decision to administer subsequent vaccine doses should be a shared decision between patient and allergist. Third, this evidence reinforces a growing consensus that vaccine/excipient skin testing has low utility to identify persons at risk of an allergic reaction to the vaccine and is not necessary. Tuong et al. show discordance between vaccination and skin testing outcomes.

Admittedly, the trade-offs between suboptimal infection immunity through partial vaccination and the risk of an allergic reaction from additional vaccine doses are not ideal. However, the complications of even a severe allergic reaction are entirely (and easily) manageable in the office setting with epinephrine in the great majority of cases. When anaphylaxis risk is compared with the risk for complications of COVID infections

that could result from absent or impartial immunity, an appropriate perspective can be maintained. Fatality from anaphylaxis, including vaccine-associated anaphylaxis, is exceedingly rare; moreover, this is a risk that a well-trained allergist can hedge and should be able to manage, and should be an option for a patient to consider [5]. More data are emerging regarding the outcomes of revaccinating patients with first-dose mRNA COVID-19 vaccine allergic reactions (including immediate severe reactions), showing that there is a low risk of severe reactions on the second dose [7, 8]. Additional data have suggested that skin testing to detect IgE-mediated sensitization to PEG is of low utility [9]. Despite a contraindication to administering a second dose to someone with a history of a first-dose reaction or a reaction to a vaccine excipient, studies such as Tuong et al. and others [7–9] are important to help demonstrate that revaccination with the same vector COVID-19 vaccine can be performed safely, under the supervision of an allergist, with consent and a shared decision-making paradigm of care.

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and has received honoraria for lectures from ImSci and MedLearningGroup. Elissa Abrams is a collaborator with the Institute for Health Metrics and Evaluation. She is an employee of Public Health Agency of Canada (PHAC), but the views expressed are her own and not those of PHAC. Marcus Shaker is a member of the Joint Taskforce on Allergy Practice Parameters; has a family member who is CEO of Altrix Medical; is an associate editor for the *Annals of Allergy, Asthma, and Immunology*; and serves on the editorial boards of the *Journal of Allergy and Clinical Immunology in Practice* and the *Journal of Food Allergy*. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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