



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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

### PEG skin testing for COVID-19 vaccine allergy



To the Editor:

I read with great interest the special article entitled “mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach” by Banerji et al in the *Journal of Allergy and Clinical Immunology: In Practice*.<sup>1</sup>

I would like to ask the authors to justify their recommendation for polyethylene glycol (PEG) skin testing for those patients in the “higher risk” for reaction to vaccine category.

The authors state that they do not recommend skin testing with the vaccine because of “lack of information about sensitivity or specificity (and) unclear safety of skin testing.”

The authors also state that PEG skin testing “could be considered” and “may be of value in shared decision making” in spite of also stating that “there is no confirmation IgE mediated reactions to PEG are responsible for reported reactions to the...COVID-19 vaccines.” Therefore, a skin test could be helpful when positive but does not rule out allergy when negative.

Allergists performing PEG skin testing can therefore be deluding themselves until they stumble across a false negative. If lack of information about sensitivity is a reason not to skin test with the vaccine, why isn't it a reason not to skin test with PEG?

Bryan D. Stone, MD

Mass General Brigham Community Physicians Group.

No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication January 28, 2021; accepted for publication February 12, 2021.

Corresponding author: Bryan D. Stone, MD, Pentucket Medical at Riverwalk, 500 Merrimack St, Lawrence, MA 01843. E-mail: [bstone@pmaonline.com](mailto:bstone@pmaonline.com).

#### REFERENCE

1. Banerji A, Wickner PG, Saff R, Stone CA Jr, Robinson LB, Long AA, et al. mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach. *J Allergy Clin Immunol Pract* 2021;9:1765-6.

<https://doi.org/10.1016/j.jaip.2021.02.016>

### Reply to “PEG skin testing for COVID-19 allergy”



To the Editor:

We would like to thank Dr Bryan Stone for his correspondence<sup>1</sup> to our manuscript “mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach” in the *Journal of Allergy and Clinical Immunology: In Practice*.<sup>2</sup>

Current CDC guidance advises that any individual with an immediate or severe allergic reaction to the mRNA vaccine or any component of the vaccine (eg, polyethylene glycol [PEG] or polysorbate) should speak to an allergist before they receive the vaccine. Before the development of mRNA COVID-19 vaccines, allergy to PEG in addition to PEG cross-reactivity with polysorbate 80 was uncommonly diagnosed in the field of drug

hypersensitivity. However, reports of severe immediate reactions to the mRNA COVID-19 vaccines, clinically compatible with anaphylaxis, have raised public concern. Although the cause of these reactions is not clear, PEG IgE-mediated allergy remains one possibility. There are well-described cases of IgE-mediated allergy to PEG in the literature, and these cases have positive skin testing to PEG.<sup>3,4</sup> PEG is also the only component of the currently available mRNA COVID-19 vaccines with a known nonirritating skin testing concentration reported in the literature.<sup>3</sup> We do not have data on nonirritating skin testing concentrations for the mRNA vaccines themselves. These mRNA vaccines have been released under emergency use authorization and are not licensed products for skin testing. Another factor to consider is that the vaccine remains a scarce and limited resource in contrast to PEG and polysorbate skin testing reagents that are widely available.

Given that there are no FDA-approved mRNA COVID-19 vaccines without PEG, consideration of skin testing with shared decision making offers a viable approach for individuals either with a clinical history suggestive of an IgE-mediated allergy to PEG or a potential anaphylactic reaction to the first dose of the mRNA COVID-19 vaccines (because PEG is the only available testable component). Although negative skin testing when using nonirritating skin testing concentrations does not definitively rule out allergy, a positive skin test is highly suggestive of true allergy. If skin testing is negative, this provides an additional data point that an IgE-mediated allergy was not identified. As such, a non-IgE mechanism, potentially prevented or minimized with premedication such as antihistamines, may have been the reaction mechanism. Negative skin testing can also address allergy fears in less concerning cases, providing visual reassurance for both the patient and provider that it would be reasonable to proceed with vaccination under close observation. Skipping skin testing altogether may miss rare cases of true IgE-mediated allergy especially when considering a group of individuals with a high-risk history. Negative PEG skin testing also is the first step toward providing reassurance that other drugs and products containing PEG will be tolerated. To confirm PEG tolerance, an oral challenge to PEG3350 may also be considered.

Our anecdotal experience in individuals with a history of an immediate reaction to PEG or a derivative to date is reassuring; individuals with negative PEG skin testing have been successfully vaccinated without incident. Similarly, we have evaluated individuals who reacted to the first dose of the mRNA vaccine, had negative PEG skin testing, and subsequently tolerated the mRNA COVID-19 vaccine. Both of these groups otherwise would have been excluded from either initial vaccination or vaccination completion based on CDC guidance.

We would highlight that our algorithm for PEG skin testing, if negative, is followed by a challenge to the vaccine in a closely monitored setting where anaphylaxis can be managed. Currently, the positive and negative predictive value of PEG skin testing for reactions associated to the COVID-19 mRNA vaccines are unknown. We are using skin testing both to ensure that patients potentially allergic to PEG are not unnecessarily excluded from vaccination with the mRNA COVID-19 vaccines and to identify

the only testable IgE culprit in the currently available mRNA COVID-19 vaccines. When allergy testing is negative, we suggest shared decision making between the patient and allergist to proceed with vaccination.

*Aleena Banerji, MD<sup>a,b</sup>*  
*Elizabeth Phillips, MD<sup>c</sup>*  
*Rebecca Saff, MD, PhD<sup>a,b</sup>*  
*Paige G. Wickner, MD, MPH<sup>b,d</sup>*  
*Lacey B. Robinson, MD, MPH<sup>a,b</sup>*  
*Anna R. Wolfson, MD<sup>a,b</sup>*  
*Paul Williams, MD<sup>e</sup>*  
*David A. Khan, MD<sup>f</sup>*  
*Kimberly G. Blumenthal, MD, MSc<sup>a,b,g</sup>*

<sup>a</sup>Division of Rheumatology Allergy and Immunology, Department of Medicine, Massachusetts General Hospital, Boston, Mass

<sup>b</sup>Harvard Medical School, Boston, Mass

<sup>c</sup>Department of Medicine, Vanderbilt University Medical Center, Nashville, Tenn

<sup>d</sup>Division of Allergy and Immunology, Department of Medicine, Brigham and Women's Hospital, Boston, Mass

<sup>e</sup>Allergy Division, University of Washington School of Medicine, Seattle, WA

<sup>f</sup>Department of Internal Medicine, Division of Allergy & Immunology, University of Texas Southwestern Medical Center, Dallas, Texas

<sup>g</sup>Edward P. Lawrence Center for Quality and Safety, Massachusetts General Hospital, Boston, Mass.

No funding was received for this work.

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication February 11, 2021; accepted for publication February 12, 2021.

Corresponding author: Aleena Banerji, MD, MGH, Cox 201, 100 Blossom Street, Boston, MA 02114. E-mail: [abanerji@mgh.harvard.edu](mailto:abanerji@mgh.harvard.edu).

## REFERENCES

1. Stone B. PEG skin testing for COVID-19 Allergy. *J Allergy Clin Immunol Pract* 2021.
2. Banerji A, Wickner PG, Saff R, Stone CA Jr, Robinson LB, Long AA, et al. mRNA vaccines to prevent COVID-19 disease and reported allergic reactions: current evidence and suggested approach. *J Allergy Clin Immunol Pract* 2021;9:1765-6.
3. Stone CA Jr, Liu Y, Relling MV, Krantz MS, Pratt AL, Abreo A, et al. Immediate hypersensitivity to polyethylene glycols and polysorbates: more common than we have recognized. *J Allergy Clin Immunol Pract* 2019;7:1533-40.e8.
4. Wenande E, Garvey LH. Immediate-type hypersensitivity to polyethylene glycols: a review. *Clin Exp Allergy* 2016;46:907-22.

<https://doi.org/10.1016/j.jaip.2021.02.015>