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11-2022

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#### Recommended Citation

Pitt J, Shopper C, Dowling P, Miller C, Sherman A, Aljubran S. Current practices in delaying testing for IGE-mediated food allergy after anaphylaxis. *Journal of Allergy and Clinical Immunology: Global*. 2022;1(4):312-313. doi:10.1016/j.jacig.2022.05.010

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# Current practices in delaying testing for IgE-mediated food allergy after anaphylaxis



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**Background:** General recommendations for delaying allergy testing, especially skin testing, in the weeks following anaphylaxis have been proposed owing to concern for false-negative results. However, no specific guidelines exist to aid clinicians in the decision regarding when to perform postanaphylactic food allergy testing and which test to use. The current practices of allergists regarding a delay in testing for food allergy after anaphylaxis are unknown.

**Objective:** We aimed to quantify the use of different approaches to postanaphylactic food allergy testing among allergists across the United States.

**Methods:** A clinical scenario was presented to 82 allergy and immunology fellowship program directors via e-mail survey. They were asked whether they avoid skin prick and/or blood-specific IgE testing in a child in the 6 weeks following suspected food-induced anaphylaxis owing to concern for false-negative results.

**Results:** The survey response rate was 33%. Of the 27 respondents, 4 (14.8%) avoid both blood and skin testing, 7 (25.9%) avoid skin testing only, and 16 (59.3%) do not avoid any testing.

**Conclusion:** Given the paucity of published evidence, a spectrum of opinions exists regarding testing in the weeks following food-induced anaphylaxis. About 40% of the allergy and immunology fellowship program directors in the United States who responded to the survey in this study avoid some allergy testing in the first 6 weeks after food-induced anaphylaxis owing to concern for false-negative results. (*J Allergy Clin Immunol Global* 2022;1:312-3.)

**Key words:** Food hypersensitivity, anaphylaxis, skin tests, diagnosis

## Abbreviation used

PAMA: Postanaphylaxis mast cell anergy

to by many names, including refractory period, empty mast cell syndrome, tachyphylaxis, and postanaphylaxis mast cell anergy (PAMA). PAMA has been proposed to involve transient depletion of mast cell mediators and diminished mast cell sensitivity following an anaphylactic reaction.<sup>1</sup> This does not, however, provide an explanation for decreased levels of specific IgE in the blood. This phenomenon has been described in only scant case reports and studies with very small sample sizes.<sup>2-4</sup> These studies have been conducted primarily in Hymenoptera-induced and perioperative drug-induced anaphylaxis. In 1 important study, about 43% of the results of skin prick tests and 25% of specific IgE tests were negative in the week following anaphylaxis due to Hymenoptera.<sup>2</sup> As a result, there are guidelines to delay allergy testing after Hymenoptera- and drug-induced anaphylaxis. There are also general recommendations to consider delaying allergy testing after anaphylaxis, regardless of the cause.<sup>5</sup> The timing of these recommendations varies, and whether they should apply to food-induced anaphylaxis is not known. The European Academy of Allergy and Clinical Immunology guidelines recommend performing skin tests at least 2 weeks after Hymenoptera-induced anaphylaxis. The guidelines further recommend that if the results of the testing are negative but clinical suspicion is high, the testing should be repeated after 6 to 8 weeks.<sup>6</sup> Regarding anaphylaxis during general anesthesia, however, the British Society for Allergy and Clinical Immunology guidelines recommend a different approach. They recommend that allergy testing be performed once the patient has been stabilized but also call for clinicians to remain scrupulous and retest at a later date if the initial test results are negative and suspicion is high.<sup>7</sup> The National Institute of Allergy and Infectious Disease guidelines for the diagnosis of food allergy discuss skin prick and blood-specific IgE testing but do not comment on whether to wait a certain number of weeks after anaphylaxis or whether testing can be performed when the patient is first referred.<sup>8</sup>

The primary objective of this study was to assess the variations in current practices of US allergists regarding a delay in postanaphylactic food allergy testing. Allergy and immunology fellowship program directors were chosen as a representative group because they are considered thought leaders who are training the next generation of allergists and they are a cohort with publicly available e-mail addresses. Given the lack of published data specific to testing after food-induced anaphylaxis, our survey questioned whether these thought leaders extrapolated observations regarding non-food-induced anaphylaxis to also apply to anaphylaxis induced by food. The survey also helps raise the question of whether this is a valid extrapolation.

## INTRODUCTION

False-negative results of skin prick and/or blood-specific IgE allergy testing occur in some individuals in the weeks following some anaphylactic reactions. This phenomenon has been referred

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Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication March 10, 2022; revised May 14, 2022; accepted for publication May 22, 2022.

Available online August 12, 2022.

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2772-8293

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<https://doi.org/10.1016/j.jacig.2022.05.010>

**TABLE I.** Ages of the respondents

Age (y)	No. (%)
<30	0 (0%)
30-39	6 (22.2%)
40-49	13 (48.1%)
50-59	6 (22.2%)
≥60	2 (7.4%)

## RESULTS AND DISCUSSION

Of the 82 program directors who were e-mailed, 27 responded (a 33% response rate). Most of the respondents were in the 40- to 49-years age group (Table I). We found that about 40% of respondents (95% CI = 22.2%-59.3%) avoided *some* type of testing during the 6 weeks following food-induced anaphylaxis. Specifically, 4 of 27 respondents (14.8%) avoid both blood and skin testing, 7 of 27 (25.9%) avoid skin testing only, and 16 of 27 (59.3%) do not avoid either blood or skin testing in the 6 weeks following anaphylaxis due to food allergy (Table II).

Although PAMA is not a new concept, many questions remain regarding its precise pathophysiology and which other factors may result in false-negative results of skin prick and/or blood-specific IgE testing early after anaphylaxis. These early false-negative testing results have been documented primarily in Hymenoptera-induced and perioperative drug-induced anaphylaxis, so the extent to which it occurs with food-induced anaphylaxis is unknown. Some evidence suggests that tryptase levels may not be as elevated in food-induced anaphylaxis as with other causes of anaphylaxis.<sup>9</sup> Lower tryptase levels may indicate less mast cell degranulation. There is also evidence that food-induced allergic reactions may induce a basophil-predominant response.<sup>10</sup> This too could result in decreased mast cell degranulation. These factors suggest that the results of the available skin prick testing may be less affected by PAMA. However, other evidence suggests that tryptase levels are similarly elevated in food-induced anaphylaxis and anaphylaxis due to other causes, so this remains unclear.<sup>11</sup> PAMA also does not explain why the results of blood-specific IgE testing may be falsely negative. A second mechanism that results in depletion of allergen-specific IgE must also exist, although there are no known published studies examining this mechanism. Further research is needed to investigate this process.

This survey was vulnerable to selection bias, including age bias. Although the response rate was similar to that for other published surveys, the total number of respondents remains small given the small number of allergy fellowship program directors compared with the number of practicing allergists. There is also a lack of scientific evidence to inform clinical decision making. These limitations prevent widespread generalization of the survey results. However, these data do suggest differences in clinical practice and teaching across allergy and immunology fellowships in the United States. With more than 40% of the program directors surveyed stating that they avoid some type of food allergy testing in the 6 weeks following anaphylaxis, the concept of PAMA is likely to permeate current allergy fellows and influence their diagnostic evaluations in the future.

**TABLE II.** Practices of the respondents

Practice	No. (%)	95% CI
Avoid neither bloods nor skin tests	16 (59.3%)	40.7%-77.8%
Avoid blood tests only	0 (0%)	N/A
Avoid skin tests only	7 (25.9%)	9.4%-42.5%
Avoid both blood tests and skin tests	4 (14.8%)	1.4%-28.2%

N/A, Not applicable.

We conclude that the decision regarding whether to test a patient in the weeks following food-induced anaphylaxis and which test to use is highly variable among allergy fellowship program directors. A review of the literature suggests that we do not know whether extrapolation of data regarding false-negative testing results after anaphylaxis due to other agents should be applied to food-induced anaphylaxis. Given the spectrum of opinions and paucity of published evidence, further studies are needed to examine the rate of false-negative results of skin prick and blood-specific IgE testing in the weeks following food-induced anaphylaxis. This may serve to guide the development of clinical guidelines and consensus for the timing of post-anaphylaxis food allergy diagnostic testing.

**Clinical implications: There is limited information regarding the rate of false-negative test results in the 6 weeks following food-induced anaphylaxis. Current practices of allergists regarding whether to test during this time vary.**

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