

# Using oral food challenges to provide clarity and confidence when diagnosing food allergies

Justin Greiwe, M.D.<sup>1,2</sup>

## ABSTRACT

*A verified food allergy can be an impactful life event that leads to increased anxiety and measurable effects on quality of life. Allergists play a key role in framing this discussion and can help alleviate underlying fears by promoting confidence and clarifying safety concerns. Correctly diagnosing a patient with an immunoglobulin E (IgE) mediated food allergy remains a nuanced process fraught with the potential for error and confusion. This is especially true in situations in which the clinical history is not classic, and allergists rely too heavily on food allergy testing to provide a confirmatory diagnosis. A comprehensive medical history is critical in the diagnosis of food allergy and should be used to determine subsequent testing and interpretation of the results. Oral food challenge (OFC) is a critical procedure to identify patients with an IgE-mediated food allergy when the history and testing are not specific enough to confirm the diagnosis and can be a powerful teaching tool regardless of outcome. Although the safety and feasibility of performing OFC in a busy allergy office have always been a concern, in the hands of an experienced and trained provider, OFC is a safe and reliable procedure for patients of any age. With food allergy rates increasing and analysis of recent data that suggests that allergists across the United States are not providing this resource consistently to their patients, more emphasis needs to be placed on food challenge education and hands-on experience. The demand for OFCs will only continue to increase, especially with the growing popularity of oral immunotherapy programs; therefore, it is essential that allergists become familiar with the merits and limitations of current testing modalities and open their doors to using OFCs in the office.*

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**N**avigating the world of food allergies can be confusing and frustrating for patients, caregivers, and health care providers alike because there is no standardized approach for diagnosing this condition. Food allergy reactions and food allergy testing are commonly misinterpreted or misdiagnosed. This often takes the form of equating a positive test result by using a serum food specific immunoglobulin E (sIgE) blood test or skin-prick test (SPT) to having an allergy. These tests detect IgE antibodies to foods but are not typically intrinsically diagnostic and are not predictive of reaction severity.<sup>1,2</sup> Conditions that mimic allergic reactions such as acute urticaria, atopic dermatitis,

irritable bowel syndrome, lactose intolerance, or gluten sensitivity can further confuse the clinical picture.

Testing and treatment plans can vary drastically, depending on the specialist being seen, and can include nonstandardized and unproven procedures such as food sIgG testing, applied kinesiology, and electrodermal testing. Misinformation from online forums and food allergy Web sites as well as drastic practice variations within the allergy community send mixed messages to parents and patients, and has likely led to an overinflation of the actual rates of IgE-mediated food allergies within the United States.<sup>3–5</sup> To provide more accurate information, allergists need to provide thoughtful, up-to-date, evidence-based guidance that relies less heavily on skin and serum sIgE testing and more on a good medical history and clarification with oral food challenges (OFC). A patient's medical history should hold just as much credence as the laboratory and skin findings and these tests should not be interpreted as an absolute indication or contraindication for conducting an OFC.

OFCs are an indispensable tool for accurately diagnosing clinically relevant food allergy with ingestion of meal-sized portions of the concerning food. There are many reasons to perform OFCs, the most obvious being to help identify the food that caused the initial allergic reaction. Other reasons to pursue OFCs include monitoring for resolution of a food allergy, updating the status of a food allergy, relieving parental or patient

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From the <sup>1</sup>Bernstein Allergy Group, Inc, Cincinnati, Ohio, and <sup>2</sup>Division of Immunology/Allergy Section, Department of Internal Medicine, The University of Cincinnati College of Medicine, Cincinnati, Ohio

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Address correspondence to Justin Greiwe, M.D., Bernstein Allergy Group, 8444 Winton Rd, Cincinnati, OH 45231

E-mail address: jcgreiwe@gmail.com

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anxiety,<sup>6,7</sup> determining if a patient is a candidate for oral immunotherapy (OIT), and assessing the status of tolerance to cross-reactive foods (*i.e.*, tree nuts in peanut allergy or non-crustacean shellfish (mollusks) in crustacean shellfish allergy).<sup>8</sup> Although double-blind placebo controlled OFCs are ideal, open (nonblinded) challenges remain the method of choice in most offices due to practicality and time limitations.

Regrettably, OFCs are generally underused in clinical practice, as described in a recent workgroup report,<sup>9</sup> despite being considered the criterion standard for diagnosing food allergies. The most common barriers to providing OFCs in the office reported by allergists seem to be mainly logistical concerns and include a lack of time, lack of staff, and lack of office space. Other barriers include apprehensions over reimbursement or risk of adverse events.<sup>9,10</sup> Interestingly, most respondents (~63%) performed only  $\leq 5$  OFCs per month. Although safety remained a top priority among allergists who offer OFCs, only 60% reported having a standardized protocol for stopping challenges and treating reactions, and only 56% had emergency medicine ready and available should a reaction occur. Based on the data collected by the survey in the workgroup report,<sup>9</sup> a lack of training and experience continues to be a major issue that prevents widespread utilization of OFCs in the office. There is a definite hesitancy in challenging infants specifically and a concern by the investigator that obtaining written consent before OFC is not universal, especially given the recent fatality in 2017.<sup>11,12</sup>

More targeted efforts are recommended, including expanding OFC fellowship training opportunities, observing higher risk challenges and concerted efforts to increase comfort among allergists performing challenges, especially in infants. This could take the form of more focused OFC education on the infant population through the American Academy of Allergy, Asthma & Immunology (AAAAI) Practice Management Workshop or other educational workshops offered by the AAAAI or American College of Allergy, Asthma & Immunology (ACAAI) annual meetings. OFCs are not prudent or necessary if the patient has a convincing history of clinical reactivity and positive sIgE testing result. In most clinical scenarios, OFCs should be recommended when there is, at the very least, a 50% likelihood that the food challenged will be tolerated based on available data and clinical history.

SPT and serum sIgE testing seem to be sensitive, although not specific for diagnosing food allergies. For example, SPT to foods have a high negative predictive value (>95%) but an overall positive predictive value of only ~50%.<sup>13</sup> A negative SPT effectively confirms the absence of an IgE-mediated process; however, food allergy cases are rarely that simple. Many patients come to the office with positive testing but no clinical

history of ingestion or reaction (*i.e.*, broad panel food testing in patients with moderate or severe atopic dermatitis or acute or chronic urticaria). These panel tests are inappropriate for a food allergy evaluation and are not recommended. More confusing still are patients who have low or undetectable values on skin and/or serum sIgE testing and still have a clinical reaction on exposure to the concerning food. To add another layer of complexity, some patients have negative SPT results but positive serum testing results or vice versa.

When interpreting food allergy testing, some practitioners rely too heavily on results of skin and serum sIgE testing when deciding which patients should undergo an OFC. Perry *et al.*<sup>13</sup> provide a useful real-life example of how the clinical history can affect OFC results. In this study, two groups were analyzed: group 1 had a clear history of a previous reaction to peanut, whereas group 2 had an unclear history or a positive test response only. For group 1, the trend for increasing failure rate with an increasing peanut sIgE level was statistically significant ( $p < 0.01$ ), with 76% of patients passing challenge with an IgE level of  $< 0.35$  kUA/L and none passing with a level of  $> 5$  kUA/L.<sup>13</sup> For group 2, 88% of patients passed with a negative peanut sIgE level of  $< 0.35$  kUA/L, whereas 77% passed with a level of  $> 5$  kUA/L.<sup>13</sup> For those included in this study who were avoiding peanut without a history of clinical reactivity, it is apparent that, even with positive testing, a large proportion of these patients passed an OFC. It is also important to recognize that even a sIgE level less than the limit of detection does not guarantee a successful challenge outcome, with approximately one-third of challenges in such patients failing in this study.<sup>13</sup>

A larger SPT wheal size ( $> 8$  mm) or higher food sIgE levels are associated with persistent food allergy but exceptions to the rule occur. Positive and negative predictive value diagnostic cutoffs have been devised based on sIgE to common food allergens; however, these values can vary widely, depending on the study, specific food, and population being examined.<sup>14</sup> Different factors can affect the accuracy of a given food allergy test result and need to be considered when interpreting results. Factors that modulate the interpretation of allergy test results can include a history of an immediate reaction to the tested food, the patient's age, ethnicity, atopic status, and geographic location.<sup>15</sup> Consequently, all these elements need to be considered when deciphering allergy test results and should compel the clinician to avoid viewing SPT or serum sIgE values in isolation.

Ultimately, current testing modalities are inadequate and often unreliable, which leads to the apprehension that currently exists in our field about offering OFCs. Experience and clinical judgment still play a major role in the management of food allergies

and whether OFCs are offered. There are several factors that can influence the decision to move forward with an OFC and can include something as straightforward as a history of a serious and/or recent allergic reaction or can be purely practical, such as not having enough time, staff, or office space to complete the procedure. Patient preferences and the importance of the concerning food culturally and nutritionally should also be considered when weighing risks and benefits of OFC. The rate of change of SPT or food sIgE levels over time can help predict the likelihood that a food allergy has resolved. For example, if a patient currently has a low level of food sIgE and experienced a > 50% decline within the past year, it would suggest that this patient would have a higher likelihood of passing an OFC.<sup>15</sup>

With the development of better diagnostic tools, the goal is to simplify the decision-making process and provide patients and clinicians with more accurate data on which to determine if OFC is necessary. The sIgE value to allergen components has been an encouraging step toward improving the accuracy of food allergy diagnostics, particularly for peanut, in which Ara h2 is a strong predictor of disease. High IgE levels to Gal d1 (ovomucoid) and Bos d8 (casein) are associated with more persistent allergy as well and result in increased reactivity to both heated and concentrated forms of egg and milk.

More recently, basophil activation testing is growing in popularity and is being used by some specialist centers to guide diagnostic and treatment decisions, especially in cases in which the history, SPT, and/or sIgE level are not definitive or if OIT is being considered. Although not widely commercially available at this time, basophil activation testing is considered to have better specificity and analogous sensitivity when compared with skin and serum sIgE testing, and can be used as a “virtual food challenge” to help reduce the number of OFCs required for an accurate diagnosis.<sup>16</sup> It can also help to discriminate between allergy and tolerance, determine resolution of a food allergy, and allow for monitoring of immunotherapy.<sup>16</sup> Other testing methods that are being investigated in the research setting include allergen-specific to total IgE ratios, allergen-specific IgG4 to IgE ratios, IgE to allergen peptides, and T-cell assays.<sup>15</sup>

Experiencing or witnessing an anaphylactic reaction to a food can be a traumatic experience for both the patient and his or her caregivers.<sup>17,18</sup> The fact that anaphylaxis can be life threatening, unpredictable, and occur with the common act of sharing a meal can place a heavy burden on those affected and their families. Patients and parents often feel as though they are on high alert, and this constant vigilance can take its toll both socially and psychologically.<sup>19–22</sup> Some parents are unwilling to allow their child with food

allergy to attend sleepovers, social events, school trips, or parties because of they are unable to control the environment and are concerned about accidental exposures. Unfortunately, this fear can be extensive, touching all members of the family and fostering an environment of anxiety and social isolation, especially in adolescents.<sup>23</sup>

There are many myths about the mechanism of how food allergies may induce an allergic reaction, and both caregivers and patients can often exaggerate the level of risk faced by their food allergy.<sup>24,25</sup> Although anaphylaxis can be life threatening and should be taken seriously, fatalities are a rare occurrence.<sup>26</sup> Parental anxiety can be curbed by better education and guidance from an allergist who provides high-quality and reliable information.<sup>27</sup> With a better understanding of the symptoms of anaphylaxis, the risks involved, and how to use appropriate treatment, those affected by food allergies can take back control and feel confident that they will be able to handle any situation that could arise in the future.

Patients and their parents can leave the office after a food allergy diagnosis with mixed emotions, ranging from relief to a sense of hopelessness. Their mindset, whether positive or negative, can often be influenced by the treating allergist messaging when framing the food allergy discussion. Fear-based appeals are a common approach used by health care providers to dissuade unhealthy behaviors and motivate positive behavioral changes. This approach is popular because it is assumed fear is a powerful motivator for change; however, this assumption is misguided. In fact, analysis of research results suggests using fear-based appeals to motivate long-term behavior change may cause harm, which leads to increased feelings of anxiety, incompetence, and negativity toward health care providers.<sup>28,29</sup>

Alternative communication methods that work to increase patient self-efficacy are more involved and difficult to implement in a busy practice because they take time and effort to cultivate. Motivational interviewing is a perfect example of an approach that builds self-confidence and encourages patients to be active rather than passive participants in their health care.<sup>30</sup> In this model, the physician is encouraged to act as a partner and support network rather than as an authoritarian and alarmist, with the goal of encouraging autonomy. The standard approach to a new food allergy diagnosis would be to have a serious talk about consequences: “You have a peanut allergy; if you don’t take this seriously and strictly avoid all nuts moving forward you might have a serious reaction and die.” Although this approach will undoubtedly grab the family’s attention, it will likely fail to motivate compliance and might even backfire and lead to increased anxiety, denial, or hopelessness.

A more effective approach might be to say, “Having food allergies means you are at a high risk for a reaction if you were to be exposed, but there are a lot of things you can do to avoid a reaction or even prevent it—like reading food labels, having a food allergy action plan, carrying an epinephrine autoinjector with you at all times, and learning more about OIT. If you are interested, I’m going to give you some recommendations for online educational resources as well as food allergy support groups that can help you navigate your new diagnosis.” Providing the patient with a direct referral to reliable Web sites and vetted support groups that have positive messaging can be life changing. It has been my experience that feeling connected to others, sharing experiences, and meeting other families who are in the same situation can be incredibly impactful. The goal with this approach is to empower parents and patients with the confidence and knowledge they need to meet any challenge, instilling a healthy respect for food reactions without crippling them with fear.

One of the biggest concerns for parents and patients when coming in for OFC is the risk of a reaction. This trepidation can affect the allergist as well, especially when it comes to infant challenges because they are nonverbal and more difficult to objectively monitor.<sup>9</sup> Despite perceived concerns, analysis of the data suggests OFCs, including infant OFCs, are both safe and practical in a clinical setting.<sup>12</sup> It is important to keep in mind that, with increased utilization of OFCs as a diagnostic tool, in-office reactions are inevitable. Providing a detailed synopsis of the challenge procedure and possible outcomes can help alleviate most worries before the first dose is ingested. If a systemic response does occur, it is important for the allergist to take advantage of this opportunity to provide real-time feedback and serve as an example of how to handle an allergic reaction efficiently and with composure.

The priority is timely administration of epinephrine and stabilization of the patient, but, if deemed appropriate, it can be beneficial to allow the patient or the parent to administer the autoinjector him- or herself. Providing this opportunity offers valuable real-world experience and instills confidence in the family’s ability to provide self-care outside the office. While epinephrine is being administered, the treating allergist should have the patient pay attention to how it is given and if the shot is painful. Kids are frequently surprised how easy and painless the injection is, especially if this is their first experience with emergency treatment. Time should be spent after the reaction discussing how quickly symptoms responded to treatment and how to recognize the signs of anaphylaxis for future reference. It is important to remember that, regardless of the OFC outcome, results of studies showed improved quality-of-life scores for those who underwent OFCs, which

highlighted that there is perhaps more value to a failed challenge than previously perceived.<sup>6,7</sup> This experience can be a unique opportunity for impactful real-world education and, if handled correctly, can provide parents and patients with much needed confidence for treating allergic reactions in the future.

Although it seems obvious that a failed challenge can be used as a teaching point, a passed challenge has educational value as well and can be used as an opportunity for counseling and dietary guidance. Failing to address the next steps after a passed challenge can lead to continued avoidance of the challenged food that has been linked to recurrence of food allergy.<sup>31–33</sup> Based on previous studies, ~25–30% of patients who were previously allergic continued a food avoidance diet despite a negative challenge, with peanuts and tree nuts being the most common culprits. There are several reasons for not consuming a food regularly after a passed challenge and can include aversion to taste, fear of subsequent reactions, and the food that was not previously a routine part of the family’s diet. Given this concerning pattern of behavior, it is very important to address any potential barriers to continued inclusion in the diet at the end of the OFC visit. Patients who successfully tolerate food challenge should be instructed to keep the food in their diet regularly to maintain tolerance. Although there are no standardized protocols for regular ingestion, the typical approach involves eating the challenged food approximately three times a week to maintain tolerance.

## CONCLUSION

The benefits of offering OFCs in the office can have long-lasting positive effects on parents, patients, and allergists alike, irrespective of the challenge outcome. Providing this service will help meet the increasing demand for OFCs as advances in food allergy research, treatment, and diagnostics continue to evolve and improve. Expert panels have developed clinical guidelines through institutions, *e.g.*, the National Institute of Allergy and Infectious Diseases,<sup>34</sup> to address the prevention of food allergies, *e.g.*, peanut. The success of initiatives such as this as well as emerging therapies, *e.g.*, OIT, are predicated on both access and willingness to perform OFCs in allergists’ offices across the country. With the establishment of multiple new food allergy centers across the United States, implementation of early introduction guidelines<sup>34</sup> that involve OFCs for infants at high risk and advances in OIT, the demand for OFCs will only continue to increase. Although OFCs can improve quality of life, clarify unnecessary dietary restrictions, and alleviate fear and anxiety, much still needs to be done about the accuracy of diagnostic testing and how the information

provided by these tests can be combined with the clinical history to more precisely identify optimal candidates for challenges.

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