

# Atopic dermatitis and food allergy: To Test or not to test

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## ABSTRACT

*One of the most challenging clinical scenarios in the field of allergy and immunology is the patient with uncontrolled atopic dermatitis (AD) and potential food allergy. These two diagnoses often coexist, but false-positive testing to foods is also prevalent. Physicians and other health care professionals may be concerned that not testing enough foods could lead to worsened AD severity or future systemic food reactions. However, testing too many foods can cause unnecessary food avoidance with varied subsequent consequences. Adding to this dilemma, patients and families with AD often request food allergy testing or present with test results in need of interpretation. The best path forward for these patients is nuanced, but evidenced-based medicine indicates that “less is more” when it comes to food allergy testing in patients with AD. This review explores when food testing is indicated based on the latest research and guidelines in food allergy and AD.*

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Managing atopic dermatitis (AD) can be exceedingly challenging in patients who are highly atopic, especially those with a real or potential concomitant, immunoglobulin E (IgE)-mediated food allergy. AD and food allergy and/or sensitization often coexist, and the prevalence of both is increasing over time.<sup>1,2</sup> According to the dual allergen exposure hypothesis, cutaneous exposure *via* a disrupted epidermal barrier leads to food allergy development. In contrast, oral intake in larger quantities may be protective.<sup>1</sup> Based on this theory, patients with AD are more likely to be allergic to foods. Indeed, infants with severe eczema are at the highest risk for developing food allergies according to a joint North American guideline.<sup>3</sup> Patients with difficult-to-manage AD usually have other markers of atopy, including a high total IgE level, some of which are likely to target foods. However, it is vital to differentiate sensitization (positive test result) from true allergy (immediate, IgE-mediated symptoms with ingestion) in this patient population. A false-positive food allergy testing is not

without potential harms. Therefore, it is of upmost importance to determine which patients with AD need testing and to which foods.

The first steps in managing moderate-to-severe AD are optimizing the skin care and medication regimens. This includes plentiful use of emollients and moisturizers, limitation of environmental triggers if applicable, and utilization of topical therapies. These steps should be accomplished before considering extensive food allergy testing or avoidance diets in patients without a history of immediate food reactions.<sup>1</sup> Some patients and families are hesitant to use topical corticosteroids, and, although these are generally safe and effective, other treatments are available, including topical crisaborole (approved  $\geq$  3 months of age), topical calcineurin inhibitors (approved  $\geq$  2 years of age), and topical ruxolitinib (approved  $\geq$  12 years of age). In more-severe cases, systemic therapies, such as oral Janus kinase inhibitors (approved  $\geq$  12 years of age), dupilumab (approved  $\geq$  6 months of age), and tralokinumab (approved  $\geq$  18 years of age), can be considered.<sup>4</sup> Because food sensitization is believed to be induced by cutaneous exposure, there is interest in preventing the development of food allergy through early or prophylactic use of topical emollients or corticosteroids. Studies examining this have so far been mixed. More studies are needed to determine which patients may benefit from this approach.<sup>1,5</sup>

If a patient has symptoms consistent with IgE-mediated food allergy, skin-prick or *in vitro* specific IgE testing for the inciting food is recommended. However, when patients or families are concerned that AD may be “worsened by” foods, particularly when they cannot identify causative food(s), which foods to test, if any, becomes less clear. Patients and families also request testing to foods that have never been ingested, concerned over the potential for future systemic reactions.

Guidelines for food allergy testing in patients with AD, especially in the United States, have changed over

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time, which contributes to differences of opinion among health care professionals and confusion among patients (Table 1). As an example, a problem-based learning session at the 2023 Eastern Food Allergy and Comorbidity Conference (January 5–8, 2023, Palm Beach, FL) that discussed a child with AD and possible food allergies prompted multiple different testing strategies by the participants. In 2010, a National Institute of Allergy and Infectious Diseases Expert Panel<sup>6</sup> recommended consideration of testing for specific foods (milk, egg, peanut, wheat, and soy) in children < 5 years of age with AD that remains uncontrolled despite adequate therapy. In 2017, after the results of the Learning Early About Peanut Allergy study,<sup>7</sup> the National Institute of Allergy and Infectious Diseases added their guidelines to recommend peanut testing before introduction in infants with severe AD or egg allergy or both.<sup>8</sup> However, preemptive testing for peanut is not recommended in other nations, including Australia, Canada, and the United Kingdom.<sup>3</sup> In 2022, the American Academy of Allergy, Asthma & Immunology Allergic Skin Diseases Committee and Leadership Institute Project issued a work group report that recommended shared decision-making after optimal skin care and medication management of AD.<sup>1</sup> These guidelines go on to warn that indiscriminate food allergy testing and false-positive results can misguide patients and health care professionals. Harms of this testing strategy include increased anxiety, development of nutritional deficiencies due to avoidance diets, and progression to new IgE-mediated food reactions from previous sensitization only.<sup>1</sup> In Europe, a 2021 algorithm proposed by the European Academy of Allergy & Clinical Immunology Task Force on Food Allergy in Children with AD used similar wording to the 2010 National Institute of Allergy and Infectious Diseases guidelines,<sup>9</sup> stating that selective food allergy testing should be considered in children < 6 years of age with moderate-to-severe AD that is persistent or does not respond to therapy, or if the child is not regularly consuming common food allergens. These guidelines primarily discuss food allergy testing in young children with AD because foods seem to play a very small role in adolescent and adult AD disease severity.<sup>10</sup> In addition to this progression of recommendations over time, the definition of severe or uncontrolled AD varies among guidelines. Clinician opinions about AD severity can also vary, further obscuring the best testing strategy in these patients.

Patients and their families are often concerned that underlying food allergies or sensitivities could be contributing to the progression and severity of the AD. Skin-prick or *in vitro* specific IgE testing is commonly requested and, if done, often results “positive” to multiple foods. Allergists may feel pressured by patients and families to perform food allergy testing, even if this is

not in the patient’s best interest. The guidelines<sup>1,8,9</sup> referenced above are moving away from extensive food allergy testing, in part because the harms of this approach are becoming more well described. In patients with AD and no history of food allergy, 19% developed a new systemic food reaction after adhering to an avoidance diet based on positive testing results. Of these new reactions, 18% occurred to foods that were previously being ingested without restrictions.<sup>11</sup> Another study showed a 13.3% oral food challenge failure rate to previously tolerated foods in children with AD when following avoidance diets based on allergy testing.<sup>12</sup> By avoiding foods based solely on positive allergy testing results, it is possible to cause the real harm of developing a new clinical food allergy from a sensitization.

Families of infants and small children with AD may also be hesitant to introduce new foods due to concern over a potential reaction. Because patients with AD are at higher risk for food allergy, this seems like a valid concern. However, The Canadian Pediatric Society recommends counseling families that the risk of a severe reaction on the first exposure to a food allergen is “extremely low.”<sup>13</sup> No fatalities have been reported after the first exposure to a food allergen in infants.<sup>14</sup> In the pivotal LEAP study,<sup>7</sup> no anaphylaxis occurred in the early introduction arm.<sup>3</sup> Allergic reactions to foods in young children are milder than in older children, so delaying the introduction of foods based on allergy testing is often unnecessary and possibly harmful.<sup>3,14,15</sup> British<sup>16</sup> and joint North American guidelines<sup>3</sup> recommend against delaying the introduction of peanut, egg, and possibly other allergens past 6 to 12 months in patients at higher risk, including those with more severe AD, due to potential harms. Some allergists use food allergy testing as a means to decide the best location to introduce a new food (at home versus in the office), but an in-office food challenge can be expensive and difficult to coordinate for patients and families. If a family states they will not try a new food at home due to anxiety, a supervised feeding in the office, which is generally less time intensive than a structured oral challenge, is an option with or without previous testing.

It is the perception of some clinicians that avoidance diets based on food testing may improve the severity of AD. This perception is based on conclusions from historical scientific studies that differ from more recent data. A 1988 study suggested that AD may be worsened by food ingestion, primarily cow’s milk, egg, and peanut, in 33% of children.<sup>17</sup> However, a 2022 systematic review and meta-analysis of 599 mostly pediatric patients with AD concluded that dietary elimination may only slightly, potentially unimportantly, improve eczema severity.<sup>18</sup> In addition to potentially creating a new IgE-mediated food allergy and not substantially

Table 1 Guideline statements for FA testing in patients with AD

Year	Organization	Clinical Scenario	Recommendation
2010	NIAID Expert Panel*	Children < 5 years old with persistent AD despite optimized management and topical therapy	Consider testing for specific foods (milk, egg, peanut, wheat, and soy)
2017	NIAID Expert Panel Peanut Allergy Addendum#	Infants with severe AD, egg allergy, or both§	Strongly consider peanut testing before introduction; based on test results, introduce peanut-containing foods at home or in office as early as 4–6 months of age; Not recommended: testing other foods before introduction, may cause overdiagnosis of FA and unnecessary dietary restriction
		Infants with mild-to-moderate AD	Introduce peanut at 6 months without testing
		Infants without AD	Introduce peanut without testing per family preference and cultural practices
2021	EAACI Task Force on FA in children with AD¶	Children < 6 years old with moderate-to-severe AD that is persistent or with poor response to treatment	Recommended: careful selection of food allergens for testing
		Children < 6 years old with moderate-to-severe AD with some treatment response but not regularly and uneventfully eating potential food allergens	Recommended: careful selection of food allergens for testing
2022	AAAAI Work Group**	Removal of tolerated food to improve AD alone	Not recommended: the potential to cause true FA and may not improve AD
		Indiscriminate FA testing in patients with AD	Not recommended: false-positive results may misguide patients and unnecessary avoidance could lead to development of a true allergy and/or nutritional deficiencies

FA = Food allergy; AD = atopic dermatitis; NIAID = National Institute of Allergy and Infectious Diseases; EAACI = European Academy of Allergy and Clinical Immunology; AAAAI = American Academy of Allergy & Immunology.

\*Ref. 6.

#Ref. 8.

§Severe AD is defined as “persistent or frequently recurring eczema with typical morphology and distribution, assessed as severe by a health care provider and requiring frequent need for prescription-strength topical corticosteroids, calcineurin inhibitors or other anti-inflammatory agents despite appropriate use of emollients.”<sup>8</sup>

¶Ref. 9.

||Skin-prick or specific immunoglobulin E blood +/- component testing for select allergens. “A careful medical and dietary history of the infant/child is mandatory prior to selecting the allergens to be tested. The history seeks to determine possible allergenic triggers for the patient as well as common food allergens that have been introduced in the diet. Testing will then aim to confirm suspected allergens as being clinically relevant especially if the history is equivocal as well as to allow for safe dietary expansion if other common allergens, relevant to the patient’s geographic location, not yet been eaten.”<sup>9</sup>

\*\*Ref. 1.

improving AD severity, elimination diets may cause other harms. Avoiding many foods, potentially without justification, can increase anxiety and decrease quality of life. Emotional stress can worsen AD, and nutritional deficiencies are another potential concern.<sup>1</sup> Children with AD and food allergy have poorer growth compared with age-matched controls, likely due to decreased intake of core nutrients, such as calcium and vitamin D.<sup>1,19,20</sup> This effect on growth increases as the number of eliminated foods increases.<sup>20</sup> Therefore, avoiding foods based only on skin-prick or *in vitro* specific IgE testing has the potential to induce a true food allergy while only minimally improving AD severity, increase anxiety, and negatively impact nutritional status. The benefit of indiscriminate food testing does not seem to outweigh the risk and harms.

## CONCLUSION

Food allergy testing in patients with AD is challenging because these conditions often coexist. However, false-positive food allergy test results are common. Performing extensive testing in this patient population creates problems, potentially when none initially existed. Professional society recommendations have changed over time to recommend a “less is more” approach to food allergy testing in patients with AD. Due to the real potential harms of overzealous testing, board-certified allergist/immunologists specifically trained in food allergy are the best qualified to order and interpret this testing, especially in this higher-risk population. It is the responsibility of the physicians or other health care professionals treating these complex patients to ensure they are practicing medicine based on the most recent guidelines and first, do no harm.

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