

Updated Guidelines on Peanut Allergy Prevention in Infants With Atopic Dermatitis

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It has been said that “extraordinary claims require extraordinary evidence.”¹ In the pursuit of evidence-based medicine, we are encouraged to follow a similar standard, with an emphasis on waiting for multiple studies with good-quality data and high levels of agreement before changing any aspect of our clinical practice. The ostensible purpose is that studies can be flawed, conclusions can be incorrect, or biases can be overlooked. In such cases, acting on questionable results could imperil patients. It is for this reason that so many review articles sometimes frustratingly seem to conclude that further evidence is needed.²

Based on this standard, recently published addendum guidelines from the National Institute of Allergy and Infectious Diseases for prevention of peanut allergy in the United States³ are somewhat striking in that they make fairly bold recommendations based on results from the 2015 Learning Early about Peanut Allergy (LEAP) study,⁴ a randomized trial evaluating early peanut introduction as a preventive strategy for peanut allergy. Of note, this study was not placebo controlled, was conducted at only 1 site in the United Kingdom, and only included 640 children, though the number of participants was admittedly large for this type of study.⁴ Arguably, the LEAP study alone does not provide enough evidence upon which to base what essentially amounts to an about-face in the official recommendations for prevention of peanut and other food allergies, which emphasized delayed introduction of high-risk foods, especially in high-risk individuals.⁵⁻⁷ To better understand this shift, we need to briefly explore the context of the addendum guidelines.

As many as one-third of pediatric patients with atopic dermatitis (AD) have food allergies, thus diet often is invoked by patients and providers alike as an underlying cause of the disease.⁸ Many patients in my practice are so focused on potential food allergies that actual treatment of the affected skin is marginalized and often dismissed as a stopgap that does not address the root of the problem.

A 2004 study of 100 children with AD found that diet was manipulated by the parents in 75% of patients in an attempt to manage the disease.⁹

Patients are not the only ones who consider food allergies to be a driving force in AD. The medical literature indicates that this theory has existed for centuries; for instance, with regard to the relationship between diet and AD, the author of an article from 1830 quipped, “There is probably no subject in which more deeply rooted convictions have been held . . . than the connection between diet and disease, both as regards the causation and treatment of the latter . . .”¹⁰ More apropos perhaps is a statement from the 2010 National Institute of Allergy and Infectious Diseases guidelines on food allergy management, which noted that while the expert group “does not mean to imply that AD results from [food allergies], the role of [food allergies] in the pathogenesis and severity of this condition remains controversial.”¹¹

Prior to the LEAP study, food allergy recommendations for clinical practice in the United Kingdom in 1998¹² and the United States in 2000¹³ recommended excluding allergenic foods (eg, peanuts, tree nuts, soy, milk, eggs) from the diet in infants with a family history of atopy until 3 years of age. However, those recommendations did not seem to be working, when in fact just the opposite was happening. From 1997 until the LEAP study was conducted in 2015, the prevalence of peanut allergy more than quadrupled and became the leading cause of anaphylaxis and death related to food allergy.¹⁴ Additionally, study after study concluded that elimination diets did not seem to help most patients with AD.¹⁵ As is required in good scientific thinking, when a hypothesis is proven false, other approaches must be considered.

The idea arose that perhaps delaying introduction of allergenic foods was the opposite of the answer.⁴ The LEAP study tested the notion that peanut allergies are rare in countries where peanuts are introduced early and if telling families to delay introduction of peanuts in infants might

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actually be causing development of a peanut allergy, and the tests bore fruit. It was found that giving infants peanut-containing foods resulted in a more than 80% reduction in peanut allergy at 5 years of age ($P < .001$).⁴ What was perhaps even more interesting was the connection between AD and peanut allergy. An important idea articulated in the LEAP study is in some ways revolutionary: Rather than foods causing AD, it could be that “early environmental exposure (through the skin) to peanut may account for early sensitization, whereas early oral exposure may lead to immune tolerance.”⁴ This concept—that impaired eczematous skin may actually lead to the development of food allergies—turns the whole thing upside down.

What do these updated guidelines actually suggest? The first guideline focuses on infants with severe AD, egg allergy, or both, who therefore are thought to be at the highest risk for developing peanut allergy.³ Because of the higher baseline risk in this subgroup, measurement of the peanut-specific IgE (peanut sIgE) level, skin prick testing (SPT), or both is strongly recommended before introducing peanut protein into the diet. This testing can be performed by qualified providers as a screening measure, but if positive (≥ 0.35 kU_A/L for peanut sIgE or > 2 mm on the peanut SPT), referral to an allergy specialist is warranted. If these studies are negative, it is thought the likelihood of peanut allergy is low, and it is recommended that caregivers introduce age-appropriate peanut-containing foods (eg, peanut butter snack puffs, diluted peanut butter) as early as 4 to 6 months of age. The second guideline recommends that peanut-containing foods should be introduced into the diets of infants with mild or moderate AD at approximately 6 months of age without the need for prior screening via peanut sIgE or SPT. Lastly, the third guideline recommends that caregivers freely introduce peanut-containing foods together with other solid foods in infants without AD or food allergies in accordance with family preference.³

The results of the LEAP study are certainly exciting, and although the theoretical basis makes good scientific sense and the updated guidelines truly address an important and growing problem, there are several issues with this update that are worth considering. Given the constraints of the LEAP study, it certainly seems possible that the results will not be applicable to all populations or foods. More research is needed to ensure that this robust finding applies to other children and to explore the introduction of other allergenic foods, which the LEAP study investigators also emphasized.⁴

In fairness, the updated guidelines clearly state the quality of evidence of their recommendations and make it clear that expert opinion is playing a large role.³ For the first guideline regarding recommendations for those with severe AD and/or egg allergy, the quality of evidence is deemed moderate, while the contribution of expert opinion is listed as significant. For the second and third guidelines regarding recommendations for mild to moderate AD and those without AD, respectively, the quality of evidence is low and expert opinion is again listed as significant.³

Importantly, delineating severe AD from moderate disease—which is necessary because only severe AD warrants evaluation with peanut sIgE and/or SPT—can be difficult, as the distinction relies on a degree of subjectivity that may vary between specialists. Indeed, 2 publications suggest extending the definition of severe AD to include infants with early-onset AD (< 3 months of age) and those with moderate AD not responding to treatment.^{16,17}

Despite these reservations, the updated guidelines represent a breakthrough in understanding in an area truly in need of advancement. Although the evidence may not be exactly extraordinary, the context for these developments and our deeper understanding suggest that we do indeed live in extraordinary times.

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