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Review

Oral food immunotherapy in patients with atopic dermatitis

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Key Messages

- Allergists offering oral immunotherapy (OIT) to young children are often faced with challenges in initiating and continuing OIT due to unpredictable changes in atopic dermatitis (AD) severity and control.
- Delays in starting OIT occur because of uncontrolled AD risk expansion of the number of food allergies due to unnecessary avoidance of multiple foods.
- Optimizing AD management and education before and during OIT is essential.
- Parents may ascribe AD flares to OIT doses, even though the degree to which OIT may lead to AD flares needs to be further studied.
- Discussion with parents and caregivers using a shared decision-making approach can guide allergists on whether to continue OIT using a modified buildup schedule, pause, or use adjunctive biologics to improve AD control and OIT adherence.
- Further evidence is needed to better understand the risk of AD exacerbation during OIT and optimal management. Current literature in this area is sparse, and as such, conditional recommendations are based on very low certainty evidence.

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ABSTRACT

Atopic dermatitis (AD) is one of the main risk factors for infants in the development of food allergy. Oral immunotherapy (OIT) in early childhood has been found to be highly effective and safe in preschoolers with and without AD, especially in young infants. Delays in initiation of OIT in infants and children due to uncontrolled AD risk expansion of the number of foods children develop allergy to through unnecessary avoidance of multiple foods. Parents and caregivers may attribute eczema flares to OIT doses, which physicians usually ascribe to non-food triggers such as weather changes, psychological stress, and infection. There is a lack of published literature confirming OIT as a trigger of AD flares, and the degree to which OIT may be associated with AD flares needs to be further studied. We describe 8 case scenarios with varying degrees of AD flare before and during OIT. We propose management algorithms for children with preexisting concurrent AD and food allergy who are being considered for starting OIT and children with AD flares during OIT. Optimizing AD control strategies and providing adequate AD care education before starting OIT can reduce confusion for both parents and allergists if rashes arise during OIT, thus improving adherence to OIT.

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Introduction

Infant atopic dermatitis (AD) is a significant risk factor in the development of food allergy. The "dual allergen exposure hypothesis" postulates that the dysregulated atopic infant skin barrier is a primary induction site of food allergy.[1,2] Conversely, early gastrointestinal exposure to food proteins promotes tolerance. In the gastrointestinal tract, dendritic cells present food proteins to naive CD4+ T cells in the mesenteric lymph nodes, with subsequent differentiation of regulatory T cells.[1] Despite clear evidence that early introduction of priority food allergens, such as peanut and egg, is effective in preventing high-risk infants with AD from developing food allergies,[3,4] there remains a significant number of infants whose primary preventive approach fails.[5] Families of these children with early onset food allergies may seek active treatment with food oral immunotherapy (OIT).[6,7]

Although low certainty evidence suggests that food triggers may play a small role in AD,[8] the degree to which poorly controlled AD hampers OIT success is poorly studied. Furthermore, the frequency with which OIT exacerbates AD is also similarly informed by scant evidence (Table 1). While awaiting further research to address this lack of data, clinical experience suggests reasonable approaches to patients in whom AD is (or becomes) a barrier to OIT. Using clinical vignettes, this article will review approaches to consider when AD limits OIT utilization. Importantly, all approaches should be considered as conditional suggestions within a paradigm of patient preference-sensitive care (ie, shared decision-making [SDM]).

Risk of Expansion of Food Allergy If Oral Immunotherapy Is Not Offered to Patients With Food Allergy and Atopic Dermatitis

Case 1A: Case of Extensive Food Avoidance and Development of More Food Allergies Beyond the Initial One

The parents of a 7-month-old female infant with peanut allergy and moderate uncontrolled AD have opted for strict avoidance of peanut. Skin prick testing (SPT) result revealed peanut sensitization (10 mm) but negative results to tree nuts. Despite the allergist offering observed ingestion to tree nuts in the office to facilitate their introduction, her parents remained hesitant for her to try them due to fear of cross-contamination with peanut. At 4 years old, she had an anaphylactic reaction due to accidental exposure to cashew, and repeat SPT result revealed strong sensitization to peanut (16 mm), cashew (10 mm), and pistachio (8 mm). This progression of history and conversion of SPT suggests that an expansion of her food allergies may have been influenced by tree nut avoidance in an at-risk phenotype.

Case 1B: Case of Early Oral Immunotherapy Facilitating Early Introduction of Other Priority Food Allergens for Primary Food Allergy Prevention

A 6-month-old male infant with peanut allergy and moderate but controlled AD initiated peanut OIT at 8 months. SPT result only revealed sensitization to peanut (8 mm), with negative testing result to tree nuts, but his parents were hesitant to introduce tree nuts due to concerns about cross-contamination with peanut. During peanut OIT, he had several minor allergic reactions, none requiring treatment. Within a couple months of starting peanut OIT, as confidence and protection with peanut OIT increased, the parents were comfortable with an observed ingestion of tree nuts in the office following which they were able to continue tree nuts regularly, decreasing the risk of tree nut allergy.

Young children with preexisting food allergy and AD are at risk for the list of foods they have allergy to expanding (case 1A), due to lack of regular exposure to allergenic foods they have not tried yet. This may be attributed to caregiver hesitancy and worries about cross-contamination, hesitancy that may be harmful long term in the at-risk patient (case 1B).

The Pronuts study was a prospective study evaluating the presence of concurrent peanut, tree nut, and sesame seed allergy in at-risk children. They noted high coexistence of peanut, tree nut, and sesame seed allergies (60.7% [n = 74/122; 95% CI 51.4%-69.4%]) confirmed by oral food challenge.[9] Of relevance, the investigators noted a secondary spread of the development of nut allergy associated with avoidance. This observation is consistent with the importance of early and consistent nut introduction, especially in at-risk patients.

OIT has been revealed in several randomized controlled trials and multiple real-world studies as highly effective and safe in preschoolers with and without AD, especially in young infants.[10–17] This approach may foster confidence within the family to proceed with early introduction and primary prevention of other allergenic foods that have not been introduced yet. This early and sustained introduction is likely most important in children with risk factors such as AD.

Importance of Optimizing Atopic Dermatitis Control Before and During Oral Immunotherapy

Case 2A: Case of Atopic Dermatitis Optimized Before Oral Immunotherapy Initiation

A 3-year-old girl was known to have a history of peanut anaphylaxis and moderate AD. SPT result revealed strong sensitization to peanut (11 mm) and cashew (12 mm). Despite appropriate skin

Table 1
Oral Immunotherapy Clinical Trials That Have Documented Atopic Dermatitis as an Adverse Event

OIT clinical trial/year of publication	Food treated	AD documented as an adverse event (Y/N)	AD reported in treatment arm	AD reported in placebo arm
Caminiti et al[24]/2015[a]	Egg	Y (defined as >10 points increase in SCORAD)	0	0
Tang et al[16] (PPOIT)/2015	Peanut	Y	2.90%	0%
Giavi et al[25]/2016	Egg	Y (descriptive)	One patient experienced AD flare (considered as probably related)	N/A[b]
Blumchen et al[23]/2019	Peanut	Y (newly diagnosed or worsening of atopic diseases[c] after OIT)	4%-5%	4%-8%
De Schryver et al[26]/2019	Cow's milk	Y (descriptive)	One patient withdrew due to recurrent GI symptoms and worsening of AD	N/A[b]
Jones et al[15] (IMPACT)/2022	Peanut	Y	13%	8%

Abbreviations: AD, atopic dermatitis; GI, gastrointestinal; IMPACT, Oral Immunotherapy for Induction of Tolerance in Peanut Allergic Children; N, no; N/A, not applicable; OIT, oral immunotherapy; PPOIT, Prebiotic and peanut oral immunotherapy; SCORAD, SCOring Atopic Dermatitis; Y, yes.
[a]AD is intentionally documented as an adverse event in the study methods, but no subjects were reported to have AD in either treatment or placebo arms within the study period.
[b]No placebo arm in the study.
[c]Including AD, bronchial asthma, and allergic rhinoconjunctivitis.

hygiene, including regular moisturizing with a high-quality emollient and regular bathing, her AD had been suboptimally controlled due to significant parental concerns of using topical steroid. After SDM with the allergist, the parents agreed to using 0.05% betamethasone valerate ointment for flares followed by topical 1% pimecrolimus cream as maintenance therapy. With this approach, her AD achieved significant improvement within 2 weeks. She was started on peanut and cashew OIT, which did not result in any significant AD flare during buildup and maintenance phases. Reassessment with SPT 1 year after reaching maintenance revealed significant reduction in peanut (6 mm) and cashew (5 mm) sensitization. She was continued on her maintenance doses until further reduction of SPT sensitization at exit oral food challenge, which she passed.

Case 2B: Perioral Dermatitis Resulting in Local Reaction During Oral Immunotherapy

A 2-year-old boy with mild AD and cashew allergy began OIT at 5 mg protein in December. During the winter months, his AD worsened, primarily on the face, with predominance around the mouth. At 20 mg cashew protein, the family reported localized urticaria around his mouth after the dose. Initially, the family treated with an oral second-generation antihistamine. On one occasion, he had isolated lip angioedema and recurrences of lip dermatitis. Given the frequency of symptoms, the family questioned whether to discontinue OIT. The family was reassured and instructed to apply a thick emollient, such as petroleum jelly, around the mouth before dosing, and as needed to reduce the perioral dermatitis, in addition to hydrocortisone 1% ointment for flares. The dermatitis and the frequency and severity of local symptoms both improved, and the patient was able to successfully complete OIT buildup.

AD can impose significant physical, emotional, and psychosocial impact to the patient and family. It is important to counsel parents and caregivers on the importance of managing AD through the regular use of emollients, steroidal and nonsteroidal topical medications during flare-ups, topical or systemic antibiotics when indicated, and multidisciplinary care with dermatologists, if necessary.[18] Optimizing AD control strategies and providing adequate AD care education before starting OIT can reduce confusion for both parents and allergists if rashes arise during OIT, thus improving adherence and confidence with continuing the OIT (cases 2A and 2B).

Caregiver-Reported Worsening of Atopic Dermatitis During Oral Immunotherapy Requires Individualized Contextual Management

Case 3A: Case of Atopic Dermatitis Flares Unlikely to Be Related to Oral Immunotherapy

A 3-year-old girl with a history of mild AD and peanut anaphylaxis was managed with peanut OIT. She has a background of recurrent mild AD flares and mild focal infection that was managed with topical mometasone ointment and topical antibiotics. As she went through her peanut OIT buildups from 1 mg to 40 mg peanut protein, she had AD flares more frequently with significant pruritis at night. This worsening coincided with a significant drop in their city's relative humidity and intercurrent viral infections. The allergist suggested suspending further OIT dose escalation. However, her parents stopped her OIT dosing completely for 5 weeks. Despite cessation, her AD flares remained unchanged. An SDM approach was adopted, and it was decided that OIT would be stopped until her AD control was improved.

Case 3B: Case of Eosinophilic Esophagitis and Atopic Dermatitis Flares Possibly Correlated With Oral Immunotherapy Dose Escalation

A 3-year-old girl had a history of severe AD and severe gastroesophageal reflux disease and laryngomalacia affecting feeding as an infant, requiring percutaneous gastrostomy and fundoplication. Her condition gradually improved, and she resumed oral feeding. She also had multiple food allergies, including peanut, almond, cashew, hazelnut, walnut, cow's milk, and egg. Her parents opted for single-food peanut OIT first to build up their confidence in the program, which was successful, and she has been on peanut maintenance dosing for nearly 9 months. She subsequently received 5 food OIT buildup (almond, cashew, walnut, hazelnut, and cow's milk) with concurrent maintenance peanut OIT. She had mild acute reactions during initial buildup and mild reflux symptoms at 80 mg protein per nut, which resolved with esomeprazole. When she reached 240 mg protein per nut, she developed significant reflux symptoms, compatible with possible eosinophilic esophagitis (EoE). Urgent endoscopy was unavailable and her OIT was paused for 8 weeks, with symptoms resolving completely. The allergist had a thorough discussion with the family using an SDM approach, and the family was very keen to continue with OIT due to food anaphylaxis being their primary concern.[19] The allergist recommended continuing with peanut maintenance and reducing to 2-food OIT (cashew and walnut), by restarting at 80 mg protein with a slower and longer buildup time of 4 to 8 weeks of intervals. She did not experience any further gastrointestinal symptoms but had substantial pruritis (especially at night) as her buildup resumed. The duration of sleep interruption was dose dependent, which was worst at 160 mg protein. It became significantly less when she stepped back to 80 mg protein. Despite multiple attempts to increase the dose and explore other possible confounding factors (such as weather changes, concurrent infection, and psychological factors), the patient and the family were unable to further endure the sleep disruption. The allergist and family later decided to maintain her cashew and walnut OIT dosing at 80 mg protein daily for 3 to 4 months and reassess her SPT reactivity to guide further treatment decisions.

In a systematic review and meta-analysis, Oykhman et al[8] studied 10 randomized controlled trials (n = 599) evaluating dietary elimination for the treatment of AD. Low certainty evidence suggested that dietary elimination may slightly improve AD severity (50% with vs 41% without dietary elimination improved the SCOring Atopic Dermatitis [SCORAD] index by a minimally important difference of 8.7 points, risk difference of 9% [95% CI 0-17]). No credible subgroup responses were identified, when comparing empiric food elimination vs elimination guided by specific IgE testing. Recognizing that food avoidance may also increase the subsequent risk of food allergy, the Allergy Immunology Joint Task Force on Practice Parameters 2023 Atopic Dermatitis Guideline provided a conditional recommendation against dietary manipulation to improve AD, instead favoring more effective therapies with lower risk.[20] It is important to highlight that a conditional recommendation is a navigational signal for SDM, and as this case highlights management of perceived dietary triggers in AD may require "n of 1 trials," as discussed in the 2023 AD guideline, especially when caregivers are convinced of an association.[20]

When OIT is initiated in a child with AD, there is potential for a parent to attribute AD flares to OIT doses. The challenge in evaluating patients with AD is teasing out whether OIT is the causative factor in an AD flare (cases 3A and 3B). In a study of 40 patients comparing multiple- vs single-food OIT by Bégin et al,[21] 1 participant dropped out of the study due to AD flare. A recent case report described a 7-year-old boy with a background of severe AD as a toddler and severe asthma, who received multiple-food OIT with omalizumab as adjunct. He developed psoriasiform eczema 1 month after OIT initiation, eventually requiring a pause in the OIT. His OIT was later successfully resumed by switching to dupilumab as the adjunct.[22] Otherwise, there has been a lack of similar reports in other OIT clinical trials.

A PubMed search was performed using the keywords "food oral immunotherapy" and "clinical trials" for articles published between 2015 and 2024. A total of 173 articles were searched, and 56 studies

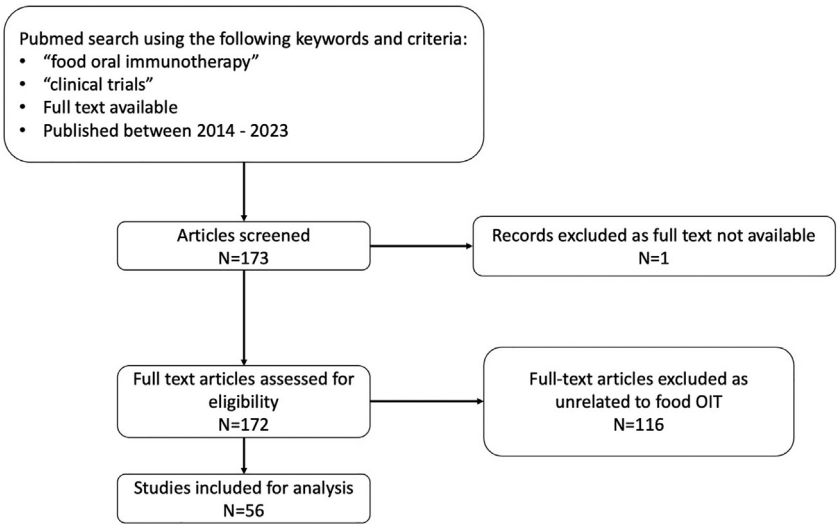

Figure 1. Flow diagram on PubMed search for food OIT clinical trials documenting atopic dermatitis flare as one of the adverse events. OIT, oral immunotherapy.

were clinical trials related to food OIT (Fig 1). Only 6 of those studies have documented AD flare as an adverse event[15,16,23-26] (Table 1). Only 1 study by Caminiti et al[24] clearly defined AD flare as a more than 10-point increase in SCORAD during OIT, but no subjects in either the treatment or the placebo arm were reported to have AD flares within the study period.

On the basis of the lack of published literature describing OIT as a trigger of AD flares, the degree to which OIT may be associated with AD flares needs to be further studied. The contemporary allergist can work with the family and tailor OIT protocols according to the child's skin condition, such as building up more slowly during periods of increased AD for the child. An SDM approach can be adopted,[27] similar to managing gastrointestinal symptoms encountered during OIT.[19] Figures 2 and 3 are proposed management algorithms for children with preexisting AD and food allergy who are being considered for starting OIT and children with AD flares during OIT, respectively.

Role of Biologics in Patients With Severe Atopic Dermatitis and Other Severe Atopic Conditions Who Desire Oral Immunotherapy

Case 4A: Severe Atopic Dermatitis in a Child Controlled With Dupilumab Before Initiating Oral Immunotherapy

A 7-year-old boy with severe AD who failed all topical therapies despite good adherence was also confirmed to have peanut, cow's milk, walnut, and pecan allergies based on history of reactions and SPT result (peanut 8 mm, cow's milk 12 mm, walnut 8 mm, and pecan 5 mm). Subcutaneous dupilumab was initiated with a loading dose of 600 mg followed by 300 mg every 4 weeks. He was able to achieve satisfactory AD control. Regular dupilumab was continued during his OIT buildup. Peanut, milk, and hazelnut OIT buildup was carried on smoothly without significant AD flares. Furthermore, the parents had accidentally given extra peanut and milk (estimated to be at least >25% to 50% of the expected dose) for nearly a week due to wrong measurements during home dosing at the 160 mg and 240 mg

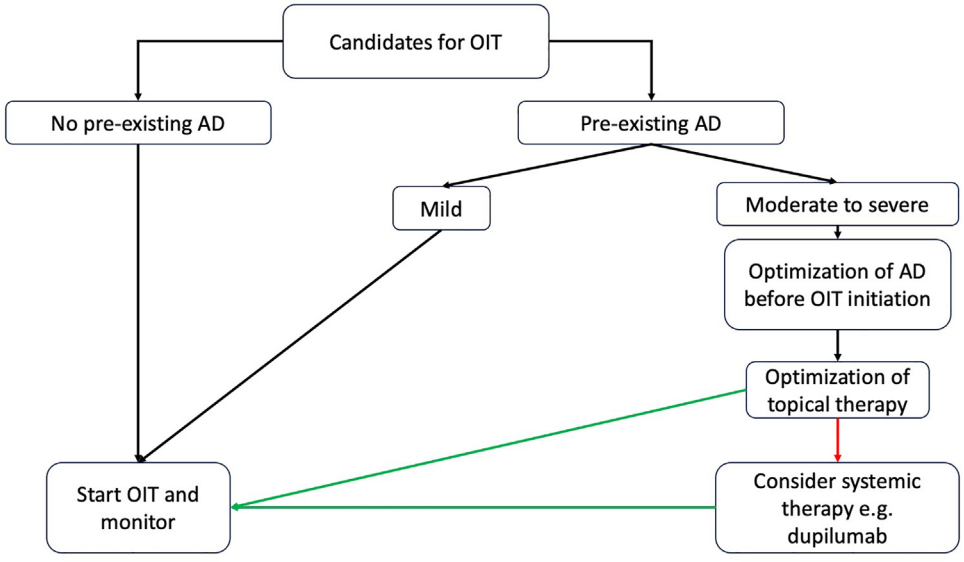

Figure 2. Proposed algorithm for the initiation of OIT in patients with preexisting AD. Green arrows indicate successful intervention. Red arrows indicate failed intervention. AD, atopic dermatitis; OIT, oral immunotherapy.

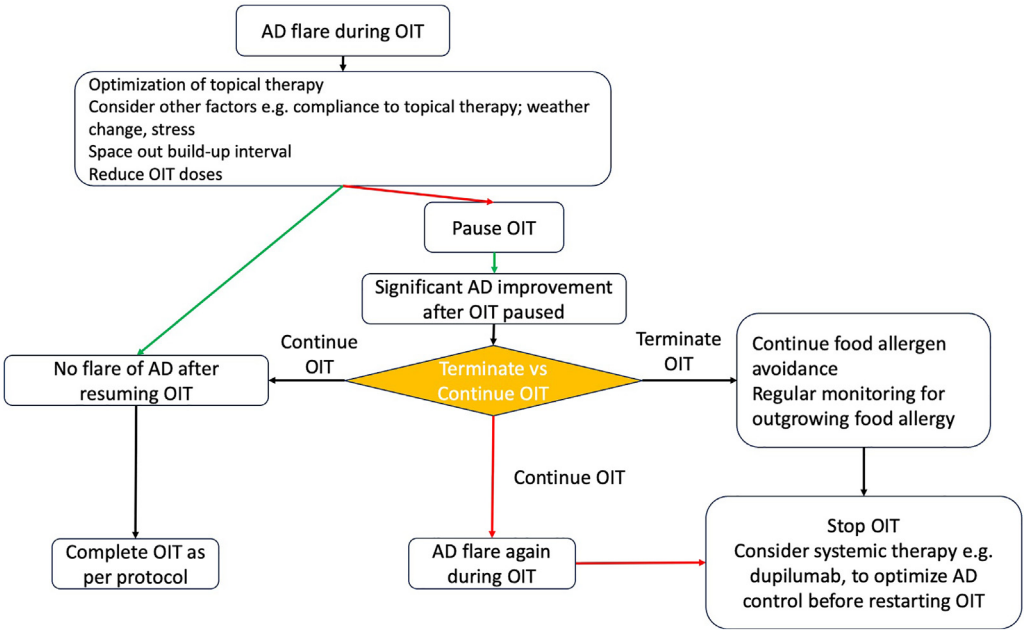

Figure 3. Proposed algorithm for patients on OIT experiencing flares of AD. Green arrows indicate successful intervention. Red arrows indicate failed intervention. AD, atopic dermatitis; OIT, oral immunotherapy.

protein stages without resulting in any allergic reactions despite not having antihistamine premedications. He completed the OIT buildup and entered the maintenance phase smoothly.

Case 4B: Infant With Severe Atopic Dermatitis, Severe Asthma, and Multiple Food Allergy

A 16-month-old boy has a history of anaphylaxis to cow's milk and egg and confirmed allergy to peanuts, tree nuts, and lentils. He has longstanding severe AD. He was admitted to the hospital for severe bronchiolitis at 11 months and subsequently developed severe asthma with multiple emergency department visits for wheezing. A course of OIT to cow's milk, egg, peanut, cashew, and lentil was attempted, but he developed mild anaphylaxis to the OIT (urticaria plus vomiting) after 3 weeks. He also encountered persistent difficulties with AD and asthma control during OIT despite regular use of topical and inhaled corticosteroids. OIT was stopped. With dupilumab being approved by the Food and Drug Administration (FDA) down to 6 months of age for severe AD, the allergist offered dupilumab for the primary purpose of treating severe AD, but with important concurrent aims of improving asthma control and allowing safer and more expedient OIT buildup as well.

For the subset of children with severe AD whose families desire OIT, control of AD before starting OIT may be difficult/impossible using conventional medical management of AD without a biologic. For moderate-to-severe AD that has failed topical treatments, novel systemic medications such as dupilumab have been found to be effective and safe in infants as young as 6 months old.[28] Dupilumab has recently been approved by the FDA, Health Canada, and the Department of Health of Hong Kong for severe AD down to 6 months of age, the same age food allergy often manifests. Dupilumab may offer rapid control of severe AD (cases 4A and 4B). In addition, it treats concomitant severe asthma and EoE, all of which could occur in children with severe AD.[29,30] Rial et al[31] recently reported a case of a 30-year-old woman who received dupilumab for severe AD developing tolerance to 2 foods that induced previous anaphylaxis, with this tolerance being confirmed by oral challenge. Currently, clinical trials are in progress to evaluate the effectiveness of dupilumab in food OIT.[32,33]

With the recent approval of dupilumab for the treatment of EoE, it remains to be revealed whether this medication may be beneficial as an adjunct to prevent gastrointestinal symptoms and pathology during the OIT process. It is conceivable that dupilumab may be used to both enhance OIT directly through its modulation of B-cell food-specific IgE production, leading to a significant reduction in food-specific IgE,[33,34] and indirectly through its clinical improvement in asthma, esophageal eosinophilia and improvement in AD, an approach that would have been of benefit for case 4B.

Omalizumab was recently approved by the FDA for treating food allergy, but the approval and the supporting data did not address outcomes in those with concomitant AD. The recently published OUtMATCH study has revealed that omalizumab is superior to placebo in increasing the reaction threshold for peanut and other priority food allergens (cashew, milk, egg, walnut, wheat, and hazelnut) in patients with multiple food allergies older than 1 year old. However, subjects with poorly controlled AD were excluded from the study.[35] Patients with similar clinical presentations in cases 4A and 4B would not be expected to achieve better control of their AD while using omalizumab as an adjunct for OIT. Although some smaller scale studies have reported that omalizumab is effective in treating severe AD as an off-label medication, systematic review and meta-analysis of published studies have revealed discrepant results for omalizumab in treating AD.[36] Further studies should investigate whether using omalizumab as an adjunct for food OIT would simultaneously lead to an improvement of AD.

Conclusion

AD and food allergy are frequently associated with one another, and allergists offering OIT to young children are often faced with the challenges in initiating and continuing OIT due to unpredictable changes in AD control. The degree to which OIT may lead to AD flares needs to be further studied. Optimizing conventional AD management and education is essential. In patients with AD, discussion with parents and caregivers using an SDM approach can guide allergists on whether to continue OIT using a modified buildup schedule, pause, or use adjunctive biologics during OIT to achieve better AD control.

Disclosures

Dr Chua received honorarium from Pharmaniaga, Sanofi, and Menarini and is an advisory board member on maternal immunization against respiratory syncytial virus of Pfizer. Dr Mack has provided consultation and speaker services for DBV, ALK, and Alladapt and is an investigator for DBV, ALK-Abello, Dermavant, Arcutis, and Amgen. Dr Shaker is a member of the Joint Task Force on Practice Parameters, serves on the editorial board of the *Journal of Allergy and Clinical Immunology In Practice*, is an associate editor of *Annals of Allergy, Asthma, and Immunology*, and serves on the Board of Directors of the American Academy of Allergy, Asthma, and Immunology (views expressed are his own). Dr Chan has received research support from DBV Technologies; has been a member of advisory boards for Pfizer, Miravo, Medexus, Leo Pharma, Kaleo, DBV, AllerGenis, Sanofi Genzyme, Bausch Health, Avir Pharma, AstraZeneca, ALK, and Alladapt; and was co-lead of the CSACI oral immunotherapy guidelines.

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References

1. Kulis MD, Smeekens JM, Immormino RM, Moran TP. The airway as a route of sensitization to peanut: an update to the dual allergen exposure hypothesis. *J Allergy Clin Immunol*. 2021;148(3):689–693.
2. Brough HA, Nadeau KC, Sindher SB, Alkotob SS, Chan S, Bahnson HT, et al. Epicutaneous sensitization in the development of food allergy: what is the evidence and how can this be prevented? *Allergy*. 2020;75(9):2185–2205.
3. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 2015;372(9):803–813.
4. Skjerven HO, Lie A, Vettukattil R, Rehbinder EM, LeBlanc M, Asarnoj A, et al. Early food intervention and skin emollients to prevent food allergy in young children (PreventADALL): a factorial, multicentre, cluster-randomised trial. *Lancet*. 2022;399(10344):2398–2411.
5. Soriano VX, Peters RL, Moreno-Betancur M, Ponsonby AL, Gell G, Odoi A, et al. Association between earlier introduction of peanut and prevalence of peanut allergy in infants in Australia. *JAMA*. 2022;328(1):48–56.
6. Chua GT, Greenhawt M, Shaker M, Soller L, Abrams EM, Cameron SB, et al. The case for prompt salvage infant peanut oral immunotherapy following failed primary prevention. *J Allergy Clin Immunol Pract*. 2022;10(10):2561–2569.
7. Mullins RJ, Dear KBG, Tang MLK. Changes in Australian food anaphylaxis admission rates following introduction of updated allergy prevention guidelines. *J Allergy Clin Immunol*. 2022;150(1):140–145.e1.
8. Oykhman P, Dookie J, Al-Rammahy H, de Benedetto A, Asiniwasis RN, LeBovidge J, et al. Dietary elimination for the treatment of atopic dermatitis: a systematic review and meta-analysis. *J Allergy Clin Immunol Pract*. 2022;10(10):2657–2666.e8.
9. Brough HA, Caubet JC, Mazon A, Haddad D, Bergmann MM, Wassenberg J, et al. Defining challenge-proven coexistent nut and sesame seed allergy: a prospective multicenter European study. *J Allergy Clin Immunol*. 2020;145(4):1231–1239.
10. Chua GT, Soller L, Kapur S, McHenry M, Rex GA, Cook VE, et al. Real-world safety and effectiveness analysis of low-dose preschool sesame oral immunotherapy. *J Allergy Clin Immunol Glob*. 2024;3(1):100171.
11. Erdle SC, Cook VE, Cameron SB, Yeung J, Kapur S, McHenry M, et al. Real-world safety analysis of preschool tree nut oral immunotherapy. *J Allergy Clin Immunol Pract*. 2023;11(4):1177–1183.
12. Soller L, Abrams EM, Carr S, Kapur S, Rex GA, Leo S, et al. First real-world safety analysis of preschool peanut oral immunotherapy. *J Allergy Clin Immunol Pract*. 2019;7(8):2759–2767.e5.
13. Soller L, Abrams EM, Carr S, Kapur S, Rex GA, Leo S, et al. First real-world effectiveness analysis of preschool peanut oral immunotherapy. *J Allergy Clin Immunol Pract*. 2021;9(3):1349–1356.e1.
14. Soller L, Carr S, Kapur S, Rex GA, McHenry M, Cook VE, et al. Real-world peanut OIT in infants may be safer than non-infant preschool OIT and equally effective. *J Allergy Clin Immunol Pract*. 2022;10(4):1113–1116.e1.
15. Jones SM, Kim EH, Nadeau KC, Nowak-Wegrzyn A, Wood RA, Sampson HA, et al. Efficacy and safety of oral immunotherapy in children aged 1-3 years with peanut allergy (the Immune Tolerance Network IMPACT trial): a randomised placebo-controlled study. *Lancet*. 2022;399(10322):359–371.
16. Tang ML, Ponsonby AL, Orsini F, Tey D, Robinson M, Su EL, et al. Administration of a probiotic with peanut oral immunotherapy: a randomized trial. *J Allergy Clin Immunol*. 2015;135(3):737–744.e8.
17. Toit GD, Brown KR, Vereda A, Irani AM, Tilles S, Ratnayake A, et al. Oral immunotherapy for peanut allergy in children 1 to less than 4 years of age. *NEJM Evid*. 2023;2(11). EVIDoa2300145.
18. Butala S, Paller AS. Optimizing topical management of atopic dermatitis. *Ann Allergy Asthma Immunol*. 2022;128(5):488–504.
19. Chua GT, Chan ES, Invik R, Soller L, Avinashi V, Erdle SC, et al. How we manage gastrointestinal symptoms during oral immunotherapy through a shared decision-making process—a practical guide for the community practitioner. *J Allergy Clin Immunol Pract*. 2023;11(4):1049–1055.
20. Chu DK, Schneider L, Asiniwasis RN, Boguniewicz M, De Benedetto A, Ellison K, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE- and Institute of Medicine-based recommendations. *Ann Allergy Asthma Immunol*. 2024;132(3):274–312.
21. Bégin P, Winterroth LC, Dominguez T, Wilson SP, Bacal L, Mehrotra A, et al. Safety and feasibility of oral immunotherapy to multiple allergens for food allergy. *Allergy Asthma Clin Immunol*. 2014;10(1):1.
22. Frugier C, Samaan K, Graham F, Paradis L, Des Roches A, Bégin P. Atypical eczematous lesions triggered by oral immunotherapy in a patient with a familial history of psoriasis. *J Allergy Clin Immunol Pract*. 2021;9(9):3479–3480.
23. Blumchen K, Trendelenburg V, Ahrens F, Gruebl A, Hamelmann E, Hansen G, et al. Efficacy, safety, and quality of life in a multicenter, randomized, placebo-controlled trial of low-dose peanut oral immunotherapy in children with peanut allergy. *J Allergy Clin Immunol Pract*. 2019;7(2):479–491.e10.
24. Caminiti L, Pajno GB, Crisafulli G, Chiera F, Collura M, Panasci G, et al. Oral immunotherapy for egg allergy: a double-blind placebo-controlled study, with postdesensitization follow-up. *J Allergy Clin Immunol Pract*. 2015;3(4):532–539.
25. Giavi S, Vissers YM, Muraro A, Lauener R, Konstantinopoulos AP, Mercenier A, et al. Oral immunotherapy with low allergenic hydrolysed egg in egg allergic children. *Allergy*. 2016;71(11):1575–1584.
26. De Schryver S, Mazer B, Clarke AE, St Pierre Y, Lejtenyi D, Langlois A, et al. Adverse events in oral immunotherapy for the desensitization of Cow's milk allergy in children: a randomized controlled trial. *J Allergy Clin Immunol Pract*. 2019;7(6):1912–1919.
27. Greenhawt M. Shared decision-making in the care of a patient with food allergy. *Ann Allergy Asthma Immunol*. 2020;125(3):262–267.
28. Paller AS, Simpson EL, Siegfried EC, Cork MJ, Wollenberg A, Arkwright PD, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2022;400(10356):908–919.
29. Aceves SS, Dellon ES, Greenhawt M, Hirano I, Liacouras CA, Spergel JM. Clinical guidance for the use of dupilumab in eosinophilic esophagitis: a yardstick. *Ann Allergy Asthma Immunol*. 2023;130(3):371–378.
30. Bacharier LB, Maspero JF, Katelaris CH, Fiocchi AG, Gagnon R, de Mir I, et al. Dupilumab in children with uncontrolled moderate-to-severe asthma. *N Engl J Med*. 2021;385(24):2230–2240.
31. Rial MJ, Barroso B, Sastre J. Dupilumab for treatment of food allergy. *J Allergy Clin Immunol Pract*. 2019;7(2):673–674.
32. Fiocchi A, Vickery BP, Wood RA. The use of biologics in food allergy. *Clin Exp Allergy*. 2021;51(8):1006–1018.
33. Sindher SB, Fiocchi A, Zuberbier T, Arasi S, Wood RA, Chinthrajah RS. The role of biologics in the treatment of food allergy. *J Allergy Clin Immunol Pract*. 2024;12(3):562–568.
34. Spekhorst LS, van der Rijst LP, de Graaf M, van Megen M, Zuithoff NPA, Knulst AC, et al. Dupilumab has a profound effect on specific-IgE levels of several food allergens in atopic dermatitis patients. *Allergy*. 2023;78(3):875–878.
35. Wood RA, Togias A, Sicherer SH, Shreffler WG, Kim EH, Jones SM, et al. Omalizumab for the treatment of multiple food allergies. *N Engl J Med*. 2024;390(10):889–899.
36. Wang HH, Li YC, Huang YC. Efficacy of omalizumab in patients with atopic dermatitis: a systematic review and meta-analysis. *J Allergy Clin Immunol*. 2016;138(6):1719–1722.e1.