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REVIEW ARTICLE

The Role of Diet Modification in Atopic Dermatitis: Navigating the Complexity

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Abstract

Diet has long been understood to have an intricate association with atopic dermatitis, although much remains unelucidated. Skin barrier dysfunction with dysbiosis and consequent impairment of immune tolerance likely underly the pathogenesis of coincident atopic dermatitis and food allergy. There is a wide range of possible skin reactions to food, complicating the diagnosis and understanding of food allergies. Many patients, parents, and providers incorrectly suspect diet as causative of atopic dermatitis symptoms and many have tried elimination diets. This frequently leads to inaccurate labeling of food allergies, contributing to a dangerous spiral of inappropriate testing, referrals, and dietary changes, while neglecting established atopic dermatitis treatment essentials. Alternatively, certain dietary supplements or the introduction of certain foods may be beneficial for atopic dermatitis management or prevention. Greater consensus on the role of diet among providers of patients with atopic dermatitis is strongly encouraged to improve the management of atopic dermatitis.

Key Points

Diet is intimately related to atopic dermatitis, although it is much more complex and interrelated than it may initially appear.

Both avoiding and supplementing foods have evidence for addressing or preventing concomitant atopic dermatitis and food allergies and is a promising area of research.

Unnecessary dietary exclusion can result in patient harm; thus, elimination diets should be reviewed and recommended judiciously by healthcare providers.

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1 Introduction and Relevance

Dating back to at least the 19th century, diet has been implicated in the pathogenesis of atopic dermatitis (AD). Food allergies (FAs) and AD, both part of the atopic triad, are clearly associated with one another, although asthma, rounding out the triad, is a stronger risk factor for FAs than AD [1]. The association between AD and FAs is most significant in young children and those with more severe disease. The prevalence of FAs in patients with AD has been reported as high as 50.7%, warranting a careful evaluation for FAs in this population [2]. Much effort has been devoted to unraveling the interaction between the two, yet there is still a great deal of speculation as to causative mechanisms and the exact role of FAs in the development and severity of AD.

This uncertainty impacts patients and providers alike. Patients and parents are increasingly questioning the role of diet in mediating this skin condition. Many incorrectly feel that diet or FA is the "root cause" of AD, with the majority of affected children having attempted dietary eliminations to treat their skin condition [3, 4]. However, data suggest that excluding foods in unselected patients offers no benefits [5]. Furthermore, unnecessary food elimination diets can, perhaps counterintuitively, cause iatrogenic FAs resulting in new immunoglobulin E (IgE)-mediated FAs to previously tolerated foods, even resulting in anaphylaxis [6, 7]. Some patients with AD may eliminate foods from their diet without

receiving any assessment by a specialist to determine if the symptoms they are concerned about are consistent with an IgE-mediated FA, [4] increasing the risk of unguided elimination diets and poor outcomes. Other adverse effects of attributing AD symptoms to FA include inordinate specialist consultation, indiscriminate testing, nutritional deficiency and lifestyle challenges from elimination diets (an additional stressful intervention especially for children), and neglect of established AD treatment essentials.

Diet is becoming an increasingly popularized explanation for inflammatory conditions such as AD, both in medicine and in media. A recent study suggests that about half of patients with AD have discussed diet with a health professional [4]. However, the majority of these patients felt the discussion was unhelpful or very unhelpful. Even less common was receiving dietary counseling from a dietitian, experienced by only 17% of adults with modified diets [4]. These findings suggest that there may be confusion on the part of both provider and patient surrounding perceived FAs and the role of dietary changes in AD.

2 Food-Induced Skin Reactions

Adverse food reactions encompass a wide-variety of immune-mediated and non-immune-related conditions, including anaphylaxis, oral allergy syndrome, celiac disease, eosinophilic esophagitis, delayed-type food reactions, food intolerance, and irritant contact dermatitis to foods [8] (Table 1). Patients commonly refer to all adverse food reactions as allergies. A true IgE-mediated FA involves the development of IgE antibodies upon exposure to a food allergen—a process known as sensitization—with subsequent IgE-mediated symptoms. It should be noted that the pathophysiology of AD is distinct from such allergies and does not involve IgE.

The conflation of many terms involving adverse food reactions, largely non-IgE mediated, with a true FA can lead to confusion and potential harm to patients. For example, food may come into contact with young children's skin while eating and parents may perceive the corresponding rash as a FA causing AD, when it is actually a local irritant contact dermatitis. Providers should be cautious of self-reported FAs and always clarify specific symptoms with patients, as multiple studies have demonstrated that 50–90% of presumed FAs are not true allergies [9]. One study found that while 20.4% of people in a large sample population reported a food intolerance, only 1.4% of tested individuals had a positive double-blind, placebo-controlled food challenge constituting a true IgE-mediated allergy [10].

While multiple testing modalities exist for identifying FAs, the gold standard of diagnosing a true FA is a positive double-blind, placebo-controlled food challenge. This is an outpatient procedure performed under close clinical supervision. A suspected food allergen is ingested in predefined increasing increments. Objective symptoms consistent with an IgE-mediated reaction during the challenge confirm an IgE-mediated FA [11]. Examples of IgE-mediated allergic symptoms include rash, urticaria, swelling, pruritus, sneezing, itching, wheezing, laryngeal manifestations, subjective gastrointestinal symptoms, emesis, and diarrhea, along with cardiovascular collapse and altered mental status [8]. While the rash and pruritus may be confused for an eczema flare, they have fundamentally different mechanisms. Ideally, the food challenge procedure is double blind, meaning the patient receives the food allergen and a placebo hours or days apart and neither patient nor provider is aware of which product the patient is receiving.

Despite being the gold standard, food challenges may be cumbersome to perform in clinical practice and epicutaneous skin prick testing (SPT) to food extracts and serum-specific IgE (sIgE) are commonly used in vitro diagnostic approaches to diagnose FAs, both relying on the presence of food-specific IgE [12]. While positive IgE serum testing indicates sensitization to an allergen and potentially a true FA if the sensitization is associated with IgE-mediated symptoms, AD is not an IgE-mediated allergic symptom. Positive sIgE and epicutaneous testing have high false-positive rates in patients with AD. In patients with AD, SPT to foods have a negative predictive value of 90–95%, yet a positive predictive value of less than 50%; these tests may be more useful in ruling out rather than diagnosing FA [13–15]. Therefore, testing relying on the presence of food sIgE is impractical without a suggestive immediate reaction history, and would not predict eczematous responses to the tested food.

In support of this concept, 1186 positive double-blind, placebo-controlled food challenges were studied and researchers found that children with a history of AD exacerbation as their only symptom of a FA reacted to a food challenge as often as the placebo group [16]. The study concluded that history of an AD flare without symptoms of an IgE-mediated FA was unlikely to represent a true FA. However, the study did find that children with a history of AD were significantly more likely to be sensitized to foods than children without previous AD, although this sensitization is frequently asymptomatic [16]. The mechanism responsible for this finding may involve the disrupted skin barrier seen in AD, leading to increased transcutaneous or epicutaneous sensitization of food allergens. As previously discussed, being sensitized likely does not translate to having an eczematous flare. A true eczematous allergic reaction, which may be represented as a delayed-type allergy, is rare and difficult to prove [17]. Therefore, AD and FAs may be related, but not in the way that many patients may perceive that they are (see Table 1).

Table 1 Types and characteristics of adverse food reactions. Adapted from Rustad et al. [75]

Condition	Food allergy		Delayed-type hypersensitivity			Non-allergic food reactions	
Types	At risk for anaphylaxis	Not at risk for anaphylaxis (oral allergy syndrome)	Celiac	Eosinophilic esophagitis	Delayed-type cutaneous	Intolerance	Irritant contact dermatitis to foods
Definition	An IgE-mediated clinical response to a food in someone who is sensitized [60]	An IgE-mediated manifestation affecting the oropharynx [61]	Autoimmune response to a gluten molecule [62]	Multifactorial inflammatory disorder with deficiency mucosal barrier of the esophagus [52]	T-cell-mediated inflammatory reaction (with or without involvement of IgE) [60]	Non-immune-mediated food reaction [63]	Non-specific response of the skin to direct chemical damage, does not involve antigen/allergen-specific T cells [64, 65]
Timing	Immediate, within 2 hours [60]	Immediate symptoms on contact with raw fruits/vegetables [61]	Median time to reaction is 1 hour, but can be delayed for 12+ hours [66]	Delayed, days to weeks [67]	Delayed, 24–48 hours after exposure [60]	Varies [63]	Minutes to hours after exposure to irritant [68]
Severity	Can be life threatening, very severe [60]	Subsides within minutes after the food is swallowed [69]	Serious, permanent condition that can be life threatening [62]	Serious, though not usually life threatening [52]	Less severe than immediate reactions [60]	Varies [63]	Varies [65]
Diagnosis	History and IgE antibodies to allergen or positive skin-prick test and clinical symptoms [60]	Positive history and skin-prick test [69]	IgA anti-tTGA, duodenal biopsy is gold standard [70]	Endoscopy with esophageal biopsies [52]	Atopy patch test [60]	Clinical symptoms without IgE antibodies to allergen or positive skin-prick test [63]	Diagnosed by history including location, appearance of rash, inciting food, and lack of IgE-mediated symptoms
Clinical manifestations	Urticaria, angioedema, flush, pruritus, hoarseness, cough, anaphylaxis [60]	Tingling, pruritus, erythema, or angioedema of the lips and tongue, throat itching or tightness [61]	Abdominal pain, diarrhea, fatigue, headache, irritability [66]	Reflux, abdominal pain, and food impaction; no cutaneous findings [52]	Atopic dermatitis, protein contact dermatitis, late-phase oral allergy syndrome [60]	Varies, may include itching, flushing, nausea, vomiting, diarrhea [63]	Well-demarcated lesions, typically confined to the area of contact with the irritant, burning more prominent than itch [65]
Examples	Milk, egg, peanut, shellfish [71]	Raw fruits and vegetables [61]	Wheat, rye, barley, spelt, kamut [62]	Milk, egg, wheat, soy [72]	Dairy, soy, rice, wheat [73]	Lactose intolerance, histamine reactions, MSG, food additives, gluten outside of celiac, irritable bowel disease [63]	General food products, acidic or spicy foods, bakery products, fruits/nuts/vegetables, meat/poultry [74]; strawberry, citrus, and tomato most commonly reported

DH dermatitis herpetiformis, *IgE* immunoglobulin E, *MSG* monosodium glutamate, *tTGA* tissue transglutaminase

3 Epithelial Dysfunction and FAs

A dysfunctional skin barrier plays a central role in the pathogenesis of numerous diseases, including AD [18]. The "leaky skin" may stem from loss-of-function mutations in the *FLG* gene which codes for filaggrin, a key protein linking keratin in the skin and supporting skin barrier function [19]. Filaggrin-poor skin is thought to allow penetration of, and increased sensitization to, allergens, as initially observed in murine models [20]. This phenomenon of epicutaneous exposure to allergens contributing to FAs has been demonstrated in clinical studies as well. A case-control study identified that filaggrin mutations represented a significant risk factor for IgE-mediated peanut allergy [21]. In the Australian HealthNuts study, infants diagnosed with AD in the first year of life were six times more likely to have an egg allergy and 11 times more likely to have a peanut allergy by 12 months of age [22].

Like skin, the intestinal epithelium is part of our innate immune system and serves to protect the body from environmental threats. Thus, the gastrointestinal tract can demonstrate similar "leaky" properties as our skin epithelium, with subsequent increased intestinal permeability and reduced protection [23]. While not completely understood, it is thought that an abnormal gut barrier allows the passage of antigens from ingested contents, which triggers an inflammatory response in predisposed patients [24]. This theory has been put to the test in studies examining the severity of intestinal barrier dysfunction in individuals with AD vs healthy individuals. Results not only showed a relationship between gastrointestinal tract health and AD, but indicated a positive association between gut barrier dysfunction and the severity of AD [25, 26].

Of note, barrier disruption is only one component of epithelial dysfunction predisposing to AD. Dysbiosis, or microbial imbalance, has also been implicated in skin and gut pathologies. On the skin, dysbiotic environments are conducive to the proliferation of *Staphylococcus aureus*, a pathogen known to exacerbate AD via multiple virulence factors [27, 28]. High carriage rates of *S. aureus* are found on AD skin, with recent analyses showing colonization in 70% of affected individuals [29]. Similarly, the natural flora of the intestinal microbiome plays a critical role in digestion, nutrient absorption, facilitation of toxin metabolism, and protection from pathogens. Alterations in the intestinal microbiome can lead to epithelial dysfunction by altering the immune system and causing increased inflammation [30, 31].

It would then follow that maintenance of a healthy gut microbiome may prevent AD exacerbation. This has yet to be borne out in the literature, but some studies suggest the use of probiotics in patients with moderate-to-severe AD improves the gut barrier [26] and could improve AD symptoms. In one study of 220 children with moderate-to-severe AD, subjects were randomized to receive various probiotics compounds or placebo. Children who received any form of probiotics showed lower SCORAD (SCORing Atopic Dermatitis) scores than the placebo group ($p < 0.001$) [32]. Despite this compelling study, multiple systematic reviews of other trials have found no significant difference in AD outcomes with the use of ingested probiotics [33, 34].

4 Preventing FAs

Interestingly, the interaction of food allergens with the dysfunctional epithelium of the skin and the gastrointestinal tract can result in opposing immune responses. This phenomenon is known as the dual-allergen exposure hypothesis and suggests the following: (1) epicutaneous food sensitization occurs through an impaired skin barrier, which allows allergen penetrance and cytokine dysregulation, culminating in a clinical FA and (2) early exposure to food allergens via ingestion promotes immune tolerance, potentially preventing the development of FAs [35]. Perhaps most convincing of the cutaneous component of this theory are the results of studies in which allergen-containing compounds were applied to inflamed skin. In the Avon Longitudinal Study of Parents and Children, application of peanut-containing skin preparations on inflamed skin was significantly associated with the development of peanut allergy [36]. Similarly, a Japanese study of wheat-containing soap users found subsequent development of a hydrolyzed wheat protein allergy [37].

This dual-allergen exposure hypothesis contradicts prior recommendations for solid food avoidance in the first 6 months from the 1980s [38]. Current evidence shows that AD generally arises before the development of food sensitization. Combined with the finding that FA is more prevalent in those with severe and chronic AD, there is clear support for a hypothesis that it is AD causing FAs, rather than the other way around [39, 40].

Discussion of food tolerance is not complete without mention of the notable Learning Early About Peanut Allergy (LEAP) study. The LEAP study was the first randomized controlled trial to study the introduction and avoidance of dietary peanuts in infants [41]. This landmark study consisted of a double-blind placebo-controlled trial in which infants aged 4–11 months with moderate-to-severe AD and/or an egg allergy were randomized into consumption and non-consumption groups. Five years later, results showed a significantly lower incidence of peanut allergies in the consumption group when compared with the avoidance group. This suggested that infants with

allergic potential tolerated peanuts after early oral exposure to the allergen [41]. In short, this study introduced the idea that FAs could be prevented by exposure to the intestinal immune system, thus pushing out the conservative strategy of allergen avoidance. This idea has been further supported by the Enquiring About Tolerance (EAT) study, a randomized trial of early introduction of six allergenic foods: cow's milk yogurt, peanut, hard-boiled egg, sesame, whitefish, and wheat; early introduction proved to be preventive against the development of FAs, as well as celiac disease, for high-risk infants [42, 43].

Thus, for children with AD and other conditions predisposing to FAs, the results of the LEAP study have sparked hope in the prevention of FAs via structured allergen introduction. The National Institute for Allergy and Infectious Disease has drawn on the LEAP study to develop guidelines for peanut allergy prevention in the USA. Given the high risk of introducing peanuts to children with unknown FA histories, it is crucial to accurately classify patients into a risk level using their severity of AD as a proxy. The SPT and IgE results can guide clinical decision making: SPT reactions 8 mm or greater and IgE levels ≥ 0.35 kU_A/L indicate a probable allergy and potentially warrant referral to an allergist [56].

Controversy remains surrounding the testing of high-risk children. In patients with a high baseline risk of FA, SPT or measurement of the peanut-specific IgE level has been recommended before introducing peanut protein to the diet [55]. However, testing of high-risk children results in delayed peanut introduction, compounding the problem of food avoidance. Furthermore, due to an already strained allergy workforce, introduction can be delayed while the child awaits an allergy evaluation. In the LEAP study, the majority (about 87%) of high-risk infants were deemed able to safely introduce peanuts without a specialist evaluation; delaying introduction would be unnecessary in most cases. Most reactions to peanuts before 12 months are mild, with no anaphylactic reactions with home introduction in a cohort of 5276 infants [44]. Screening all infants with eczema and/or an egg allergy would likely not be cost effective and would still miss about 23% of peanut allergies [44]. It is also difficult for parents to determine whether their child is "high risk", as this term was specifically defined for research, rather than clinical, purposes. Many may feel their child is "high risk" and unnecessarily delay peanut/food introduction or seek a specialist evaluation.

Recommendations are still much debated and in flux regarding the best approach for timely introduction of peanuts between the ages of 4 and 11 months. Currently, the provider's decision of testing for peanut SPT or sIgE should consider the advantages and disadvantages for the individual high-risk infant patient.

5 Recommendations for Managing and Advising Patients with AD About Diet

Given the individual variation in symptoms and history among patients, as well as unclear clinical recommendations, it can be challenging for clinicians to advise their patients with AD about diet. Allergy specialists likely focus more on allergic triggers, and evidence suggests they may be more likely to use dietary manipulation for the management of AD than dermatologists and pediatricians [45].

In order to provide consensus on AD management, experts in both allergy and dermatology have created guidelines. A Joint Task Force (JTF) was created in 2012 to develop a parameter for AD diagnosis and treatment, representing the American College of Asthma, Allergy and Immunology; the American Academy of Asthma, Allergy and Immunology; and the Joint Council of Allergy, Asthma and Immunology [46]. The American Academy of Dermatology (AAD) created similar guidelines in 2014 [1]. However, it should be noted that these guidelines are several years old in a rapidly changing area, and there are both benefits and risks to FA testing, especially given that it causes delays in food introduction. Significantly, these guidelines were developed prior to the publication of the LEAP study and related key research findings.

The guidelines of the JTF and AAD share some similarities. Both recommend against food elimination based solely on allergy testing. Patients with positive skin or specific IgE test results may be only sensitized, and consequently not truly react allergically to the oral intake of foods. However, if a patient has a true IgE-mediated FA with a history of type 1 hypersensitivity symptoms, avoidance of the triggering food is recommended to avoid anaphylaxis. Even in these patients with clinically relevant FAs, food avoidance is unlikely to improve their AD [9].

These now out-of-date guidelines suggested that if children have AD refractory to optimal treatment, relevant and limited FA testing may be considered. For children aged younger than 5 years with persistent AD, this may include evaluation of FAs to milk, egg, peanut, wheat, and soy, according to JTF guidelines. In addition, the JTF recommends IgE testing if a FA is clinically suspected. For many patients, this approach could result in avoidance of a food that is clinically tolerated in the patient. In contrast, the AAD recommends a diagnostic elimination diet or controlled oral food challenge if a specific FA is suspected rather than testing. Additionally, the AAD guidelines emphasize the importance of obtaining a thorough history of patient environmental allergies and FAs, upon which to base the need for allergy assessment.

Since the publication of the JTF and AAD guidelines, food avoidance has become increasingly dissuaded, as FAs

may be treatable and food elimination carries a great risk of inducing iatrogenic FAs. Oral immunotherapy has demonstrated efficacy for treating IgE-mediated FAs, including peanut allergy [47–49]. Patients with AD who are tolerating a food without any symptoms of an IgE-mediated reaction should not be subjected to unnecessary allergy testing and avoidance. Healthcare providers must explicitly warn families of the risk of new iatrogenic FA before embarking on an allergy work-up or elimination diet in patients without a history of immediate FA.

5.1 Dietary Choices for Improving AD?

As discussed, avoiding foods is not generally supported for the management of most patients with AD. Yet, there are a few elimination diets being studied for other inflammatory medical conditions. The Six-Food Elimination Diet, is the empirical elimination of milk, wheat, soy, eggs, peanut/nuts, and fish/seafood. Another specialized diet being studied is the Autoimmune Protocol (AIP) diet, an expanded Paleolithic (popularly known as "paleo") diet. The AIP diet draws from dietary changes studied in inflammatory bowel disease, and aims to avoid foods, additives, and medications that potentially provoke intestinal inflammation. Food groups avoided in the AIP diet include dairy, eggs, all grains, legumes, nightshades (tomatoes, peppers), coffee, alcohol, nuts and seeds, refined/processed sugars, oils, food additives, as well as nonsteroidal anti-inflammatory drugs.

Both the Six-Food Elimination Diet and AIP are intended to reduce inflammation and have shown promise as adjunctive treatment in autoimmune and inflammatory conditions such as inflammatory bowel disease [50] and autoimmune thyroiditis [51]. The Six-Food Elimination Diet has been utilized in the treatment of eosinophilic esophagitis [52]. No evidence exists currently on the applicability of these diets for AD. The potential benefits of these diets on reducing inflammation must be balanced with the previously discussed risks of elimination diets as well as increased grocery cost and complexity [53]. Elimination diets should be performed with input from nutrition experts such as dietitians, especially in young children at risk of growth and nutritional deficiencies.

However, the question remains whether any specific foods or supplements exist that, when added to the diet, could have beneficial effects on AD. This is an area under investigation, but several studies show promising results.

5.1.1 Oolong Tea

In an open study of 118 patients with recalcitrant AD aged 16–58 years, drinking oolong tea three times daily after meals was associated with a marked-to-moderate improvement in 63% of participants [54]. The positive effects were first observed after 1–2 weeks of treatment, and a good response was still observed in 54% at 6 months. While knowledge on the pharmacologic properties for oolong tea is incomplete, it is hypothesized that its therapeutic effect is a result of the anti-allergic properties of the polyphenols found in this tea.

5.1.2 L-Histidine

Filaggrin is well established to be impaired in the skin barrier of those with AD. Its precursor, profilaggrin, was previously known as a "histidine-rich protein"; hence, it has been speculated that histidine supplementation could be a therapeutic target. A 2017 in vitro study and double-blind, placebo-controlled randomized controlled trial in 24 adults with AD demonstrated that 4 g/day of oral L-histidine supplementation significantly improved both filaggrin formation and skin barrier function in vitro, and clinically significantly reduced AD severity by 34% after 4 weeks when compared with placebo [55]. The clinical effect of L-histidine paralleled that of mid-potency topical corticosteroids, the cornerstone of traditional AD treatment, without the side effects of long-term topical steroid use.

5.1.3 Hempseed Oil

A randomized crossover study of 20 adult patients with AD found that daily consumption of 2 tablespoons of hempseed oil over 20 weeks was associated with decreased skin TEWL, dryness, itchiness, and use of topical medications, compared with an olive oil control [56]. Hempseed oil is a rich source of omega-6 and omega-3 polyunsaturated fatty acids. The study subjects had significant changes in plasma fatty acid profiles in addition to the improved measured AD symptoms, hence, it is postulated that the clinical improvements originate from these beneficial fatty acids in the oil.

5.1.4 Overall Considerations for Supplements

A 2019 systematic review found that vitamin E and D supplementation have the strongest evidence for benefitting AD management, probiotics may aid in preventing infantile AD, and that preliminary evidence suggests certain fatty acids, including hempseed oil, may help decrease AD severity. Nonetheless, the authors reiterate the idea that further research, specifically randomized controlled trials, are needed and that a small sample size is a common limitation of many studies [57]. Most dietary supplements have low-to-minimal side effects and are inexpensive, and consequently may be reasonable for patients to try if they choose without substantial risk. However, the cost of adding multiple supplements or vitamins to one's diet long term can quickly add up and may offset any potential benefit. Furthermore,

it should be noted that certain supplements, such as vitamin D, may be seriously harmful in excess. It is important for providers to be aware of any supplements, vitamins, or minerals that a patient takes, and to discuss the risks and benefits to set appropriate expectations for patients while preventing adverse effects. See Table 2 for a summary of selected dietary modifications and supplements.

Providers and patients should also be aware that there is considerable evidence for placebo and nocebo effects in dermatology, particularly for itch in AD [58]. Verbal suggestions for itch treatments can influence expectations and self-reported itch, regardless of subject awareness of the placebo [59]. Nocebo effects could be at play regarding the attribution of foods as causative of symptoms; this could contribute to inaccurate claims or self-diagnoses of FA, inordinate testing, and unnecessary food avoidance, as discussed previously [59]. Skin improvement during food avoidance or elimination may be coincidental and/or reflect the placebo effect. Being more conscious of one's diet could be a confounding factor, as patients may simultaneously make healthier food choices, impacting both overall and skin health and inflammation.

The placebo and nocebo effects could be partly responsible for the inconsistency of results and difficulty in studying dietary supplements for AD, as well as the variability of individual results and expectations of patients. Yet, if it occurs for a particular patient, the placebo effect could augment a potentially beneficial dietary supplement and further improve patient quality of life.

6 Conclusions

A strong, though complex, link between FAs and AD clearly exists and should continue to be a focus of investigation though evidence demonstrates both temporally and mechanistically that AD contributes to FA development, rather than the reverse. Infants and children with a predisposition to atopy should receive medical and nutritional guidance when relevant to modulate, and potentially prevent their risk and symptoms. Healthcare providers for patients with AD should regularly explore their patients' ideas of their diet and its interplay with their skin. For example, asking about any dietary changes they have made or are considering, and providing evidence-based recommendations and dietitian referrals when applicable. Families and patients should be counseled on the risks of elimination diets and made aware of the different food reactions to minimize inaccurate FA self-diagnosing and unnecessary avoidance of foods. Delays in food introduction directly contribute to the risk of FA in children with AD, and such delays must be avoided. More interdisciplinary discussion and consensus on the role of FAs and diet, and consequent management, between the

Table 2 Selected potential dietary modifications and supplements for AD

Supplement	SFED/AIP diet	Oolong tea	L-Histidine	Hempseed oil	Probiotics	Vitamin E	Vitamin D
Proposed mechanism	Anti-inflammatory	Anti-allergenic	Improving filaggrin and skin barrier function	Improving cutaneous fatty acid profile, anti-inflammatory	Prevent or correct disease-implicated microbial imbalances	Potent antioxidant, improving immune response	Possibly immunomodulatory, decreased cell proliferation, improved epidermal barrier
Evidence from literature	Has not been studied for AD	Marked-to-moderate improvement [54]	In vitro: improved filaggrin formation, skin barrier function In vivo: reduced AD severity [55]	Decreased TEWL, dryness, itchiness, and use of topical medications [56] May decrease AD severity [57]	No significant difference in symptom severity in established AD, more promising for AD prevention in infants [57]	Significant improvement in AD symptoms, pruritus, extent of lesions Correlated with reduced IgE levels [57]	Significant improvement in AD symptoms, especially when combined with vitamin E [57]
Recommendation	Not currently recommended for AD	Insufficient evidence for general recommendation	Insufficient evidence for general recommendation	Insufficient evidence for general recommendation	Insufficient evidence to recommend for established AD Could consider as prevention in at-risk infants [57]	Some evidence to support its use as monotherapy in mild-to-moderate AD, but further research needed	Strongest evidence for benefitting AD, but further research needed [76] May be harmful in excess

AD atopic dermatitis, *AIP* Autoimmune Protocol, *IgE* immunoglobulin E, *SFED* Six-Food Elimination Diet, *TEWL* transepidermal water loss

different medical providers of patients with AD, mainly dermatology, allergy, and pediatrics/primary care, would have a major impact on improving the efficacy, efficiency, and cost of healthcare for those with AD.

Declarations

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