Dermatologists and pediatric dermatologists frequently treat patients with atopic dermatitis (AD), and patients and guardians often associate AD with food allergies. A common misconception is that dietary restrictions will resolve the disease. The role of diet is evolving in the discussion of AD. The American Academy of Dermatology (AAD) has recently provided recommendations on diet and therapies for AD. This article reviews recent scientific data on the role of foods and dietary modifications in the management of AD as both an intervention and as prevention. **Cutis. 2016;97:227-232.**

**Pathogenesis of AD**

Atopic dermatitis (AD) is the leading diagnosis among pediatric dermatologists, and this condition is commonly seen worldwide by dermatologists and allergists. There is a widespread misconception held by many patients and their guardians who believe that AD is caused by a food allergy. Although AD is related to and part of the atopic complex of disorders associated with food allergies, the role of diet in AD is not well defined. Previously it was recommended to delay early exposure to foods, but now it is recommended to do the opposite in certain situations. In fact, delaying exposure to certain types of foods can increase the likelihood of food allergies (eg, early exposure to peanut butter lowers the statistical chance of developing peanut allergies). This article reviews recent data on the role of diet in AD regarding disease activity as well as new and emerging data on dietary modifications for prevention and intervention. Emerging data on the relationship between AD and food allergies also are presented.

**PRACTICE POINTS**

- Test children younger than 5 years with moderate to severe atopic dermatitis (AD) for food allergies if they have persistently severe AD or known food-induced reactions.
- Food elimination diets are not recommended for management of AD.
- There is not enough evidence supporting the use of complementary and alternative medicine, probiotics/prebiotics, or supplements for the treatment of AD.

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and mucosal sensitization.\textsuperscript{4,5} Another source of percutaneous exposure to allergens is macroscopic breaks in the skin caused by scratching, which allows dendritic termini of Langerhans cells to be exposed to percutaneous antigens\textsuperscript{4,6} through binding to high-affinity IgE receptors.

Langerhans cells exposed to allergens can trigger either an immediate or delayed-type (type I or type II) reaction (sensitization phase) in the lymph node causing inflammatory activation (elicitation). Inflammatory activity in AD is broad and complex and includes the release of IL-4, elevated IgE levels, and eosinophilia, which trigger the helper T cell T\textsubscript{H}2 and T\textsubscript{H}17 cascade of cytokines, including IL-2, IL-4, IL-5, IL-8, IL-10, IL-13, IL-17\alpha, tumor necrosis factor \alpha, and IFN-\gamma.\textsuperscript{7-9} with the latter worsening barrier defect via downregulation of intercellular substances (eg, filaggrin) and intercellular adhesion expression (eg, claudin 1).\textsuperscript{6,7,10}

Atopic dermatitis does not exist in isolation. The barrier dysfunction associated with AD allows for sensitization to allergens, including those found in food and/or the environment. The atopic march, which occurs via barrier abnormalities facilitating sensitization, can result in further atopy, such as food allergies, environmental allergies, asthma, and eosinophilic esophagitis.\textsuperscript{11}

\section*{AD and Food Allergies}

Many patients and guardians believe AD is caused by a food allergy and that diet restrictions will resolve the disease. Although the latter is not true, in reality many patients with AD do have food allergies. Approximately 40\% of infants and young children with moderate to severe AD and 8\% of the general population of children will manifest a specific IgE-based food allergy. Food-specific IgE can be triggered or exacerbated by AD through the induction of hives, cutaneous activation of mast cells, increased “spontaneous” basophil histamine release, and food-related lymphocyte-proliferative responses measurable by food patch testing.\textsuperscript{12} Allergists generally recommend avoidance of or use of heavily denatured food (in the case of a milk/egg allergy) in the setting of documented IgE-mediated allergens.\textsuperscript{13} Food allergies in AD can manifest with flares, hives, pruritus, and/or other cutaneous symptoms in the absence of flaring AD disease.

Guidelines from the American Academy of Dermatology (AAD)(Table) for the management of AD have recently recommended testing for food allergies in children younger than 5 years who have intractable AD or known food-induced reactions.\textsuperscript{14} This technique will largely identify children at risk for anaphylaxis but may not yield information contributing to AD improvement. Furthermore, withdrawal of allergens with known IgE-mediated response was classified by the AAD as having consistent good-quality patient-oriented evidence, and asking about allergic reactions as well as acting on a reported allergic history had inconsistent or limited-quality patient-oriented evidence. It is believed that atopy can progress, or march, into a food and/or environmental allergy at any point in life; therefore, testing for a food allergy should be considered in all patients.
with recent onset of severe and/or persistent AD and/or food-aggravated AD due to a lifetime risk of sensitization. A food introduction plan may require collaboration with an allergist, especially in high-risk patients (eg, those with known food reactions, family history of food allergies, severe atopy).

**Prevention of AD Through Dietary Modification**

The National Institute of Allergy and Infectious Diseases consensus group published guidelines on food allergies that affect AD management, including avoidance of proven allergens but not random elimination of food allergens in AD; the group identifies AD and family history of AD as risk factors for food allergies. The best data in support of avoidance of documented food allergens to reduce AD severity has been found for egg white allergy and avoidance. Active egg allergy also is linked to staphylococcal superantigen IgE sensitizations, but the reason for the link is not yet clear. For the pediatric population, exclusive breastfeeding until 4 to 6 months of age and introduction of solids within the first 4 to 6 months as well as avoidance of maternal dietary restriction during pregnancy and lactation was further endorsed, with use of hydrolyzed formulas as an alternative to exclusive breastfeeding in infants who are not exclusively breastfed.

A Cochrane review of maternal dietary restrictions during pregnancy found no benefit of maternal prenatal dietary restriction on AD prevalence in the first 18 months of life but did note an association with lower mean gestational weight. There is currently an effort to produce foods, such as soybeans and corn, that are genetically modified to reduce exposure to the allergenic component, but it is possible that when large-scale challenges occur, these foods also will be allergenic.

In the case of a modified apple, some promising reduction in allergy symptoms has been reported. In the case of a modified apple, some promising reduction in allergy symptoms has been reported.22 Inactivation of staphylococcal superantigen IgE sensitizations,17 but the reason for the link is not yet clear. For the pediatric population, exclusive breastfeeding until 4 to 6 months of age and introduction of solids within the first 4 to 6 months as well as avoidance of maternal dietary restriction during pregnancy and lactation was further endorsed, with use of hydrolyzed formulas as an alternative to exclusive breastfeeding in infants who are not exclusively breastfed.

**Complementary and Alternative Medicine**

The AAD guidelines do not recommend complementary and alternative medicine (CAM) to treat AD, but it remains a commonly used therapy in the United States. A 2014 analysis of data from the 2007 US-based national health interview survey of 9417 children (age range, 0–17 years) demonstrated that 46.9% of children used 1 or more CAM, of which 0.99% used CAM specifically for AD. In this study, herbal therapy, vitamins, homeopathy, diet, and movement techniques were associated with increased prevalence of AD. Some herals have been shown to be beneficial in AD, hepatotoxicity has been reported with some herbal therapies. Complementary techniques with evidence-based support include massage therapy, relocation to an alternative climate, acupuncture that rivals cetirizine in efficacy, and supportive nutritional advice.

**Factors Affecting the Incidence of AD**

Atopic dermatitis is of greater prevalence in children in developed wealthy nations such as the United States, supporting the role of enhanced hygiene and overall good health through vaccination as a possible contributor to the rise in AD prevalence in the last 4 decades. Alternatively, viruses such as respiratory syncytial virus may trigger AD, suggesting vaccination against the virus may reduce the risk for AD. Overall, vaccination improves life expectancy and should be conducted on schedule without reservation. Other aspects of hygiene that could conceptually affect prevalence of AD are raw food ingestion and the effects of foodborne microbes on the intestinal microbiome in relationship to AD development. Probiotics have been tested for this purpose.

Probiotics and prebiotics have been theorized to work through a reduction in inflammation; these agents have some evidence in their favor, but they were not endorsed in the AAD guidelines despite showing promise in meta-analysis. In particular prenatal and postnatal (maternal and child) supplementation of Lactobacillus rhamnosus shows promise. Food elimination diets and supplements including vitamin D, selenium, fish oil, borage oil, and zinc were not found to be beneficial and were not recommended in the AAD guidelines.

Percutaneous exposure to peanuts, possibly in household dust, may be the mechanism of peanut sensitization in AD via an inherent adjuvant effect of peanut protein. The recent LEAP (Learning Early About Peanut Allergy) trial randomized 530 infants aged 4 to 11 months to peanut-avoidant versus peanut-exposed diets for 60 months. The results showed statistically reduced (approximately one-twelfth of the risk) peanut allergy even in infants known to be sensitized (approximately one-third of the risk). It is now recommended in countries with a high prevalence of peanut allergies to introduce peanuts to an infant’s diet between 4 and 11 months of age (evidence level 1 [highest level of evidence]), with referral to an allergist for introduction in known sensitization cases and severe AD. In the setting of known or documented peanut
allergy and for evaluation of potential food allergies, an allergist should be consulted.

Other interventions have been described as promising in mouse models. Those supplements include Lithospermum erythrorhizon,57 Platycodeon grandiflorus,58 Hypsizygus marmoreus,59 fortified ginseng extract,60 polyunsaturated fatty acids,61 and galactooligosaccharide.62 Prebiotic oligosaccharides also are promising for early prevention of AD symptoms in infants, but otherwise these agents have remained largely untested in AD.63 None of these therapies have been endorsed by the AAD, and the long-term safety and efficacy in humans remains to be proven.

Risks of Dietary Restriction
Dietary restrictions in treating AD can have negative consequences, including reduced birth weight when initiated in pregnancy,19 osteomalacia from vitamin D deficiency,49 and nutritional deficiencies (eg, calcium, phosphorus, iron, vitamin K, vitamin D, zinc, vitamin A, B1, B2, B6, niacin, cholesterol, and/or vitamin C deficiencies).45 Excess dietary intake of vegetables in individuals with extensive food allergies can result in carotenemia.46 Protein-restricted diets from use of rice milk or dietary protein restriction can result in kwashiorkor-like protein malnutrition and marasmus.47-49 Nutritional deficiencies in the skin; therefore, nutrition counseling and/or supplementation is recommended for patients with food-restricted diets.

Avoiding Fragrance in Food
Food intolerance often is reported by AD patients. In allergies, food intolerance refers to side effects such as gastrointestinal symptoms; in dermatology, food intolerance can include itching, systemic flares of allergic contact dermatitis (eg, fragrance allergy), or true IgE-mediated allergies such as oral allergy syndrome. Oral allergy syndrome (pollen-food allergy syndrome) is an epitope-spread phenomenon related to an allergy to tree pollen, causing broad allergy to specific groups of fruits and nuts.50 Food triggers in AD include kiwi, milk, apple, tomato, citrus fruits, tree nuts, and peanuts. Oral allergy syndrome is common in food-sensitive AD patients (51.2%) followed by gastrointestinal symptoms (23.5%) and worsening AD (11.4%).51 Sensitization to fragrance can cross-react with foods (eg, balsam of Peru and tomatoes).52 A tomato allergy can be detected either by a skin-prick test or a food patch test in this setting.53 An allergist should be consulted if oral allergy syndrome is suspected.

Conclusion
Food allergies are more common in AD patients and patients should be referred to an allergist for evaluation and management. Strict dietary practice is not recommended, while avoiding proven food allergens in AD could be beneficial. Dermatologists should be aware that patients with dietary restrictions may lack key nutrients, manifesting with nutritional deficiencies in the skin; therefore, nutrition counseling may be needed in the most severe AD/allergy patients. This field is evolving; therefore, ongoing study and evaluation of interventions as they relate to AD will be needed to assess best practices for diet in AD over time.

REFERENCES


