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Review of Evidence for Dietary Influences on Atopic Dermatitis

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Abstract and Introduction

Abstract

Atopic dermatitis (AD) is a chronic inflammatory skin disease affecting children and adolescents worldwide. The relationship of AD to diet has been a matter of curiosity for many years. Here we look at the evidence in the literature of the association between AD and diet, and the effectiveness of elimination diets and diet supplementation in the management of AD. Several studies have found an association between clinical food allergy and AD, and more recent investigations have also suggested that dietary elements may promote late AD exacerbations. Diet elimination trials in select patients who are clinically allergic to eggs have shown promise in reducing symptoms. Additionally, elimination of food additives in a subgroup of patients was found to be beneficial. Finally, diet supplementations with evening primrose oil and an omega-3 fatty acid (docosahexaenoic acid) may be appropriate in certain AD candidates.

Epidemiology

Atopic dermatitis (AD), often referred to as eczema, is a relapsing pruritic inflammatory skin condition that affects a range of 1–22% of children and adolescents worldwide,[1] and approximately 11% of children in the US.[2] The incidence of the condition appears to be increasing, with the strong predictors of high prevalence being metropolitan living, black race, and an educational level greater than high school.[2] Healthcare services have also seen more of the condition in the last several decades, as the number of office visits for eczema increased from 620,000 in 1997 to 1.7 million in 2003.[3]

Pathophysiology of Atopic Dermatitis

Atopic dermatitis is often placed within a cluster of atopic diseases, along with asthma and allergic rhinitis. The traditional model for the pathophysiology of the disease describes hypersensitive immunological reactivity of mast cells, dendritic cells, immunoglobulin E (IgE) production, and a predominant T helper type 2 (Th2) cell response to environmental triggers. In this model, skin sensitization is similar to the airway sensitization seen in asthma.

AD is now predominantly considered a disorder of epidermal barrier structure and function, rather than a downstream consequence of immunologic hypersensitivity, as previously thought. We now consider epidermal barrier failure as the main driving force behind the subsequent release of pro-inflammatory mediators.[4] Filaggrin gene defects are at the center of this mechanism. Those with filaggrin loss of function mutations (FLG) were more likely to have dry skin even in the absence of clinical eczema (OR 8.50, 95% CI 1.09–66.58), and were more likely to subsequently develop clinical eczema by 3 months of age (OR 4.26, 95% CI 1.34–13.57). In addition to their association with AD, filaggrin gene defects also increase the risk of developing allergic sensitization and allergic rhinitis. Furthermore, they increase the risk of developing asthma in those with established AD.[5] Thus, the current understanding of the pathophysiology of AD represents a complex interplay between genetics, skin barrier structure and function, as well as sensitization to environmental exposures. Those with genetic predisposition are at increased risk of developing AD with particular exposures.[6]

Clinical Features

Most individuals with atopic dermatitis have an onset of the disease before the age of 7,[7] and the condition will clear in nearly 40% of patients by adulthood. The condition manifests as dry skin, pruritus, and secondary changes to the

skin as a result of chronic rubbing or scratching. The type and location of lesions varies with the stage of the disease, often presenting in extensor surfaces and cheeks in infants, as opposed to a flexural or palmar/plantar distribution in older children, adolescents, and adults. The UK working group's diagnostic criteria for atopic dermatitis are the most consistently validated ().[8]

Table 1. UK diagnostic criteria for atopic dermatitis

Must exhibit evidence of pruritic skin in addition to 3 or more of the following:
• General dry skin in the last 12 months • Visible flexural involvement* • History of flexural surface involvement* • Personal history of asthma or allergic rhinitis** • Onset <2 years of age***

*For children <18 months of age, can be met by cheeks and/or extensor involvement

**History of atopic disease in first degree relative in children <4 years of age

***Does not apply to children <4 years of age

Association With Allergic Disease

Allergic associations remain a common finding in many patients diagnosed with AD. Eichenfield et al. found that up to 80% of children with AD will eventually develop asthma and allergic rhinitis, and recommended that AD be treated with guidelines much like those currently used for asthma therapy.[9] In a study in Japanese nursery school children, Fukiwake et al. found that elevated serum IgE levels, maternal history of atopy, as well as past history of asthma and food allergy were all linked to developing AD in children up to 6 months of age.[10]

Association With Diet

The relationship between AD and food allergies in particular has been of great interest. In a study published this year from the International Study of Asthma and Allergies in Childhood (ISAAC), consumption of three or more servings of fast food was linked to development of asthma, rhinoconjuctivitis, and AD.[11] As with any other cross-sectional study, the temporal association of diet to AD was not established in this study, and no causal conclusion was possible, but the findings relay an important public health question: Are certain foods related to the development or exacerbation of AD? And if so, will restricting diets lead to improvement of symptoms?

Food allergies can manifest through different immunological mechanisms. In the skin, they can progress acutely via an IgE mediated response, or in a subacute manner via a non-IgE mediated mechanism. Skin manifestations specific to foodexacerbated AD are considered to occur through both an IgE and a non-IgE mediated reaction. Therefore, some reactions occur within minutes to hours of ingestion, while others may take days to appear. IgE mediated food allergen sensitization is often evaluated via skin prick testing (SPT) or in vitro testing for foodspecific IgE, the latter being a less sensitive test.

The rate of food allergen IgE sensitization in infants with eczema is variable in different populations. Garcia et al. found a rate of 61% in a study of 44 infants. The severity distribution of AD in this study included 32% of patients with mild,

64% with moderate, and 4% with severe AD, with the most frequent sensitization observed to egg.[12] High levels of sensitization to wheat, soy and peanuts are commonly observed in other similar studies.[13] Hill et al. found that among a cohort of infants who had IgE mediated positive skin prick testing to food allergens, 56% were categorized as having AD. Additionally, they noted that in those diagnosed with severe AD, the prevalence of IgE sensitization was 69%. The relative risk of an infant with AD having IgE mediated food allergy was 5.9 for those who were most severely affected.[14]

Allergen sensitization alone, however, does not prove that a clinically significant food allergy exists. Positive skin prick testing indicates presence of IgE antibody, with a positive predictive accuracy of 50% depending on the food being tested.[15] Clinical reactivity must be assessed via double-blind placebo-controlled food challenges (DBPCFC) for suspected IgE mediated allergy or elimination and reintroduction of foods for suspected non- IgE mediated allergies in order to categorize patients as those with clinically significant food allergies. Eller et al. found large discrepancies between sensitization and confirmed food hypersensitivity. This study also found that children with AD were not more IgE sensitized than healthy children, but did have more persistent sensitization. Based on these results, the authors recommended standardized oral challenges for confirmation of food allergy in future studies.[15] In another study, 32% of children in a birth cohort with AD were sensitized to a food allergen, but only 18% demonstrated clinical reactivity.[16]

In those who do exhibit clinical food allergy, immediate reactions occurring via an IgE mediated mechanism are well documented throughout the literature. In the above study, the severity of AD was demonstrated to be higher in children with clinical food allergy than those without clinical allergy. In a prospective cohort study among 63 children referred for dermatological care for AD, Eifenmann et al. found that 37% of children categorized as having moderate to severe AD had clinically significant IgE mediated food hypersensitivity.[17]

The occurrence of non-IgE mediated reactions have been a subject of debate for some time. Non-IgE mediated skin reactions to food ingestion tend to occur within hours to days of ingestion of the offending foods. The assessment of this type of reaction is not well established, making measurement of reactivity more difficult. Evidence suggests that particular foods correlate with late AD exacerbation. Breuer et al. conducted 106 doubleblind placebo-controlled food challenges to cow's milk, hen's egg, wheat, and soy in 64 children with AD, and found that 46% of the challenges were associated with eczematous reaction 24 hours after ingestion.[18] Uenishi et al. investigated irregular aggravation of skin lesions in 69 children aged 3–15 years with AD via challenge tests. Seventy-five percent of the subjects had confirmed challenge-positive tests 48 hours after ingestion, with the predominant offending foods of chocolate, cheese, and yogurt. Specific IgE antibodies to the offending foods were found to be mostly negative. Additionally, the study excluded offending foods from patients' diets for 3 months, improvement of skin lesions was assessed in a follow-up visit.[19]

Dietary Elimination

Elimination diets as a general treatment in unselected patients with AD are not recommended, as evidence has not demonstrated improvement in symptoms. However, a select group of patients with clinically relevant food allergy may benefit from particular dietary restrictions. A Cochrane systematic review based on nine randomized controlled trials concluded that eliminating egg from the diet in those who had positive specific IgE to eggs proved beneficial.[20] As such, the American Academy of Dermatology recommends egg restriction in the subset of patients with AD who are found to be clinically allergic to eggs.[21] Food additives elimination has been studied in adult patients with AD, in which investigators imposed restrictions on preservatives such as sorbic acid and coloring agents such as tartrazine in study participants' diets for 6 weeks. Results showed that a subgroup of patients in the study clinically improved after removal of these food additives, while only a small group clinically responded to a double-blind additive challenge with the same food substances.[22]

Dietary Supplementation

Studies on various dietary supplementations have found that evening primrose oil may be beneficial in those who do not use high potency steroids.[23] Docosahexaenoic acid (DHA) has been shown to be of benefit in decreasing the severity of eczema in a small randomized controlled trial that had a large dropout rate.[24] Fish oil, vitamin D, and vitamin E supplementation have shown symptom improvement in several randomized trials. However, evidence was found to be of questionable clinical significance, as many of the studies were small with a low number of participants and poor quality.[25]

Conclusion

The pathophysiology of atopic dermatitis represents complex interactions between genetics, physiology, and the environment. The relation of AD to food allergens signifies the crucial role of environmental exposures in the development and severity of the disease. Several studies have shown that sensitization to food allergens is significantly correlated with the disease. Furthermore, clinically significant food allergies have been linked with IgE mediated dermatologic reactions in those with AD. Late non- IgE mediated reactions have also been documented with AD exacerbations 24 to 48 hours after exposure to the offending food. Dietary eliminations for those with known allergy have demonstrated improvement in AD symptoms, while some dietary supplementations appear to decrease the severity of the disease. These findings suggest that diet and AD may be linked in a pathophysiologic manner. Future studies should further investigate the specific mechanisms that contribute to these relationships in order to facilitate clinical management of AD.

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