

# The Relationship between Atopic Dermatitis and Food Allergy


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## ABSTRACT

Atopic dermatitis (AD) is a chronic inflammatory skin disorder characterised by an inadequate skin barrier. This can be caused by a variety of reasons such as hereditary predisposition and immunological dysregulation. AD affects 20% of infants, it is the most common chronic inflammatory skin disease in this group, and 3% of adults. It typically manifests as moderate disease, with two-thirds of people with AD unlikely to develop sensitivity to environmental allergens; nonetheless, there have frequently been connections with atopic diseases, particularly IgE-mediated food allergy (FA). Allergy is confirmed with a food challenge test before restricting this in the diet. Up to one-third of children with early-onset AD experience an atopic march, which is characterised by the later development of atopic disorders including asthma, allergic rhinitis and/or rhinoconjunctivitis, food allergies, and hay fever. As a result, AD and food allergy are linked, and recent research shows that AD develops before food sensitisation, and food allergy relates to atopic dermatitis of varied severity.

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## 1. INTRODUCTION

Atopic dermatitis (AD), often known as atopic eczema, is a chronic inflammatory skin disorder, the most common in children. It frequently begins before the age of five and is relapsing-remitting, with many people improving by adolescence. It is distinguished by a deficient epidermal barrier [1], [2]. The pathophysiology is linked to factors such as filaggrin gene mutations, low humidity, and cutaneous imbalance, all of which induce a decrease in filaggrin expression and hence impact epidermal functioning [3]. The barrier allows allergens and irritants to pass through, triggering an immunological response. Th2, th22, th17, and th1 cytokine pathways can all be activated, with th2 expressing the most IL-4, IL-5, and IL-13 while also elevating IgE and peripheral eosinophilia [4]. Radioallergosorbent testing (RAST) looks at the blood to assess for specific IgE antibodies to known or already suspected antigens and can be used to confirm specific allergens which mount a hypersensitivity response [5], [6] (Figs. 1, 2). AD is diagnosed based on a comprehensive clinical picture—often dry, itchy, erythematous skin, and in many cases, a history of an allergen, confirmed by RAST testing, which triggered dermatitis.

AD occurs in 21.5% of children in their first year of life, 43.2% spontaneously outgrow the disease and 18.7%

persist into severe AD with a likely atopic march including FA, asthma, and rhinitis [7]. Although predominantly in children, AD can also occur in adulthood.

Food allergies (FA) are estimated to affect 3–10% of children and can have a negative influence on quality of life [7]. Adverse food reactions can be immunological (IgE) mediated, with symptoms appearing two hours after intake. This is common in the case of eggs, cow's milk, soya, peanuts, fish, and shellfish [8], [9]. Symptoms involve dermal erythema, pruritis, urticaria, and upper respiratory congestion, as well as rhinorrhoea [10]. If the reaction is severe enough, there may be angioedema of the lips and tongue, which can lead to anaphylaxis. It can also be non-IgE mediated, which manifests a delayed response and can also present in other conditions like AD or food protein-induced enterocolitis [11]. The delay makes an association with an allergen less clear thus a comprehensive history is essential, as is frequently exploring a food diary with significant events such as transferring from formula feed to solid food [2]. It can also be a combination of reactions with both immediate and delayed manifestations.

The association of FA and AD was first explored in 1983 when Sampson used double-blind oral food challenges in 26 children with elevated total IgE [12]. A strong association was found between IgE-mediated food allergy and

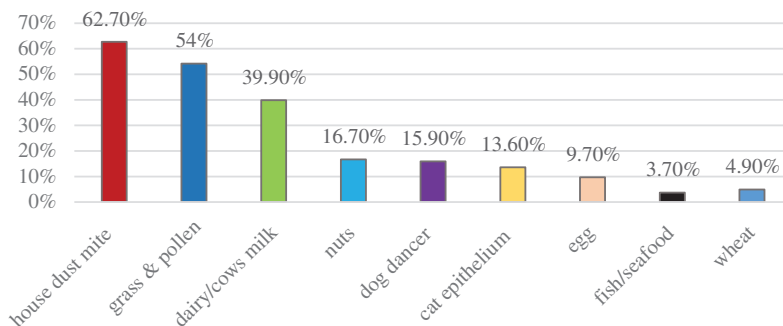


Fig. 1. This figure shows the percentage of raised specific IgE levels for each allergen tested in 81 adults with atopic dermatitis [5].



Fig. 2. This figure highlights the individual-specific IgE levels among patients who tested positive for RAST testing in 133 children with eczema [6].

atopic dermatitis. Specific IgE antibodies can be measured using radioallergosorbent testing, which has been deemed valuable for the investigation and management of atopic dermatitis [8]. In this trial, trigger foods were eliminated 2 weeks before the trial. In fifteen of the children, there was FA and 57% of patients with AD had a positive reaction to food. More recently, a population cohort study of over 4000 children highlighted infants with AD were six times more likely to have FA to cow milk, egg or peanut at age 12 months compared to those without AD [13]. We shall explore the relationship between FA and AD and comment on the advances made in this research, predominantly focusing on studies which involve children.

## 2. METHOD

The literature was searched using Pubmed and the Cochrane Library with focused search terms ‘food allergy’ AND ‘atopic dermatitis.’ This paper explores one review article on the advancing methods for FA and AD prevention, a systematic review on complementary feeding and food allergy, and a report from the National Institute of Allergy and Infectious Diseases workshop on AD and the atopic March. The papers identified were published from 2017 to 2020 to include relevant and current advancements.

## 3. DISCUSSION

A 2020 review, which focused on recent advancements in AD and FA, looked at the mechanisms and therapeutic

advancements in the management of AD and FA. With regards to FA, the review commented on precision and personalised medicine for food allergy and particularly the role of biomarkers for early prediction of severe FA [14]. Currently, the method for treatment of FA is strict avoidance with the use of rescue pack medication if there is an allergic reaction. However, newer methods in current research include adding anti-IgE as a biological agent to improve food intolerance, which effectively reduces allergic side effects. Nanoparticles or DNA vaccines have also been investigated in a study which involved using CpG-coated nanoparticles with a peanut extract in a mouse model for peanut allergy; this significantly protected the mice from anaphylaxis. The use of early introduction of the allergen has been a route to prevention, with evidence that early egg introduction reduces the risk of developing egg allergy. The use of systemic IL-2/anti-IL-2 complexes was used on mice too which showed promising responses and suppressed side effects [14]. Like FA, the review also commented on oral immunotherapy for AD protection whereby administration of increasing amounts of allergens later provided protection against AD by the expression of Th2 inflammatory responses and the skin barrier functioning. Additionally, a study commented on the medical benefit of topical ivermectin, often used for scabies and rosacea, to provide protection against AD by priming the allergen-specific T cells [15].

A 2019 systematic review explored the relationship between the introduction of complementary foods and beverages (CFBs), and the amounts of CFBs consumed with the development of food allergy, atopic dermatitis,

asthma, and allergic rhinitis [16]. In total seventy-eight articles were identified via 4 databases. 31 of these articles focused on the timing of CFBs and 47 looked at the types and quantity consumed. The CFBs explored were common allergenic foods such as peanuts, tree nuts, shellfish, eggs, cow milk products, and wheat. In twenty studies, the relationship between the introduction of CFBs and atopic dermatitis was explored. However, in half of these studies, the population was already at high risk of atopic disease due to familial or paternal history. Fifteen of the studies commented on no significant relationship between the introduction of CFBs and the risk of AD development. In five of the studies, there was an exploration of the relationship between the age of tree nut or peanut introduction and the risk of later AD. Later introduction was associated with a lower risk of AD at 4 years. Another study commented on earlier nut introduction and decreased risk of AD. One study commented on no significant association between the age of peanut or tree nut introduction and risk of AD at 2, 3, or 4 years. The overall argument was that there was no relationship between the timing of introduction of allergenic foods and the risk of development of FA, AD or childhood asthma. There was limited evidence to suggest that the introduction of allergenic food in the first year of life may prevent peanut and egg allergy. The review concluded that the evidence was limited to quantifying a relationship between a varied diet and atopic disease.

In a 2017 report from a workshop sponsored by the Division of Allergy, Immunology and Transplantation of the National Institute of Allergy and Infectious Diseases the mechanisms and interventions for AD and the atopic march were discussed with reflection on developmental relationships between AD, FA, and airway allergic diseases [17]. In one part of the report, there was an association between AD and FA in human subjects. Infantile AD in the first 6 months of life was associated with the development of FA, as well as immediate hypersensitivity to food. Earlier forms and more severe forms of AD were associated with a higher risk of AD. Data from the Learning Early About Peanut Allergy (LEAP) study highlighted that of 321 children with AD, 76% had 1 allergic disease and 40% had FA at the age of 5 [18]. This study included 640 infants in total aged 4–11 months old. The cohort had egg allergy, severe eczema, or both. Those who had a peanut-free diet had higher rates of peanut allergy. However early peanut introduction in high-risk children, aided in the prevention of peanut allergy formation. The mechanism linking AD and FA was a dysfunctional epithelial barrier which allowed for cutaneous exposure to the environmental allergen resulting in FA, likewise, to patients with AD their impaired skin barrier allowed penetrating food allergens. There is also a genetic relationship between FA and AD. The FLG (filaggrin gene) maintains the skin's barrier and was associated with peanut allergy and independently AD. The review commented on high-level exposure to environmental peanut dust and increased sensitisation to peanuts, highlighting the genetic and environmental relation, as well as how early exposure can help to prevent later FA.

#### 4. LIMITATIONS

The data discussed is limited in various ways. The systematic review discussed involved a skewed population with a familial or paternal history of atopic disease in over half of the patients. Thus, conclusions are likely to be on a genetic basis and for patients with undiagnosed AD, the relationship to develop FA at a later stage is likely to be explored due to genetic history.

The data is also limited by the focus on children, although this was mainly due to a lack of studies on the adult population with AD or FA, it is limited to comment on adult or adolescent relation between AD and FA. A 2020 review showed a varied prevalence of FA in patients with AD and reflected on studies of food-triggered AD in older children and adults which although few, showed little association, with limited benefit using elimination diets. Food-triggered AD was more common in infants and young children who had existing severe AD [19].

#### 5. CONCLUSION

The association of AD and FA are commonly seen in children. Genetic and environmental factors including reduced filaggrin, filaggrin mutation, and IL-4 receptor alpha chain polymorphisms contribute to a change in the immunological phenotype which increases or decreases susceptibility of developing FA. Quantifying how severe or if there is early-onset AD in children can determine the likelihood of the development of atopic disease. Early preventative strategies such as the introduction of such foods in infants can help to prevent FA in children with known AD.

#### CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

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