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The Evaluation and Management of Food Allergy in Atopic Dermatitis

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Atopic dermatitis (AD) is a form of eczema that generally begins in early infancy and is characterized by extreme pruritus, chronically relapsing course, and distinctive morphology and distribution. AD is typically the first clinical manifestation of a child prone to develop atopic disease, with 50% of all AD developing in the first year of life and 80% by 5 years of age. Approximately 80% of children with AD develop asthma or allergic rhinitis; many lose their AD with the onset of respiratory allergy. The acute rash of AD is typically an erythematous, papulovesicular eruption, occasionally with weeping and crusting that is more commonly seen in early life. It typically progresses to a subacute form marked by erythema and scaling papules, and, especially in older patients, to a chronic form characterized by thickened, lichenified skin and fibrous papules.[1] The distribution of the rash varies with age,[2] involving the cheeks and extensor surfaces of the arms and legs in infancy, the flexor surfaces in the young child, and flexor surfaces, hands, and feet in the teenage patient and young adult. Atopic dermatitis is identified by a constellation of symptoms. Standard diagnostic criteria exist[3] and are an accepted standard for diagnosing atopic dermatitis, and the SCORAD Index[4] adapted by the European Task Force on Atopic Dermatitis provides a standardized method for gauging severity.

The pathogenic role of allergy in atopic dermatitis has been debated since Besnier first described the eczematous rash that has become known as AD. However, recent studies delineating the immunopathogenic role of immunoglobulin (Ig)E-bearing antigen-presenting cells (eg, Langerhans cells and other dendritic cells) in establishing the initial Th2 lymphocytic response and of the IgE-mediated late-phase response in provoking cutaneous inflammation, numerous clinical studies demonstrating the provocation and resolution of skin symptoms in a subset of AD patients with the introduction and elimination of allergen, and the development of a murine model of a food-induced eczematous rash leave little doubt about the pathogenic role of allergy in some AD patients.[5]

Immunopathology of Atopic Dermatitis

Approximately 85% of patients with AD have elevated serum IgE levels, and about 85% of these have evidence of specific IgE antibodies to food and inhalant allergens.[6] The immunopathogenic role of allergen-specific IgE antibodies in AD involves a number of cell types. Receptors for IgE antibodies have been identified on B cells, T cells, monocytes, macrophages, dendritic cells, eosinophils and platelets.[7–9] Langerhans cells, "professional" antigen-presenting cells in the skin, are more numerous in atopic dermatitis lesions, possess allergen-specific IgE antibodies on their surface,[10], and are highly efficient at promoting Th2 responses to allergens.[11,12] Utilizing in situ hybridization, cytokines expressed in lymphocytes found infiltrating skin lesions in AD have been shown to reflect an allergic milieu. In acute lesions (less than 3 days) infiltrating T lymphocytes express predominantly the Th-2 cytokines, interkuekin (IL)-4, IL-5, and IL-13, while T cells in chronic lesions express predominantly IL-5 and IL-13[13,14]. This is in distinct contrast to classic Type IV cellular responses, such as tuberculin test (PPD) or rhus dermatitis (poison ivy), where cells express primarily mRNA for interferon γ and IL-2, but not IL-4 and IL-5[15].

The Th-2 cytokines promote chronic allergic inflammation by upregulating adhesion molecules on vascular endothelial cells, eg, vascular cell adhesion molecule-1 (VCAM-1), E-selectin and intercellular adhesion molecule-1 (ICAM-1),[16] up-regulating high-affinity receptors for IgE antibodies on Langerhans cells and other antigen-presenting cells, recruiting eosinophils and other inflammatory cells to the site, and promoting local synthesis of IgE antibodies. Adhesion molecules are not typically expressed in the skin of nonatopic individuals, but are expressed in normal appearing skin of AD patients and are markedly upregulated in skin lesions or following epicutaneous application of allergen in sensitized, AD patients.[17] Keratinocytes do not express MHC class II antigens, a sign of interferon-γ stimulation typically seen in delayed-type cell meditated reactions.[18] The high-affinity receptors for IgE on Langerhans cells, through bound IgE antibodies, play a

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special role as "nontraditional" receptors on these antigen-presenting cells.[19] IgE-bearing Langerhans cells are 100- to 1000-fold more efficient at presenting allergen to T cells (primarily Th-2 cells) and activating T cell proliferation.

Although identification of relevant provocative allergens is often problematic due to the multiple "trigger" factors known to elicit flares of AD, evidence at the cellular and molecular level strongly implicates an allergic component in AD, especially in children. Patients with AD generally have elevated levels of total[20] and food protein-specific IgE antibodies.[21] Blinded oral food challenges in food-allergic AD patients lead to sharp increases in plasma histamine concentrations,[22] activation of plasma eosinophils,[23] and infiltration of eosinophils and elaboration of eosinophil products in acute skin lesions.[6,24,25] In vitro stimulation of peripheral blood mononuclear cells from AD patients with IgE-mediated milk-induced skin symptoms led to proliferation of T cells bearing the cutaneous lymphocytes antigen (CLA), which was not seen in patients with milk-induced gastrointestinal disease[26] or asthma. Food antigen-specific[27] (and aeroallergen-specific[28]) T cells have been cloned from active skin lesions and normal skin of patients with AD. Food antigen-specific T cells have been routinely identified from peripheral blood in subjects with relevant food protein-induced AD.[26,29,30]

Mechanisms involving IgE antibodies, other than direct IgE allergen activation of cutaneous mast cells, are also believed to play a role in the inflammation of eczematous skin. Children with AD and food hypersensitivity who were chronically ingesting foods to which they were allergic were found to have high "spontaneous" basophil histamine release from peripheral blood basophils in vitro compared to patients with AD and no food allergy or to normal controls.[31] When placed on an appropriate food allergen elimination diet for 1 year, food-allergic children experienced good clearing of their eczematous rash and a significant fall in spontaneous basophil histamine release (38.0 ± 9.6% to 4.3 ± 2.1%; $P < 0.01$). Peripheral blood mononuclear cells from food-allergic subjects with high spontaneous basophil histamine release were found to elaborate a 23 kD cytokine termed histamine-releasing factor (HRF) that could activate basophils from food-sensitive, but not food-insensitive children.[32] Several isoforms of IgE are secreted,[33] and it has been postulated that histamine-releasing factor interacts specifically with some isoforms of IgE. Passive sensitization experiments using basophils from nonatopic, control donors and IgE from food-allergic patients revealed that these basophils could be rendered sensitive to histamine-releasing factor.[31] Passive transfer of IgE from non-food-allergic individuals to these same basophils failed to render the basophils sensitive to histamine-releasing factor.

Although eosinophils are not prominent in histologic sections of AD lesions, as seen in allergen-induced asthma, immunohistochemical staining of AD skin has revealed prominent deposition of eosinophil major basic protein and eosinophil-derived neurotoxin in active eczematous lesions. Major basic protein is a cytolytic protein secreted almost exclusively by eosinophils capable of damaging skin epithelial cells[34] and promoting mast cell degranulation.[35] Biopsies of eczematous skin lesions from AD patients demonstrated extensive extracellular major basic protein deposition in a fibrillar pattern in the superficial dermis, not found in uninvolved skin sites in these same patients.[24] Similar studies in patients with contact dermatitis (rhus dermatitis) revealed no dermal deposition of major basic protein. These studies provide further evidence of an IgE/Th2-induced cutaneous reaction. Infiltrating lymphocytes are capable of releasing a variety of interleukins that may promote mast cell proliferation (IL-3), cell surface expression of Fcε receptors and IgE synthesis (IL-4), eosinophil proliferation (IL-5), etc.

Clinical Studies of Food Hypersensitivity and Atopic Dermatitis

A number of early reports suggested that food proteins could provoke eczematous skin rashes. As early as 1915, cases were reported of patients who experienced improvement in their eczematous skin lesions after avoiding specific foods.[36] Shortly thereafter, additional studies[37,38] described two series of patients who experienced clearing of their skin when foods eliciting positive skin tests (food-specific IgE) were removed from their diets. Subsequently, a series of classic experiments[39,40] unequivocally demonstrated that ingested food allergens readily penetrate the gastrointestinal mucosa and are transported via the circulation to cutaneous mast cells. Sixty-five normal adults were passively sensitized with intracutaneous injections of serum from a patient with severe fish allergy and serum from a normal donor.[39] The volunteers ate fish on the following day, and within 90 minutes, 61 out of 65 developed a wheal and flare reaction at the site injected with serum from the fish-allergic patient but not at the site from the normal control. Similar results were found in a series of experiments conducted in 66 normal children with serum from an egg-allergic subject.[40] Investigators also studied the absorption of food antigens from various locations along the gastrointestinal tract and other sites, such as the nose, eye, and urinary bladder.[41] They concluded that "the absorption of unaltered protein into the circulation is a normal, physiologic phenomenon occurring in nonatopic as well as atopic individuals, at all ages, and with many allergens."[41] Recent studies in rodent models indicate that allergic patients may develop even more rapid symp-

toms due to facilitated absorption resulting from IgE molecules present on gut epithelial cells.[42,43]

A 1936 report[44] emphasized the role of pruritus in food-induced eczematous symptoms. A child with AD and wheat allergy was admitted to the hospital when his skin was clear and covered with a thick crinoline bandage on his left arm and leg. The child was fed two wheat crackers, and within 2 hours he developed pruritus and scratching. The following morning the child had typical eczematous lesions on the open skin, but under the bandages the skin appeared clear. Similar trials were reportedly repeated in several other children. Such studies would not be acceptable today, but these studies clearly demonstrated that food proteins are rapidly absorbed and transported throughout the body and that they can elicit pruritus and skin symptoms in AD patients with food allergy.

In the past two decades, a number of approaches have been taken to address the relevance of food allergy in atopic dermatitis. The weight of the evidence fulfill Koch's postulates of causality, supporting a pathogenic role for food hypersensitivity in a subset of children and adolescents with atopic dermatitis: removal of the causative agent leads to resolution of the disorder, introduction of the causative agent provokes the disorder, and avoidance of the causative agent prevents the disorder. Appropriate studies in adult patients are inadequate to draw any conclusions, but most investigators agree that food hypersensitivity plays a very minor (if any) role in adult AD. As with other chronic, atopic disorders (eg, asthma), a variety of factors may trigger eczematous flares (wheezing in the case of asthma), making such studies complicated to control adequately.

A number of studies have reported the beneficial effect of removing foods suspected of provoking symptoms in children with AD.[45–47] Utilizing a similar trial design, a study in older patients[48] reported improvement in some patients while eliminating milk and egg from their diet, but overall no statistically significant difference was seen in 40 patients completing the crossover trial. In a prospective follow-up study of 34 patients with AD, 17 children diagnosed with multiple food allergies by double-blind placebo-controlled oral food challenges were placed on an appropriate allergen elimination diet and experienced a marked improvement in their eczematous rash at 1–2 years and 3–4 years follow-up. These children showed significantly greater improvement than 12 similar AD patients who did not have food allergy and 5 children with food allergy and AD who did not adhere to their diet.[49] Another prospective, blinded, randomized controlled trial looked at egg elimination in young children presenting to a dermatology clinic with AD and a positive radioallergosorbent test (RAST) to egg (majority under age 2 years).[50] At the close of the study, egg allergy was confirmed by oral challenge, and 55 egg-allergic children were ultimately identified. A physician blinded to the dietary instructions evaluated the children. There was a significant decrease in both area affected (from 19.6 to 10.9%; $P = 0.02$) and symptom scores (SCORAD: 33.9 to 24.0; $P = 0.04$) in the children avoiding egg only compared to controls (percent involved, 21.9 to 18.9%; P = NS) symptom score (36.7 to 33.5; P = NS).

Several investigators have attempted to provoke eczematous skin changes by challenging patients with AD and suspected food allergy. In studies of children primarily with suspected food allergy and asthma, one group[51] reported that four of seven children with a history of AD developed skin rashes within 2 hours of administration of a double-blind placebo-controlled oral food challenge (DBPCFC). Utilizing a similar protocol, this author and his colleagues evaluated 470 patients with moderate to severe AD for evidence of food hypersensitivity utilizing DBPCFCs.[52–55] Subjects ranged in age from 3 months to 24 years with a median age of 4.1 years. The median clinical score for the group was 15 (range 0 to 30) at the time of their first admission to a clinical research unit, based upon a standardized clinical scoring system.[52] Family history was positive for atopic disease in 91% of subjects. At the initial evaluation, 39% had allergic rhinitis and asthma, and 41% had either allergic rhinitis or asthma. Serum IgE concentrations were elevated in 376 patients (80%), with a median IgE level of 3410 IU/mL and a range of 1.5–45,000 IU/mL. All patients were admitted to the clinical research unit to provide a stable, low-allergen environment. Foods administered during DBPCFCs were selected on the basis of skin test (and RAST) results and/or a suggestive history of food allergic reactions. Foods selected for the challenge protocol were excluded from the patient's diet for 7 to 14 days before admission. The initial 220 patients were routinely prick skin tested to a battery of 20 food extracts (Greer Laboratories, Lenoir, NC) on the day of admission to confirm previous results, standardize skin test data, and determine which foods would be administered in the DBPCFCs. While on the clinical research unit, patients were treated with hydrating regimen and low-potency topical steroids and anti-Staphylococcal antibiotics to reduce eczematous symptoms. Utilizing this regimen and a highly restricted diet, erythema and pruritus could generally be controlled in 3 to 4 days. During the admission, three to four DBPCFCs were conducted.[56] The clinical research center dietician determined the order of all challenges using a randomization scheme. Only the dietician was aware of the contents of individual challenges until the code was broken. Each challenge was evaluated and scored using a previously published symptom score sheet.[52] All negative DBPCFCs were confirmed by feeding the food openly to the patient before the time of discharge to ensure the accuracy of the blinded challenge and to

Table 1. Outcome of food challenges in 470 children with atopic dermatitis

• Median age	4.1 yrs
• Elevated serum IgE	376 [80%]
• Total number of food challenges	1,776
• Negative challenges	1,062
• Positive by history (majority peanut & nut)	
• Positive challenges	714
-Cutaneous symptoms	529 [74%]
Skin only	195 [27%]

Table 2. Common food allergies

Infants/Children	*Older Children/Adults*
Cow's milk	Peanut
Egg	Tree Nuts (Cashews, Walnut, etc.)
Peanut	Fish
Soy	Shellfish
Wheat	
Tree Nuts	
Fish	
Shellfish	

assure the patient (and parent) that the food can be ingested safely. In the initial 1000 food challenges performed, there were five reactions during the open feeding following negative DBPCFCs (<1% false-negative results). Three children, two aged 4 years and one aged 2 years, developed symptoms after drinking milk.

In the initial evaluation of 470 children with atopic dermatitis, a total of 1776 DBPCFCs have been conducted (Table 1). DBPCFCs were not conducted in 193 instances because clinical history indicated a "convincing" account of a major anaphylactic reaction (mostly to peanuts and nuts). History was considered convincing when a patient experienced severe respiratory symptoms (laryngeal edema and/or wheezing) and/or hypotension within minutes of ingesting an isolated food and required emergency care by a physician. In each case where the challenge was not performed, the patients had a markedly positive prick skin test to the food in question. No patient experienced a severe anaphylactic reaction during DBPCFC, although about one half the patients required oral diphenhydramine for severe pruritus and several patients required subcutaneous epinephrine for respiratory symptoms. Of the 1776 DBPCFCs performed, 714 were positive and 1062 were interpreted as negative. Cutaneous reactions developed in 74% of cases and consisted of a pruritic, erythematous, macular, or morbilliform rash, primarily in previous predilection sites. Symptoms confined exclusively to the skin occurred in only 30% of the reactions. Typical urticarial lesions were rarely seen and generally consisted of only a few lesions. Intense pruritus often provoked vigorous scratching that frequently resulted in superficial excoriations and occasionally bleeding. Gastrointestinal symptoms were seen during one half of the positive reactions, even though history rarely revealed previous gastrointestinal symptoms in the patients. The gastrointestinal symptoms seen consisted of nausea, abdominal pain, or both, plus vomiting, diarrhea, or both. Respiratory symptoms most frequently involved the nasal airway and were seen in 45% of the positive DBPCFCs. Respiratory symptoms included nasal congestion, rhinorrhea, sneezing, tightness of the throat, hoarseness and/or wheezing.

The food challenges typically provoked symptoms between 5 minutes and 2 hours of starting the blinded challenge. Symptoms associated with the immediate response were generally abrupt in onset, readily apparent, and lasted for 1–2 hours. Several patients experienced a second episode of increased cutaneous pruritus and transient morbilliform rash 6 to 10 hours after the initial positive challenge. These symptoms were less prominent than the immediate symptoms and tended to last for several hours. In our early studies, most patients (80%) reacted to only one to three foods, even though many reports have suggested that children with atopic dermatitis are sensitive to a large number of foods. In the past 5 years, children often have reacted to more than three foods. Most children in the earlier study had positive prick skin tests to several foods (mean: 3.5; range: 0–10), but only about one third of positive skin tests correlated with clinical reactions during food challenges: 169 children (36%) reacted to only one food, 122 (26%) reacted to two foods, 85 (18%) reacted to three foods, 47 children (10%) reacted to four foods, and 47 patients (10%) reacted to five or more different foods. Five foods (egg, peanut, milk, wheat, and soy) accounted for about 80% of the positive clinical responses (Table 2).

Studies using the DBPCFC clearly demonstrate an immediate, IgE-mediated food hypersensitivity reaction in a subset of children with AD. Such distinct food-induced symptoms are rarely seen under normal circumstances because foods are generally not ingested on an empty stomach following prolonged periods of food allergen avoidance. Repeated ingestion of a food allergen results in a "down regulation" of the immediate response.[57] The second onset of pruritus and rash in some children following DBPCFC is suggestive of a "late-phase" component of an IgE-mediated response.

A study in the 1930s reported a decrease in the incidence of AD in breastfed infants.[58] Since that time, there have been numerous conflicting reports about the relative benefit of breastfeeding infants to prevent or delay the onset of atopic disease. An analysis of studies addressing this issue 20 years ago noted the poor quality of published studies and suggested no benefit of breastfeeding in the prevention of AD.[59] Since that time, however, a number of well designed prospective studies have been performed, and as noted in a recent

meta-analysis of prospective studies,[60] breastfeeding appears to reduce the prevalence of AD in high-risk populations.[60] It is clear that the potential benefit of breastfeeding can be complicated by transmission of food antigens in maternal breast milk.[61,62] Several investigators have demonstrated the beneficial effect of eliminating certain foods from the maternal diet during lactation,[63–67], but overall, this is limited to infants from atopic families and generally limited to foods such as peanuts and nuts.

Delayed introduction of solid foods beyond 4 months of age has been shown to decrease the prevalence of AD. In a prospective, nonrandomized study of 1265 unselected neonates, the effect of solid food introduction was evaluated over a 10-year period.[68,69] A significant linear relationship was found between the number of solid foods introduced into the diet by 4 months of age and subsequent atopic dermatitis. There was a threefold increase in recurrent AD at 10 years of age in infants receiving four or more solid foods compared to infants receiving no solid foods before 4 months of age. No relationship was noted between asthma and the introduction of solid foods. A prospective, nonrandomized study comparing breastfed infants receiving their first solid foods at 3 months or 6 months of age revealed reduced AD and food allergy at 1 year of age in the group avoiding solids for the 6-month period.[70] Further follow-up at 5 years, however, revealed no significant difference.[71]

Diagnosis of Food Allergy in Patients with Atopic Dermatitis

Approximately 40% of children with moderate to severe AD who attended a university pediatric dermatology clinic were found to have food allergy.[72] In general, the more severe the AD and the younger the patient, the more likely food allergy is contributing to the symptoms.[73] While parents can sometimes attribute worsening of eczematous symptoms to the ingestion of certain foods, most often the history is not particularly informative, especially in cases of severe AD. A number of factors can lead to worsening of the eczematous rash, eg, *Staphylococcus* infection, irritants, heat and humidity, etc., so it is often difficult to identify the ingestion of a food allergen as the cause of an eczematous flare. In our series of nearly 500 children with moderate to severe AD, only 35–40% of parental historical accounts of food allergy could be verified by DBPCFCs. Egg allergy is the most frequent cause of food-induced eczematous symptoms, affecting two thirds of children with food allergy and AD in our series.[6] Overall, egg, milk, peanut, soy and wheat account for about 90% of food allergy in children with AD. Therefore, in infants and young children with moderate to severe AD, an empiric trial of egg and milk exclusion may be warranted. In infants receiving breast milk, it is important that the mother completely exclude these foods from her diet as well. In young infants, this approach may be successful, but in older infants and young children consuming a more generalized diet, more definitive diagnostic tests are generally necessary (See Fig. 1).

Prick/puncture skin tests are useful for determining the presence of specific IgE antibodies to various foods and other allergens. After discontinuing antihistamines for a sufficient length of time, a bifurcated needle or lancet is used to puncture the skin through a glycerinated food extract and appropriate positive (histamine) and negative (saline-glycerine) controls. A local wheal and flare response indicates the presence of food-specific IgE antibody. Prick skin tests are most informative when they are negative because the negative predictive value of the tests is very high (over 95%), while the positive predictive value is less than 40%.[53,74,75]. Thus, a positive skin test in isolation cannot be considered proof of clinically relevant food hypersensitivity, while a negative test virtually rules-out IgE-mediated food allergy to the food in question. Intradermal allergy skin tests with food extracts should not be used because they give an unacceptably high false-positive rate and a greater risk for adverse reactions to testing.[74] The protein in commercial extracts of some fruits and vegetables are prone to degradation, so fresh extracts of these foods are more reliable.[76]

Although slightly less sensitive than prick skin tests, in vitro tests for specific IgE antibodies (RAST) may be more practical than prick skin tests for the screening of food allergies in most office settings and can be used while the patient is taking antihistamines and does not depend on having an area of eczematous-free skin for testing. Like skin tests, a negative result is fairly reliable in ruling out an IgE-mediated reaction to a particular food, but a positive result has low specificity. Quantitative measurements of food-specific IgE appear to be more useful in predicting clinical reactivity. As shown in Table 3, "decision points" have been established that provide >95% confidence that a patient has symptomatic food allergy.[77,78] An oral challenge would be needed to confirm reactivity for children with levels falling below the 95% predictive decision point.

Studies using both skin prick tests and atopy patch testing with foods have been reported by a number of groups and have shown value in identifying patients with delayed onset of symptoms;[79–83] children with immediate reactions generally had positive skin prick tests while those with late reactions were more likely to have positive patch tests to the relevant foods. Further studies with patch testing are needed to standardize the reagents and procedures and to confirm these results before making general recommendations.

The DBPCFC remains the "gold standard" for diagnosing food hypersensitivity in chronic atopic disorders

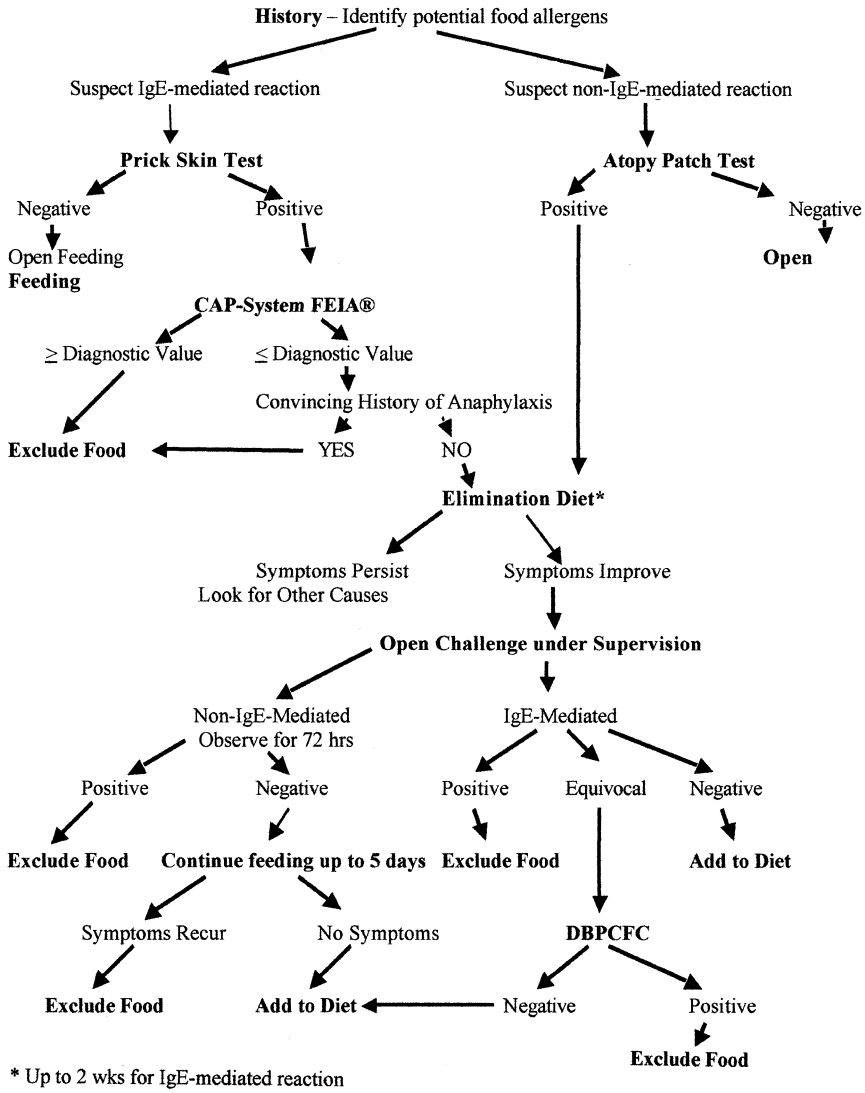

Figure 1. *Approach to diagnose food allergy in patients with atopic dermatitis.*

such as atopic dermatitis. In the typical office practice, however, a careful history and evidence of food antigen-specific IgE antibodies [prick skin tests, RASTs] may indicate foods that can be eliminated for a 2- to 3-week dietary trial. Symptoms may be recorded in a diary during the trial period. If unequivocal improvement is documented, foods felt least likely to be responsible for reactions (eg, foods other than egg, peanut, milk, soy, and wheat) are added back to the diet. However, any food suspected of causing a severe anaphylactic reaction should never be administered at home because of the potential for inducing anaphylactic shock.[84] If a clear deterioration in the patient's AD occurs when a food is added back, it should be removed from the diet. If cause and effect can be established, the patient should remain on the avoidance diet unless it requires elimination of more than one "major" food (egg, milk, soy, wheat) and/or two or more "minor" foods (all others). If severe symptoms persist on the elimination diet and food allergy is still in question, a brief trial (1–2 weeks) of an extensively restricted diet

Table 3. Serum food-specific IgE levels indicative of clinical reactivity

Food	*Decision Point* [IgE = kU_a/L]*	*Rechallenge Value*
Egg	≥7.0	≤1.5
[children <2 yrs of age[89]]	≥2.0	
Milk	≥15.0	≤7.0
[children <2 yrs of age[90]]		
Peanut	≥14.0	≤5.0†
Fish	≥20.0	
Tree Nuts	≥15.0	

** Patients with food-specific IgE values less than the listed as decision point values may be clinically reactive and should be challenged to clarify the clinical status. Unless history strongly suggests tolerance, a physician-supervised food challenge should be performed to determine if the child can ingest the food safely.*

† If no reactions after 3rd birthday.

may be implemented. If the dietary elimination results are equivocal or several foods are implicated, blinded oral food challenges should be performed once the patient's skin has been sufficiently cleared (may require hospitalization) to interpret challenge outcome. Multiple dietary restrictions are rarely necessary.

Management of Food Hypersensitivity in Patients with Atopic Dermatitis

Once food hypersensitivity is diagnosed, therapy consists of placing the patient on a diet completely eliminating all forms of the offending food allergen. Instructing the patient and family to read food labels to avoid "hidden" sources of the suspect food and to avoid potential sources of allergen contamination is critical.[85] The major reason why dietary management fails in food-allergic patients is inadequate patient instruction by the treating physician. Helpful information may be obtained from the *Food Allergy and Anaphylactic Network* (phone: 800-929-4040; e-mail: www.foodallergy.org), a lay organization based in Fairfax, VA. Antihistamines and corticosteroids may modify the symptoms of food hypersensitivity after an accidental ingestion, but they have no prophylactic role in the treatment of food allergy. A controlled, blinded trial of oral cromolyn in AD patients with "challenge-proven" food hypersensitivity demonstrated no therapeutic benefit.[86] Treatment of food hypersensitivity with oral desensitization, immunotherapy, and rotational diets also has not been proven to be effective in controlled trials. Early studies of recombinant humanized anti-IgE antibody therapy in food-allergic patients appear promising and may eventually play a role in the treatment of food-allergic patients with AD.

Natural History of Food Hypersensitivity in Atopic Dermatitis

Approximately one third of children with atopic dermatitis and food allergy will "lose" (or "outgrow") their clinical reactivity to food over 1 to 3 years.[87] Three factors appear to be important in determining the probability of patients losing their clinical reactivity: the food to which the patient is allergic, ie, patients allergic to peanuts, nuts, fish, and shellfish are not likely to lose their clinical reactivity, whereas those allergic to soy, wheat, milk and egg are much more likely to develop clinical tolerance; the level of specific IgE antibody to a particular food, ie, the higher the level of food antigen-specific IgE the less likely that clinical tolerance will develop in the subsequent few years;[88] and the degree to which the patient adheres to the elimination diet, ie, patients ingesting small amounts of allergen or having frequent accidental ingestions are less likely to develop clinical tolerance. Monitoring the level of food-specific IgE antibodies may be useful in determining when a patient has "outgrown" his/her food allergy.[77,78] Prick skin test results do not correlate with loss of clinical reactivity and may remain positive for many years after the food has been reintroduced into the diet. It is recommended that patients be rechallenged at set intervals (eg, egg, every 2–3 years; milk, soy, wheat, every 1–2 years; foods other than peanut, nuts, fish, and shellfish, every 1–2 years) to determine whether their food allergy persists. To date, no patients have experienced a recurrence of allergic symptoms or worsening of eczema once food hypersensitivity was "lost."

Despite years of debate and some persistent dissenting voices, it is now apparent that food hypersensitivity plays a significant pathogenic role in up to 40% of children with moderate to severe atopic dermatitis,[72] and that elimination of the responsible food leads to marked improvement in eczematous symptoms in the majority of these children.[6,50] The significance of food allergy in adults with AD remains to be established. The prevalence of food allergy in the United States and Europe appears to be increasing, and children with AD have the highest incidence of food allergy of any identifiable patient group. If asthma is also present, these patients are at highest risk for developing severe food anaphylactic reactions. Since the majority of children with AD develop asthma, and since "outgrowing" food allergy appears to require food allergen avoidance, it is imperative that physicians identify these food allergic children early and place them on appropriate elimination diets, regardless of whether they believe the food allergy in playing a pathogenic role in a child's atopic dermatitis. Successful management of food allergy often requires the services of a dietitian who is knowledgeable about food allergy and appropriate elimination diets. With the information and support groups available today, allergen elimination diets are no longer as onerous as in the past.

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