allergic rhinitis or asthma;[2] (3) Serum IgE concentrations are elevated in about 80% of children with atopic dermatitis;[3] (4) Most children have positive immediate skin tests and radioallergosorbent tests (RAST) to various dietary and environment allergens.[15]

The pathogenic role of food hypersensitivity in atopic dermatitis has been disputed for nearly a century. In a recent study, however, approximately one third of children seen in university dermatology and allergy clinics had food hypersensitivity contributing to their skin symptoms.[1,5] Approximately 60% of these patients had a positive reaction to double-blind, placebo-controled food challenge to one the food allergens tested. In Sampson study[6] a link between immediate food hypersensitivity and cutaneous symptoms in some children with atopic dermatitis was provided when 14 of 26 children were found to develop cutaneous erythema and pruritus shortly after the ingestion of food antigen administered in a double-blind-placebo controlled food challenge. Therefore the purpose of this study was to determine whether immediate food hypersensitivity plays a part in the pathogenesis of atopic dermatitis in a pediatric population and, if so, whether skin testing is useful in diagnosing that hypersensitivity in these patients.

Methods

Thirty children with age from infancy to 12 years old between November 1987 and December 1992, referred for evaluation of atopic dermatitis were enrolled in the study. All subjects had a history of atopic dermatitis which was defined as a pruritic, chronic or chronically relapsing, non-infectious dermatitis of typical morphology and distribution based on the suggestions by Hanifin and Lobitz (cited 3); dating back to infancy and most who were controlled with regimens of topical steroids, antihistamines and systemic steroid fulfilled for the diagnosis of atopic dermatitis.

The eczema was regarded as severe if it was generalized and/or if there were need for hospitalization, as moderate if localized and required frequent application of steroids ointments and as mild if no or only mild steroid ointments were needed for 1 t o 3 days. For this study we evaluated 30 children using a standard questionnaire, skin prick test (SPT) and determination of total eosinophils.

An episode of bronchial obstruction was accepted only if the diagnosis was made by a physician and three or more episodes of bronchial obstruction were regarded as asthma. Rhinitis was considered to be allergic if it appeared at least twice after exposure to a particular allergen. Positive exposure to an allergen was defined as an obvious reaction within 1 hour after exposure on at least 2 occasions.

Skin tests were performed on the volar area of the forearm in all children with a battery of 20 different food antigens Standard glycerinated extracts from Dome-Hollister Stier in a concentration of 1: 20 (weight/volume) were applied by the prick

technique; mean diameters of erythema and wheal reactions were recorded. Wheal reaction 3mm or greater than the negative control were considered positive.

If no more than a few foods are suspected as the cause of symptoms, the initial elimination diet can consist simply of removing these foods. If removal of one or several foods from the diet is not successful in eliminating symptoms, initiation of a severely limited diet for a short periods of time had been done and followed by the return of each suspected food 3 weeks later. Continuation of symptoms while patients are on restricted diets indicates that the symptoms are not caused by food.

Results

Thirty children, 15 males and 15 females were enrolled in the study (Table 1). Patients ranged in age from 4 months to 12 years. The family history was positive for atopic disorders (allergic rhinitis, asthma, atopic dermatitis) in 18 (60%) patients. 15 (50%) in one of their parents and 3 (10.6%) both parents had a history of atopic disorders.

In addition to atopic dermatitis, 6 (20%) children had asthma, 4(13.3%) had allergic rhinitis, 4(13.3%) had both allergic rhinitis and asthma, 1 (3.3%) had urticaria and another 1(3.3%) had both asthma and urticaria. In 14 (46.6%) children with atopic dermatitis had no history of any other allergic disease. Skin prick test were not done in 11 infants and children under 2 years of age and the result of the remaining 19 children are as follows:

A total of 24 elimination diet and food challenge children were performed, 6 depends on history only, because they did not come back for the second control; 19 (63.3%) (two depends on history) were interpreted as positive. Agreement between challenge oral tests and the results of skin tests was found in 26.5% of patents (5 out of 19). The onset of symptoms usually occurred within 4-6 hours of ingesting food antigens and no significant delayed reaction were noted. The skin symptoms which were seen mostly are diffuse erythematous macular or morbilliform rash and pruritus.

11 foods accounted for all the positive challenge and/or history. Of these children, seven (36.8%) to one food, four (21%) to two foods, three (15.8%) to three foods and five (26.3%) to four or more foods. Egg accounted for 40.6%, fish for 52.6% and shrimp for 40.6%. Of the 19 skin tests performed, 12 (63.2%) yielded positive reaction. Egg accounted for 50%, shrimp accounted for 33% and fish for 25%.

Discussion

The clinical significance of food hypersensitivity in atopic dermatitis has been debated for a number of years, but increasing evidence suggest a pathogenic role for IgE-mediated hypersensitivity mechanism. Sampson and McCaskill[6] have shown that foods

play a pathogenic role in some children with atopic dermatitis. Approximately 60% of the children they challenged had positive food reaction.

Table 1. Distribution of the children with atopic dermatitis

Age (yr.)	No. of patients		
< 1 yr.	2	-	2
1-	2	7	9
2-	4	4	8
5-	4	4	8
>10	3	-	3
	15	15	30

Table 2. Family history of allergic diseases

	< 1yr	1-	2-	5-	10-	Total
1 of their parents	1	3	4	6	1	15 (50%)
both parents	-	1	1	-	1	3 (10%)
no family history	1	6	2	2	3	12 (40%)

Table 3. History of other allergic diseases ever experienced

History of allergy	1 yr.	1-2 yr.	2-5 yr.	5-10 yr.	>10 yr.	Total
Asthma	-	2	1	2	1	6
Allergic rhinitis	-	-	1	1	2	4
Asthma and allergic rhinitis	-	-	1	1	2	4
Urticaria	1	-	-	-	4	
Asthma and urticaria	-	-	1	-	-	1
No history	2	5	3	4	1	14

Engman et al (cited by 6) suggested in 1936 that the ingestion of a food might play a role in exacerbation of atopic dermatitis. They hospitalized a child with wheat hypersensitivity who remained on a wheat-free diet until his skin symptoms were clear. After the symptoms were clear, the child was allowed wheat in his diet. This challenge

resulted in severe scratching and the development of typical lesions of atopic dermatitis. These studies and others like to suggest that foods do participate in exacerbating the dermatitis.

Table 4. Results of skin prick test to 20 batteries of food allergens in 19 patients age 2-12 years old with atopic dermatitis

Negative reaction	7 (37%)
Positive reaction	12 (63%)
■ Egg	
■ Shrimp	
■ Fish	
■ Chocolate	
■ Peanut	
■ Crab	
■ Strawberry	2
■ Milk	1
■ Wheat	1
■ Chicken	1
■ Pork	1
■ Beef	0

Table 5. Food inducing positive challenge in 19 of 30 children with atopic dermatitis

Food challenge	0-	1-	2-	5-	10-	Total
■ Egg	-	2	4	1	1	8
■ Fish	-	3	3	3	1	10
■ Shrimp	-	-	3	4	1	8
■ Crab	-	-	2	2	-	4
■ Egg & fish in breastmilk	1	1	-	-	-	2

The lesions are considered to be the consequence of immediate IgE-mediated food hypersensitivity, producing a pruritic rash, and then leads to severe scratching and

lichenification and the typical skin changes in atopic dermatitis.

The proposed mechanism by which adverse food reactions exacerbate skin symptoms is the late-phase IgE response. Two to 4 hours after ingestion of the antigen there is a progressive accumulation of eosinophils and neutrophils, which reach a maximum concentration at 6 to 8 hours and the skin symptoms which was heralded by pruritus and consisted of an erythematous macular or morbilliform rash were followed. More evidence suggests that other mediators released during IgE hypersensitivity responses, such as mast cell-derived prostaglandins and leukotriens or eosinophil "major basic protein" may also contribute to the skin changes seen.

A child (especially younger than 7 years old) with atopic dermatitis unresponsive to routine therapy (topical steroids, antihistamines and occasional systemic steroids) appears to have greater than a 50% chance of having food hypersensitivity.[8] Such children should therefore undergo appropriate evaluation.

In the past, and even more recently some investigators have suggested that children with atopic dermatitis are allergic to a wide variety of food antigens. These statements generally were based on results of skin tests or RAST tests, clinical impressions, or dietary exclusion and challenge studies.

Although many of our patients had many positive skin prick test reaction to food antigens, 36,8% of the children experienced a positive oral challenge to only 1 food, 21% to 2 foods and 32.1% to 3 foods or more. Although according to SPT, egg accounted for 50%, shrimp accounted for 33% and fish to 25%, according to oral food challenge egg accounted for 40.6%, fish for 52.6% and shrimp for 4.6% and only 5 of out 19 patients (26.3%) who according to food challenge were positive had also a positive skin prick test to the same food. Most scientist agree that the most appropriate means of diagnosing food hypersensitivity in patients with atopic dermatitis starts with a careful medical history and physical examination directed at distinguishing food hypersensitivity from other causes of adverse reactions to food.

Skin tests and in vitro tests for antigen-specific IgE are used in selected cases to support the clinical diagnosis and confirmation of the diagnosis may be obtained by oral elimination and challenge with suspected food. Before any diet is initiated, it is useful for the patient to remain on the usual diet for 1 to 2 weeks. During that time the patient records the type and amount of foods ingested and the occurrence and character of food reactions.

Foods are suspected as the cause of symptoms, the initial elimination diet can consist simply of removing these foods. If removing of one or several foods from the diet is not successful in eliminating symptoms, if multiple food sensitivities are suspected, or if the symptoms are unlikely to be caused by foods, initiation of a severely limited diet is sometimes warranted.

Severe elimination diets, especially in children, can be used for only short periods of time. Extensive elimination diets for infants under 3 months of age include milk

substitute alone and elimination of the mother diet; 3-6 months of age, milk substitute and rice cereal; 6 months to 2 years, milk substitute, cereals, certain fruits, eggs, chocolate and peanuts. Continuation of symptoms while patients are on restricted diets indicates that the symptoms are not caused by foods. If symptoms resolve on the restricted diets, provocation can be started 3 weeks later and foods provoking symptoms should be removed. Although the procedure described is lengthy, it is direct and applicable to patients evaluation with a minimum confusion.

A number of in vivo and vitro technique procedures are used in the diagnosis of food allergy. These techniques include skin testing, RAST and ELISA. Skin prick test may be considered an excellent means of excluding IgE-mediated food allergies but is only suggestive of the presence of clinical food allergies with some exceptions. First, IgE-mediated sensitivity to a great number of fruits and vegetables is frequently not detected because of the liability of the responsible allergen.[5,9] Second, children less than 1 years of age may have IgE-mediated food allergy in the absence of positive skin test result and infants less than 2 years of age may have smaller wheal, presumably because of a lack of skin reactivity. Third, individuals may have positive skin tests in the absence of food allergy (false positive) and allergy to food in negative skin tests (false negative) and patients should never be advised that they are allergic to certain foods solely on the basis of skin tests.[5]

Radioallergosorbent tests (RAST) and similar in vitro assays such as enzyme-linked immunosorbent (ELISA) assays are considered slightly less sensitive than skin prick tests.[1,5] One study that compared Phadebas RAST (Pharmacia AB, Uppsala, Sweden) with double-blind, placebo controlled food challenges found skin prick tests and RAST's have similar sensitivity and specificity when a Phadebas score of 3 or greater was considered positive. Oral food challenge (double-blind food challenge) may be used occasionally for the diagnosis of food intolerance if the correlation between specific foods and symptoms remain unclear. It need not be used if the medical history, physical examination, skin testing and dietary studies have resulted in a diagnosis. Although double-blind placebo-controlled food challenge provides a scientifically acceptable means of diagnosing adverse food reactions, such challenge may be impractical for general clinical use.[6]

In conclusion, in some children food hypersensitivity does play a pathogenic role in atopic dermatitis. This hypersensitivity to food is generally limited to one or two antigens and may be lost after several years. Appropiate elimination diets should not pose the nutritional hazard. Children appropriately diagnosed and given restricted diets can be expected to show significant improvement in their clinical course. Skin testing with the prick technique may be some aid in diagnosing food allergy, but a high rate of clinically insignificant positive skin tests and a small rate of false negative test can occur.

And in some children whom food hypersensitivity can not be documented, other factors such as temperature extremes, stress, contact with house dust mite, animal dander, possibly pollen allergens and unknown factors should be considered.

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