

Atopic Dermatitis: The Attack of Food Allergens

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Abstract

Atopic Dermatitis (AD) is a multifactorial disease and hereditary, environmental and immunological components are involved in its etiopathogenesis. Until now, no specific skin signs, no diagnostic histologic features and no characteristic laboratory markers were described in AD. In the recent years considerable attention has been focused on the immunological abnormalities associated with AD and multiple and interrelated immune aberrations are reported. The aim of the present paper is to summarize the current knowledge on immunological abnormalities in AD. In addition, personal data on T-cell subsets and Poly Morphonuclear Neutrophils (PMN) chemotaxis in children suffering from severe AD and Hyper Immunoglobulinemia E syndrome (HIES), will be reported. Although the investigations performed by many Authors and our results show a wide variety of different immunological abnormalities in AD, the biological significance of these abnormalities in relation to the pathogenesis of AD remains unclear.

Keywords: Asthma; Egg; Reactions; Diarrhea

Introduction

More than 50 years ago Food Allergy (FA) was suggested as a contributing factor in AD. It was shown that Cow's Milk (CM) feeding predisposed to the development of AD while breast-fed babies had a prevalence of eczema seven times lower than that of CM-fed babies [1]. Later on, it was reported that children with a family history of allergy and soy formula fed during the first six months of life had less eczema and asthma in comparison with CM-fed children [2]. In a double-blind, cross-over study, Atherton et al demonstrated a marked improvement of AD in 21 2-8-yr-old children receiving a CM- and egg-free diet. It was noted that 14/20 patients responded more favourably to the antigen-avoidance diet employing a soy formula as CM-substitute, whereas only one had a more favourable response to a not CM- and egg-free diet [3].

The contributory role of both CM and egg was confirmed in subsequent studies. We have evaluated the efficacy of a CM- and/or egg-free diet in 59 children suffering from severe AD [4]. The elimination of CM and/or egg for 4 weeks resulted in the healing, or marked improvement of skin lesions in 47/49 children. Sampson has evaluated 210 children in Double-Blind Placebo-Controlled Oral Food Challenges (DBPCFC): 235 (36%) were positive; 130 children (62%) reacted to at least one food. Overall, 174/235 positive reactions (75%) involved the skin [5].

In a recent study of ours, 154 challenge tests were done in 146 children aged 6 mo-10 yrs (median 24 mo): 101 with CM, 45 with egg and 8 with other foods. In the 146 children who underwent the challenge test with CM and/or egg 61 (42%) were positive. 42/101 challenges with CM (42%) and 19/45 with egg (42%) were positive. 30/116 children were subjected to both challenge tests (CM and egg). The following symptoms (immediate or delayed) were elicited by challenge tests: AD worsening in 30 cases (49%), pruritus in 28 (46%), rash/erythema in 26 (43%), urticaria in 14 (23%), asthma in 9 (15%), lip edema in 5 (8%), diarrhea in 4 (6%), vomiting in 2 (3%) [6].

Allergic reactions to CM, egg, and peanut are often incriminated in the etiology of AD. In the children studied by Sampson, eggs, peanuts and CM provoked 70% of the positive DBPCFCs. Less than 15% of children reacted to more than two foods [5]. Employing two foods for challenges, we have obtained a similar percentage of positive reactions (75%) [6]. Children with AD are frequently reported to be allergic to a

wide variety of foods. This opinion is generally supported by the high number of positive skin and RAST tests to foods found in children with AD. Although children eat a wide variety of different foods: CM, egg and wheat, which are the most common foods consumed in the Italian diet, and accounted for more than 93% of the positive responses. These data should be taken into account to eliminate the nutritional problems of too restrictive a diet. Foods frequently reported to induce hypersensitivity such as citrus fruit, chocolate, strawberries, did not elicit positive responses in our patients [5,6].

Natural history of atopic dermatitis due to food allergy

As yet, retrospective and longitudinal studies have been carried out by many authors to assess the factors which may significantly affect the AD outcome. Widely varying estimates ranging from 20-80% of patient improvement during adolescence and adulthood have been reported, probably due to different selection criteria. However, most studies suggest that adolescents tend to outgrow the disease in a percentage between 40 and 50%. The prevalence of respiratory allergy in AD patients has been evaluated between 30 and 55% [7]. Recently we have carried out a long-term (5 years), prospective study on 56 children. AD was due to FA in 82% of cases, in whom the offending foods were CM and egg in 69% of children. 43% of patients still had AD at the last follow-up. Tolerance toward CM and egg was reached at age 4 years. In addition 50% of patients had bronchial asthma and/or allergic rhinitis during the follow-up. The following parameters were significantly associated with persisting skin lesions: age of onset of AD after the sixth month of life ($p=0.023$); widespread or not-typical (reverse pattern) skin lesions ($p=0.0001$); persisting food intolerance ($p=0.0007$), total ($p=0.0001$) and specific IgE ($p=0.0001$), the relationship between development of tolerance and symptoms ($p=0.0026$) and between

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tolerance and development of additional allergies (p=0.035). Family history of atopy, sex, skin test responses, severity of skin lesions, had no predictive value. Positive skin tests and/or IgE to inhalant allergens at the first examination appeared to have a predictive value for the development of respiratory allergy (p=0.0007) [8].

Ford and Taylor found in 25 young children with AD and egg hypersensitivity, as confirmed by DBFC, and followed-up to 2.5 yrs that hypersensitivity resolved in 11 children and persisted in 14 [9].

Although the difference is widely varying between one study and the other, the data suggest that children with FA diagnosed at older ages do not tend to outgrow the illness. As recently reported by Sampson, 75 children on avoidance diet were rechallenged after 1-2 yrs and 38/121 (31%) rechallenges were negative. The food(s) eliciting hypersensitivity responses influenced the development of tolerance. For example, <25% of reactions to CM, egg, and peanut were lost during the above period, whereas 1/2 of soy sensitivity and 2/3 of other food allergies were outgrown in the same period. In summary, 18/75 (25%) children lost clinical FA after 1-2 years, and other 4 lost any evidence of hypersensitivity after an additional 1-yr avoidance diet. Therefore, approximately 1/3 of FA children with AD will outgrow their clinical hypersensitivity in 1-3 yrs on condition that they are maintained on an appropriate allergen elimination diet [5].

The importance and necessity of the elimination of foods inducing clinically documented FA is further demonstrated by the different AD course in children following or not a restricted diet. In a group of 34 children followed prospectively for 3-4 yrs, 17 of whom with FA diagnosed with DBPCFC and maintained on a restricted diet (diet group), and 17 either with no FA confirmed or not complying with their restricted diet, it was shown that the diet group fared much better clinically than the non-diet group (p<0.001). In addition, total serum IgE levels decreased significantly over the study course only in the diet group (p = 0,037) [5].

Diagnosis of food allergy in children with AD

A “diagnostic” oligoantigenic elimination diet should be given for no more than 4-weeks since there are so far no laboratory tests for the diagnosis of FA which obviate the need for careful clinical assessment. The elimination diet can be adapted to the suspected sensitivities of the single patient. A home-made meat diet is employed by us with good results and infants’ compliance (Tables 1 and 2). This diet can be adapted to the individual patient that is vegetables, other types of fruit and meat, wheat flour and other nutrients can be added to the diet according to the age and weight of the child, and the physician’s judgement. This is one of the major advantages of this diet.

Several factors may contribute to the lack of reliability of elimination diets in AD due to FA, since small quantities of triggering allergens may be heedlessly or inadvertently ingested by, or may reach food allergic

S.No	Properties of Soy-proteins-based Formulas
1	No minute amount of cow milk proteins.
2	No cross reactivity with cow milk protein.
3	Lower immunogenicity (IgE Abs) than cow milk proteins.
4	Lower allergenicity than cow milk proteins.
5	Similar antigenicity (IgG Abs) to cow milk proteins.
6	Nutritional adequacy similar to cow milk formulas.
7	Better palatability than highly Hydrolysate Formulas.
8	Less expensive than highly Hydrolysate Formulas.

Table 1: Properties of Soy-proteins-based Formulas.

Ingredients	Units
Lamb meat	100
Olive oil	40 gms
Pre-cooked rice flour	70 gms
Water until to	1litre
Calcium gluconate	300 mg
NaCl	300 mg
Vitamine D	400 U/l

Table 2: Home-Made Meat Based Formula (Rezza Diet).

children. Negligible quantities of residual Sensitizing Food(S) (SF) may “contaminate” other foods due to inadequate cleaning of kitchen utensils, pots, etc., or to clumsy attempts to separate or eliminate an SF from the others, or to direct or indirect contact between two foods, e.g. when one uses the same pots or trays to serve different courses. The SF may also unnoticedly reach the sensitive child either touching or licking kitchen utensils, bottles, tableware, glasses, cups, etc. with residues of SF, or inhaling the fumes during cooking or baking of SF, or being unknowingly in the vicinity of or during serving of SF at a table, or in a restaurant, etc., or opening wrappings or cans containing the SF or inadvertently touching them, and even kissing the lips of, or being kissed by persons who have consumed the SF, or receiving caresses by someone who touched them. In addition, in the restaurants or at parties the sources of various food ingredients and the presence of offending allergens in them are frequently unknown [10]. Lecithin can be prepared from either eggs or soybeans but its protein or allergen contents are unknown. Starch, a common food ingredient, can be made from corn, wheat, tapioca and several other sources, but the protein content is again unknown. Cross-reactions may sometimes occur between closely related foods. Cross-reactions are perhaps more likely between the eggs of different birds such as chicken, turkey, duck, and goose and the milk of various species such as CM and goat milk. The exclusion of all types of eggs and milk should be advocated in elimination diets when the above foods are among the suspected ones. Cross-reactions may also occur between CM proteins and CM proteins hydrolysates, as reported by us in five babies with IgE-mediated CM allergy [11]. When a child shows a clear-cut improvement after the 4-wk diet, he can undergo a challenge test. The procedure is not risk-free. David reported anaphylactic shock in four children. We also observed in 18 children severe immediate reactions after the challenge test: 9 with CM and 9 with egg [6,12].

Reliability of skin tests and RAST in atopic dermatitis

Both diagnosis and treatment are difficult since the much in vogue diagnostic items, ST and RAST yield varying results in term of sensitivity, specificity, predicted positive and negative values. We have evaluated sensitivity (0.66), specificity (0.80), and positive (0.10) and negative predictive accuracy (0.79) of RAST to soy in 143 children with AD, while the prevalence of RAST to food and Dpt was as follows: Egg 49% (70), CM 34% (49), soy 24% (35), wheat 22% (31) and Dpt 18% (26). We have recently demonstrated that considering sensitivity, specificity, and positive and negative predictive accuracy of ST and RAST of both CM and egg as regards immediate and total reactions, ST sensitivity is high (0,88 for CM and 1,00 for egg for immediate reactions and 0,88 for CM and 0,95 for egg for total reactions). However specificity is low (0, 25 for CM and 0, 27 for egg for immediate reactions and 0, 30 for CM and 0, 38 for egg for total reactions). In addition, the ST positive predictive values are low (0, 15 for CM and 0, 30 for egg for immediate reactions and 0, 46 for CM and 0,60 for egg for total reactions). Since history is unreliable especially as regards the immediate reactions

predictivity, challenge tests in children with positive ST should always be done with caution. The ST high negative predictive accuracy (0, 93 for CM and 1.00 for egg) permits to exclude immediate reactions following the challenge test. RAST sensitivity is lower than that of ST. RAST specificity is better than ST, however neither can be utilized at the clinical level. In addition RAST negative predictive accuracy is lower than that of ST and consequently scarcely useful for FA diagnosis. Its use should be limited to those cases in whom antihistaminic administration cannot be discontinued or dermographism is remarkable or lichenification fails to allow ST evaluation [6].

Conclusion

Since the observation that cow's milk-fed infants had eczema 7 times more than breast-fed babies, the possibility of preventing atopic diseases in high risk babies has been shown by prospective studies done by several groups of investigators. We point out that in order to prevent the development of AD in high risk babies, since we cannot change the atopic inheritance after birth, perhaps we can start early and effective preventive measures giving not only dietary manipulations based principally on prolonged breast feeding and/or soy-protein formulas, or casein hydrolysates, but also hygienic environmental engineering [13-16]. Finally we would stress that in addition to food allergens inhalant allergens such as house dust mite and pollens may exacerbate AD [15-18].

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