ATOPIC DERMATITIS : IS FOOD IMPORTANT IN ITS PATHOGENESIS?

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Atopic dermatitis (AD) is an inflammatory skin disorder affecting 5% to 10% of children, with evidence showing that its prevalence is still increasing. At the moment, the role of food in the pathogenesis of AD has not been completely elucidated, although it has been shown that food can induce or aggravate the symptoms of AD in a number of patients. On the other hand, not all children with AD have food allergy. This report highlights some of the recent developments in the role of food in the pathogenesis of AD.

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Introduction

Although AD is the most common chronic skin disease in children, its pathogenesis remains largely unexplained. Studies on its prevalence have estimated that 5% to 10% of all children suffer at one time from AD, and there is evidence showing that its prevalence is still increasing. The increase of AD goes together with the increase in prevalence of atopy. A number of environmental factors have been implicated. The hygiene hypothesis states that insufficient exposure to certain infectious agents during childhood increases the risk of developing atopic diseases, including AD. In a recent population study on a large group of 1-year-old children, it was found that 25% of them have symptoms of AD (Van Bever, unpublished data). Data from Singapore show that its prevalence is about 5% to 10% in children above the ages of 6 to 7 years. Studies in twins point to a hereditary disposition, but expression of it seems to be dependent on a multitude of environmental factors. Observations from bone marrow transplantation have identified the marrow as the site of the primary defect in AD.

Clinical presentations

- AD has no specific skin signs and comprises a number of atypical dermatological characteristics such as erythema, excoriation, scratching lesions, lichenification, and hypopigmentation.

- Children do not have symptoms from birth, but they usually appear before the age of 3 months.

- The lesions appear before the age of 1 year in 80% of the children and before the age of 5 years in 90% of children.

- The most invariable symptom is pruritus which can sometimes be very intense and cause severe insomnia.

- The distribution profile of the disease varies with age and is characterized by the predominance of certain skin lesions.

- The diagnosis of AD is generally not difficult, but in some cases the symptoms are poorly defined. In this event the diagnostic criteria of Hanifin and Lobitz are useful.

- The severity of AD can be assessed by usage of the scoring system SCORAD (Scoring Atopic Dermatitis), which might be important in the follow-up of the disease or in standardisation of criteria of severity as needed in clinical trials.

- The clinical course is characterized by variability and unpredictability. The asymptomatic intervals usually become extended as the child ages. It is estimated that in 60% of children with severe AD requiring hospitalization, symptoms will
persist above the age of 20. In 95% of milder cases, symptoms disappear before the age of 20.

Several aspects of AD have particular clinical and social importance. These include cutaneous infections, common warts and molluscum contagiosum, ocular complications, contact dermatitis, and sleep disturbances inducing learning difficulties.

**IgE-mediated hypersensitivity in AD**

Most AD patients have signs of atopic respiratory disease, such as asthma or rhinoconjunctivitis. Usually, the respiratory symptoms begin later than the skin symptoms and many clinicians have noted the peculiar and unexplained tendency for AD and asthma to alternate in their courses. This phenomenon is not constant, however, as both can flare simultaneously.

The highest levels of IgE have been detected in patients suffering from both AD and asthma. It is not yet known whether there is a causal relationship between these high levels and AD, or whether this is just an expression of the atopic constitution. In some patients, however, IgE is important in the pathogenesis of AD, while in others it is not. The following observations have been made:

- Increased total serum IgE has been recorded in about 80% of patients. In addition, there is a correlation between total serum IgE and severity of AD.

- Positive skin prick tests and positive specific IgE to a number of inhaled allergens, especially house dust mite, and food allergens are found in the majority of patients.

- Positive family antecedents of atopic diseases are found in the majority of patients.

- Of subjects with AD, 50% to 80% suffer also from asthma and/or rhinoconjunctivitis.

**Skin prick testing or determination of specific IgE?**

The presence of specific IgE or a positive skin prick test to an allergen still does not mean that the AD lesions are triggered by this particular allergen. The prick test and the determination of specific IgE via RAST or CAP are both known to yield false positive and false negative results. A possible explanation for the false negative results is that the allergen can induce skin lesions by non-IgE-dependent mechanisms. On the other hand, a positive prick test corresponds to a clinically detectable allergy (by a provocation test) in only about 25% of AD patients. Moreover, in young children prick test are more frequently negative than in older children.
The search of specific IgE offers no more diagnostic possibilities than the skin prick test. These two tests are comparable in specificity and sensitivity. If both specific IgE determination and skin prick test are used together in one patient, the diagnostic precision remains the same as for separate interpretation of each test.

However, in children with severe AD, covering the greatest part of the body, interpretation of results of skin prick testing becomes difficult, sometimes even impossible. In these children, determination of specific IgE should be performed.

**Double-blind placebo-controlled provocation tests = golden standard**

Anamnestic features usually contain insufficient information to establish a clear link between exposure to an allergen and the appearance of AD lesions. Parents often report their child to be “allergic” to a particular food, but when a provocation test is carried out, this food seldom seems to have any effect on the skin lesions. The opposite is often equally true: clearly positive provocation results are obtained by foods which the parents did not suspect.

At the moment, the best method to demonstrate that an allergen triggers AD is the double-blind placebo-controlled provocation test (DBPCPT). In children with severe AD, challenged by Sampson and McCaskill, 63 children out of 113 (56%) showed positive reactions to food, using the DBPCPT. Cow's milk, eggs, and peanuts were responsible for 72% of the positive DBPCPT. In another study, on 25 children with severe AD, we could demonstrate, by DBPCPT, that foods are able to induce exacerbations of AD in 24 out of 25 of the subjects. In that same study it was also found that food additives, tyramine and acetylsalicylic acid were able to cause exacerbations of AD. In children with mild to moderate AD, the role of foods seem to be less important. In a study by Burks on 165 children with mild to moderate AD, it was found that 60% of the patients had positive skin prick tests to food and only 39% showed positive DBPCPT. Moreover, most positive reactions were found in the younger age group.

Taken together, it seems that food allergy can play a role in AD. Most positive reactions to food occur in young children with severe types of AD.

**Role of inhaled allergens**

In a great number of patients with AD, positive reactions (prick test and specific IgE) to a number of inhaled allergens can be found. These reactions are not usually directly linked to the skin symptoms; they are merely a manifestation of the atopic constitution. There is as yet no clear evidence that inhaled allergens trigger AD directly, i.e. after inhalation. There are, however, anecdotal reports of AD induction after contact with pets or pollen. In a study of Platts-Mills et al. it was shown that AD improved by cleaning the patient's bedrooms.
On the other hand, it was demonstrated that inhaled allergens, applied epicutaneously by patch test, may penetrate the skin and induce eczematous skin lesions. These skin reactions which are delayed in time (positive after 24-72 hours) did not occur in allergic asthma and allergic rhinitis, and, therefore, seemed to be specific for AD. Microscopy of the patch test reactions shows many similarities to the clinically involved skin in AD. Therefore, inhaled allergens are believed to be involved only by direct contact in a number of patients with AD who have a concomitant allergy to inhaled allergens, especially to house dust mite. It is consequently reasonable to advise elimination of these inhaled allergens in some patients with AD.

**Role of food allergens**

As already mentioned, the strangest stories are told concerning food and AD. At the moment, the golden standard in diagnosing food allergy is the DBPCPT, as both anamnestic features and determination of allergy (by prick test or IgE-determination) frequently show false positive and false negative results. In view of the fact that it is difficult to demonstrate the existence of a food allergy, the following rules and procedures are recommended:

- Food is important as a trigger factor in children with severe AD. The role of food in children with mild eczema is unknown.
- Certain foods can induce AD by various mechanisms, including IgE-mediated mechanisms.
- Prick tests and specific IgE determination are frequently false positive and false negative. They may act as a guideline in defining the atopic state, but often they are useless as routine tests.
- If the clinician relies on the results of prick tests and IgE determination, inadequate diets will be prescribed, resulting in poor compliance and ineffectiveness.
- Since DBPCPT are often impossible to perform, a trial diet is justified in selected patients with severe AD, who are unresponsive to a standard treatment of moisturizers, topical corticosteroids and antihistamines.

**Conclusions**

AD is a complex disease in which a great number of environmental factors are involved, including food allergens and inhalant allergens. In young children with severe AD, food allergens, such as cow's milk and hen's eggs, should be considered as triggering factors. In older children, however, the role of food seems to be less important. In these patients inhaled allergens, such as house dust mite, might trigger the chronic lesions.