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Correlation between Clinical and Immunological Findings in Atopic Dermatitis

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Many immunological alterations have been reported in atopic dermatitis, and it is likely that in some cases they are capable of worsening the clinical course of atopic dermatitis (AD). More frequently these alterations are responsible for conditions associated with AD such as asthma, food allergy and infections. It seems probable that in some cases they are evidence of a preclinical allergic manifestation. However, in most cases, it is likely that the immunological alterations do not affect significantly the clinical course of the disease. *Key words: Atopic dermatitis; T-lymphocyte; IgE.*

Many immunological alterations have been reported in atopic dermatitis (AD), even though none of them is present in all cases of the disease. The aim of this lecture is to discuss the influence that the commonest immunological alterations have on the clinical manifestations of AD. We will first consider T-lymphocyte deficiency. There is much clinical evidence suggesting that there is a T-lymphocyte deficiency in AD subjects, the most important being their greater susceptibility to various infections and a low frequency of allergic contact dermatitis, the later being more evident in the first years of life (2).

Certain infections are more frequent in AD subjects; Kaposi's herpetic eruption is the most severe, sometimes lethal. Normally, most individuals come into early contact with herpes simplex virus, but the disease is observed almost exclusively in subjects with AD. This is why nineteen out of twenty recently observed cases of this infection were seen in AD subjects. Other cutaneous infections, such as impetigo, are more frequent in AD subjects. It is likely that in certain cases of AD a minimal T-lymphocyte deficiency may contribute to the increased susceptibility to infection.

On the other hand, there is no clear link between the clinical course of AD and T-lymphocyte deficiency: we observed mild cases of AD complicated by severe viral or bacterial infections. This is probably why AD children with T-lymphocyte deficiency respond to thymic extracts and levamisole, becoming less susceptible to infection and showing some improvement of the immunological parameters, whereas their AD in most cases does not improve significantly (6). From a clinical point of view, AD in children with T-lymphocyte deficiency does not differ significantly from common forms of AD, except for cases of the so-called HyperIgE syndrome, which will be discussed later. Besides a higher frequency of infections, immediate allergic reactions such as asthma och food allergy, are more frequently encountered in AD children with T-lymphocyte deficiency (6).

Another early clinical observation leading to the hypothesis of a T-lymphocyte deficiency in AD subjects, is the fact that only 10% of children with atopic dermatitis suffer from allergic contact dermatitis, even though these children are continuously exposed to pharmacological and chemical stimuli. This percentage increases considerably with age (2).

This minority of AD subjects who later develop allergic contact sensitivity usually have clinical characteristics that are different from other AD subjects. In these subjects the onset of AD occurs later, at about 5 years of age, and females are affected more frequently than males. The onset of allergic contact sensitivity can be observed in most cases from the age of 8 years onwards. The eczematous lesions are more frequently located on the

hands and feet and in most cases it is difficult to say to what extent an eczematous lesion is due to AD and to what extent it is due to allergic contact dermatitis. Another important difference of these AD subjects is a lower frequency of bronchial asthma and food allergy, probably due to lower average levels of IgE (2).

We will now consider the influence of total and specific IgE levels on the clinical manifestations of AD. Increased levels of total blood IgE in the umbilical cord were considered as the most accurate parameter for assessing the risk of atopy in newborns (4). In order to investigate whether toxic erythema of the newborn was a precocious manifestation of atopic diathesis, we determined the IgE levels of these children at birth. We did not find any significant difference in the IgE levels of newborns with toxic erythema as compared to those of normal controls: we therefore concluded that toxic erythema of the newborn, even though characterized by urticaria-like lesions and eosinophilia, is not linked with atopy. In order to answer the question whether AD in subjects with increased levels of total IgE differs from AD in subjects with normal levels of IgE, we compared the clinical findings of 2 different populations, both affected by AD, but with different levels of IgE: the first population had total IgE levels of more than 1 000 u/ml, the other had total IgE levels of less than 100 u/ml. The onset of AD was significantly later in patients with normal levels of IgE, whereas the severity, the duration, the sites involved and the clinical course of the disease was almost identical in the 2 populations. The most important clinical finding was a significantly higher incidence of asthma and other immediate reactions in the population with high levels of total IgE.

Hyper IgE syndrome is characterized by chronic recurrent eczematous lesions, very high levels of IgE and increased susceptibility to infections: it is uncertain whether it represents a separate syndrome or an exaggeration of clinical and biological manifestations of AD. The dermatitis of these subjects is not always severe, often located on unusual sites such as the groin, the pubic region, armpits and scalp (8); these children may also present coarse features, prognathism and failure to thrive. With regard to specific IgE, it is well known that about 70% of subjects with AD have IgE antibodies against the most common environmental allergens. We will discuss the influence of specific IgE antibodies against foods, grass pollens and dermatophagoides on the clinical course of AD. Specific IgE antibodies against cow's milk and egg white can be detected in about 40% of subjects with AD, especially in the first years of life. On the other hand, clinical reactions attributable to foods are reported by the patients or provoked by challenge tests in less than 10% of AD cases (1). The most frequent reaction is a contact urticaria involving the lips, then the face and other sites, sometimes followed by vomiting and/or asthma. An exacerbation of AD may also be observed in these patients, even though it is difficult to demonstrate definitely. These subjects are mainly children who do not tolerate cow's milk. In these cases, it is unlikely that AD is triggered off only by food. In fact, it is more common to observe a worsening of preexisting AD which then persists irrespective of exposure to food. It is also far from certain that the mechanism whereby foods aggravate AD is of a purely allergic nature. This is why the adverse reaction does not materialize under all conditions but depends on whether the offending food has been introduced in the autumn when the child is unwell or in the summer when the skin is better.

It has been recently suggested that subjects with AD; have serum IgE immune complexes, the antigenic portion of which is of alimentary origin (3). When confirmed in a large number of subjects, these studies could explain the problem of the latency period (up to 6–8 hours) between ingestion of food and exacerbation of the eczema in some atopic subjects. Specific IgE against respiratory allergens such as grass pollens and dermatophagoides can be found in about 40% of subjects with AD, this percentage increases with age. Some of these subjects have hay fever, recurrent urticaria/angioedema, periennal rhinitis or

bronchial asthma. Minor symptoms such as itching or contact urticaria after contact of the skin with house dust or grass pollens can be observed in AD subjects with specific IgE antibodies against inhalant allergens. It is likely that in some other cases specific IgE against respiratory allergens are evidence of preclinical sensitization, but in most cases they have no clinical importance, merely representing the response of a hyperproductive antibody organism to previous contact with an environmental allergen. However, AD in subjects with specific IgE against respiratory allergens is not different from other cases.

In order to assess the role of respiratory allergens in the course of AD, we studied the levels of specific IgE against these allergens in 3 different populations of subjects with AD. The first group improved during the summer, the second group worsened during the summer and the third group had persistent symptoms throughout the year. The levels of specific IgE antibodies against dermatophagoides and grass pollens were almost identical in all 3 populations: it is therefore unlikely that inhalant allergens play an important role in the course of AD. In a second experimental study we vaccinated 7 children affected by atopic dermatitis and presenting specific IgE against dermatophagoides but without respiratory allergic symptoms. These children and 14 non-vaccinated controls were followed for a period of 3 years: vaccination did not improve the clinical course of AD, whereas specific IgE against dermatophagoides decreased and asthmatic symptoms could be prevented. The conclusions to be drawn from these studies were that respiratory allergens do not affect the clinical course of AD. Recent investigations have demonstrated that some allergens such as penicillin, chicken extracts and dermatophagoides (7) are capable of eliciting both immediate hypersensitivity reactions and other types such as type IV and so-called cutaneous basophil hypersensitivity reactions (5). A delayed hypersensitivity reaction to dermatophagoides was demonstrated in AD children. We were not able to confirm these results in a preliminary study carried out on 50 subjects with AD: 26 of them presented immediate positive reaction to dermatophagoides, whereas none of them showed a delayed reaction when tested with dermatophagoides by scratch-patch test.

In conclusion, it is likely that numerous and complex allergic factors are capable in some cases of worsening the course of AD; in most cases they are responsible for conditions such as asthma, infections and food allergy associated with AD. However, one should remember that numerous non-allergic stimuli are capable of affecting the clinical course of AD, a disease which is genetically determined.

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