

The role of IgE in the pathogenesis of atopic dermatitis

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The mean level of serum IgE in patients with atopic dermatitis (AD) is higher than in patients with allergic asthma or allergic rhinitis. The spectrum of allergen-specific IgE varies with age, starting with IgE for food allergens such as cow's milk, egg, or peanut in infancy and for environmental allergens after the age of 1 year. The clinical observation that cow's milk allergen avoidance in young sensitized children and environmental allergen exposure intervention measures such as mattress covers may improve the course of AD suggests a role for allergens in the pathogenesis of AD. The high serum levels of allergen-specific IgE suggests a role for IgE in the mechanism involved in allergic inflammation in patients with AD. Furthermore, the presence of allergen-specific Th2 cells in the circulation and in the skin of these patients suggests an inflammatory mechanism in which both allergen specific IgE and T cells are involved. The route by which allergens influence the course of AD may be the respiratory tract, the gastrointestinal tract, or the skin. A clinical proof of the latter route is the observation that erythematous rashes and itch may be induced by skin contact of AD patients with animal dander or saliva. The atopy patch test (APT) is used as a test for eczematous skin reactions to aeroallergens in AD. Understanding the mechanism involved in the APT may offer more insight into the mechanism involved in AD. This paper gives a summary of the state of the art of the APT.

The atopy patch test (APT)

The APT is specific for patients with AD. In this test, an aeroallergen is applied onto the skin in a

concentration as used in the prick test. The test is read after 24 and 48 h and, if positive, shows erythema, induration, and sometimes even vesicles. The histology resembles an eczematous response. The test is positive in about 50% of the patients with AD and elevated allergen-specific serum IgE. To obtain this percentage, it is necessary to decrease the diameter of the stratum corneum by 10–15 times by tape stripping before application of the patch test (1).

The mechanism behind the APT is based on the presence of IgE molecules bound to the $F_{c\epsilon}R_1$ on dendritic cells (DC) in patients with AD. An allergen is able to bind to allergen-specific IgE on DC and can be presented to allergen-specific T cells (2). Evidence that this occurs *in vivo* is only indirect. Allergen-specific T cells belonging to the Th₂ type can be cultured from positive APT sites (3). During the APT, there is within the first 24 h an upregulation of Th₂-derived cytokines such as interleukin (IL)-4 (4); furthermore, the occurrence of an APT reaction is related to the presence of IgE-positive DC in the epidermis.

The nonlesional skin of patients with AD is already primed skin. Endothelial cells show an increased expression of ICAM-1, E-selectins, P-selectins, and, to a lesser degree, VCAM-1. Furthermore, non-lesional skin shows a long-term T-cell memory. Identical allergen-specific T cells can be detected in nonlesional skin over many years in the same patient, even during clinical remission (5).

Allergen-specific T cells derived from the skin express CLA. However, during the inflammatory process of the APT, there is no increase in the number of CLA-positive T cells (6). This suggests that the already present CLA-positive, allergen-

specific T cells in nonlesional skin become activated due to allergen presentation by DC in the skin. The increase in the number of T cells during the APT reaction is due to the influx of CLA-negative cells. These cells produce cytokines such as interferon-gamma (IFN- γ); during the later phase (after 24 h) of the APT, an increase in the number of IFN- γ -producing T cells can be observed. The cytokine pattern of the late phase of the APT is similar to that of lesional AD skin.

The composition of the cellular influx during the APT differs from the cellular influx during the late phase of the skin reaction to intradermally applied allergen. This late-phase (24 h) reaction is dominated by the influx of neutrophils and eosinophils (7). Neutrophils are not observed in the skin during the APT reaction; they are also absent in lesional AD skin.

Conclusion

In summary, the APT offers a model whereby to study allergic inflammation in AD patients. The eczematous response occurs earlier than in a classical type IV response. This is probably due to the presence of T cell-memory cells in nonlesional skin; the initial phase of the reaction is dominated by Th₂-type T cells and switches subsequently to Th₁-type T cells. The cytokine pattern in chronic AD skin lesions is also dominated by Th₁-type T cells. The mechanism behind this switch in reaction pattern is not known. A possible candidate is IL-12 released by macrophages and eosinophils (8).

The APT teaches us that eczematous responses can be induced by allergens in AD patients. IgE

bound to Fc ϵ R₁-positive DC and allergen-specific, CLA-positive Th₂ cells play a major role.

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