

Authors' affiliations:

A. Kapp, T. Werfel, Hannover, Germany

The most common skin diseases which may be caused or triggered by allergens are eczematous diseases (i.e., allergic contact dermatitis, atopic dermatitis). Allergic contact dermatitis is mostly caused by haptens which lead to the stimulation of specific T cells. If it is possible to eliminate the identified allergens, this disease can be almost completely cured. This is not always true of atopic dermatitis (AD), a chronic skin disease which may be associated with or triggered by a variety of pathogenic factors. Based on the research of the last decade, there is increasing evidence that T-cell responses to environmental or food allergens play a major role in the propagation of AD (1).

Proliferative responses can be elicited in T cells with inhalant allergens, particularly house-dust mites and pollen. Such responses are remarkably elevated in sensitized patients with AD in the circulating T-cell subpopulation expressing the skin homing molecule "cutaneous lymphocyte antigen" (CLA), a fact which points to an allergen-dependent mechanism targeting specific T cells in the skin. Inhalant allergens may directly trigger eczematous skin lesions in AD: we have recently shown that such lesions are associated with specific T-cell responses (2). Moreover, in addition to IgE-dependent mechanisms, IgE-independent mechanisms may also be involved in eczematous reactions to food and food-related allergens in AD. In the proliferative response of blood lymphocytes, we found significant differences between AD patients who reacted to milk with worsening of AD and control groups, and were able to generate casein-specific T-cell clones from these patients (3). New results point to a role of birch-pollen-associated food allergens in the course of the skin disease in more than 30% of sensitized patients with AD. This finding is associated with an allergen-specific T-cell response which can be detected in lesional skin upon oral provocation (4). Ongoing

To cite this article:

Kapp A. & Werfel T. Allergic inflammation: skin.
Allergy 1999, 54, 23-24.

Copyright © Munksgaard 1999

ISSN 0105-4538

studies directly address the major role of T-cell-mediated responses also in the so-called intrinsic variant of AD, which is characterized by the absence of specific IgE responses to protein allergens, and which is, therefore, still a diagnostic challenge in clinical practice.

The majority of allergen-specific T cells derived from skin lesions that have been provoked in patients with AD by epicutaneous application of inhalant allergens produce predominantly type-2 cytokines such as IL-4 or IL-5. A polarized type 2-cytokine pattern was previously regarded as a specific feature reflecting immune dysregulation in AD (5), but later it became clear that it is confined to early atopy patch test reactions characterizing the initial phase of the inflammatory process in AD. Allergen-specific T cells from the blood or from "spontaneous" skin lesions secrete both

type-1 and type-2 cytokines. However, the expression of IFN- γ predominates over IL-4 in chronic skin lesions and older patch test reactions in AD, pointing to a switch to a type-1 cytokine pattern (6). This phenomenon is apparently not a unique finding in AD, since IL-4 is found both on the mRNA and on the clonal level in nickel-induced early patch test reactions. The switch from a type-2 to a type-1 cytokine pattern is, therefore, not related to "atopy" and instead represents the time course of skin lesions (i.e., change from acute to chronic eczema) (7). A number of factors may be involved in the T2/T1 switch in older skin lesions. IL-12 appears to be a predominant mediator. Recently, eosinophils, which are actively involved in the inflammatory process in AD (8, 9), were identified as a source of this relevant molecule (10).

References

1. Werfel T, Kapp A. Environmental and other major provocation factors in atopic dermatitis. *Allergy* 1998;**53**:731–739.
2. Wistokat-Wülfing A, Schmidt P, Darsow U, et al. Atopy patch test reactions are associated with T-lymphocyte mediated allergen-specific immune responses in atopic dermatitis. *Clin Exp Allergy* 1999;**29**:513–521.
3. Werfel T, Ahlers G, Schmidt P, et al. Milk-responsive atopic dermatitis is associated with a casein-specific lymphocyte response in adolescent and adult patients. *J Allergy Clin Immunol* 1997;**99**:124–133.
4. Reekers R, Busche M, Wittmann M, Kapp A, Werfel T. Birch pollen related food triggers atopic dermatitis with specific cutaneous T-cell responses to birch pollen antigens. *J Allergy Clin Immunol* 1999 (in press).
5. Kapp A. Atopic dermatitis – the skin manifestation of atopy. *Clin Exp Allergy* 1995;**25**:210–219.
6. Grewe M, Bruijnzeel-Koomen CA, Schöpf E, et al. A role for Th1 and Th2 cells in the immunopathogenesis of atopic dermatitis. *Immunol Today* 1998;**19**:359–361.
7. Werfel T, Hentschel M, Kapp A, Renz H. Dichotomy of blood and skin-derived interleukin-4 producing allergen specific T-cells and restricted V β repertoire in nickel mediated contact dermatitis. *J Immunol* 1997;**158**:2500–2505.
8. Kapp A. The role of eosinophils in the pathogenesis of atopic dermatitis – eosinophil granule proteins as markers of disease activity. *Allergy* 1993;**48**:1–5.
9. Wedi B, Raap U, Lewrick H, Kapp A. Delayed eosinophil programmed cell death *in vitro*: a common feature of inhalant allergy and extrinsic and intrinsic atopic dermatitis. *J Allergy Clin Immunol* 1997;**100**:536–543.
10. Grewe M, Czech W, Morita A, et al. Human eosinophils produce biologically active IL-12: implications for control of T cell responses. *J Immunol* 1998;**161**:415–420.