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On Definition and Framework of Atopic Dermatitis

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Based on experience in connection with working and discussing differential diagnostic problems, a definition of atopic dermatitis (AD) seems to be needed. This should include the relation to atopy: it is obvious that the person developing this skin disease is an atopic individual. At the same time it is of importance to emphasize that the ensuing skin inflammation is of a specific character, since atopic persons may also develop skin lesions which have no relevance to their genetic constitution and immunological behaviour. When defining the special traits of AD, the prominent and clinically basic symptom, the itch and subsequent morphological changes should be mentioned in first hand, whereas a delayed-type skin reaction, based on cellular infiltrate and immunobiochemical alterations should also be considered. The term of eczema is much debated (1) and in this case a too broad concept and not covering all morphological events. It is, however, deeply rooted in the dermatological literature, and, as compromise, "eczematous inflammation" is mentioned (see table I).

Secondly, a pathomechanistic model of AD is presented. There are several designs in the literature which summarize the different events in the mechanism of AD (2–7), or covering some aspects of it, like the events on the cell level (8). The aim of presenting a new model is to attempt to put the, especially from the clinical point of view leading trait of the disease, i.e. the itch, in the center of the pathomechanistic pathways. The design considers genetic as well as environmental factors and consequences of the impaired immunoregulation including biochemical alterations, changes in cell functions and the release of inflammatory mediators. As a consequence of the atopic state the production of higher IgE levels, elicited by different allergens occurs in the majority of the cases, resulting in type-I hypersensitivity manifestations. Mostly attributed to alteration in the sub types of T cells, a paradoxical situation emerges: while deficiency of suppressor and cytotoxic T cells leads to impairment of cell-mediated immunity with its important consequences, predominantly T helper cells, in cooperation with antigen-presenting cells, including Langerhans cells, and other cells, create the infiltrate, typical for a delayed-type response.

On the other hand, I want to emphasize that the inflammation, elicited by immunological alterations occur in a skin which is impaired in several of its functions; in other words: the atopic events appear in an abnormally reacting skin. These functional alterations of the skin in the AD patient include changes in sebum production, sweat inhibition, barrier function and result, among others, in increased staphylococcal colonisation and in general reduced resistance to contact irritants. It has been shown, that, compared to the skin of nonatopic persons, alterations are present in the non-lesional skin of patients with AD, although it is clinically symptom-free

The only obvious common link between the immunological and non-immunological traits, i.e. itch, should be put in the center of the pathomechanistic events when designing a model. Itch is also a typical sign in both type-I and type-IV responses and is their important clinical consequence (another link may be the Langerhans cell (9), see Table 2).

A further intention was to discuss which of the etiological or provoking factors are of primary or secondary character in the mechanism of AD. The use of the term "primary" is rather problematic, since it frequently may be assumed that there exists a preceeding factor or event to a fact which is called "primary". Thus I have chosen to make a distinction between events influencing or depending on the course of AD. In the latter case, the changes following the clinical course are obviously a consequence of the intensity of the clinical phase of the disease. In some details, the data do not yeat allow a classification into these principles and these aspects are symbolized with a question mark (Table 3).

Table 1. *Definition of AD*

Atopic dermatitis is a specific dermatitis in the abnormally reacting skin of the atopic resulting in itch with sequelæ as well as in eczematous inflammation

Table 2. *Mechanism of AD: attempt to synthesis*

cAMP = cyclic 3,5,-adenosinemonophosphate, PDE = phosphodiesterase, PML = polymorph leukocytes, Mono = monocyte, IgE/s = IgE in serum, Ts = suppressor T cell, Th = T helper cell, Tcyt = cytotoxic T cell, Teff = T effector cell

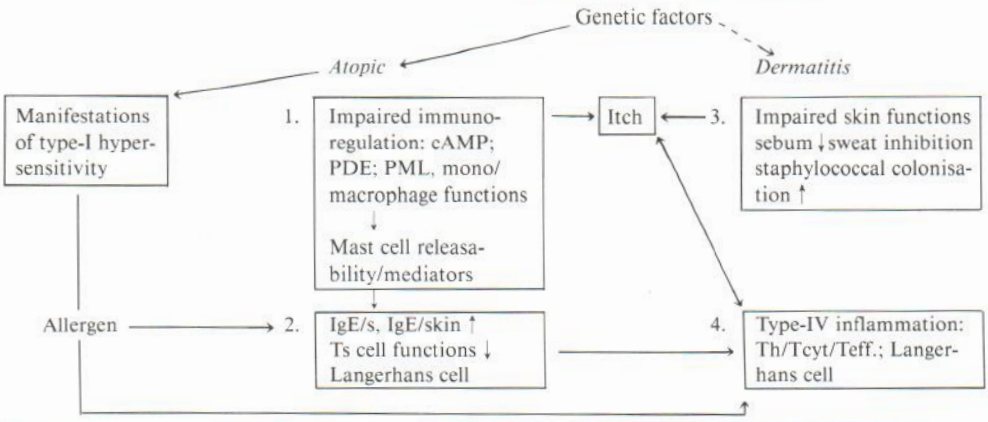

Table 3. *Putative primary and secondary immunological and pathophysiological events in the mechanism of AD*

Putative primary events (influencing the course of AD)	Putative secondary events (dependent on the course of AD)
1. Increased itch	1. Itchy skin
2. Increased PDE activity	2. High IgE production
3. Dry skin/reduced lipid secretion, Str. corneum alteration/increased TWL/reduced water content/ impaired barrier function, lower resistance to irritants, increased staphylococcal colonisation	3. Reduced cell mediated immunity
4. Mast cell releasability (?)	4. Reduced antiinfectious resistance/ reduced chemotaxis
5. Disturbed metabolism of linoleic acid in serum lecithin (?)	5. Vascular disturbances
	6. Sweat disturbances (?)

(?) = possibly pertinent to the other group.

Table 4. *Synopsis for the clinician*

Most stimuli either on allergic or nonimmunological basis reaching the skin outwards or inwards (incl. emotional influences) elicit or maintain *itch*

We have an immunological *imbalance*; therefore:
- Low defense against living agents
- Many positive immediate reactions with variable clinical significance

We have a *dysfunctioning* skin, therefore:
- The skin is dry
- Overcolonized with staphylococci
- Sweating leads to itch

Lastly, an ambition is mentioned in order to explain in a short and simple manner the important clinical consequences of the complex theoretical aspects of AD for the clinician, which he/she in turn can then point out for their patients (Table 4).

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