45.1 Introduction

Whereas the pathomechanisms of atopic respiratory diseases such as hay fever or extrinsic bronchial asthma are rather well-established, the exact role of various pathogenetic factors in the development of atopic eczema is still controversial. Especially in regard to the role of allergy, this becomes apparent in the confusion regarding terminology of this disease: since the term “atopy” has now been restricted to the IgE-associated forms of these diseases, there is no longer an “intrinsic” variant of “atopic” eczema. The consensus of the World Allergy Organization recently published consequently now names this disease only “eczema,” leaving the “atopic eczema” for the IgE-associated form and the term “nonatopic eczema” for what was formerly called the “intrinsic” type of AE (Chap. 1).

As logical as this seems in theory, in practice the problem is not solved. Eczema can start as the nonatopic form and only later on will IgE-antibodies develop. We have to keep in mind that “nonatopic eczema” is a negatively defined term without a specific positive marker for this variant (Chap. 29). It reflects the basic lack of knowledge regarding the etiopathophysiology of eczema.

Let us briefly reflect on the most important features which either alone or in combination play a role in the development of this disease. Animal models may help in molecular understanding (Chap. 43).

45.2 Genetic Predisposition

The well known genetic predisposition manifesting as familial occurrence of eczema, asthma, and hay fever have been known for almost a century and gave rise to the first description of the term “atopy” by Coca and Cooke. Classical genetics have shown a concordance rate in homozygous twins of approximately 85% compared to 30% in heterozygous twins (Chap. 23). 70% of eczema patients have family members with atopic diseases.

When both parents suffer from atopic disease and the same organ manifestation (e.g., both father and mother have eczema), the child has a risk of 70%–80% of developing eczema. If, however, the two parents suffer from different atopic diseases (e.g., the father asthma and the mother eczema) the incidence of atopic diseases in the children is only 30%.

New approaches in molecular genetics have described various gene loci showing close association with eczema (Chaps. 24, 25). It is of special interest that some of these gene loci are not connected to any known biological function. While some are closely related to immunological parameters such as the cytokine cluster on chromosome 5q, others also show obvious association to psoriasis, a clearly distinct skin disease; these genes might encode for other factors relevant for inflammation in the skin.

This clear-cut genetic influence sometimes gives rise to the misleading concept of an inborn, hereditary disease which, therefore, should be incurable. This is not only theoretically and empirically wrong, but also very frustrating for the patient and his family, when this prognostic information sounds like a verdict. The chromosomes cannot be changed at the moment; however, the itchy skin lesions can be very well treated. Nobody would say that streptococcal angina is incurable only because it may occur again!
Disturbed Skin Barrier Function ("Dry Skin")

The commonly described “dry skin” (Chap. 15) of an eczema patient involves a complex mixture of various factors with at least three quite different dimensions, namely:

1. Rough vs smooth
2. Lipid-rich vs lipid-poor
3. Moist vs low in water content

In a more modern view, this feature can be better described as disturbed barrier function, most likely on the basis of altered intercellular epidermal lipids (Chap. 37). Most of these lipids are ceramides, which are produced by various enzymes, some of them found to be altered in the skin, for example sphingomyelinasem, betaglucocerebrosidase, and sphingomyelin-deacylase. Proteases or protease inhibitors may also play a role in explaining the disturbance of barrier function, which can be measured as increased transepidermal water loss (Chap. 38). These protease inhibitors might under normal conditions inactivate environmental substances such as the major allergen from house dust mite or microbial toxins.

While many authors regard dry skin as a genetic feature of eczema, others point correctly to the variable nature of this dryness, which can change with time in many patients during exacerbation and remission. It is an attractive hypothesis that the dryness of the skin reflects only the sequelae of an otherwise invisible inflammation (Chap 19, 20).

Psychosomatic Interaction and Autonomic Nervous System Dysregulation

Many of the stigmata of atopic diseases go along with a dysregulation in the autonomic nervous system, best described by the concept of the $\beta$-adrenergic blockade from Szentivanyi together with $\alpha$-adrenergic and cholinergic hyperreactivity. This phenomenon might also explain the altered releasability of vasoactive mediators (e.g., histamine or leukotrienes) in this disease (Chap. 34).

The vasoactive mediators that seem to be more easily released such as histamine or eicosanoids not only have pro-inflammatory activities, but also anti-inflammatory effects via receptors on the lymphocyte surface. It may be speculated that increased levels of some of these mediators may contribute to the immune deviation characteristic for atopic diseases.

The role of psychosomatic influences in eczema may also be explained partly by this concept. Stress of any kind is able to release similar mediators involved in itch pathogenesis (e.g., histamine) as released during an allergic reaction. A doctor who neglects the role of the psyche in eczema will inevitably have difficulties in patient management. However, it is clear that atopic eczema is not a “psychological” disease; psychological phenomena may amplify the disease intensity or trigger exacerbations similar to asthma. In children, it is especially important to consider the parent–child interaction, which may be problematic in many families. Therefore, eczema school programs focus also particularly on the psychosomatic influence and use psychosomatic modalities in the management of eczema patients, who can be trained in “eczema school” programs (Chaps. 59, 63).