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COMMON IMMUNOCHEMISTRY IN ATOPIC DERMATITIS AND BRONCHIAL ASTHMA

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Abstract. Atopic dermatitis and bronchial asthma are closely associated with respect to hereditary factors, epidemiology and occurrence in the same individuals. Both depend on more or less common genetic and environmental traits. Both are typical multifactorial diseases. They have also much in common as regards the complex immunological and chemical mechanisms involved. This becomes particularly evident when comparable subgroups of patients with either atopic dermatitis and bronchial asthma are investigated.

Key words: Atopic dermatitis; Bronchial asthma; *Immediate* hypersensitivity; IgE; Atopy; Immunology; Immunochemistry

Children with infantile atopic dermatitis (AD) run a considerable risk of developing respiratory allergy and bronchial asthma (BA). 50–80% of infants and toddlers with AD have developed BA by 6 years of age (13, 16, 18). In this respect some traits are particularly predictive. In the vast majority of AD infants and children who later develop BA, the respiratory disease is more or less influenced by reaginic allergy (1, 3). Allergy is defined as immunological hypersensitivity which is harmful to the tissues or disruptive of the physiology of the host. There is ample evidence that most reaginic antibodies belong to immunoglobulin E (IgE). Elevated serum and skin IgE and IgE antibodies may be found in a high proportion of children with AD as well as with BA. Particularly high values are found in patients with severe AD, with seasonal allergic asthma and with combinations of AD and allergic asthma or bronchial lability, respectively (7, 15, 18).

The role of IgE-mediated allergy is well documented for several instances of AD and BA (1, 3, 16, 17, 19, 21). However, discussion of the role of IgE immunology in the two diseases can become more than lively on the slightest provocation. When there is so much divergence of opinon, there must be cause for re-evaluation in the light of newer information.

Some of the controversy as regards the role of allergy in AD and BA may be attributed to non-qualified use and non-discriminating interpretations of skin testing and radio-allergosorbent tests (RAST). This applies to both AD and BA. Much of the disagreement may also be due to differences in subpopulations studied. In BA, several subpopulations may be distinguished according to the involvement of immunological and non-immunological factors, respectively (3). A similar distinction may be appropriate even in AD, although the distribution may be quantitatively different in the two diseases.

Comparable subgroups of patients with AD and BA, respectively, have much in common as regards both immunology and biochemistry (Table I).

Itch is the main symptom of AD. Itch may be triggered by many factors, but is a main and prominent feature of allergy. It is the first and most persistent symptom of IgE-mediated reactions in the skin following direct skin testing and passive transfer *a.m.* Prausnitz-Küstner. Itch is also the most frequent skin symptom occurring during inhalant provocation tests in patients with both AD and BA (18). It is also the first—and in some patients, the major—symptom of a local allergic reaction in the nose. For BA, it is possible that in the bronchi the itch reflex is replaced by that of cough..

The wheal and flare reaction as seen in the reversible initial stage of the positive skin test reaction, is set off mainly by histamine released by local mast cells. In the bronchi, allergen challenge results in swelling of the mucosa and bronchial muscular spasm. In the first stage, this is easily reversible in the same way as the initial allergic wheal and flare reaction in the skin. However, in BA as in AD a combination of allergy with special tissue factors seems to be a necessary prerequisite for an acute exacerbation of the disease. Presence of one factor does not exclude the causative

Table I

	Atopic dermatitis		Bronchial asthma	
	Extreme immunol. sub-group	Extreme biochem. sub-group	Extreme immunol. sub-group	Extreme biochem. sub-group
A. *Immunological traits*				
Atopic (IgE) heredity	+	+/−	+	+/−
Elevated skin and serum IgE	+	−	+	−
Serum IgE antibodies	+	−	+	−
Positive skin tests to allergen	+	−	+	−
Positive allergen challenge	+	−	+	−
Non-significant allergies	+	(+)	+	(+)
Incomplete immunological information	+	+	+	+
B. *Biochemical traits*				
Acute and chronic inflammation	+	+	+	+
Abnormal response to histamine	+	+	+	+
Abnormal response to acetylcholine	+	+	+	+
Abnormal response to other biochemical agents	+	+	+	+
Tissue hyper-reactivity	+	+	+	+
Decreased cellular response to adrenergic stimuli	+	+	+	+
Altered autonomic regulation	+	+	+	+
cAMP/cGMP imbalance	+	+	+	+
C. *Clinical traits*				
Occurs in same individual	+	+	+	+
Multifactorial	+	+	+	+
Changeable features	+	+	+	+
Vicious circles	+	+	+	+
Threshold mechanisms	+	+	+	+

role of others. This is amply illustrated for AD by the classical description by Engman et al. (10) of a child with confirmed wheat hypersensitivity. Half his body was protected by dressings and, following ingestion of a wheat cracker, atopic dermatitis lesions appeared, but only on the unprotected areas. This case is consistently referred to, to emphasize the importance of trauma through scratching in the development of AD lesions. It may also, however, be used to emphasize the importance of allergy followed by scratching. If neither is removed in the child, who is usually not bandaged, the child will have eczema.

Neither the pathological anatomy of atopic eczema nor the pathological morphology of BA can be explained by the effects of the immediate and reversible stage of the IgE-mediated reaction as described up to this point (1, 14). However, our concept of the immunochemistry of IgE- and allergen-mediated reaction has been far too naive up to now. Too much consideration has been devoted to the first immediate and reversible stage of biodynamics following allergen + IgE-mediated mast cell release of mediators. The immunochemistry of IgE-mediated reaginic reactions is much more complex. The mast cell acts not only as a transistor and amplifier for the immunological reaction into the immediate and rapidly reversible biochemical reaction as described. It seems to be a leading element also in secondary sub-acute to chronic inflammatory reactions (5, 6). In this respect, it comprises both humoral and cellular aspects of inflammation. In fact, some of the patho-morphological traits found in AD have much in common with the characteristic traits of subgroups of BA (Table I). Many of these traits may be fairly well explained by the tissue reaction set off in the secondary inflammatory stage initiated by mast cell release of biochemically active agents. Clinically, manifestations of the secondary inflammatory stage can be demonstrated both in the skin and in BA (4, 11, 20). The two diseases also have other, possibly related immunological traits in common. Depression of cell-mediated immunity and defective T-cell function as

well as reduced adrenergic responses in lymphocytes are described for both (9, 12, 22).

Neither BA nor AD can be explained by IgE immunology alone. The main non-immunologic characteristic trait in both is hyperirritability and overresponsiveness of the tissues to a number of irritant stimuli. Bronchial hyperreactivity may also be found in patients with uncomplicated AD (15). It is possible that the clinical manifestations depend on genetic regulation of IgE immunology and genetic regulation of particular biochemical tissue reactivities combined (2, 23).

Future research concerned with BA has to concentrate on distinct subpopulations, the one used as control for the other. Data available so far with respect to AD seem to indicate that this should also be the case for this disease. The links between AD, atopic allergy and BA are very strong. This calls for active prophylactic measures to be undertaken in the AD child to prevent or postpone allergic sensitization of the respiratory passages. More should be done to investigate which factors may influence this trend. For a prospective study of etiologic factors in BA, the infant presenting with AD provides the perfect case.

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