

Natural history of "intrinsic" atopic dermatitis

E. Novembre*, A. Cianferoni, E. Lombardi, R. Bernardini, N. Pucci, A. Vierucci

Key words: asthma; atopic dermatitis; natural history; skin prick test.

It is well known that allergy plays a pathogenic role in the development of atopic dermatitis (AD) (1). However, approximately 20% of AD patients suffer from a skin disease that clinically resembles the skin lesions and the distribution pattern of AD, but is not associated with atopic status. This kind of "intrinsic" AD (iAD) seems to differ from the classical or "extrinsic" form (eAD) both in the T-cell cytokine production and in the immunohistology (2, 3), but no data are available about its natural history.

In this study, we investigated the persistence of AD and the development of respiratory allergic diseases in a group of children seen at the ages of 2 and 11 years according to the skin prick test (SPT) reactivity to allergens at those ages.

The parents of 111 children with AD evaluated at our allergy unit in 1989-90 were asked for re-evaluation of the children about 9 years later. Seventy percent of the children (77/111) underwent clinical history, and SPTs to food (egg white, wheat, milk, tomato, codfish, and soy [Lofarma, Milan, Italy]) and inhalant

allergens (dust mite, cat, dog, *Alternaria*, grass pollen, *Parietaria*, mugwort, olive pollen, and *Cupressus sempervires* [Lofarma]). AD was diagnosed according to Hanifin & Rajka (4).

The presence of asthma and SPT reactivity was studied as previously described (5, 6).

According to the SPT results, we defined the following groups:

- 1) "early atopic", i.e., those children who were already SPT positive at age 2 and were still SPT positive at age 11
- 2) "late-onset atopic", i.e., those who were negative at age 2 but became SPT positive by the age of 11
- 3) "nonatopic", i.e., those who were SPT negative at the ages of both 2 and 11.

We considered patients SPT negative at age 2 as having iAD.

The data were analyzed by the statistical program SPSS 6.0 for Windows with the chi-square and chi-square for trend tests. A two-sided type 1 error lower than 0.05 was considered statistically significant.

Seventy-seven AD patients, with a mean age ($\pm$ SE) of 24.1 ± 2.28 months at the first evaluation, and 132 ± 3.24 months at the second evaluation, were identified. At diagnosis, all of them had AD (77/77), 22% (17/77) had asthma, and 64% (49/77) had at least one positive SPT. At 11 years of age, 46% of them had AD (36/77), 43% (33/77) had asthma, and 84% had (65/77) at least one positive SPT.

Forty-nine out of the 77 (64%) studied children had early atopy, 16/77 (21%) had late-onset atopy, and 12/77 (15%) were nonatopic.

None of the nonatopic children developed asthma by age 11 (0/12), compared with the 25% (4/16) and the 59% (29/49) of the late-onset and early atopic children, respectively (chi square for trend, $P < 0.0002$). AD was still present by age 11 in 67% (8/12) of nonatopic AD as compared with 44% (7/16) and 43% (21/49) of the late-onset and early atopic children (Fig. 1). Altogether, the 28 AD children

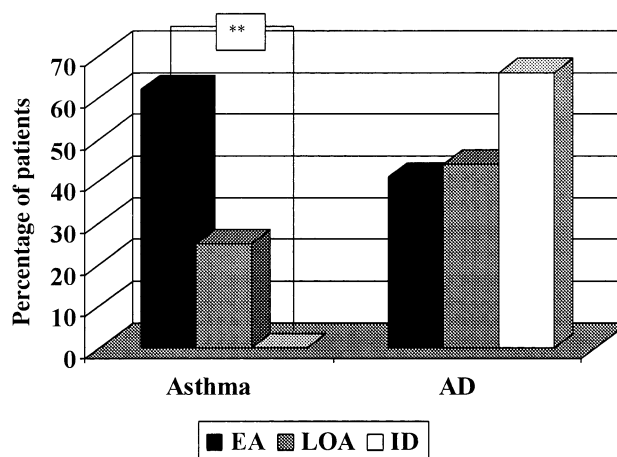


Figure 1. Prevalence of asthma and atopic dermatitis at age 11 according to early-atopic (EA), late-onset (LOA), and "intrinsic" dermatitis status. ** $P < 0.0002$ (chi square for trend).

with negative SPT at age 2 had a prevalence of asthma at age 11 of 14% (4/28), compared to 60% (29/49) for the early atopic ones ($P < 0.0003$).

AD is a common illness that develops early in childhood (4). iAD is a condition different from eAD, because allergy seems not to play a major role in its pathogenesis (1, 7). However, a strict distinction cannot be made because of the possibility that iAD may develop into eAD during the course of time. In fact, we have found in this study that more than half of patients SPT negative at the onset of AD, became SPT positive by the age of 11. Therefore, in many cases, the so-called iAD is not a true entity but only a transition stage in the natural history of AD. However, subjects with negative SPT at the onset of AD have a much lower risk of developing asthma much lower than the early atopics. On the other hand, the atopic status seems not to be important for AD persistence. In conclusion, children with SPT-negative AD by the age of 2 years have a significantly lower risk of developing asthma than SPT-positive ones. This feature might be useful to select children with AD who need prevention or early treatment of asthma.

*Allergy and Clinical Immunology Unit
Department of Pediatrics
Anna Meyer Hospital
Via Luca Giordano 13
50132 Florence
Italy
Tel. (+39-055) 5662461
Fax: (+39-055) 570380

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SIT in Croatia

V. Milavec-Puretić*, J. Lipozenčić, N. Di Biagio, I. Lakoš-Jukić

Key words: hypersensitivity; immediate diagnosis; immunologic tests; immunotherapy.

● SPECIFIC immunotherapy (SIT) (hyposensitization) is the practice of administering gradually increasing quantities of a specific allergen to allergic patients (insect sting-induced reactions – anaphylaxis, rhinoconjunctivitis, bronchitis, asthma, and atopic dermatitis caused by inhalatory allergens) until a maintenance dose is reached or the symptoms disappear.

A 15-year evaluation of immunotherapy.

The principle of preparing modified vaccines is to reduce or remove allergenicity and to preserve or increase immunogenicity. In this way, the capacity to modulate the immune system and to maintain clinical efficacy is preserved (1). Physical modification includes absorption and inclusion of allergens as depot vaccines, as with aluminum (2), calcium phosphate, tyrosine, and liposomes (3). Chemical modification refers to the so-called allergoids. Combinations of chemically and physically modified vaccines include tyrosine-adsorbed, glutaraldehyde-modified vaccines and aluminum hydroxide-adsorbed formaldehyde vaccines.

Contraindications for SIT include immunodeficiency diseases, malignancies, severe uncontrolled asthma, cardiovascular disorders, age under 5 years, advanced age, and pregnancy. Hypersensitivity to Hymenoptera venom is an exception.

During a 15-year period (1985–99) at the Department of Dermatology and Venereology (Allergy Unit), Zagreb University Hospital Center, Croatia, allergen SIT was used in 185 allergic patients with the following diagnoses: allergic rhinitis, allergic conjunctivitis, pollinosis, bronchial asthma, atopic dermatitis with sensitization to inhalatory allergens, and urticaria with Quincke's edema.

Allergen mixtures of tree and grass pollen and weeds, and single allergens (house dust and dust mite) were used (Table 1).

Therapy was administered twice weekly with increasing doses of allergen vaccines in concentrations I to IV, followed by the maintenance dose, with due consideration of contraindications as recommended by WHO. Pretreatment examinations included the prick test and serologic analyses (total and specific IgE). During allergen SIT, the following clinical and laboratory examinations were regularly performed: