

# Comparison of Transepidermal Water Loss, Capacitance and pH Values in the Skin between Intrinsic and Extrinsic Atopic Dermatitis Patients

Atopic dermatitis (AD), with the prevalence rate of around 10 to 15%, is characterized by an intensely pruritic skin lesions with typical distribution and morphology. Recently, AD is divided into extrinsic type (ADe) and intrinsic type (ADi) according to the laboratory findings and associated diseases. ADe is well-known for high IgE level, positive response to food- or aero-allergens, whereas ADi has clinically similar skin lesions and distribution patterns of AD with normal serum IgE levels, negative in vitro test for environmental or food allergens and without associated atopic diseases. To instrumentally evaluate the differences of skin involvement and functions between ADi and ADe, we checked the transepidermal water loss (TEWL), capacitance and pH in both types of childhood AD and age-matched control. The proportion of ADi was around 20% in all AD patients (10/51). Our experiment suggested possible differences between ADi and ADe. Antecubital fossa is a famous involvement site of childhood type of AD, where both types of AD patients showed higher TEWL and decreased capacitance. ADe patients showed increased TEWL in all sites and lower hydration in 4 sites, whereas ADi patients showed no significant differences of TEWL and hydration in forehead, cheek, and back of leg.

Key Words : Dermatitis, Atopic; Transepidermal Water Loss; Capacitance; Hydrogen-Ion Concentration

Suk-Jin Choi, Min-Gyu Song,  
Whan-Tae Sung, Dong-Youn Lee,  
Joo-Heung Lee, Eil-Soo Lee, Jun-Mo Yang

Department of Dermatology, Samsung Medical  
Center, Sungkyunkwan University School of  
Medicine, Seoul, Korea

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## Address for correspondence

Jun-Mo Yang, M.D.  
Department of Dermatology, Samsung Medical  
Center, Sungkyunkwan University School of  
Medicine, 50 Ilwon-dong, Kangnam-gu, Seoul  
135-710, Korea  
Tel : +82-2-3410-3541, Fax : +82-2-3410-3869  
E-mail : jmyang@smc.samsung.co.kr

## INTRODUCTION

Atopic dermatitis (AD) is characterized by an intensely pruritic skin disease with typical distribution and morphology. The age of onset is nearly always within the first 5 yr of life, and lifetime prevalence in children is roughly 10 to 15% in industrialized countries (1). Although the etiology remains obscure, atopy can be defined as a familial hypersensitivity of skin and mucous membranes against environmental substances, which is associated with increased IgE production and/or altered nonspecific reactivity in the skin of patients with AD and in the lungs of patients with asthma.

Recently, AD is divided into two subgroups according to the laboratory findings and associated diseases. In analogy to the extrinsic and intrinsic types of asthma (2, 3), the term "intrinsic type of AD" (ADi) has been proposed as a counterpart to the term "extrinsic type of AD" (ADe) (4-6). Nonallergic AD, nonatopic eczema, or nonatopic AD (7) are used interchangeably with ADi, which is found in a relevant proportion of all AD patients at a frequency of 15-45% (8). The ADe is so-called IgE-associated dermatitis and is frequently related with allergic bronchial asthma or allergic rhinoconjunctivitis. On the other hand, ADi has clinically similar skin lesions and distribution patterns of AD, but has normal serum

IgE levels. These patients are negative in vitro for environmental or food allergens and are not associated with other atopic diseases, such as asthma or allergic rhinoconjunctivitis. Even though patients with ADi tend to have a late onset of the disease (9-11), there are neither molecular markers nor clinically diagnostic tools for distinguishing ADi from ADe (8).

With the development of new technology, there have been trials to evaluate the skin involvement and functions of AD patients instrumentally, with special focus on disrupted skin barrier functions (12). However, there is no report to compare the skin conditions between ADi and ADe patients.

To obtain the objective data to distinguish ADi from ADe, we evaluated transepidermal water loss (TEWL), capacitance and pH of the skin of childhood ADi, ADe, and healthy control of the same age group.

## PATIENTS AND METHODS

### Study population

Fifty-one patients, aged 7-13, (mean  $\pm$  SD = 8.87  $\pm$  1.98 yr), 29 males and 22 females, affected by AD according to the criteria of Hanifin & Rajka (13), and 8 healthy age-matched

children (mean  $\pm$  SD =  $9.25 \pm 1.98$  yr) were included in this study. Healthy controls, who did not have any symptoms or signs of AD, were recruited from out-patient department. No patients had clinical signs of concomitant ichthyosis vulgaris. History of respiratory atopy (allergic rhinitis or asthma) was observed from all patients, and metacholine provocation test was done on the patients who had the history of asthma. Although we did not check the scoring atopic dermatitis (SCORAD) index in these patients, all the patients recruited in this study had the typical childhood type AD skin lesion and similar clinical findings.

All the subjects were instructed to refrain from using oral, topical medicines and moisturizers for at least 3 days prior to the study. Informed consent was obtained from all patients and control individuals, and the study was approved by Samsung Biomedical Research Institute Medical Ethics Committee.

### Laboratory measurements

To investigate whether the patients were ADi or ADe, we took the blood from all the patients to check total IgE titer, eosinophilic cationic protein (ECP) and eosinophil counts. All AD patients were checked either with specific IgE titer (Pharmacia CAP system fluoroenzymeimmunoassay, Uppsala, Sweden) towards Dermatophagoides species, dust and some kinds of foods including milk, egg, meat, chicken and pork and/ or with prick test towards inhalant allergens and pollens.

### Instruments and study procedure

Instrumental measures were performed at 8 different sites-

**Table 1.** Laboratory findings of ADi and ADe patients (mean  $\pm$  SD)

	Intrinsic (n=10)	Extrinsic (n=41)
Total IgE	99.3 $\pm$ 70.0	591.8 $\pm$ 616.9*
ECP	47.6 $\pm$ 50.0	76.7 $\pm$ 54.1
Blood eosinophils	258.8 $\pm$ 45.4	446.0 $\pm$ 232.7*
Positivity to CAP test	0% (0/10)	54% (21/39)
Positivity to prick test	0% (0/10)	96% (22/23)

\*Significant difference between intrinsic and extrinsic groups ( $p < 0.05$ ).

**Table 2.** TEWL values ( $\text{g/m}^2 \text{ h}$ ) in children of AD and control (mean  $\pm$  SD)

TEWL	Control (n=8)	ADi (n=10)	ADe (n=41)
Forehead	10.9 $\pm$ 3.17	24.2 $\pm$ 18.1	21.9 $\pm$ 12.9*
Cheek	14.7 $\pm$ 9.04	24.3 $\pm$ 11.7	24.6 $\pm$ 13.7*
Volar forearm	10.2 $\pm$ 2.56	15.7 $\pm$ 6.85*	19.6 $\pm$ 10.1*
Dorsal forearm	9.89 $\pm$ 1.61	14.2 $\pm$ 5.15*	18.8 $\pm$ 11.9*
Antecubital fossa	13.9 $\pm$ 5.00	24.4 $\pm$ 12.8*	26.7 $\pm$ 14.5*
Abdomen	10.4 $\pm$ 0.95	18.2 $\pm$ 6.73*	22.8 $\pm$ 13.1*
Interscapular	11.2 $\pm$ 3.33	18.4 $\pm$ 12.6*	20.0 $\pm$ 11.4*
Back of leg	16.5 $\pm$ 8.17	21.9 $\pm$ 18.8	28.8 $\pm$ 18.8*

\*Significant difference between control and AD group ( $p < 0.05$ ).

forehead, cheek, antecubital fossa, volar side of the forearm, dorsal side of the forearm, abdomen, interscapular region, and back of leg-according to Seidenari and Giusti (12).

TEWL was measured using a Tewameter TM210 (Courage + Khazaka electronic GmbH, Germany) according to the guidelines of Pinnagoda *et al.* (14). The skin surface hydration and pH were determined by a corneometer CM 820 and skin-pH-meter (Courage + Khazaka electronic GmbH, Germany), following the instruction of the manufacturer.

All evaluations were performed on subjects in reclining position after a 30 min acclimation period in a room with the temperature set at 21-22°C and humidity at 45-50% in the following order: TEWL, capacitance, and pH measurements.

### Statistical analysis

ANOVA with multiple comparison and Duncan-Turkey test were used for assessing differences among 3 groups. Only the  $p$  value less than 0.05 is statistically significant.

## RESULTS

According to the laboratory data (Table 1), we separated AD patients into ADi (n=10) and ADe (n=41). Total IgE and blood eosinophilia were significantly higher in ADe patients than ADi. 92.7% (38/41) of ADe patients showed allergy to dust, mite or some kinds of foods. Thirteen patients from ADe

**Table 3.** Capacitance values in children of AD and control (mean  $\pm$  SD)

Capacitance	Control (n=8)	ADi (n=10)	ADe (n=41)
Forehead	74.4 $\pm$ 3.81	70.2 $\pm$ 17.0	63.2 $\pm$ 13.8*
Cheek	60.4 $\pm$ 11.4	68.0 $\pm$ 14.3	64.0 $\pm$ 13.2
Volar forearm	60.3 $\pm$ 3.88	58.6 $\pm$ 11.0	58.2 $\pm$ 11.4
Dorsal forearm	55.1 $\pm$ 9.33	56.6 $\pm$ 7.49	56.8 $\pm$ 10.9
Antecubital fossa	77.1 $\pm$ 20.7	53.5 $\pm$ 13.0*	57.3 $\pm$ 13.5*
Abdomen	58.0 $\pm$ 9.52	56.8 $\pm$ 9.52	55.6 $\pm$ 10.4
Interscapular	77.4 $\pm$ 12.6	67.8 $\pm$ 13.5	67.1 $\pm$ 11.7*
Back of leg	64.8 $\pm$ 14.4	56.7 $\pm$ 10.6	52.1 $\pm$ 14.2*

\*Significant difference between control and AD group ( $p < 0.05$ ).

**Table 4.** PH values in children of AD and control (mean  $\pm$  SD)

pH	Control (n=8)	ADi (n=10)	ADe (n=41)
Forehead	5.10 $\pm$ 0.63	4.97 $\pm$ 0.41	5.26 $\pm$ 0.70
Cheek	5.06 $\pm$ 0.48	5.24 $\pm$ 0.50	5.39 $\pm$ 0.65
Volar forearm	5.09 $\pm$ 0.58	5.18 $\pm$ 0.43	5.27 $\pm$ 0.62
Dorsal forearm	5.15 $\pm$ 0.63	5.22 $\pm$ 0.46	5.37 $\pm$ 0.83
Antecubital fossa	5.05 $\pm$ 0.65	5.14 $\pm$ 0.56	5.20 $\pm$ 0.61
Abdomen	4.89 $\pm$ 0.55	5.53 $\pm$ 0.26*	5.28 $\pm$ 0.49*
Interscapular	4.98 $\pm$ 0.78	5.21 $\pm$ 0.37	5.15 $\pm$ 0.62
Back of leg	4.90 $\pm$ 0.56	5.17 $\pm$ 0.38	5.30 $\pm$ 0.71

\*Significant difference between control and AD group ( $p < 0.05$ ).

group had allergic rhinitis and six had asthma according to metacholine test. The ECP was somewhat higher in ADe patients, but there was no significant difference between the two groups.

In TEWL, all 8 sites of ADe patients and 5 sites of ADi patients were significantly different from those of control subjects. Forehead, cheek and back of leg of ADi patients did not show any differences in comparison with those of control (Table 2). On the other hand, capacitance values showed differences in several sites-forehead, antecubital fossa, interscapular area and back of leg-in ADe patients and only in antecubital fossa in ADi patients (Table 3). pH values of AD patients somewhat shifted to alkalinity, showing significant difference only in abdomen in both types of AD (Table 4).

## DISCUSSION

AD has been thought to be caused by both genetic background and environmental factors. With recently increasing prevalence of AD, a lot of studies have been done to identify the causes of the disease and reported that increasing air-pollution may be a major external factor, especially in ADe. ADi, which occupies around 15-45% of all AD patients and does not have any kind of allergy, is indistinguishable morphologically from ADe by naked eyes. The instrumental evaluation of skin morphology and function provided us with more objective and precise data than using naked eyes. The clinical and instrumental comparisons of eczematous skin in its impaired barrier function and susceptibility to irritants have been thoroughly documented. Increased water loss and reduced hydration in contrast to normal skin have been reported from eczematous skin lesions (15, 16), hands of AD patients (17), sites of flexural eczema (18) and allergic and irritant patch test sites (19).

In our experiment, the proportion of ADi patients was around 20% and was consistent with previous reports. ECP, a protein present in eosinophil granules, is cytotoxic to parasites and is secreted by activated eosinophils during allergic and inflammatory reactions (20). Kapp et al. (21) found that ECP serum levels are increased in patients with moderate to severe AD compared with non-atopic control subjects. Correlation of eosinophil count or ECP with IgE is still controversial. In our study, ADe patients showed somewhat higher, but statistically insignificant ECP compared with that of ADi. TEWL is increased due to any kind of impaired barrier functions in the skin. Seidenari and Giusti (12) reported higher TEWL in involved skin sites compared with uninvolved sites in AD patients. On the other hand, Abe et al. (18) reported no difference between involved and uninvolved sites of AD. Our study showed that higher TEWL values were observed in all sites of ADe and 5 sites of ADi patients. The face and leg of ADi patients showed no difference from those of control subjects. The hydration of stratum corneum in AD pa-

tients was significantly lower than that of normal control (22), and even the uninvolved skin of AD differed from uninvolved psoriatic skin and control (23). The hydration was decreased in face, antecubital fossa, interscapular and leg of ADe, but only in antecubital fossa in ADi in our study. The normal values of pH were reported 4.0-5.5 on the forehead and 4.3-5.9 on the cheek in white people. High pH is frequently associated with high TEWL, and high TEWL is associated with low hydration (24). This finding was usually correlated with experimentally induced irritant dermatitis (24), but there were no correlations among these parameters in AD (12). In our study, only abdomen showed significant difference of pH compared with normal controls in both type of AD.

Although the study group is rather small, it is the first time to try to differentiate the differences of barrier function and skin distribution between ADi and ADe. Putting all these data together, we may conclude that there may be differences between ADi and ADe. Antecubital fossa is a famous involvement site of childhood type of AD, and both type of AD patients showed higher TEWL and decreased capacitance in this site. ADe patients showed increased TEWL in all sites and lower hydration in 4 sites, whereas ADi patients showed no significant differences of TEWL and hydration in forehead, cheek and back of leg. Although the skin lesions of ADi look very similar to those of ADe in naked eyes, the face and leg of ADi patients may be less severe based on our results. To confirm these findings, a large group of study will be needed in the near future.

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