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Objective Assessment of the Skin of Children Affected by Atopic Dermatitis: A Study of pH, Capacitance and TEWL in Eczematous and Clinically Uninvolved Skin

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In order to obtain objective data on skin functions in subjects with atopic dermatitis (AD), according to the different phases of the disease, we evaluated the skin of children with AD instrumentally and compared it to that of healthy subjects of the same age group. One hundred patients, aged 3 to 12, and 21 healthy children were studied by means of measurements of pH, capacitance and transepidermal water loss (TEWL) at 8 different skin sites. At the moment of the investigation 55 children out of 100 presented skin lesions on at least one of the assessed skin areas, whereas 45 had been free from eczema for at least 1 month. Considering all skin sites together, significant differences were found between mean values of pH, capacitance and TEWL of eczematous skin, both in respect to those referring to apparently healthy skin in the same patients and in respect to the skin of control subjects. Moreover, TEWL, pH and capacitance values referring to uninvolved skin of AD patients significantly differed from those of healthy subjects. Finally, when values referring to patients with skin lesions and to patients without lesions were separately considered, significant differences concerning the parameters of uninvolved skin were observed. These data show that, in subjects with AD, skin functions undergo fluctuations according to the phase of the disease and support the hypothesis that the presence of active eczema determines an impairment of the barrier of uninvolved skin, even at sites far from active lesions. ***Key words: skin barrier function; phase of AD.***

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A decisive break-through in the definition of atopic dermatitis (AD) occurred upon the adoption of standardized diagnostic criteria (1). Successively, efforts have been made to establish common standards for the clinical evaluation of the severity of the disease and of pruritus, to be used as a basis for objective assessment of therapeutic studies (2–6). However, the quantification of the extension of the dermatitis, as well as the assessment of the degree of skin lesions and symptoms, often lack in inter- and intra-observer reproducibility.

Technology and knowledge have, over the years, enabled the instrumental evaluation of skin morphology and functions, leading to an objective and reproducible description of healthy and diseased skin. The skin of patients affected by AD has been studied in order to describe the micro-surface reliefs (7, 8), the water content (9–12) and the evaporation rate through the epidermis (13–18) and to determine susceptibility to irritant substances (16–20). Data on children with AD are, however, scarce, and little is known about uninvolved skin in subjects in different phases of the disease (14).

We instrumentally evaluated the skin of children with AD and compared it to that of healthy subjects of the same age group. The aim of our study was to obtain objective data on skin functions in AD subjects, according to the different phases of the disease, to be proposed for supporting subjective monitoring of the course of the dermatitis and the therapeutic response in children affected by AD.

PATIENTS AND METHODS

Study population

One hundred patients, aged 3 to 12, (mean ± sd = 4$^{8}/_{12}$ ± 3$^{4}/_{12}$), 49 males and 51 females, affected by AD according to the criteria of Hanifin & Rajka (1), and 21 healthy children (mean ± sd = 5$^{9}/_{12}$ ± 2$^{1}/_{12}$), entered the study. At the moment of the investigation 55 children out of 100 presented skin lesions (acute or chronic eczematous inflammation) on at least one of the assessed skin areas (active dermatitis), whereas 45 had been free from eczema for at least 1 month (inactive dermatitis). Their skin appeared normal or dry. No patients showed clinical signs of concomitant ichthyosis vulgaris.

The subjects were instructed to refrain from using topical drugs or moisturizers for 3 days prior to the study.

Instruments and study procedure

Evaluations were carried out from October 1993 to March 1994. Instrumental measurements were performed at 8 different skin sites, including predilection sites and skin areas generally not affected by dermatitis, i.e. forehead, cheek, antecubital fossa, volar side of the forearm, dorsal side of the forearm, abdomen, interscapular region and back of the leg. Values referring to skin sites showing eczematous lesions were considered separately.

Transepidermal water loss (TEWL) was measured using an evaporimeter EP1 (Servo Med, Sweden), which is based on vapour pressure gradient estimation. An insulating glove for holding the probe and the protection cover without the screen and grid was employed during measurements. The built-in damping filters were used to smooth the fluctuations in TEWL, in order to register a TEWL value during a 30-s period after stabilization, which was considered as the measured value (21).

The skin surface hydration was determined by a corneometer CM 820 (Courage + Khazaka, Germany). The instrument measures the electrical capacitance of the stratum corneum. Since water has the highest dielectric constant in the skin, an increase in the water content will raise the capacitance values, which are displayed in arbitrary units by the instrument.

A pH meter with a flat surface glass electrode (pH 90, Schwarzhaupt Medizintechnik, Germany), based upon the electrochemical method, was used to measure the pH of the test sites.

All evaluations were performed after a 30-min acclimation period on reclining subjects in a room with the temperature set at 21–22°C and humidity at 45–50% in the following order: TEWL measurement, capacitance measurement and pH measurement. It was not always possible to keep small children quiet until all evaluations were carried out; therefore some measurements are missing, as indicated by the

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Table I. *TEWL values (g/m² h) in children affected by AD and in control subjects (mean ± sd)*
The number of assessed areas is in parenthesis.

	Healthy skin of control subjects	Uninvolved skin of AD patients	Involved skin of AD patients
Forehead	7.18±3.03	10.36±6.31 (80)	34.29±21.12 (7) a,b
Cheek	6.59±2.21	8.61±3.57 (70)	32.26±19.05 (23) a,b
Volar forearm	4.06±1.98	7.71±4.13 (82) b	27.50±12.93 (10) a,b
Dorsal forearm	3.24±1.39	6.53±4.40 (75) b	25.20±17.29 (10) a,b
Antecubital fossa	5.82±2.43	10.09±5.27 (65)	34.40±21.20 (20) a,b
Abdomen	7.18±4.25	8.40±5.07 (77)	28.57±13.05 (7) a,b
Back of the leg	5.00±4.29	6.96±3.81 (80)	26.00±17.38 (16) a,b
Interscapular region	5.12±1.90	7.93±5.11 (73)	32.90±18.67 (10) a,b

a = significant ($p<0.05$) in respect to uninvolved atopic skin.
b = significant ($p<0.05$) in respect to the skin of control subjects.

number of assessed cases in the Tables. At some skin areas both involved and uninvolved skin was evaluated: in this case two values for the same area were considered.

Statistics

Analysis of variance and the SNK test were used for assessing differences between values belonging to the skin of healthy subjects (SHS) and the uninvolved skin of AD patients (UAD), between SHS and the involved skin of AD patients (IAD) and between UAD and IAD. Linear regression analysis was used to calculate the correlation coefficients between the different parameters. Probabilities less than 0.05 were considered significant.

RESULTS

The results of the measurements, according to the different body locations, are illustrated in Tables I-III.

In children with AD, values referring to affected skin significantly differed from those of unaffected skin at most skin sites for all the parameters.

At uninvolved skin sites, TEWL values were significantly higher in respect to those referring to healthy children only on the forearm, whereas capacitance values differed significantly from those of non-atopics only on the cheek and the interscapular region. pH values of atopic children had shifted towards alkalinity, showing significant differences in respect to those of non-atopic subjects at forehead, volar forearm, antecubital fossa, abdomen and interscapular region.

Fig. 1 shows the results referring to all skin sites together. Values of uninvolved and eczematous skin are considered separately. Significant differences are noticeable between mean values of pH, capacitance and TEWL of eczematous skin both in respect to those referring to apparently healthy skin in the same patients and in respect to the skin of control subjects. Moreover, TEWL, pH and capacitance values referring to uninvolved skin of AD patients significantly differ from those of the healthy subjects.

If AD patient data are divided into two groups according to the presence of eczematous lesions (Fig. 2), clear differences concerning the parameters of uninvolved skin are seen: TEWL and pH values are significantly higher at uninvolved skin sites in subjects with current eczema in respect to values belonging to the group without skin lesions, whereas capacitance values are lower. Water content of the stratum corneum of uninvolved skin, as evaluated by capacitance, is lower in respect to values referring to healthy skin of control subjects only in children with active dermatitis.

No correlations were found between values of pH, TEWL and capacitance either in healthy or atopic children.

DISCUSSION

Impaired barrier function and susceptibility to irritants of eczematous skin have been thoroughly documented both clinically

Table II. *Capacitance values in children affected by AD and in control subjects (mean ± sd)*
The number of assessed areas is in parenthesis.

	Healthy skin of control subjects	Uninvolved skin of AD patients	Involved skin of AD patients
Forehead	58.5±12.1	56 ±13.6 (93)	35.1±12.1 (7) a,b
Cheek	61 ± 9.7	49 ±13 (78) b	42.9±14 (24) a,b
Volar forearm	53.7± 9.1	56.3±12.1 (89)	44.7± 8.1 (12) a,b
Dorsal forearm	52.7± 9.2	52.8±10.6 (81)	38.5±10.6 (10) a,b
Antecubital fossa	60.2± 7.6	64.6±12.9 (79)	45.2±10.5 (21) a,b
Abdomen	56.3± 8.9	52.9±11.9 (90)	42.7± 8.9 (7) a,b
Back of the leg	53.6± 8.1	51.6±11.4 (88)	38.5± 8.4 (16) a,b
Interscapular region	66.9±10.9	60 ±12.9 (84) b	43.3±10.2 (11) a,b

a = significant ($p<0.05$) in respect to uninvolved atopic skin.
b = significant ($p<0.05$) in respect to the skin of control subjects.

Table III. *pH values in children affected by AD and in control subjects (mean ± sd)*
The number of assessed areas is in parenthesis.

	Healthy skin of control subjects	Uninvolved skin of AD patients	Involved skin of AD patients
Forehead	4.67±0.39	4.99±0.66 (91) b	5.68±0.47 (7) a,b
Cheek	5.43±0.42	5.49±0.57 (76)	5.68±0.38 (23)
Volar forearm	4.86±0.45	5.23±0.74 (88) b	5.54±0.63 (11) b
Dorsal forearm	5.12±0.63	5.37±0.75 (80)	5.97±0.62 (9) a,b
Antecubital fossa	4.70±0.49	5.12±0.73 (78) b	5.57±0.87 (21) a,b
Abdomen	5.04±0.43	5.50±0.62 (87) b	5.68±0.57 (7) b
Back of the leg	5.32±0.48	5.55±0.74 (86)	5.63±0.64 (15)
Interscapular region	4.80±0.44	5.17±0.64 (82) b	5.69±0.56 (11) a,b

a = significant ($p<0.05$) in respect to uninvolved atopic skin.
b = significant ($p<0.05$) in respect to the skin of control subjects.

and instrumentally. Increased TEWL values and reduced hydration values in respect to normal skin have been reported at eczematous skin sites (22, 23), on the skin of the hands of AD patients (13), at sites of flexural eczema (14) and at allergic and irritant patch test sites (24). Our data demonstrate that the eczematous skin of children with AD differs from the skin of control subjects and from the uninvolved skin of AD patients by higher TEWL and pH values and lower capacitance values.

The uninvolved skin of AD patients has been assessed to ascertain whether proclivity to develop a dermatitis upon contact with irritants, which is characteristic of AD patients, depends on functional alterations of clinically normal skin and to clarify if this defective barrier function has a constitutional basis, or if it is mainly due to skin metabolism abnormalities subsequent to subclinical inflammation.

Several authors have described an increased TEWL at non-eczematous sites in patients with AD, both on dry and clinically normal skin (13–18). In order to investigate the relationship between skin surface lipids and TEWL in AD patients, Abe et al. evaluated 22 children aged 3–11, at two skin sites (forearm and antecubital flexure) and recorded increased TEWL values both on involved and uninvolved skin (14).

Our data confirm these observations: in our patient group, overall TEWL values at uninvolved skin sites were significantly higher in respect to those referring to healthy skin of control subjects, both in children with active dermatitis and in those without eczematous lesions at the moment of the investigation, indicating that the clinically normal skin of AD patients is functionally abnormal.

Hydration of the stratum corneum of dry skin in AD patients was found to be significantly lower than that of clinically normal skin (9,10). Berardesca et al. studied the hydration and

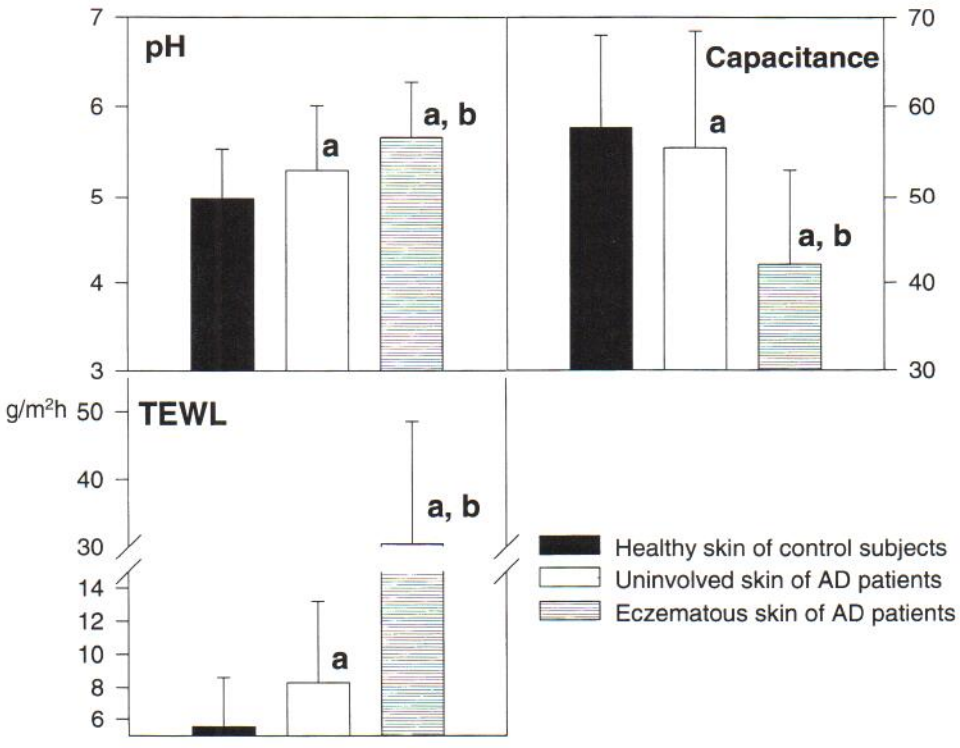

Fig. 1. pH, capacitance and TEWL values (mean ± sd) in children affected by AD (uninvolved and eczematous skin) and in control subjects. Values refer to all assessed skin locations together. *a* = significant in respect to values of healthy skin of control subjects. *b* = significant in respect to uninvolved skin of AD patients.

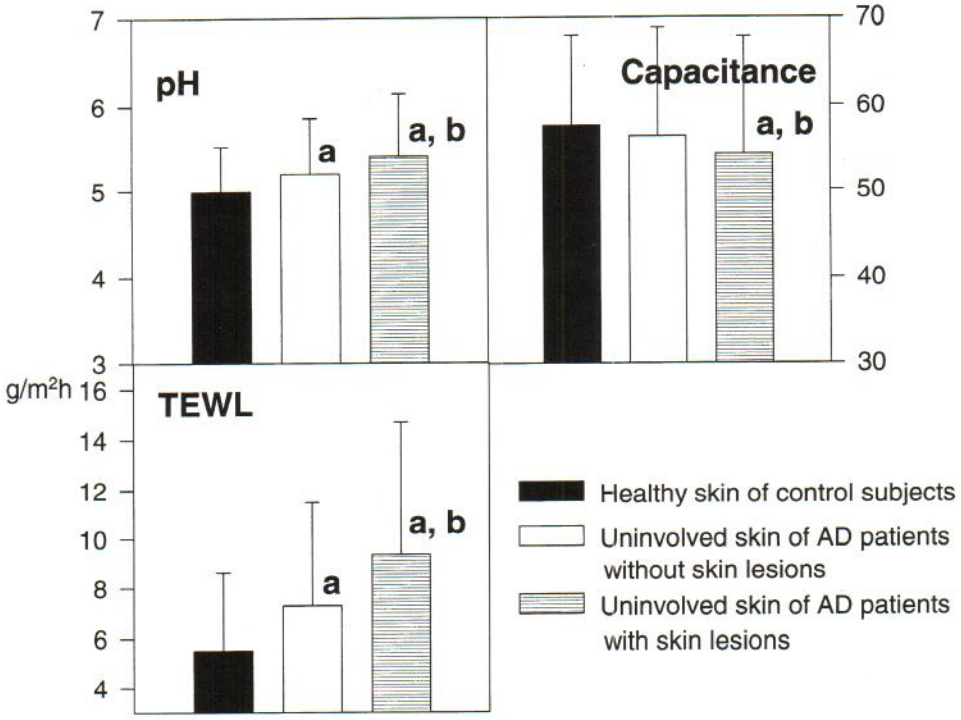

Fig. 2. pH, capacitance and TEWL values (mean ± sd) in children affected by AD and in control subjects. Values referring to uninvolved skin of AD patients are separately considered according to the presence of active dermatitis. *a* = significant in respect to values of healthy skin of control subjects. *b* = significant in respect to uninvolved skin of AD patients without skin lesions.

water retention capacity of the stratum corneum on the volar forearm of 11 subjects with AD and found that uninvolved atopic skin differs from uninvolved psoriatic and control skin by reduced capacitance and increased TEWL values (12).

In our population, differences between single site capacitance values of uninvolved skin of children with AD and those of normal skin of control subjects were not well pronounced. However, when considering values regarding different skin sites all together, one finds capacitance to be significantly lower.

The mechanism underlying the skin's buffering capacity is far from clear. In a recent review of factors predisposing to cutaneous irritation, skin surface pH was found to be correlated with the severity of experimentally induced irritant dermatitis (25). It is also known that many forms of dermatitis cause an increase in pH (26). Children with different skin diseases have been found to have altered pH levels not only at sites of skin lesions, but also on unaffected surfaces (27).

Our data show a shift in pH values towards alkalinity both at eczematous skin sites and on the uninvolved skin of AD patients, significant differences in respect to the skin of control subjects being present at most of the skin sites examined.

However, no correlations, as evaluated by Pearson's correlation test, were observed between pH values and TEWL and capacitance values of uninvolved and involved skin.

A most interesting aspect of our data is based on the observation that, when subdividing values referring to pH, capacitance and TEWL according to the presence of skin lesions, we observed significant differences between the patients with active dermatitis and those with inactive dermatitis. Moreover, whereas the skin of subjects with current disease showed significantly lower capacitance values, uninvolved skin in patients without lesions appeared to have a normal water content, in comparison with the skin of healthy subjects.

These data show that, in AD subjects, skin functions undergo fluctuations according to the phase of the disease and support the hypothesis that the presence of active eczema determines an impairment of the barrier of uninvolved skin, even at sites far from active lesions. Yet, partial alterations of TEWL and pH values were also present at clinically uninvolved skin in 45 children who had been free from eczema for at least 1 month, indicating that the skin is functionally abnormal even prior to or following the active phase of the disease. From this we can deduce that susceptibility to irritants in AD patients can be ascribed both to a primary defect of epidermal differentiation and functions and to the presence of subclinical inflammation induced skin damage, as evidenced by a further impairment of the barrier during the active phase of the disease.

In conclusion, in childhood too, the skin of subjects affected by AD shows modifications, which can be easily assessed using non-invasive techniques. An objective evaluation of skin alterations in AD patients could successfully support standardized clinical assessment based on scoring indexes combining extent, severity and subjective symptoms.

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