

Susceptibility of Atopic Dermatitis Patients to Irritant Dermatitis Caused by Sodium Lauryl Sulphate

TOVE AGNER

Department of Dermatology, Rigshospitalet, Copenhagen

Basal transepidermal water loss, skin thickness, blood flow and skin colour were examined before and after exposure of 28 patients with atopic dermatitis and 28 healthy controls to sodium lauryl sulphate. Transepidermal water loss was measured with an evaporimeter, skin thickness by ultrasound A-scanning, blood flow by laser Doppler flowmetry and skin colour by a chroma meter using the L^* , a^* and b^* values, respectively. Patients with atopic dermatitis were found to have higher basal transepidermal water loss than controls ($p < 0.0001$), and had an inclination towards an increased basal skin thickness ($p = 0.056$). No statistically significant differences were found with respect to basal blood flow or skin colour. The skin response to sodium lauryl sulphate was found to be statistically significantly increased in atopic patients compared with controls when evaluated by visual scoring and by increase in skin thickness, but not by increase in transepidermal water loss, blood flow or skin colour. **Key words:** *Transepidermal water loss; Laser Doppler; Ultrasound; Colour measurement.*

(Accepted November 26, 1990.)

Acta Derm Venereol (Stockh) 1991; 71: 296–300.

T. Agner, Department of Dermatology, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark.

A history of atopic dermatitis (AD) is known to predispose to hand eczema (1), and an increased susceptibility to irritants in patients with AD has been described (2). Moreover, increased transepidermal water loss (TEWL) in patients with AD has been reported (3, 4, 5), although not found in adult subjects with a childhood history of AD but no atopic lesions in adult life (6).

This study was undertaken to examine basic physiological parameters such as TEWL, skin thickness, blood flow, and skin colour, and the skin reactivity to sodium lauryl sulphate (SLS) in patients with AD as compared to controls.

MATERIAL AND METHODS

Twenty-eight patients with atopic dermatitis (AD), 9 males and 19 females, median age 27 years (range 21–44) were included in the study. The patients were recruited from the Department of Dermatology, Rigshospitalet, and the study was carried out in the period December–April 1989/90. Inclusion criteria were age > 18 years, and presence of AD according to the diagnostic criteria of Hanifin & Rajka (7). Patients with involvement of the flexor site of both upper arms were excluded (one arm had to be free of eczema lesions in order to perform the testing on uninvolved skin). Also, patients with other major diseases or patients receiving light therapy were excluded from the study. Treatment of active eczema lesions with topical steroids or tar was accepted, but the actual test site must not have been affected by eczema or have received any kind of treatment within the preceding 3 weeks.

All patients had suffered from AD since childhood, and 22 patients had other atopic manifestation(s) (allergic asthma or allergic rhinitis). The severity of the disease was evaluated by a simple scoring system as suggested by Queille-Roussel et al. (8). The scoring system takes into account *a*) the intensity of the various skin lesions (erythema, edema, vesicles, excoriations, crusts, scaling, lichenification, xerosis, pruritus and loss of sleep) graded on a scale from 0–7 (0 = non lesion, 7 = extremely severe), as well as *b*) the extent of the surface area involved (each of the following areas was scored from 0–3 according to the degree of involvement: face, scalp, buttock, anterior and posterior aspects of the trunk, arms, hands, legs, knees, feet). Thus, the maximum score for *a* and *b* combined was 100. In the present study, median total score number for the included patients was 36 (25/75 percentiles 28–43).

Twenty-eight healthy subjects with no history of AD or other skin diseases, matched according to sex and age, served as controls (median age 27, range 21–45). Exposure in a solarium was not accepted. Controls were examined at the same time of year as patients. Females were not tested prior to or during the menstrual phase (from day 25 until day 5 in the menstrual period) (9).

Informed consent was obtained from all participants, and the study was approved by the local medical ethics committee.

Test procedure

Uninvolved skin on the flexor side of the upper arm was chosen as test region. Closed patch tests with 60 μ l of aqueous solutions of 0.50% SLS (SLS Sigma, 99% purity)

Table I. Median values and 25/75 percentiles for basal values of transepidermal water loss (TEWL), skin thickness, blood flow, and skin colour indicated by $L^*a^*b^*$ -values.

	Basal values		
	Atopic dermatitis	Controls	<i>p</i>
TEWL (g/m ² h)	9.5 (6.6–11.2)	5.3 (4.3–6.1)	<0.0001
Skin thickness (mm)	1.08 (0.92–1.19)	0.96 (0.91–1.04)	n.s.
Blood flow (a.u.)	7 (5–9)	7 (5–8)	n.s.
Skin colour L^*	63.1 (61.6–64.9)	63.9 (62.1–65.3)	n.s.
a^*	6.1 (5.2–7.2)	6.3 (5.7–7.6)	n.s.
b^*	16.0 (13.3–17.0)	15.5 (13.3–16.9)	n.s.

p-values for differences between patients and controls are calculated by Wilcoxon's test for unpaired samples. n.s. indicates *p* > 0.05.

on filter discs were applied using large Finn chambers[®] (diameter 12 mm) on Scanpore[®] tape. Adjacent normal skin served for control purposes. Test chambers were removed after 24 h, and evaluation of the test reactions was commenced 1 h after removal.

The reactions were evaluated by visual scoring according to the following scale: 0, no reaction; ½, slight scaling or very weak erythema; 1, weak erythema, possibly slight infiltration; 2, marked erythema, infiltration, possibly vesicles and crusting; 3, pronounced erythema, infiltration, possibly vesicles, bullae, pustules and/or pronounced crusting. The following non-invasive bioengineering methods were used to measure basic physiological parameters and to quantify the skin response to SLS (measurements performed 1 h after removal of patch tests):

Transepidermal water loss (TEWL) was measured using an Evaporimeter (Servo Med[®] EP1, Stockholm, Sweden). The principle of the apparatus has been described earlier (10). The sensors of the Evaporimeter (pairs of hygrosensors and thermistors), mounted in the open chamber of the probe, determine the water vapour pressure gradient above the skin, in order to quantify the diffusion of water through the skin, i.e. the TEWL. A protective cover (no. 2107, supplied with the Evaporimeter) was used. All measurements were performed inside an incubator to avoid convection of air, according to the guidelines of the Standardization Group of the European Society of Contact Dermatitis (11).

Skin thickness was measured with a 20 MHz A-mode pulsed ultrasound scanner (Dermascan A[®], Cortex Technology, Hadsund, Denmark) (12, 13). By measuring the distance between the acoustic echoes from stratum corneum and from the dermis/subcutis interface, respectively, the thickness of epidermis and dermis combined was determined. To calculate skin thickness, an acoustic velocity of 1580 m/s was used, and the value was expressed in mm.

Superficial blood flow was measured with a laser Doppler flowmeter (Periflux Pf2B[®], Perimed, Stockholm, Sweden). Operating principles for this instrument are described by Tenland (14). The instrument was adjusted to a bandwidth of 20 Hz–12 kHz and a gain at 10. A 2.5 cm (w) × 10 cm (l) × 1.5 cm (h) plastic block with a hole for the probe and Velcro straps for fastening around the arm was used to

keep the probe stable during measurements without the use of adhesive tape.

Skin colour was measured with a Minolta Chroma Meter CR-200 (Osaka, Japan). The method is based on illumination of the skin by Xenon flash light. A protective shield was interpreted between the probe and the skin. The skin surface colour is quantified using the CIE (Commission Internationale de l'Éclairage) system (15). The colour is expressed in a three-dimensional coordinate system L^* expresses the brightness (integrated reflection of light from the surface) ranging from total black (low values) to pure white (high values). The a^* and b^* are the two colour coordinates: a^* represents the colour range from green (–) to red (+) and b^* represents the colour range from blue (–) to yellow (+). The true colour of the skin is an admixture of L^* , a^* and b^* (16, 17).

All visual scorings and instrumental recordings were performed by the author. The measurements were carried out in the following order: skin colour, blood flow, TEWL, and skin thickness. Since ultrasound examination involves wetting of the skin, which might influence the other measurements, this examination was undertaken last. Disturbances in the laboratory during measurements were kept at a minimum. The relative humidity varied between 30 and 45%, and the room temperature was kept at 20–22°C. The skin temperature during measurements was in all instances within the range 29–31°C, measured on skin in the test region. Skin temperature measurements were performed using a skin thermometer with a hand-held thermocouple probe, Comarck 2001[®] (Comarck Electronics, Rustington, Sussex, England). Measurements were expressed as the mean value of two recordings (evaporimetry and colorimetry) or three recordings (laser Doppler flowmetry and ultrasound). Variations in quantification of irritant patch test reactions by non-invasive measuring methods and comparison between methods have been presented elsewhere (18, 19).

Statistics

Wilcoxon's test for unpaired samples was used for comparison between groups. Spearman's test was used for correlation studies. The chosen level of significance was *p* < 0.05.

Table II. Median values and 25/75 percentiles for transepidermal water loss (TEWL), skin thickness, blood flow and redness of the skin (a^*) after exposure to SLS.

Visual scoring	Values after exposure to SLS		$p < 0.05$
	Atopic dermatitis 1 (1-2)	Controls 1/2 (1/2-1)	
TEWL (g/m ² h)	18.7 (16.0-25.1)	14.0 (12.3-17.9)	<0.005
Δ TEWL	10.7 (6.6-14.5)	9.0 (7.1-11.6)	n.s.
Skin thickness (mm)	1.42 (1.29-1.56)	1.17 (1.10-1.33)	<0.001
Δ Skin thickness	0.36 (0.25-0.47)	0.20 (0.16-0.28)	<0.005
Blood flow (a.u.)	21 (15-42)	14 (10-34)	n.s.
Δ Blood flow	12 (7-31)	8 (4-28)	n.s.
Skin redness (a^*)	9.29 (7.55-10.99)	8.98 (7.72-11.46)	n.s.
Δ Skin redness	3.10 (1.47-4.73)	2.77 (1.56-4.33)	n.s.

Δ -values indicate the difference before and after exposure to SLS. p -values for differences between patients and controls are calculated by Wilcoxon's test for unpaired samples. n.s. indicates $p > 0.05$.

RESULTS

Median values for basal TEWL, skin thickness, blood flow and skin colour (L^* , a^* and b^* values) are given in Table I. Basal TEWL was found significantly higher for AD patients than for controls ($p < 0.0001$). No statistically significant difference between the groups was found according to skin thickness, blood flow or skin colour.

Values after exposure to SLS are given in Table II. An increased reactivity to SLS in AD vis-à-vis controls was found as measured by visual scoring ($p < 0.05$) and by increase in skin thickness ($p < 0.005$). The same trend was found for blood flow and a^* , although not statistically significant. No statistically significant difference in L^* or b^* -values after exposure to SLS was found between the groups (data not shown). TEWL after exposure to SLS was found significantly elevated in AD patients vis-à-vis controls ($p < 0.005$). However, the increase in TEWL (Δ TEWL) did not differ significantly between the two groups (Table II).

A significant positive correlation between basal TEWL and TEWL after exposure to SLS was found for AD patients ($R = 0.72$, $p < 0.001$) and for controls ($R = 0.79$, $p < 0.0001$) (Fig. 1). The correlation coefficient between basal TEWL and Δ TEWL was 0.24 and 0.65 for AD patients and controls, respectively. No correlation was found between severity score and skin reactivity as measured by visual scoring or any of the non-invasive methods ($p > 0.05$).

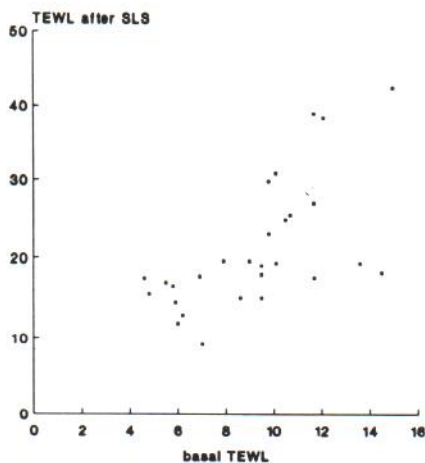
DISCUSSION

Examination of uninvolved, clinically normal skin in patients with AD of moderate severity showed increased TEWL as compared with matched controls. The increase in basal TEWL in AD patients is described elsewhere (3, 4, 5), and is confirmed in the present study. In an earlier study (6) basal TEWL measured on the upper arm in hand eczema patients with a childhood history of AD, but without other atopic manifestations in adult life than hand eczema, was found normal. Thus, although increased basal TEWL is doubtless associated with AD, TEWL values may undergo changes related to the course of the disease.

Though not statistically significant, there was a tendency for increased basal thickness of the skin in atopics vis-à-vis controls ($p = 0.056$). This may reflect a gradual thickening of the skin due to numbers of episodes of (sub)clinical inflammation of the skin. However, no histopathological studies were carried out to confirm this assumption. The ultrasound method is a very precise method for determination of full skin thickness, but does not allow differentiation between epidermis and dermis, and conclusions about the thickness of the stratum corneum/epidermis/dermis alone can thus not be drawn.

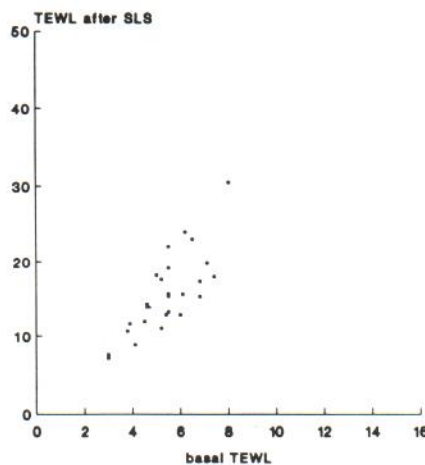
A fair skin complexion as a predictor of skin susceptibility has been reported earlier (20, 21) but was not found here to be associated with AD (Table I). Skin complexion as determined by the L^* -value of the chroma meter depicts the content of melanin in the skin, but is also influenced by the haemoglobin

Atopics TEWL



Spearman correlation analysis, $R = 0.72$

Controls TEWL



Spearman correlation analysis, $R = 0.79$

Fig. 1. Correlation between basal TEWL and TEWL after exposure to SLS for patients with atopic dermatitis and for controls. The Spearman coefficients of correlation were $R = 0.72$ ($p < 0.001$) and $R = 0.79$ ($p < 0.0001$), respectively.

content. Moreover, structural conditions such as scaling and position of collagen fibres in the dermis may to a major degree influence the reflection and scattering of the Xenon flash light and thus influence the L^* , a^* and b^* values (22).

The enhanced reactivity of the skin in atopics as confirmed statistically by visual scoring and by in-

crease in skin thickness (Table II) is in agreement with earlier reports (2). The lack of statistical evidence for elevated blood flow values or augmented skin redness is probably due to these methods being less sensitive (19). Although total TEWL values after SLS exposure were found higher in patients with AD than in controls, no significant difference in the increase of TEWL due to SLS exposure (Δ TEWL) was found between the groups (Table II).

This observation is supported by the poor correlation between basal TEWL and Δ TEWL in patients with AD ($R = 0.24$). Thus, although a positive correlation was found between basal TEWL and SLS-TEWL in atopics, basal TEWL did not to a major degree influence or reflect the magnitude of the skin response to SLS, as measured by Δ TEWL. This is in contrast to the present findings in controls, where a clear association between skin barrier function and response to SLS was found. Thus, due to the basically impaired barrier function in the atopic patients, the magnitude of the skin response to SLS may to a greater degree depend upon the current inflammatory reactivity of the skin, and cannot be predicted from basal TEWL values. However, it can be concluded that the function of the barrier in patients with AD is significantly inferior to the barrier in controls, before as well as after exposure to SLS.

REFERENCES

1. Meding B, Swanbeck G. Epidemiology of different types of hand eczema in an industrial city. *Acta Derm Venereol (Stockh)* 1989; 69: 227-233.
2. Frosch P. Current topics of contact dermatitis. Berlin: Springer Verlag, 1989; 385-398.
3. Werner Y, Lindberg M. Transepidermal water loss in dry and clinically normal skin in patients with atopic dermatitis. *Acta Derm Venereol (Stockh)* 1985; 65: 102-105.
4. Van der Valk PGM, Nater JP, Bleumink E. Vulnerability of the skin to surfactants in different groups of eczema patients and controls as measured by water vapour loss. *Clin Exp Dermatol* 1985; 10: 98-103.
5. Tupker RA, Pinnagoda J, Coenraads PJ, Nater JP. Susceptibility to irritants: role of barrier function, skin dryness and history of atopic dermatitis. *Br J Dermatol* 1990; 123: 119-205.
6. Agner T. Basic physiological characteristics and susceptibility to sodium lauryl sulphate in patients with hand eczema and controls. *Br J Derm*, in press.
7. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Acta Derm Venereol (Stockh)* 1980; Suppl 92: 44-47.
8. Queille-Roussel C, Raynaud F, Saurat JH. A prospective computerized study of 500 cases of atopic dermatitis.

- itis in childhood. *Acta Derm Venereol* (Stockh) 1985; suppl 114: 87-92.
9. Agner T, Damm P, Skouby SO. Menstrual cycle and sensitive skin. *J Am Acad Dermatol*, in press.
 10. Nilsson GE. On the measurement of evaporative water loss. Linköping University Medical Dissertations, No. 48, 1977.
 11. Pinnagoda J, Tupker RA, Agner T, Serup J. Guidelines for transepidermal water loss (TEWL) measurement. *Contact Dermatitis* 1990; 22: 164-178.
 12. Serup J. Localized scleroderma (Morphoea). Thickness of the sclerotic plaques as measured by 15 MHz pulsed ultrasound. *Acta Derm Venereol* (Stockh) 1984; 64: 214-219.
 13. Serup, J. Ten years' experience with high frequency ultrasound examination of the skin: Development and refinement of technique and equipments. Altmeyer P, ed. Bochum: Karger [in press 1990].
 14. Tenland T. On laser Doppler flowmetry. Methods and microvascular applications. Linköping Medical Dissertations, No. 136. 1982.
 15. Robertson AR. The CIE 1976 color difference formula. *Color Research and Application* 1977; 2: 7-11.
 16. Queille-Roussel C, Poncet M, Schaefer H. Quantification of skin colour changes induced by topical steroids on normal skin using the Minolta chroma meter. Abstract presented at the 8th International Symposium on Bioengineering and the Skin, Stresa, 13-16 June, 1990.
 17. Serup J, Agner T. Colorimetric quantification of erythema. *Clin Exp Dermatol* 1990; 15: 267-272.
 18. Agner T, Serup J. Individual and instrumental variation in patch test reactions. *Clin Exp Dermatol* 1990; 15: 29-33.
 19. Agner T, Serup J. Sodium lauryl sulphate for irritant patch testing: A dose response study using bioengineering methods. *J Invest Dermatol* 1990, 95: 543-547.
 20. Frosch PJ, Wissing C. Cutaneous sensitivity to ultraviolet light and chemical irritants. *Arch Dermatol Res* 1982; 272: 269-278.
 21. Agner T. Basal transepidermal water loss, skin thickness, skin blood flow and skin colour in relation to sodium-lauryl-sulphate-induced irritation in normal skin. *Contact Dermatitis*, in press.
 22. Rox Anderson R, Parrish JA. The optics of human skin. *J Invest Dermatol* 1981; 77: 13-19.