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Abnormalities of Cutaneous Microcirculation in Atopic Eczematics

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There are signs of abnormal microcirculation in atopics, yet reliable methods for its non-invasive measurement are scarce so far. Since the phenomenon of dermographism (D) elicited by blunt stroking of the skin reflects the functional response of cutaneous vessels to pressure, we studied the haemodynamics of D using laser-Doppler microfluxometry (LDF) and infrared thermography (IR-TH) in patients with atopic eczema (n=23) and in healthy controls (n=21) under standardized investigative conditions. Only in-patients not treated with corticoids were selected. LDF values showed a marked reduction in the intensity of hyperaemia in the patients as compared with the controls, according to the visual degree of the dermographic blanching effect (white, delayed white, indifferent; pink). A reduction of the radiating skin temperature vis-à-vis the controls was measured by IR-TH. These results yield evidence that dermographic pallor of atopic skin depends on the strength of local vasoconstriction, possibly including altered blood flow in cutaneous shunt vessels. ***Key words: Pale dermographism; Laser-Doppler fluxometry; Thermography.***

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There are several signs of disturbed cutaneous microcirculation in atopic skin, viz. some susceptibility to acrocyanosis, lowered skin surface temperature, disturbances of cutaneous thermoregulation, paradoxical blanching phenomenon with i.c. acetylcholine injection, and in particular the eliciting of white dermographism (1–4). However, some patients with atopic eczema (AE) also show pink or delayed white dermographism (D). In any case, some kind of pallor is typical of atopic skin and can be accentuated by linear stretching with a spatula or other suitable tool.

The local microcirculatory dynamics underlying the phenomenon of pale or white D have not yet been sufficiently elucidated. Various hypotheses, e.g. exaggerated vasal constriction (5–7) and/or pericapillary edema (8, 9) have been proposed, yet the diversity of methods used to investigate the vascular mechanism operating in D has hampered a convincing explanation of the phenomenon.

In order to quantify the stretching pressure of D reproducibly, we constructed an easily usable device named 'Dermographometer' (Fig. 1). Details of this tool and its use for studying the patterns of D have been published elsewhere (3, 10). By applying the apparatus it became feasible to study several parameters of cutaneous microvascular reactivity to defined skin stretching pressure using laser-Doppler microfluxometry (LDF) as well as infrared thermography (IR-TH).

SUBJECTS AND METHODS APPLIED

The study included 23 in-patients (14 females, 9 males, age range 13 to 42 yr, mean 21.9 yr) suffering from AE according to the diagnostic criteria as stated by Hanifin & Rajka (11). All the patients reported both personal and family history of atopy, all showed increased concentrations of IgE in serum (>150 U/ml) as well as 'delayed blanch' skin reaction to i.c. acetylcholine and epicutaneous application of nicotinic acid ointment. Corticoid treatment, either systemic or topical, was withdrawn at least one month before entering the study. None of the patients was allowed to take antihistamines or other drugs influencing neurovegetative reactivity within 2 days of the study, nor were they allowed to smoke within at least 3 h before. All measurements were made under the same conditions, including day time, room setting, constancy of room temperature (22°C ± 1°), and keeping the subjects at rest for 20 min in order to become adapted to the examination. Two days before, the lumbar test areas were spared from any topical treatment other than mild emollients. Only areas exhibiting dry scaly or lichenified skin were chosen for examination.

Twenty-one non-atopic healthy volunteers (10 females, 11 males, age range 22 to 29 yr, mean 24.2 yr) examined under the same conditions served as controls.

For statistical evaluation, Student's t-test was applied. Limit of error probability was set at $\alpha < 0.1$. Except the 3 min value of IR-TH ($\alpha < 1.5\%$) all the calculated figures ranged far below the error probability of 0.1%.

Laser-Doppler Microfluxometry (LDF)

Measurements were done with a commercially available laser-Doppler fluxmeter (Periflux, Perimed Inc., Sweden). After 20 min of adaptation time, LDF was performed and recorded continuously for 25 min over the right lumbar area of the prone subject. The values of predermographic blood fluxes were determined by vol.% for 5 min as an arbitrary gauge. D was then elicited by conducting slowly (4 cm/s) the dermographometer by hand over the test area (right lumbar site), and the changes in local microcirculation were measured continuously by LDF and drawn simultaneously on automatically recording paper. The fitted mid-pounder of the Dermographometer (Fig. 1) yields a constant pressure of 285 g (121 g/mm^2, contact area of the pounder tip = 2.35 mm^2) to the skin surface.

Infrared Thermography (IR-TH)

The left lumbar test area was marked by 6 aluminum pin cones to obtain three definite linear distances:
l = midline of the area (stretched for *D*)

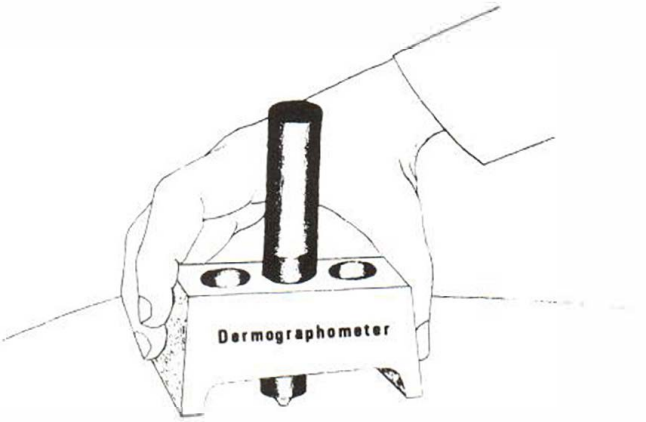

Fig. 1. Handling of the Dermographometer carrying one pounder conducted over the back skin.

Table I. *Ranges and mean data of Laser-doppler-fluxometry in atopics (I) and controls (II)*[a]

	30 sec	1 min	2 min	3 min	5 min	10 min	15 min
I.							
min	0.68	0.77	0.78	0.79	0.81	0.90	0.96
max	8.80	9.64	9.00	8.15	7.95	6.75	6.50
$\bar{x}$	3.58	3.39	3.21	2.83	2.49	2.12	1.93
s	2.34	2.24	2.32	2.21	2.00	1.28	1.21
II.							
min	5.00	6.35	5.30	4.89	4.30	4.11	3.39
max	16.00	17.80	17.20	16.40	18.80	12.00	10.13
$\bar{x}$	9.88	10.55	10.68	10.29	9.69	7.30	6.21
s	3.34	3.56	3.53	3.39	3.43	1.81	1.74

[a] Data represent increase factors (IF) related to mean pre-dermographic values (set at 0.00). Differences between mean values of atopic and non-atopic subjects are significant ($\alpha<0.01$).

C_1 and C_2 = imaginary control lines (unstretched) for the purpose of temperature comparison.

In order to determine selectively the dermographically induced changes in local warmth radiation, the changes in temperature were registered at defined time sequences. All the values obtained were considered using the formula

$$I - \frac{C_1 + C_2}{2} = \text{relative rise in temperature}$$

By calculating the different values, the elicited changes in warmth radiation in the dermographed area could be determined.

After LDF measurement, an IR camera (Philips Digital Thermography System 14–110500) was positioned over the test area, keeping the camera detector 15–20 cm distant from this region. Colour-visualized differences in warmth radiation before and after eliciting *D* were recorded by means of computer-assisted discrimination of temperature (Δt 0.1°C) and the thermic data were electronically stored. Distance of the visualized thermographic spectrum of the test area from black level (i.e. level just below the visualized lowest temperature) was chosen at 0.9 – 1.2°C.

After monitoring the pre-test colour pattern of the test area, *D* was evoked with a spatula stretched over line *I*, and changes in the pattern along this line were recorded every one minute, for 20 min. The monitored patterns of the lines *I*, C_1 and C_2 were documented by polaroid photography at 3, 5, 10 and 20 min in order to enable comparison of the test lines at definite times. The integral values of warmth radiation on and around each test line (about 1 × 10 cm) were calculated by computer-aid and increases displayed by a connected printer as differences vis-à-vis the pre-test data.

It should be noted that for IR-TH a spatula was used, since an application of the dermographometer could influence the thermographed data due to stretching the control lines C_1 or C_2 by the skids of the device itself.

RESULTS

The visual aspects of *D* during the time examined are delineated in Table I. In none of the patients was a bright red appearance of *D* observed, in contrast to the controls. Moreover, the latency times were markedly longer in the atopics (30 s to 7 min) than in the controls (6 – 15 s), and inversely the duration of visible *D* took about half the time as recorded for the controls.

Laser-Doppler Fluxmeter

Dermographically induced alteration of microcirculation resulted, in relation to the individual pre-test curve, in virtually recorded increase factors (IF) of the continuously measured blood flux. Single and mean values of IF were calculated for both the atopics and controls at different times. The data listed in Table I represent the ranges and mean IF of blood fluxes at the defined time points of calculation. There were significant differences ($\alpha < 0.01$) between the mean data of either group of subjects.

The initial mean IF in the group of patients increased by 3.6 after 30 s and then declined slightly from a plateau-phase down to 1.9. In contrast, the controls revealed a steep initial increase in microcirculation, reaching mean IF values of 9.9, 10.55 and 10.7, resp., at the first three test occasions, followed by a moderate decline down to 6.2 (at min 15). As shown in Fig. 2, the mean IF values of both groups differed during the initial 2 min about 3-fold; at min 3 just 4-fold; and even at min 15, still 3–3.5-fold.

Considering the mean LDF curves for the different subgroups of *D* (white, indifferent, pink to delayed white, pink) in the atopics, we found remarkable differences between their respective values (Fig. 3). Patients with either white or indifferent (invisible) *D* showed the slightest increases of blood flux, whereas in those with either delayed white or pink *D*, the mean IF values were intermediate to those of the controls and the two lowermost subgroups. There were some parallels in the slopes of red and pink *D* as well as of different and delayed white *D*.

Infrared Thermography

Changes in local warmth radiation elicited by *D* were selectively registered for the three defined lines. The mean pre-dermographed warmth emission of the test area ranged in the atopics between 29.1 and 34.5°C, and in the healthy controls between 30.1 and 34.5°C. Immediately after the eliciting *D*, some of the subjects (10 non-atopics, 15 atopics) revealed a

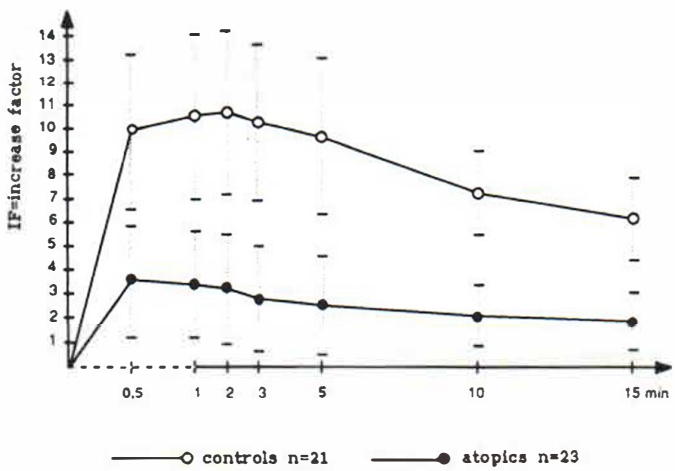

Fig. 2. Laser-Doppler Microfluxometry. Comparison of the curves (mean values) af the dermographically induced hyperaemia in atopic patients and non-atopic controls. Vertical range bars = standard deviations. IF = increase factor (relative to the pre-dermographic microcirculatory blood flux).

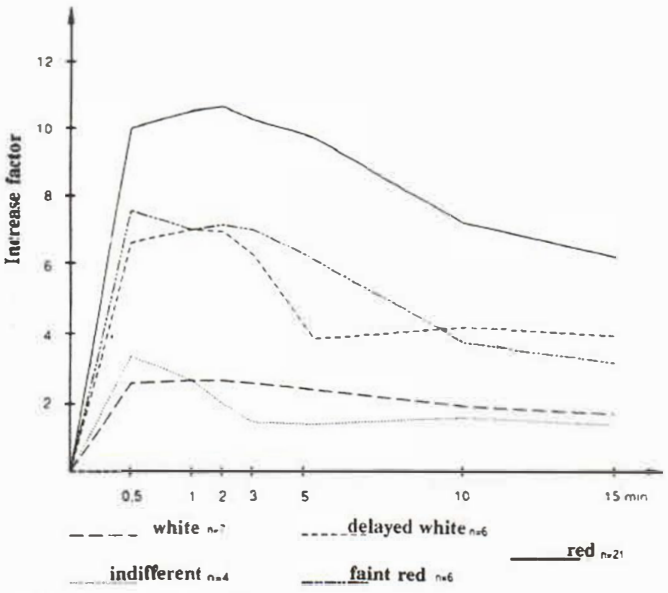

Fig. 3. Laser-Doppler Microfluxometry. Follow-up of the mean values of increase factor (IF) in red *D* (non-atopic controls) and in different subtypes of *D* in atopics.

brief drop in temperature (0.03 to 0.15°C after 1 min). However, in all the subjects some rise in temperature was found after 3 min, which approximately persisted in the atopics, yet increased slightly in the controls throughout the period of measurements. The mean values of elevated temperature in both the atopics and the controls are given in Table II.

It can also be seen from Fig. 4 that the mean rises of temperature in the controls exceeded those in the atopics about twofold after 3 min and 3.5-fold after 20 min.

DISCUSSION

Definite conclusions can be drawn from the data obtained by both laser-Doppler fluxometry and infrared thermography that atopics with dry scaly or lichenified skin do react to dermographic pressure, but evidenced only by weak hyperaemia in the cutaneous blood vessels, in contrast to significantly stronger hyperaemia in the non-atopic healthy controls who usually display a bright red *D*. All the values measured tally well with the concept of an active 'vasoconstrictory' mechanism impeding the dermographically induced vasodilation in the peripheral vessels. This view is also in agreement with the experience of vasoconstriction in acetylcholine-induced skin blanching (4, 8, 12, 13). An increased propensity to vasoconstriction, depending basically on an intrinsic 'weakness' of vascular β_2-adrenoceptors, in line with Szentivanyi's theory of β-receptor anomaly (14), may be counterbalanced by concomitant expression of α-adrenoceptors in the (pre-)terminal blood vessels.

Although our results, in particular the striking correlation between different subtypes of dermographic pallor and the extent of inhibition of IDF-monitored hyperaemia, clearly indicate the significance of mild to moderate vasoconstriction in the pathodynamics of pale *D*, such a 'throttling' of hyperaemia may operate in different segments of the cutaneous microvasculature, i.e., at precapillary sphincter cuffs and anastomosing shunt vessels. Argon laser pulses (622 nm wavelength) emitted from the piezo-electric crystal probe of the LDF device penetrate the skin down to 1–1.2 mm depth, and Doppler-sonic reflections can be obtained from blood cell fluxes in all the vessels localized within the sonographed tissue sector (15, 16). It is the complex interplay of different segments of dermal microvasculature due to the release and synergistic action of different neurotransmitters and cell-mediated substances with corresponding cell receptors, that adapts the local blood supply to the metabolic requirements of the tissue (17).

Table II. *Ranges and mean data of infrared-thermography*[a]

	3 min	10 min	20 min
Atopic subjects			
min	−0.075	−0.210	−0.295
max	0.490	0.420	0.415
$\bar{x}$	0.123	0.082	0.097
s	0.138	0.166	0.166
Control subjects			
min	0.135	0.160	0.015
max	0.530	0.805	0.690
$\bar{x}$	0.269	0.187	0.346
s	0.104	0.187	0.177

[a] Increases in warmth radiation (in °C). Except for the mean values at min 3, those at 10 and 20 min differed significantly ($\alpha<0.01$).

It can hardly be decided whether the different grades of determined suppression of dermographically induced hyperaemia are caused mainly by constriction of percapillary sphincter cuffs, or also by simultaneous changes in blood shift through adjacent shunt vessels. It should also be noted that IR-TH comprises infrared waves radiating from both the superficial and deep layers of dermis and subcutis. Thus, the results of LDF and IT-TH are only comparable to a limited extent, due to distinct parameters of measurement as well as to different skin compartments whence the signals to be recorded are emitted. Nevertheless, each method yields valuable data which can be interpreted as indicators of vascular mechanisms regulating the local blood circulation. In the present study, the coinciding results of laser-Doppler fluxometric and thermo-

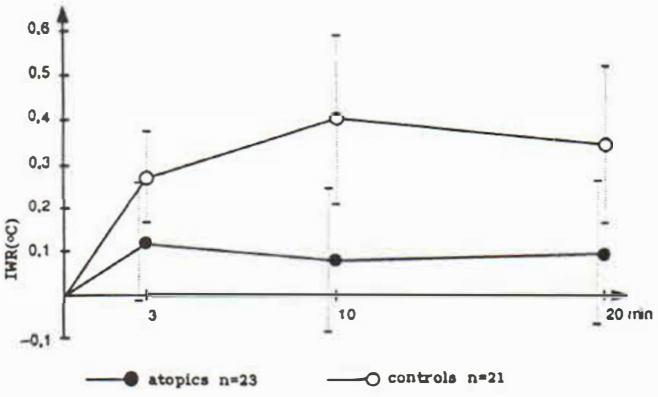

Fig. 4. Comparison between atopics and controls of infrared-thermographically determined warmth radiation. IWR = increase of warmth radiation (°C).

graphic measurements provide convincing evidence of enforced vasoconstrictory activity leading to the pale appearance of *D* in atopic skin.

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