Increased Subcutaneous Adipose Tissue Blood Flow in UVB-inflamed Human Skin

The Existence of a Cutaneous–subcutaneous Reflex Mechanism?

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In 4 healthy subjects a skin area 10 mm in diameter was exposed to twice the minimal erythema dose of UVB. Subcutaneous blood flow (SBF) in the area was measured by the local 133-Xenon washout technique before and 8, 24, 48 and 72 h after induction of inflammation. Local skin temperature (TS) was monitored with electrical thermocouples. SBF gradually increased by 400% and peaked 24 to 48 h after induction of inflammation, while TS peaked after 8 h (+3°C). The disparity in skin temperature and subcutaneous blood flow indicates that TS is not the governing factor in the increase in SBF. As release of

inflammatory mediators from the cutis influencing the subcutis and a local effect of UVB on subcutis are unlikely, we suggest the existence of a cutaneous–subcutaneous vascular reflex mechanism as an explanation for the increased subcutaneous blood flow.
Key words: Skin temperature; 133-Xenon washout.

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Shortly after induction of inflammation in human skin, the skin becomes reddened. This flare, which is a part of the inflammatory response, represents neurogenic vasodilation and is most probably mediated through the release of vasoactive neuropeptides (1, 2). This vascular phenomenon has been extensively investigated during recent decades. The role of C-fibre activation on neurogenic inflammation was recently reviewed by Lynn (3).

The presence of cutaneous–visceral reflexes, i.e. the existence of neurogenic pathways from which impulses arising in the skin produce reflex alterations in blood flow in deeper organs has been described previously (4). The present demonstration of an increased subcutaneous blood flow in UVB-inflamed human skin would suggest the existence of a cutaneous–subcutaneous vascular reflex.

MATERIALS AND METHODS

Subjects

Four healthy Caucasian subjects, age range 21–28 years, participated in the study. None was taking medication. No abnormal sensitivity to sunlight was known. Informed consent according to the Helsinki II declaration was obtained in each case.

UV-B inflammation

A bank of two Philips TL 20W/12 tubes was used as ultraviolet source. Adjacent circular sites (10 mm) on the volar aspect of the right forearm were exposed to increasing doses of UVB light. Doses varied between 0.05 and 4.0 J/cm^2, $\sqrt{2}$ increments were used. The energy composition of the tubes was UVB 2.1 W, UVC 35 mW. Energy at skin level was measured with a UVX Digital Radiometer with the UVX-31 sensor (Ultra-violet Products, Inc, California, USA). Minimal erythema dose (MED) was defined as the minimal dose of the total tube output needed to produce a distinct erythema with sharp margins 24 h after irradiation. Median MED was 0.14 J/cm^2 (0.10–0.40).

Measurement of SBF

Subcutaneous blood flow rate was measured by the local 133-Xenon washout technique (5–7). A chamber (10 mm) formed by doublesided adhesive tape and a Mylar membrane was attached to the skin. By means of a gas-tight syringe and a fine needle, approximately 0.1 ml of 133-Xenon in saline was injected into the chamber. Diffusion was allowed to take place for 3 min. Hereafter the saline was drawn back into the syringe, the chamber was removed and surplus of liquid gently dabbed away with cotton pads. The radiation was detected by a scintillation detector placed 20 cm above the labelled area. The recorded activity was fed into a gammaspectrometer printer adjusted to the 81 KeV photopeak of 133-Xenon. Activity was measured every 20 s. Some 10–30 min after labelling, 133-Xenon had been washed out of the skin and was deposited in the subcutaneous adipose tissue only. The washout then described a monoexponential curve (7). The washout rate constant, k, was computed by the least squares method after logarithmic transformation and correction for background activity. SBF was calculated by the formula:

$$SBF = k \times \lambda \times 100 \text{ (ml/100 g tissue/min)} \quad (1)$$

Where λ is the tissue-to-blood partition coefficient. A λ value of 7.0 was used (7).

Skin temperature measurements

The skin temperature was monitored with electrical thermocouples (Elektrocompaniet, Copenhagen). The median value of a five-measurement series was used in the following.

Experimental procedure

The subjects were placed in the supine position, the forearm was held at heart level and immobilized. SBF was then measured on the left arm. The temperature was measured in the labelled area. Hereafter the area was exposed to 2 × MED. SBF and skin temperature were measured again

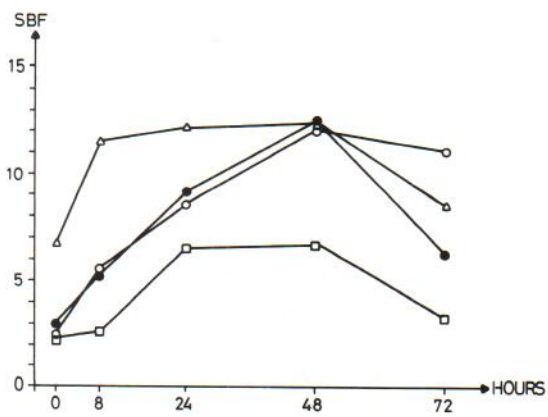

Fig. 1. A graphic presentation of the subcutaneous blood flow rates (SBF, ml/100 g tissue/min), before induction of inflammation (time 0) and up to 72 h after inflammation.

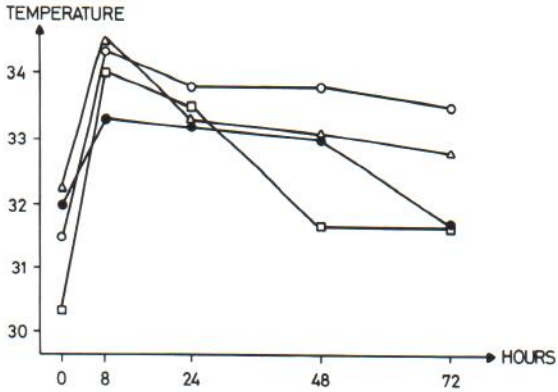

Fig. 2. The time course of the skin temperature measurements (°C).

8, 24, 48 and 72 h after irradiation. The labelling chamber (10 mm) was placed exactly in the middle of the irradiated skin area (30 mm).

RESULTS

The SBF values are presented graphically in Fig. 1. Median SBF in normal skin was 2.77 (ml/100 g tissue/min; range 2.52–6.68). It can be seen that SBF gradually increased from induction of inflammation 24–48 h, after which a decline was noticed.

Temperature recordings are shown in Fig. 2. Cutaneous temperature in normal skin was 31.8°C (range 30.3–32.2). During the first 8 h a rapid increase was seen, after which the temperature gradually decreased.

DISCUSSION

The main finding in the present study was increased SBF in UVB-inflamed human skin. The reason for this is not known, but according to the following discussion, the existence of a cutaneous–subcutaneous reflex mechanism is conceivable.

The washout of 133-Xenon is a well established technique for the measurement of subcutaneous tissue blood flow and several dissertations have used this method (8, 9, 10). The prerequisites of the tracer washout technique are 1) no recirculation, 2) equilibrium between tissue and blood, and 3) homogeneously perfused tissue. In a wide variety of situations, the above-mentioned assumptions are fulfilled. The specificity of the method is reliable as the washout of 133-Xenon from adipose tissue after atraumatic labelling corresponds to venous outflow (6). The coefficient of variation is approximately 10% (10). According to eq. 1, SBF is calculated on the basis of the washout rate constant k, and the tissue-to-blood partition coefficient λ. If the water content in the adipose tissue increases, as seen during the formation of edema, λ decreases by approximately the same magnitude as that by which the water content has increased (10). An evident clinical edema means a 10–20% increase in water content. As edema was not noticed at all, correction for this seems of no importance. Changes in temperature and haematocrit affect λ, but only to a minor degree. Increased temperature and decreased venous haematocrit as seen at high blood flow rates, however, both tend to increase λ, thereby underestimating SBF. Consequently, the observed SBF seems not to be an artefact.

Penetration of optical radiation in skin of white subjects in the range 290–320 nm (UVB) is described by Anderson & Parrish (11). As the approximate penetration depth of light at 280 nm is 1.5 μm and the corresponding 300–350 nm light values 6–60 μm, a direct UVB-induced increase in SBF is not possible. The average thickness of epidermis and dermis is approximately 1 mm. The mean skin thickness on the flexor aspect of the forearm is 0.8 mm, range 0.5–1.1 mm (12).

The possibility that vasoactive metabolites liberated in dermis increase SBF is less reasonable, seen in the light of the vascular arrangement. The blood supply to the subcutaneous adipose tissue originates chiefly from the deep subcutaneous plexus and from ascending arteries throughout the subcutaneous tissue. The upper part of the adipose tissue receives its blood supply from arterial branches of the subdermal plexus. It is therefore generally accepted that subcutaneous tissue receives its blood supply independently of the cutaneous supply. Increased venous return through subcutis from the cutis will not influence the SBF, as adipose blood flow is regulated by arteriolar tone. As recirculation does not take place, either systemically or locally, increased SBF cannot be elicited by vasoactive substances liberated in the dermis.

Increased SBF due to cutaneous–subcutaneous diffusion of vasoactive substances is a theoretical possibility. This subject was described by van der Leun (13). On the other hand a subcutaneous reaction to such diffusion processes seems less plausible as the diffusion distance is approximately 1 mm. Owing to substantial dilution during diffusion, the compounds might become biologically ineffective. Exudates from suction blisters following UVB irra-

diation have been shown to be without pharmacological effects (14). As diluted substances diffusing very short distances are ineffective, a diffusion distance of 0.5–1.1 mm would completely eliminate the biological activity of the substances.

Correlation between skin temperature and SBF has previously been demonstrated (15). when skin temperature was raised from 29° to 37°C, SBF increased by 80%. The results from the present study, however, demonstrated a much greater increase in SBF despite skin temperature being raised by only 2–3°C. The time course of the skin temperature and SBF in the inflamed skin also differs. Temperature peaked 8 h after irradiation and tended to normalize slowly during the time of observation. The trend of SBF was a sharp increase within the first 24 to 48 h, after which SBF was decreased. Consequently, the increased skin temperature does not explain at all well the SBF changes during inflammation.

One might have expected a faster process as a result of a neurogenic inflammation. However, the time course of the blood flow increase corresponds to similar findings in skin (16).

On the basis of our knowledge of UVB photobiology, the cutaneous–subcutaneous vascular arrangement and the influence of skin temperature on SBF, we suggest the existence of a cutaneous–subcutaneous vascular reflex, triggered by UV-induced inflammation.

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