ing the SSWL decay for a shorter period and calculating the endpoint as the SSWL value at a given time point, e.g. 60 min.

However, there remains the influence of sweating on vulvar SSWL measurements. The only way to eliminate the sweating factor would be to suppress sweat gland activity with anticholinergic agents locally or systemically. Since this is not practical in irritation studies, a higher variance of SSWL measurements must be anticipated in contrast to the forearm. In order not to overlook existing differences between treatments (type II error), the number of subjects may have to be higher in irritation studies on vulvar skin compared to forearm studies.

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Cutaneous Blood Flow Rates during Orthostatic Manoeuvres Measured by Laser Doppler Flowmetry

LARS JELSTRUP PETERSEN and JENS HEIN SINDRUP

Department of Dermatology, Bispebjerg Hospital, University of Copenhagen, Denmark

The validity of Laser Doppler Flowmetry for measurements of changes in skin blood flow rates during orthostatic manoeuvres was evaluated. Fifteen healthy subjects were investigated. Relative skin blood flow rates on the dorsum of the hand were measured during stepwise raising and lowering of the arm in 10 cm increments to an extreme position of 40 cm below respectively above heart level. All measurements at test levels were preceded and followed by measurements at reference level, i.e. heart level. At all levels of arm elevation, relative blood flow rates were significantly increased compared with the corresponding reference level (p=0.0005). This was unexpected in view of the autoregulatory mechanism. Highly significant blood flow rate reductions were found at all levels of arm lowering. This is in contrast to previous findings of unchanged skin blood flow rate to a point of approximately 35 cm below heart level, where the veno-arteriolar reflex is elicited. Key words: Skin blood flow rate; Local blood flow regulation; Autoregulation; Veno-arteriolar reflex.

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L. Jelstrup Petersen, Department of Medicine C, Bispebjerg Hospital, Bispebjerg Bakke 23, DK-2400 Copenhagen NV, Denmark.

Laser Doppler Flowmetry is a generally accepted method for measurement of skin blood flow rates. The method has been widely applied because of its accessibility and non-invasive character. However, due to great inter-individual variations in skin blood flow rates as well as great variations in cutaneous blood perfusion rates within very closely located skin areas (1, 2), the advantage of the Laser Doppler technique seems to be dynamic blood flow studies with the laser probe in the same location during the entire measurement.

Previously, the Laser Doppler has been used for
monitoring local regulation of blood flow rates in human skin, including the local venu-arteriolar reflex (3, 4, 5). The results, however, demonstrated that blood flow rates decrease in both lidocaine-infiltrated skin and in chronic sympathectomized patients (4, 5). According to the nature of the venu-arteriolar reflex, no such findings would be expected. Consequently, these observations suggest that Laser Doppler Flowmetry is unsuitable for measuring skin blood flow rates during major orthostatic manoeuvres. Whether the laser signal is influenced by minor changes in venous or arterial pressure is unknown. Consequently, we intended to monitor skin blood flow rates during successive orthostatic manoeuvres from 50 cm above to 50 below heart level in healthy subjects.

MATERIAL AND METHODS

Subjects
Fifteen healthy, non-smoking subjects participated in the study. Median age was 31 years, range 22–61 years. None was taking any medication. The investigation was approved by the local medical ethics committee and informed consent was obtained in each case.

Laser Doppler Flowmetry
A helium–neon laser (Pfl, Perimed, Sweden) was used. Settings were as follows: time constant 10 s, frequency limits 4 kHz. Prior to blood flow rate measurements the probe was pointed at a white surface and the pen recorder was set at zero. Then the probe was attached to the skin on the dorsum of the hand with a plastic probe holder. The holder was attached by tape.

Blood flow rate measurements
The subject was placed supine and the arm was immobilized on a horizontal bar, allowing orthostatic manoeuvres without changing the position of the laser probe holder.

During arm lowering, both arterial and venous pressures are increased whereas when the arm is raised, only arterial pressure decreases. Thus, two parameters are influenced during arm lowering whereas only one parameter is influenced during arm raising; the investigation was split into two parts: 1) arm elevation, and 2) arm lowering. The experimental setups were similar, however.

Initially, the blood flow rate was measured with the hand placed at heart level, BF\textsubscript{ref1}. Then the hand was passively moved to a test level and the signal was recorded at that level, BF\textsubscript{test}. Finally, a second reference value was obtained, BF\textsubscript{ref2}. Test values were obtained from –50 cm to +50 cm from mid-axillary line. 10 cm intervals were used. The relative blood flow rate at each test level was calculated as follows:

\[ BF_{relative} = \frac{BF_{test}}{(BF_{ref1} + BF_{ref2})^{1/2}} \]

Due to technical circumstances, only subjects with long arms were measured in the extreme positions. ±50 cm from heart level. Thirteen subjects participated in part 1, 11 persons in part 2. The experiments were performed in a constant temperature room (22–23°C).

Statistics
The two parts of the investigation were statistically evaluated by the same method. Each part comprised more than two
groups of paired data. Consequently, Friedman tests were used for the statistical evaluation.

Unchanged blood flow rate during elevation, i.e. autoregulation of blood flow, has been demonstrated up to +40 cm with the $^{133}$Xe washout technique. Above this level, the blood flow rate is reduced (6). Consequently, relative blood flow rate changes in the interval from heart level to +40 cm were tested. During arm lowering, the blood flow rate, measured by $^{133}$Xe washout method, is kept constant until approximately -35 cm, where the veno-arteriolar reflex is elicited. Further lowering does not decrease the blood flow rate (7). The test interval was then from heart level down -30 cm, where unchanged blood flow rates would be expected.

RESULTS

The results from study part 1 are presented graphically in Fig. 1, which shows that the 95% confidence limit of medians of all test levels from +10 cm to +40 cm demonstrates a uniform increase in blood flow rate. Medians and 95 percentiles at +10 cm to +40 cm were 1.33 (1.14-1.78), 1.44 (1.17-2.67), 1.67 (1.02-2.88) and 1.58 (1.14-3.73), respectively. Relative blood flow rate at +50 cm in 5 persons was 0.95 (range 0.23-2.87). BF<sub>relative</sub> differs statistically from reference level in the chosen interval ($p=0.00052$).

The results from study part 2 are shown in Fig. 2. All chosen test levels below the mid-axillary line demonstrated significantly decreased blood flow rates, as the 95 percentile of median does not include the reference value, 1.0. Ten cm below heart level, BF<sub>relative</sub> was 0.71 (95 percentile 0.44-0.93). The corresponding values at -20, -30, and -40 cm were 0.49 (0.42-0.79), 0.39 (0.29-0.65) and 0.29 (0.17-0.61), respectively. Fifty cm below heart level, the relative blood flow rate in 4 persons was 0.19 (overall range 0.04-0.32). Relative blood flow rate changes during hand lowering in the interval from heart level to 30 cm below this level demonstrated a highly significant reduction in blood flow rate ($p<0.00001$).

DISCUSSION

Autoregulation of blood flow, i.e. the ability to maintain constant blood flow rate despite an decreasing arterial pressure head, is a well-known established parameter for normal intrinsic smooth vasculature reactivity. Using the $^{133}$Xe washout technique, autoregulation has been described in several tissues, including subcutaneous adipose tissue (7) and skin (6, 8). In the present study, however, we demonstrated significantly increased laser Doppler signals when the arm was raised.

This disparity might be explained by the fact that the $^{133}$Xe washout technique measures capillary blood flow rate, whereas the laser Doppler flowmeter estimates total flux of moving structures within the range of the laser beam. As the skin on the back of the hand is very thin, the 1 mm penetration of the laser beam probably reaches the whole dermis including the subdermal plexus. Consequently, laser Doppler measurements involve all vessels in the cutaneous tissue, including postcapillary venous vessels.

When the arm is raised, venous pressure is kept constant, whereas venous blood volume is reduced as the veins tend to collapse (9). It has previously been demonstrated that blood flow rate is influenced by changes in the vessel diameter (10, 11). Due to displacement from laminar flow in the centre of the vessel, erythrocyte flux tends to be turbulent. It is not possible to say whether the increased laser Doppler signal during elevation is caused by changes in particle flux in collapsed venous vessels, or whether it is a normal vascular flow pattern which is not measured by the $^{133}$Xe washout technique. The mechanism has yet to be elucidated.

During lowering of the hand, venous and arterial pressure increase in parallel. When venous transmural pressure increases 25 mmHg, corresponding to approximately 35 cm below the heart, the capillary blood flow rate decreases suddenly by about 35%. When the arm is lowered still further, no further blood flow reduction is seen. This local sympathetic axon reflex is elicited by venous distension of all types (venous stasis, external negative pressure), as discussed in detail in the thesis of Ole Henriksen (7). The results of the present work obtained with the laser Doppler technique, however, contrast with these previous findings. Below heart level, blood flow rate fell at all test levels. Furthermore, no major blood flow rate reduction was seen in the interval from -30 to -40 cm. The results demonstrate that one cannot measure the local veno-arteriolar reflex in human skin with laser Doppler flowmetry. Similar results have been reported by other investigators (4, 5). In the study by Engelhart and co-workers (4), laser Doppler Flowmetry was used to monitor vascular sympathetic reflexes prior to and after lidocaine blockade. Abolished Vasalva manoeuvre and cold pressor test—but preserved response to venous distension—were demonstrated in lidocaine-infiltrated skin. According to the nature of the veno-arteriolar reflex, no changes in blood flow rate would be expected, as the sympathetic impulse transmission was abol-
ished. A decreased laser value during venous disten-
sion may indicate that changes in blood volume influence
the laser signal.

The results of the present work demonstrate that
orthostatic manoeuvres might invalidate the interpreta-
tion of the laser signal. As even minor deviations
from the heart level influence the laser Doppler sig-
nal, the method has to be used with care. It is evident
that laser Doppler flowmetry measures blood flow
rates related not solely to capillary blood flow rate.
The significance of changes in blood volume in the
area under study remains to be elucidated.

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Elastase-inhibiting Activity in Scaling Skin Disorders

A. CHANG, J. SCHALKWIJK, R. HAPPLE and P. C. M. van de KERKHOF
Department of Dermatology, University Hospital, Nijmegen, The Netherlands

Elastase inhibiting activity (EIA) has been observed in
normal skin as a response to surface trauma, immedi-
ately following the intra-epidermal accumulation of
polymorphonuclear leukocytes (PMN). In order to elu-
cidate the relation between EIA and inflammation, the
inhibiting activity was assessed in skin samples of
scaling dermatoses (a) without significant inflama-
tion: erythrodemic autosomal recessive lamellar
ichthyosis (EARLI), non-erythrodemic autosomal re-
cessive lamellar ichthyosis (NEARLI), X-linked recessive
ichthyosis (XLRI) and X-linked dominant chon-
droplasia punctata (XLD-CDP); (b) with predomi-
nantly mononuclear cell infiltration: atopic dermatitis;
(c) with mixed infiltration of PMN and mononuclear
cells: psoriasis and Netherton syndrome. All skin dis-
orders investigated showed an increased EIA as com-
pared with normal skin. Scales from psoriatic lesions,
EARLI and Netherton syndrome showed a statistically
significant increase in EIA above that observed in oth-
er monogenic disorders of keratinization NEARLI,
XLRI XLD-CDP and above atopic dermatitis. EIA
proved to be an indicator for abnormal keratinization
with a marked expression when a mixed infiltrate is
present in the skin. Key words: Polymorphonuclear
leukocytes; Scaling dermatoses.

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A. Chang, Department of Dermatology, University
Hospital Nijmegen, Philips van Leydenlaan 25, 6525
EX Nijmegen, The Netherlands.

Human polymorphonuclear leukocytes (PMN) con-
tain the proteolytic enzyme elastase, which is unique
and specific for these cells (1, 2). Briggaman and co-

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