The laser Doppler flowmeter and the 133-Xenon washout techniques of measuring cutaneous blood flow were compared for measuring the vasoconstrictor response of the hand during orthostatic maneuvers. Important discrepancies were detected for the two methods. When the hand was lowered by 40 cm a 40% decrease in blood flow was detected by the 133-Xenon method, while a 60% decrease was seen by the laser Doppler technique. Lowering the hand by 50 cm resulted in no further blood flow decrease when using the 133-Xenon method, but an 80% blood flow decrease was recorded with the laser Doppler method.

The laser Doppler technique is a rather new method for evaluation of blood flow in the microcirculation [1]. The method has, compared to other methods, the advantage that it can measure blood flow continuously and register sudden blood flow changes [2,3]. The method is suitable for the measurements of relative blood flow changes following a standardized stimulus as reactive hyperemia [4] and following warming/cooling procedures [3]. However, large differences in blood flow in apparently similar adjacent skin regions makes the method unsuitable for the comparison of blood flow levels from patient to patient [5]. In a previous paper, evaluating the vasoconstrictor response, a good correlation between the laser Doppler values and the 133-Xenon washout technique was found [4]. The measurements were performed in the skin fold area between 1. and 2. finger, an area consisting of two layers of cutaneous tissue. The aim of the present study was to compare the laser Doppler method with the local 133-Xenon washout technique when measuring the vasoconstrictor response on the dorsum of the hand, during orthostatic manoeuvres.

A marked decrease in blood flow was recorded by the laser Doppler technique in hands that were sympathectomized or a hand that was subjected to a nerve blockade, strategies which should eliminate the orthostatic vasoconstrictor response of superficial cutaneous vessels. The 133-Xenon technique did not detect any blood flow changes in hands without sympathetic tone. We found the laser Doppler flowmetry technique unsatisfactory for measurement of blood flow changes that occur in nutritional vessels as this method measures total skin blood flow including non-capillary vessels. J Invest Dermatol 91:451–453, 1988

PATIENTS AND METHODS
A total of fifteen subjects, aged 25 to 40, were investigated. In the first part of the study, eight suffering from Raynaud’s phenomenon (one was sympathectomized in both upper extremities 10 years before) and six without cold sensitivity participated. Informed consent was obtained prior to the experiments. The vasoconstrictor response in subcutaneous tissue is elicited when vascular transmural pressure is elevated above 25 mmHg or more [6]. In the present experiments this was obtained by lowering the hand 40 cm below heart level. In two persons additional lowering to 50 cm was performed.

In the second part of the study, the effect of local nervous blockade was investigated. In one person, a 4-cm² area on the dorsum of the hand was infiltrated with 2 ml lidocaine (10 mg/ml). To test its effectiveness, the responses to ice cold water (cold pressor test) and deep inspiration were evaluated.

133-Xenon Washout Blood flow in subcutaneous tissue on the dorsum of the hand was measured by the atraumatic epicutaneous 133-Xenon washout technique [7], using a 133-Xenon-saline solution.

After a labeling period of 4 min, the 133-Xenon-saline solution was drawn back into the syringe, and the labeling chamber and surplus of liquid were removed from the skin surface. Measurement of washout was started 35 min after the labeling period to make sure that 133-Xenon was located mainly in the subcutaneous tissue. The following experimental conditions were chosen: The subjects were recumbent, and a single study consisted of 3 periods of measurement of 133-Xenon washout. 1) The hand was placed at reference/heart level, \( t_{ref1} \); 2) the hand was lowered 40 cm, \( t_{ref2} \); and 3) finally the hand was placed at reference level \( t_{ref2} \). Each period of measurement lasted for 5 min. This triad of measurements was chosen to compensate for small changes in washout rate not related to blood flow. The emission of 133-Xenon was detected by a NaI(Tl) scintillation detector and the pulses were fed into a gammaspectrometer with a
window set around the 81-KeV photopeak of 133-Xenon. The activity was recorded at 10 sec interval.

**Laser Doppler flowmetry** The probe of the laser Doppler flowmeter (Perimed, Sweden) was fixed on the dorsum of the hand with double-sided adhesive tape, in exactly the same area as the 133-Xenon labeling was performed. The laser Doppler signals were led to a pen recorder. Blood flow was measured during the same manoeuvres as described for the 133-Xenon technique. The laser Doppler flow was recorded during several minutes in each position, until the flow value had stabilized.

The parameters for the laser Doppler were frequency limit 4kHz, time constant 3 sec, and gain x10. Zero point for the laser Doppler was obtained by placing the probe on the hand and apply suprasystolic pressure on the upper arm.

**Calculations** Mean perfusion coefficient ($f$) can be calculated from the rearranged Kety-formula: $f = k \lambda$ [100 [ml (100g min)$^{-1}$] [8], where $k$ denotes the washout rate constant in min$^{-1}$ and $\lambda$ the tissue to blood partition coefficient in ml g$^{-1}$. For the same radioactive depot, where $\lambda$ remains constant, relative blood flow equals relative 133-Xenon washout rate.

Relative 133-Xenon washout rate, $f_{relative}$, during lowering was calculated as the mean value of the values obtained on the two reference values, i.e.,

$$f_{relative} = \frac{f_{test}}{0.5(f_{ref-1} + f_{ref-2})}.$$

$k$ was calculated from the logarithmically transformed radioactivity data corrected for background activity as a function of the time according to the "least square method". A typical experiment is shown in the upper part of Fig 1.

The arbitrary laser Doppler "blood flow" values was read directly from the pen recorder. A typical experiment is shown in Fig. 2 (lower part).

**Statistics** Statistical tests included Wilcoxon rank sum test for paired and unpaired observations. As a limit of significance, a value of 0.05 was chosen.

**RESULTS**

During 40-cm hand lowering, the relative values differed significantly from 1 and relative blood flow was significantly lower with the laser Doppler method (left, Fig 3).

Additional hand lowering from 40 to 50 cm in two persons (1 and 2 in Fig 3, right), showed a further flow decrease when measured with the laser Doppler, but not with the 133-Xenon method.

In one sympathectomized patient relative blood flow at 40 cm hand lowering was 0.95 when measured with the 133-Xenon method but decreased to 0.40 when measured with the laser Doppler. Local nervous blockade abolished the reflex in the subcutaneous tissue evaluated by 133-Xenon washout (Fig 1, lower part), but a remarkable decrease of blood flow was demonstrated using the laser Doppler (Fig 2, upper part). Analgesia of the skin and abolished vasoconstriction during cold pressor test and deep inspiration were taken as evidence that effective lidocaine blockade had been achieved.

**DISCUSSION**

The decrease in blood flow during lowering is due to arteriolar constriction; the vasoconstrictor response [6]. This response is evoked when vascular transmural pressure is elevated by 25 mmHg or more. Lowering the hand 40 cm below heart level corresponds to an increase in vascular transmural pressure of about 30 mmHg. The response is observed in both cutaneous, subcutaneous, and skeletal muscle [6]. We found a decrease in relative blood flow during lowering, which corresponded well with earlier findings using the 133-Xenon method [4]. When measured with laser Doppler flowmetry, flow decrease was significantly stronger.

As shown in a previous work [9], the 133-Xenon method measures only nutritive blood flow in capillaries, and the laser Doppler method measures flow in "all blood vessels" to a depth assumed to be approximately 1 mm [5]. Therefore, besides measuring the decrease in nutritive blood flow, the laser Doppler method probably also measures a decrease in linear blood cell velocity due to stasis of blood in postcapillary vessels during lowering. This pronounced "flow decrease" overshadows the flow changes occurring in the capillaries and a false increased response is observed. This theory is supported by the facts that 1) We observed a flow decrease during further lowering of the hand (further increase in postcapillary pressure) when measured by the laser Doppler flowmeter. This was not observed by the 133-Xenon technique, which in accordance with previous investigations shows that the veno-arteriolar reflex is an on/off phenomenon [6]. 2) During local nervous blockade, vasoconstriction due to cold pressor test and deep inspiration was abolished, but a blood flow reduction induced by 40-cm hand lowering was demonstrated. 3) Flow decrease was still pronounced when measured by the laser Doppler in the lidocaine infiltrated skin and in the chronically sympathectomized patient, although no response remains in these patients [10] when measured by the 133-Xenon washout technique.
Discrepancy between the 133-Xenon washout method and laser Doppler Velocimetry in evaluation of the local vaso-arteriolar reflex in sympathectomized patients has also been found by Kastrup et al [11].

In a previous study [4] a good agreement between the 133-Xenon washout technique and the laser Doppler method was found when we measured the vasoconstrictor response in the skin fold between 1. and 2. finger. However, the discrepancy from this study might be explained by the fact that we now measured blood flow in both cutis and subcutis, whereas in the previous study we measured only in cutis. Subcutis contains more extended postcapillary vessels, which probably accounts for a more "increased" response when measured by the laser Doppler, for the reasons previously mentioned.

Therefore, we conclude that laser Doppler flowmetry is unsuitable for measure blood flow changes in nutritive vessels during orthostatic manoeuvres, because this method measures "total blood flow," including blood flow in non-capillary vessels (subpapillary venous plexus). Most certainly, blood flow changes in these vessels overshadow the reactions in the nutritive vessels.

REFERENCES


4TH INTERNATIONAL SYMPOSIUM ON THE TREATMENT OF PSORIASIS AND PSORIATIC ARTHRITIS

This conference is sponsored by the International Psoriasis Treatment Center and will be held at Dead Sea, Jerusalem, March 5–12, 1989. For further information contact: Henry H. Roenigk, Jr., M.D., Department of Dermatology, Northwestern University Medical School, Chicago, Illinois 60611.