

## SHORT REPORTS

### Transcutaneous PO<sub>2</sub> and Laser Doppler Blood Flow Measurements in 40 Patients with Venous Leg Ulcers

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The study included 40 patients with clinically venous leg ulcer(s) in one leg only and with a systolic toe blood pressure above 50 mmHg in both legs. Transcutaneous oxygen tension was measured on both lower legs at equivalent sites, on the affected leg immediately proximal to the ulcer(s). Similarly, skin blood flow was measured in both legs at a skin temperature of 32°C and 44°C by means of laser Doppler velocimetry, and for each leg the index of blood flow 44°C/flow 32°C was calculated to express the degree of blood flow increment following local hyperthermia. Transcutaneous oxygen tension measurements were significantly lower on affected legs ( $p < 0.01$ ) as was flow increment ( $p < 0.01$ ), mainly due to a high flow measurement at 32°C on affected legs rather than to a low measurement at 44°C. The results of our flow measurements suggest a state of (relative) hyperemia in the vicinity of venous leg ulcers, also confirmed by the clinical findings. This could be interpreted as an arteriolar response to lowered oxygen tension or (it could) be part of reactive reparative processes leading to increased O<sub>2</sub> consumption in the tissues. *Key word: Cutaneous blood flow.* (Received June 25, 1986.)

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In 1982 Browse and Burnand (1) introduced their theory on leakage of fibrinogen and pericapillary polymerisation to fibrin leading to the development of a diffusion barrier to oxygen in venous leg ulceration. If this theory proves to be correct, it may dramatically affect planning of future treatment regimes of venous leg ulcers.

With the development of techniques for transcutaneous monitoring of PO<sub>2</sub> (2, 3), a new noninvasive tool has become available for the quantitation of a clinical physiological parameter in patients with chronic venous insufficiency. According to the former theory one would expect low values of O<sub>2</sub>-tension in legs with venous ulceration as compared to healthy legs. The application of this technique as a means of measuring absolute values of O<sub>2</sub>-tension is however problematic. We therefore chose to design the present study in a manner that only called for comparison of values within the same individual.

## MATERIALS AND METHODS

Forty patients (median age 71 years, range 56-91 years) were investigated during a period of 2 months. All attended our out- or inpatient department for unilateral clinically venous leg ulcer(s). To reassure the predominantly venous aetiology, a determination of the systolic toe blood pressure was performed bilaterally in each patient at the hospital's clinical physiological department using previously described techniques (4). Only patients with systolic toe blood pressures above 50 mmHg were included.

Transcutaneous PO<sub>2</sub> (tcPO<sub>2</sub>) was measured by means of a transcutaneous oxygen monitor (TCM-2,

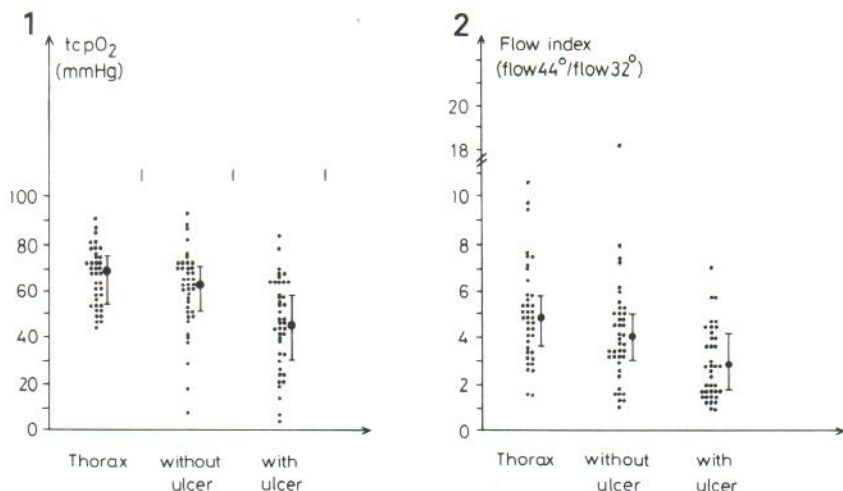


Fig. 1. tcPO<sub>2</sub> (mmHg) on chest wall (left side), legs without ulcer(s) and legs with ulcer(s).

Fig. 2. Flow index (flow 44°C/flow 32°C) on left side of chest wall, legs without ulcer(s) and legs with ulcer(s).

Radiometer A/S Copenhagen). At all measurements the electrode temperature was 44°C and before each session the electrode was calibrated. First a measurement was performed on the left side of the chest wall to yield a reference value. Subsequently, measurements were performed on both lower legs at equivalent positions, guided by the location of the ulcer(s) on the affected leg. Measurements were made approximately 1 cm from the proximal border of the ulcer(s) with the leg in a horizontal position. Oxygen tension values were read out from the digital display after an equilibration time between 15 and 20 min, i.e. when the oxygen tension value was constant. In 30 patients the circumference of the legs was measured at the same level as the tcPO<sub>2</sub> measurements.

Laser Doppler flow measurements were made on the basis of previously described techniques (5, 6). We performed measurements at a distance of 5 cm from the site described for tcPO<sub>2</sub> determinations. One measurement was performed at normal skin temperature (32°C) and one at a skin temperature of 44°C. For each set of measurements we calculated an index of flow increments: flow 44°C/flow 32°C.

#### Statistics

The non-parametric Pratt rank sum test was used for comparison of data. As level of significance  $p < 0.05$  was chosen.

## RESULTS

Fig. 1 shows a plot of the tcPO<sub>2</sub> values. The tcPO<sub>2</sub> was significantly lower on affected legs ( $p < 0.01$ ).

In Fig. 2 a plot of the flow index, flow 44°C/32°C, is shown. Flow increment following local hyperthermia was significantly lower on affected legs (Table I). Only the flow measurements of 39 patients could be evaluated. The circumference of ulcer-legs was significantly increased compared to the control-leg ( $p < 0.01$ ) (Table II).

## DISCUSSION

Although our study has the qualities of a clinical investigative approach more than a strict basic scientific approach to the problems of chronic venous insufficiency, our results clearly indicate a state of lowered oxygen tension in the skin of legs with venous ulceration. This is in accordance with the results of previous studies (7, 8).

Table I. *Flow values (mean  $\pm$  SD) (arbitrary units) at 32°C and 44°C.*

	Chest wall (left)	Legs with ulcer(s)	Legs without ulcer(s)
32°C			
Mean	16.49	23.87	15.18
SD	$\pm 8.60$	$\pm 20.93$	$\pm 11.92$
44°C			
Mean	76.03	53.82	48.85
SD	$\pm 33.12$	$\pm 26.66$	$\pm 18.49$

We found it problematic to compare absolute values of O<sub>2</sub> tension from different individuals, and therefore chose to design our study as an intraindividual comparison of oxygen tensions on legs with and without ulcer(s), the ultimate manifestation of chronic venous insufficiency. Many of our patients of course had bilateral signs of venous insufficiency, but still ulceration was associated with a significantly lower oxygen tension on the surrounding skin.

The most intriguing approach in recent time to the problems of pathogenetic factors of skin manifestations in chronic venous insufficiency syndrome, has been the studies and theories of Burnand, Browse et al. (1, 9, 10). According to this theory the leakage of fibrinogen and pericapillary polymerisation to fibrin, causing a diffusion barrier to oxygen in venous leg ulceration, could be expected to cause low oxygen tension measurements in the vicinity of venous leg ulcers. Our results are consistent with these theories, but we find it difficult to rule out several competing factors such as increased epidermal thickness, change in skin composition and oedema as the primary cause of low tcPO<sub>2</sub> values. In our study increased oedema paralleled a decreased tcPO<sub>2</sub>. Neumann et al. (7) pointed out an increased tissue metabolism as a possible cause of lowered tcPO<sub>2</sub> in chronic venous insufficiency. According to the results of our laser-Doppler flow measurements, there was a state of increased cutaneous blood flow at 32°C near to venous leg ulcers as compared with the non-ulcerated legs. The laser-Doppler technique only provides a relative estimate of blood flow. Therefore this need to be confirmed by more refined techniques. The finding might indicate the existence of reactive and reparative processes around venous leg ulcers.

Thus, it is our opinion, that further and extended studies, including histological/histochemical techniques, should be performed to elucidate and expand the theories of Burnand, Browse et al. (10). If a pericapillary fibrinogen polymerisation proves to be the major pathogenic factor in chronic venous leg ulceration, one would expect surgical intervention in the terms of radical removal of affected tissue and replacement by auto skin grafts to be the treatment of choice in long-standing venous leg ulceration.

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### Seasonal Variation in Urinary Excretion of 5-S-Cysteinyldopa in Healthy Japanese

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The urinary excretion of 5-S-cysteinyldopa was examined in 10 healthy Japanese subjects once a month during a period of one year. The mean values were highest in August (296 µg/day) and lowest in February (141 µg/day). Individual variations were so great that only a weak difference was observed ( $p < 0.05$ ). *Key words: Dopa; Sunlight.* (Received September 16, 1986.)

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Urinary excretion of 5-S-cysteinyldopa (5-S-CD) has been widely used as a biochemical marker of melanoma metastasis (1, 2). The catecholic amino acid arises from the oxidation of dopa and the subsequent coupling of dopaquinone with cysteine (3). Thus, 5-S-CD formed in melanoma tissues (4) by the action of tyrosinase is excreted in large amounts in the urine of melanoma patients (2, 4). 5-S-CD is also excreted in smaller amounts in the urine of healthy subjects, regardless of skin and hair colour (5).

Seasonal variation in the excretion of 5-S-CD was reported in healthy Swedes (6). The results showed a 3-fold increase in the mean excretion value in the summer as compared with that in the winter. We thought it necessary to study the seasonal variation in the urinary excretion of 5-S-CD in healthy Japanese, because of the difference of climate, life style and genetic background. The urinary excretion of dopa and dopamine were also examined.

### MATERIALS AND METHODS

This study included 10 healthy subjects; 7 were students of the University, aged 18-21 years (2 males and 5 females), and the other 3 were 35 (male), 38 (female) and 40 (male) years old. All the subjects lived without excessive exposure to sunlight.

Urine was collected for 24 h in bottles containing 50 ml of acetic acid and 1 g of sodium metabisulphite. 5-S-CD, dopa and dopamine were determined by HPLC with electrochemical detection as previously described (7).