PAPERS AND SHORT REPORTS

Blood flow in the skin of the foot related to posture in diabetes mellitus

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Abstract

Normal healthy subjects show a reflex rise in precapillary resistance in the skin of the foot when they rise from lying to standing. To investigate the integrity of this reflex in patients with diabetes mellitus blood flow in the plantar region of the big toe was measured, using a laser Doppler flowmeter. The responses of diabetic patients with and without peripheral sensory neuropathy and healthy control subjects matched for age and sex were studied, with the foot at heart level and the foot passively lowered to 50 cm below the heart.

In normal subjects mean blood flow recorded during the third to fourth minute of dependency fell to 18·1 (SD 11·9)% of the preceding resting flow determined with the foot at heart level. In the diabetic patients without neuropathy blood flow fell to 28·9 (18·6)% of the preceding resting flow. In the diabetic patients with neuropathy blood flow fell to 53·5 (23·7)% of the preceding resting flow, which was significantly different from the value achieved by the diabetics without neuropathy ($p<0·02$) and the healthy controls ($p<0·002$). Six normal subjects were indirectly heated to release sympathetic tone and achieve the same mean skin temperature of the foot as the diabetic patients with neuropathy, and blood flow fell to 38·7 (24·3)% of the preceding resting flow, a value not significantly different from the response seen in the patients with neuropathy.

These findings suggest that the postural control of blood flow in the foot is disturbed in patients with diabetic neuropathy, and this disturbance is compatible with a loss of sympathetic vascular tone. The resultant hyperperfusion on dependency may account for the oedema seen in some patients with neuropathy and may also act as a stimulus for the thickening of capillary basement membranes.

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Introduction

The precapillary resistance in the skin of the foot rises on standing, thereby limiting the rise in capillary pressure resulting from the vertical column of blood between the heart and the foot.[1] Evidence suggests that this vasoconstriction is mediated by a sympathetic axon reflex.[2] We examined this reflex in patients with diabetes for

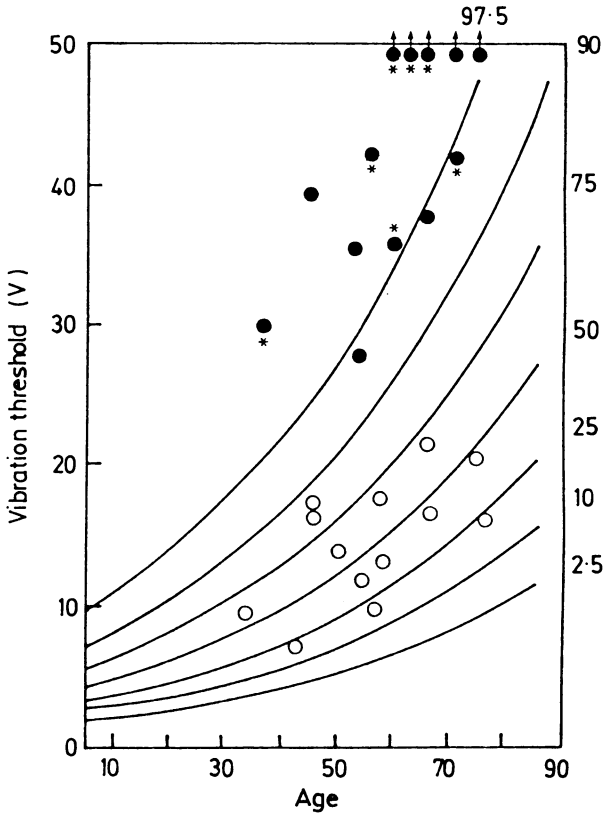

FIG 1—Centile chart of vibration thresholds in the big toe.[6] Open and closed circles represent values in diabetics in the present study without and with neuropathy, respectively. Asterisks indicate patients with autonomic neuropathy.

two reasons: firstly, oedema may occur in patients with diabetic neuropathy,[3 4] which might represent failure to limit the rise in capillary pressure on dependency; secondly, thickening of basement membranes, the histological hallmark of disease of the small vessels in patients with diabetes, is promoted by raised capillary pressure.[5] The reflex change in microcirculatory flow in the skin of the foot on dependency may be studied with a new instrument, the laser Doppler flowmeter. This technique is non-invasive and, unlike existing techniques, does not entail local heating of skin, injection trauma, or venous occlusion, all of which may disturb local vasomotor reflexes.

Patients and methods

We studied three groups of subjects: diabetics with peripheral sensory neuropathy, diabetics without neuropathy, and healthy controls matched for age and sex. Patients were classified as having neuropathy if ankle jerks were absent and vibration sensory threshold, determined with a biothesiometer (Biomedical Instrument Co, Ohio), was above the 90th centile for age when compared with published centile charts for normal subjects of varying ages (fig 1).[6] Seven of the subjects with neuropathy showed evidence of cardiac autonomic dysfunction, eight had a history of ulceration of the foot, and four had mild, unexplained peripheral oedema. Autonomic neuropathy was assessed by measuring the response of the heart rate to standing, deep breathing, and the Valsalva manoeuvre.[7] Diabetics without peripheral neuropathy had no evidence of autonomic dysfunction or history of ulceration of the foot. In all subjects foot pulses were palpable and ratios of ankle to arm systolic pressure (measured by Doppler ultrasound) were normal. The table gives details of the subjects.

Measurement of blood flow—Blood flow was measured using a laser Doppler flowmeter (Periflux, model PF1C, MkVII, Perimed Limited, Sweden). This instrument produces a voltage signal directly proportional to microvascular blood flow in superficial skin vessels.[8] Blood flow was measured in the plantar aspect of the left big toe, except in subjects who had ulceration of the foot or who had had the left foot amputated, when the other foot was used. Skin temperature was measured continuously using a Comark electronic thermometer type 1625 and copper-constantan thermocouple placed within 0·5 cm of the laser Doppler probe. Tests of blood flow were conducted in a room where the temperature was controlled (21-23°C). The subject lay recumbent on a specially constructed couch, which was hinged to permit passive lowering of either leg from the hip. Resting blood flow was recorded over two minutes after 30 minutes of acclimatisation. The leg was then lowered so that the toe was placed 50 cm below the midaxillary line, and flow was recorded between the third and fourth minute of dependency, when blood flow is stable.

Effect of skin temperature on blood flow during dependency—To examine the effect of different temperatures of the skin of the toes on the vascular response to dependency we studied a separate group of six normal subjects (mean (SD) age 49·7 (21·4) years) under the same conditions as described above, and again after indirect heating (a heat blanket pressed to the

Details of subjects in the three groups. (Values are means (SD))

	Age (years)	M:F	Duration of diabetes (years)	Plasma glucose (mmol/l)	Haemoglobin A_1 (%)
Normal controls	59·5 (13·8)	7:6			
Diabetics without neuropathy	55·2 (12·5)	7:6	15·5 (8·1)	9·5 (4·2)	9·1 (1·5)*
Diabetics with neuropathy	59·5 (11·6)	9:4	12·8 (11·3)	9·2 (2·7)	8·9 (1·1)

*Normal range: 4·0-7·5%.
Conversion: SI to traditional units—Plasma glucose: 1 mmol/l≈18 mg/100 ml.

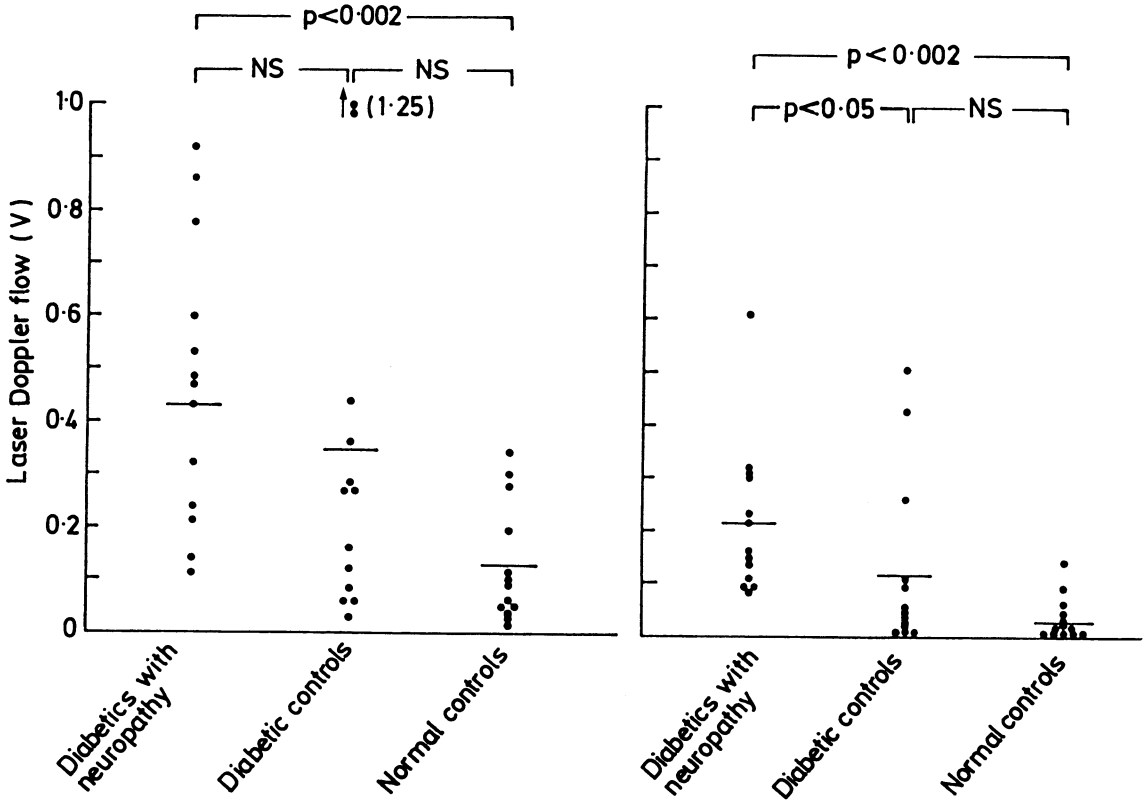

FIG 2—Blood flow in the toe recorded by laser Doppler technique with toe at heart level (left) and 50 cm below heart level (right). (Horizontal bars indicate means.)

abdominal wall) to release central sympathetic drive and raise the temperature of peripheral skin.

Statistical methods—The results are expressed as means (SD). Differences between the groups were analysed using the Mann-Whitney U test.

Results

Skin temperature—Skin temperatures measured after acclimatisation in the supine position were significantly higher in the patients with neuropathy (32·2 (2·0)°C) than in the patients without neuropathy (28·7 (3·1)°C, $p<0·002$) and the normal subjects (27·7 (3·3), $p<0·002$). There was no significant difference in values between the diabetics without neuropathy and the normal subjects.

Resting flow—Figure 2 shows resting flow values. Mean resting flow in the diabetics with neuropathy was significantly higher than that in the normal subjects (0·44 (0·23) *v* 0·13 (0·11) V (arbitrary units of flow), $p<0·02$). Mean resting flow in diabetics without neuropathy (0·34 (0·37) V) was not significantly different from that in either the control subjects or the diabetics with neuropathy.

Blood flow during dependency—Figure 2 shows measurements of flow during the third to fourth minute of dependency. Mean flow on dependency was significantly higher in diabetics with neuropathy (0·22 (0·15) V) than in the normal subjects (0·03 (0·04) V, $p<0·002$) or the diabetics without neuropathy (0·12 (0·17) V, $p<0·05$).

Percentage change in blood flow on dependency—In the normal subjects mean blood flow during the third to fourth minute of dependency fell to 18·1 (11·9)% of the original resting flow (fig 3). In the diabetic patients without

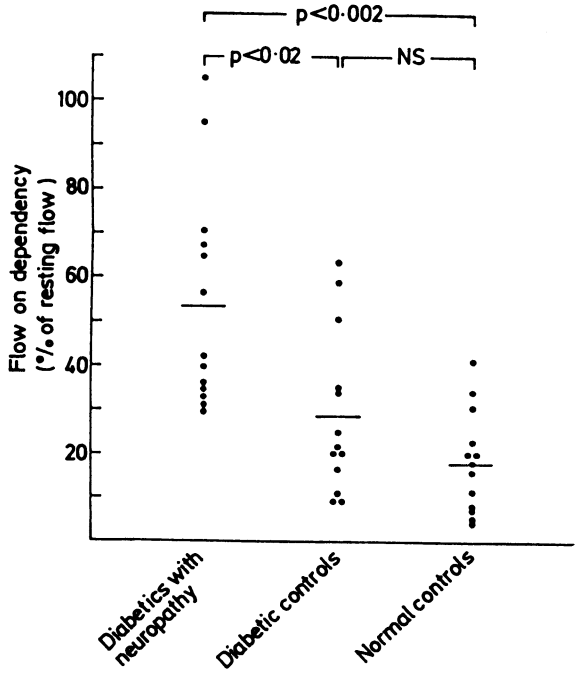

FIG 3—Flow on dependency expressed as percentage of preceding rest flow.

neuropathy blood flow fell to 28·9 (18·6)% of the original resting flow, but this was not significantly different from that achieved by normal controls. In the diabetic patients with neuropathy blood flow fell to 53·5 (23·7)% of the original resting flow, which was significantly different from the value achieved by the diabetics without neuropathy ($p<0·02$) and the healthy controls ($p<0·002$).

Effect of skin temperature on blood flow during dependency—Figure 4 summarises the percentage change in blood flow during the third to fourth minute of dependency in the six normal subjects before and after indirect heating. The values in the diabetics with neuropathy are plotted on the same graph. Before indirect heating blood flow fell during dependency to 20·9 (13·0)% of the original resting flow. After indirect heating the fall in blood flow was less in all six subjects, with a mean value of 38·7 (24·3)% of the original resting flow. The skin temperature of the normal subjects after indirect heating was not significantly different from that found in the diabetic patients with neuropathy (32·4 (2·4) *v* 32·2 (2·0)°C). Vascular

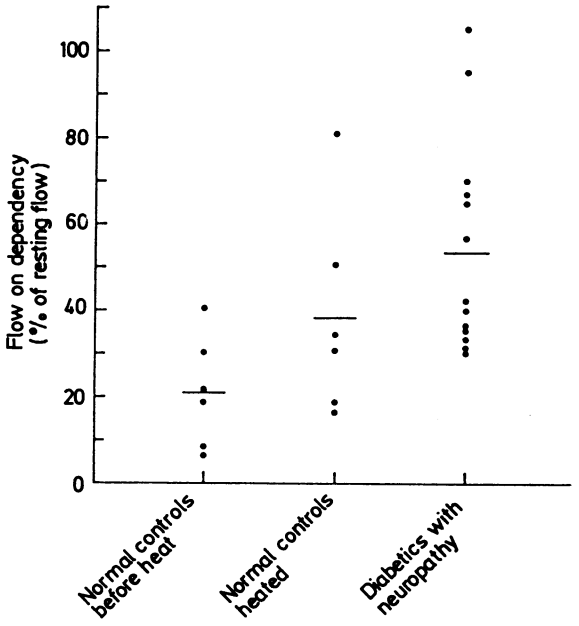

FIG 4—Vascular response to dependency in normal controls before and after skin temperature was raised by indirect body heating compared with response in group with neuropathy.

response to dependency in the normal subjects after heating was not significantly different from that observed in the diabetic patients with neuropathy (38·7 (24·3) *v* 53·5 (23·7)%).

Discussion

Most measurements of blood flow in the feet of diabetic patients have been taken with the foot at heart level. This is clearly unrepresentative of the conditions to which the peripheral circulation must adapt for most of the time. Lowering the foot below heart level elicits the venoarteriolar reflex, which results in an increase in precapillary resistance.[1,2] The non-invasive technique of laser Doppler flowmetry, though it does not provide an absolute measurement of volume flow, is well suited to determining such reflex changes in local flow as it does not damage the skin or depend on venous occlusion or local heating. Comparative studies with television microscopy, which measures flow velocity in single capillaries, suggest that the laser Doppler technique detects flow in subcapillary plexuses and shunts as well as the capillary loops, but the reflex responses determined by the two techniques are broadly comparable.[9]

The finding that skin temperature was raised in the group with neuropathy is in keeping with previous observations and presumably reflects the higher resting flow observed in this group.[10,11] This increased flow is exaggerated on dependency, the value attained being seven times that in healthy control subjects, compared with a fourfold increase when the foot was at heart level. This exaggeration indicates the failure of the venoarteriolar reflex. Although the mean fall in flow in the diabetics without neuropathy was less pronounced than that in the healthy controls, this value was distorted by three or four diabetics with particularly impaired responses. These patients might conceivably have had sympathetic neuropathy without detectable sensory and cardiac autonomic neuropathy, a hypothesis supported by the observation that the sympathetic nervous system may be more susceptible to early impairment in patients with diabetes.[12]

Indirect heating causes release of sympathetic tone and opens up peripheral arteriovenous anastomoses to promote the dissipation of heat. Our study showed that the response of blood flow to dependency in the skin of diabetic patients with neuropathy is similar to that seen in vasodilated normal skin, suggesting that the reflex failure observed may represent an abolition of sympathetic tone with persistence of arteriovenous shunting on dependency.

Considerable evidence exists to support the concept of increased shunting in the foot of diabetics,[10] but the exaggeration of this abnormality in the dependent position is a new observation.

Several inferences may be drawn from this study. Failure of precapillary vasoconstriction on dependency will result in the capillary bed being exposed to a greater hydrostatic load. This may account for the development of peripheral oedema seen in patients with neuropathy. Furthermore, chronic exposure to capillary hypertension may act as a localising stimulus to thickening of capillary basement membranes. Vracko described increasing thickness of capillary basement membrane from thigh to foot, which is particularly pronounced in patients with diabetes.[13] Both these inferences require direct experimentation to substantiate them. Preliminary results from our laboratory suggest that capillary pressure is indeed higher in the dependent foot of diabetics compared with normal subjects.

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Iron deficiency in young Bradford children from different ethnic groups

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Abstract

Haematological parameters and iron state were studied in children admitted to hospital consecutively during a six month period. A total of 147 of 598 children (24·6%) were anaemic, with haemoglobin values below the third centile of the reference range, and 131 of 400 children (32·8%) were iron deficient, with serum ferritin concentrations less than 10 μg/l. Both findings were more common in children from the Asian ethnic minority.

The "routine" full blood count is a useful tool for the presumptive identification of iron deficiency in childhood. Iron deficiency is deleterious to the health of young children. In view of its extent and degree—not exclusively among the Asian ethnic minority—a community based preventive programme on the lines of the Stop Rickets Campaign is recommended.

Introduction

Iron deficiency is common among young children and is usually determined nutritionally.[1,2] Many young children are admitted to hospital, and those of poorer socioeconomic state are over-represented among these.

Bradford Health Authority serves a population of 340 000, which includes an Asian ethnic minority of about 60 000. These consist of first and second generation migrants, almost entirely Moslems from Pakistan, with small numbers of Moslems from Bangladesh, Hindus, and Sikhs. Roughly one third of children admitted to Bradford paediatric beds are from the Asian ethnic minority.

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This report presents the haematological results and serum concentrations of the iron storage protein ferritin in children consecutively admitted to paediatric beds over six months. The children studied were aged between 6 months and 4 years. Anaemia, hypochromia, microcytosis, and iron deficiency were common findings.

Patients and methods

Every child admitted to a paediatric bed in Bradford during 1 September 1983 to 29 February 1984 was eligible for study if the age on the date of admission was at least 6 months and less than 4 years. Children admitted more than once were studied during the initial admission. The study was approved by the ethical committee.

In those children in whom a venepuncture was thought clinically necessary blood was taken for full blood count (Coulter counter method) and serum ferritin estimation (by immunoradiometric assay) in addition to clinically indicated assays. Haemoglobin electrophoresis was performed on any child whose mean corpuscular haemoglobin value was less than 25 pg.

The following children were excluded: six with β thalassaemia, three in whom β thalassaemia trait was discovered during the study, one West Indian child, two Africans, one Greek Cypriot, and one child admitted for investigation of anaemia.

Haemoglobin concentration and mean corpuscular volume were compared with age and sex specific reference ranges,[3,4] and, along with mean corpuscular haemoglobin and ferritin values, the results were also compared by age, sex, and ethnic group.

Statistical evaluation was by χ^2 test and the Mann-Whitney U test.

Results

After exclusion of the 14 children noted above, 778 children (513 white, 265 from the Asian ethnic minority) were eligible for the study. These corresponded to about 6% of the children of this age residing in the Bradford Health District.

There were no significant differences in the proportions of boys and girls, in the results between boys and girls in each ethnic group, or for the