

THE NON-INVASIVE ASSESSMENT OF THE ISCHAEMIC LIMB, WITH
PARTICULAR REFERENCE TO THERMOGRAPHY.

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Submitted for the degree of
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Statement of Originality and Ethical Approval

After extensive review of the literature, the work described in this thesis does not, to my knowledge, duplicate previous published studies. It provides an original contribution which is complementary to the work of other investigators on the subject of the non-invasive investigation of blood flow.

Although all of the methods of investigation described in this work were in clinical use at Hope Hospital, ethical approval was sought and granted by a written certificate from the Ethical Committee, Salford Health Authority for these studies.

ABSTRACT.

Skin temperature (T_{sk}) has long been used in assessing limb circulation, and in recent years thermography has been used as an accurate way of measuring T_{sk} . However, apart from the general proposition that T_{sk} must be related to that of the blood, the precise relationship between the blood supply to a limb and its T_{sk} remains poorly understood. Without this knowledge full use cannot be made of thermography in the assessment of the limb with peripheral vascular disease.

The purpose of these studies was to provide a scientific basis for the use of thermography on limbs. Previous work had indicated that T_{sk} was related to skin blood flow in the hand and foot, but not in the forearm or calf. This work has been confirmed and extended by studies on normal subjects at different ambient temperatures, and on subjects with a peripheral A-V fistula. I have shown that T_{sk} over the forearm and calf is related to the core temperature of the limb, i.e. to the arterial inflow.

An attempt was then made to see if these findings could be used to interpret the abnormal thermograms found in a group of patients with intermittent claudication, and in a group with more severe peripheral vascular disease.

In claudicants the regression line relating mean calf T_{sk} to total blood flow was parallel to, but higher than that in normal subjects, i.e. for the same blood flow, claudicants' T_{sk} was higher than in normal subjects. The

reasons for this difference are not apparent.

Thermograms in patients with more severe limb ischaemia were often difficult to interpret because of the confusion introduced by other pathologies.

Thermography is a useful adjunct in the assessment of the ischaemic limb, but is unlikely to replace more conventional methods of investigation.

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THE NON-INVASIVE ASSESSMENT OF THE ISCHAEMIC LIMB WITH
PARTICULAR REFERENCE TO THERMOGRAPHY.

FORWARD.

Despite improvements in technique and advances in instrumentation over the last 20 years, few of the methods of non-invasive investigation of the ischaemic limb have been generally accepted, either singly or in combination.

Segmental Doppler pressure measurements represent a major advance and can be helpful but have been shown to be unreliable when arteries become calcified (Wolfe, 1988; Greenhalgh, 1988).

Isotope washout techniques have reverted in recent years to the subdermal injection method rather than the epicutaneous route described by Sejrsen (1971), and as such it is invasive and will therefore not be discussed further in this thesis.

Skin perfusion pressure has its enthusiasts (Holstein et al., 1980) but it is not applicable where ulceration or gangrene is present.

Various forms of plethysmography can be informative but they only give information about regional blood flow. Since it is the cutaneous circulation which is crucial to the healing of wounds then plethysmographic techniques alone are not enough.

The development of laser Doppler flowmetry (Tenland, 1982) has provided a new method for assessing the cutaneous micro-circulation but at present can not give quantitative values.

Transcutaneous oxygen tension may indicate the state of tissue nutrition beneath the probe but oxygen availability and utilisation in ischaemic tissue is known to be different to that in normal subjects. It is also a very time-consuming study.

Thermography has much to recommend it as a technique. It is an investigation requiring absolutely no contact of any equipment with the patient, thus causing no disturbance or pain should any ulceration or gangrene be present; it is harmless to the patient and has no side effects. It is quick to perform and reproducible, and has the advantage of providing a picture of the whole limb under scrutiny and not just isolated points.

The equipment is expensive, but if definitive, reliable information can be obtained from its use, then it might allow some of the other more time-consuming or invasive forms of investigation to be dropped.

Aims of study

In these studies therefore, our aims were:

i) to establish a sound, scientific and physiological basis for the understanding of thermographic data in control subjects, with particular focus on the relationship between skin temperature and blood flow;

ii) to examine patients with peripheral vascular disease of varying severity and determine in what way and to what extent any changes in thermographic appearance might be reflected in altered blood flow;

iii) to ascertain by these means whether thermography

has a significant role to play in the non-invasive investigation of the ischaemic limb.

Skin blood flow was measured using a laser Doppler technique, and, where appropriate, total limb blood flow was measured by strain-gauge plethysmography. Transcutaneous gas tension values were used as an estimate of tissue nutrition, and traditional ankle Doppler pressure measurements were also made. Each method of investigation has been evaluated and the reason for its inclusion in this work stated.

The number of diagnostic tests currently used in the assessment of the ischaemic limb suggests that none is free from objection. A better understanding of the mechanisms of the changes produced by peripheral vascular disease should lead to the design of more reliable dynamic tests which could be used in the surgical management of these patients. With knowledge of the factors which determine the temperature of different regions of the skin in normal and diseased limbs we should be able to make better use of skin temperature in the diagnosis and care of patients with peripheral vascular disease.

INTRODUCTION.

The incidence of lower limb ischaemia. "Critical" ischaemia - concept and natural history.

Since William Harvey's description of the circulation of the blood (Harvey, 1628) and the recognition that its oxygen carrying capacity is vital for tissue nutrition (Lavoisier, 1777), the study of abnormal flow has been of prime interest to clinician and scientist alike.

Lower limb ischaemia is responsible for much pain and disability, and a great deal of costly expertise is needed in its investigation and management (Gupta & Veith, 1988). The prevalence of symptomatic arterial disease of the lower limb in Britain is estimated to be around 2% - and rising - of the population aged 45-60 (Boobis & Bell, 1982) and is responsible for around 200,000 hospital admissions per year (DHSS. HMSO, 1981).

The aim of the vascular surgeon is to prevent symptomatic ischaemia progressing to "critical" (Bell et al., 1982) or end-stage ischaemia where loss of the limb is likely or inevitable.

In patients with symptomatic peripheral vascular disease, critical ischaemia will develop in 1-3%, and between 40-70% will be dead within 5 years whether treated by amputation or reconstructive surgery (Dormandy & Thomas, 1988).

Need for careful selection of patients and operation.

In a review of seven long-term follow-up studies after

reconstruction for critical ischaemia Dormandy and Thomas (1988) demonstrated an overall limb salvage rate of 45% with an operative mortality of 4%. But they emphasise the danger of combining figures from different centres where graft materials and patient selection procedures may differ.

If revascularisation fails, there may be no alternative to amputation. Retention of the knee joint significantly improves the chances of rehabilitation, (McCollum, 1988), but only about 60% of patients having a below-knee amputation achieve primary healing. Some will eventually heal by secondary intention but approximately 15% will require re-amputation at a higher level and around 7% will die without leaving hospital (Dormandy & Thomas, 1988).

In the management of critical ischaemia with this bleak outlook there is clearly a need to choose the right operation first time to improve the quality of life for the patient, and reduce hospital stay along with post-operative morbidity and mortality. The results of revascularisation procedures depend on many factors, not least the experience of the surgical team where improved patient selection along with improved technique is likely to influence results. Thus, it is important to know which patient to operate on, which operation to perform and the likely outcome of surgery.

Investigation of lower limb ischaemia.

Investigation of peripheral ischaemia of the legs includes a detailed history and thorough examination of

the patient, assessment of the pulses and a record of any obvious ischaemic changes in the limb. Contrast angiography will provide a 'road-map' of the vasculature, but even with the advent of digital subtraction techniques (DSA), it remains an expensive, time-consuming and invasive method of investigation.

Purpose of investigation.

The aims of investigation of arterial disease are to determine:

- i) the degree of ischaemia
- ii) the extent of disease
- iii) the possibility of reconstructive surgery
- iv) the likelihood of sympathectomy being of benefit if reconstruction is not feasible
- v) the optimal site for amputation if no other option is available
- vi) the success of treatment
- vii) the progression of disease.

With these goals in mind, attempts have been made to obtain the maximum amount of accurate information from the minimum of tests, time and trauma to the patient.

Non-invasive investigation - the burgeoning of physics with physiology.

Assuming that a detailed history and thorough examination have been made, the simplest method of assessment of blood flow to the limb can be obtained by measuring systolic blood pressure down the leg using a

Doppler probe (Woodcock, 1985). However, although some authors rely heavily on this method (Holstein, 1973; Yao & Bergan, 1974; Dean et al., 1975; Barnes et al., 1976; Lee et al., 1979; Cederberg et al., 1983), others feel that it is unreliable (Lazarus, 1978; Bernstein, 1986; Wolfe, 1988; Stoner et al., 1989). The reasons for this are discussed later.

In an effort to find non-invasive methods of obtaining information about blood flow in limb ischaemia, a variety of plethysmographic techniques have been used; volume displacement (Brodie & Russell, 1905), impedance (Kubicek et al., 1974), segmental (Raines, 1978), capacitance (Holling & Verel, 1957), gravimetric (Jackson & Matthews, 1977; Humphrey et al., 1980), and strain-gauge (Whitney, 1953).

Clearance of the isotope ^{133}Xe , applied epicutaneously, has been used to determine cutaneous blood flow (Sejrsen, 1971) but more recently ^{99}Te and $[4\text{-}^{125}\text{I}]\text{i}$ odoantipyrine have been favoured and are being used by the intradermal route and thus are no longer non-invasive (Holstein et al, 1983; Spence et al, 1984).

Laser Doppler flowmetry (Tenland, 1982) and skin perfusion pressure (Holstein & Hansen, 1988) are also being used to determine skin blood flow but none of these methods has achieved wide acceptance.

The delivery of oxygen to the tissues for nutrition is one purpose of the circulation, and transcutaneous oxygen tension measurement is regarded by some as a more sensitive indicator of the degree of ischaemia (Matsen et

al., 1980; Young et al., 1981; Clyne et al., 1982; van Urk & Feenstra, 1988). But the observation that the skin of the ischaemic limb was usually cold, both subjectively and objectively, led to the investigation of temperature measurement as a method by which to assess the degree of ischaemia.

HISTORICAL BACKGROUND.

Skin temperature measurement and thermography.

The idea that temperature differences could be used to detect disease is not new; approximately 2,000 years ago Hippocrates stated that " should one part of the body be hotter or colder than the rest, disease is present in that part " (cited by Winsor & Bendezu, 1964).

Skin temperature measurements can be made in many ways using thermocouple thermometers, thermistor thermometers, bolometers, liquid crystal sheets and infra-red thermography (Ring, 1971; Clark & Edholm, 1985).

" Thermography gives a true heat photograph " wrote Barnes, one of the early pioneers, in 1963 (Barnes, 1963), but assumptions were being made about what these heat photographs meant. Skversky et al (1964) described a lack of correlation between skin temperature and blood flow through underlying muscle and fatty tissue, but they were happy to rely on the statement of Friedlander and his colleagues (1938) that skin temperature was an index of the amount of blood flow to the skin.

Over the last two decades the development of thermography has led to its expanding use in both the

industrial world and clinical practice. Initially, all thermograms were 'grey-scale' pictures, but colour thermography became available in the 1970s.

Infra-red thermography has been used in the assessment of skin flap viability in plastic surgery (Hackett, 1974), depth of burn injury (Mladic et al., 1986), neuropathy (Berholdt & Brand, 1975), breast cancer location (Draper & Boag, 1971), varicose veins (Linhagen et al., 1983), deep venous thrombosis (Browse, 1978), patency of shunts (Chevrel, 1979), intestinal viability (Moss et al., 1981), pain (Hobbins, 1984), as well as many studies investigating the ischaemic limb.

Historically, its earliest use was in the field of tumour location. Lawson, in Montreal, established, using thermography, that the skin over the site of a breast cancer was hotter than that over the contralateral normal side, but this work was not published for fifteen years (Lawson & Alt, 1965).

In England, in the early sixties, in addition to its use in tumour location, Lloyd Williams realised that infra-red radiation from the skin might show the site of incompetent perforators in patients with varicose veins. In May 1961, he obtained the first thermographs of breast cancer outside the USA, and with the help of Maxwell Cade designed a new scanner specifically for medical use (Williams, 1964; Williams et al., 1964; Cade & Barlow, 1970).

Peripheral vascular disease was one of the first fields to be explored. Skversky and his colleagues in 1964

looked at six patients with different forms of peripheral vascular disease and noted the effect of intra-arterial injection of vasodilator agents on thermograms. No mention is made of the conditions under which these measurements were made, such as environmental temperature or equilibration time before thermography was performed. Workers in other disciplines recognised the importance of a rigid protocol to obtain useful results and the early work of Mladic et al (1966) in the assessment of burn injury was an extension of Lawson's realisation of the value of thermography in this field (Lawson et al., 1961).

Wallace (1967) not only used thermography to assess depth of burns but included the investigation of peripheral vascular disease by studying patients with carotid insufficiency, as suggested by Wood (1965). These studies were based on the theory that in a case of peripheral ischaemia, the skin distal to an obstructing arterial lesion would be cooler than the proximal skin since it would be relatively under-perfused. As will be shown later, this assumption does not always hold true, especially where superficial collateral channels may increase the radiant heat emission from an ischaemic limb compared to the opposite normal limb.

Although thermographs were being made in many different conditions; thrombophlebitis, obstructive arteriosclerosis, complete and partial nerve injury, arthritis, trauma, collagen diseases and neoplasms - Winsor (1968) claimed to have studied over 1,000 subjects - only small series were reported. These outlined the

increasing range of peripheral vascular disorders for which the technique was being employed, including Raynaud's disease and phenomenon, the effect of sympathectomy, thrombophlebitis, collagen or connective tissue disorders affecting digital vessels, Buerger's disease and the influence of cigarette smoking on thermograms of the hands (Winsor, 1968; van Voss, 1968).

Thermography and tissue viability.

In the same year Patterson (1968) first raised the possibility that thermography might be useful in determining tissue viability. Using a pig model, he studied the thermographic patterns produced when skin flaps were raised on segmental vascular pedicles, and the following year Birch and others looked at the thermographic appearances of a full thickness skin graft placed onto denuded areas of rabbits' ears (Birch et al, 1969; Brånemark & Nilsson, 1969).

A new technique had arrived which apparently assessed blood flow; it was rapid to perform, easily reproducible, and more importantly, was completely harmless and without side-effects to the patient. This realisation stimulated Williams to compare thermography with the results of angiography in 15 patients with occlusive vascular disease. As a screening procedure that was free from the attendant hazards of intra-arterial angiography, it presented a desirable alternative, and in his series there was good correlation between complete occlusion with poor collateral circulation and asymmetrical thermograms with

distal cooling demonstrable on the affected side (Williams, 1969).

Assumptions made by other studies.

Buwalda (1969) postulated two arterial systems when interpreting thermograms of the lower limb in subjects with vascular disorders. He claimed that before cooling, in normal individuals, "...on the upper legs there are more hot spots than on the more distal parts. This is the picture of the skin circulation." After a 15-20 minute cooling period to an ambient temperature of 18°C, at which he made his thermograms, "...the spotted picture disappears. Then one gets a view of a certain pattern of warm and cold areas, reflecting the more or less vascularised deeper parts of the leg." Unfortunately these statements are made in the absence of any skin or limb blood flow measurements.

Thus, in much of the early work it was difficult to be certain of exactly what physiological event was reflected by thermography, or even to agree on the environmental temperature at which measurements should be carried out. Another study chose an ambient temperature of 24°C for no apparent reason (Gershon-Cohen & Borden, 1969).

In 1970 Robins and Bernstein reviewed 75 patients with peripheral vascular disease who had both digital strain-gauge plethysmography and infra-red thermography performed before and after arterial reconstructive surgery. No mention was made of ambient temperature nor was quantitative analysis made of the plethysmographic

recordings. They concluded that; "...i) the two methods were comparable in normal patients or in patients with vasospastic rather than occlusive disease; ii) in occlusive arterial disease, the two methods were parallel if there was no infection and if there was normal sympathetic nervous system activity in the extremity; iii) the results of reconstructive vascular surgery were recorded accurately by both if the above-cited conditions applied; iv) the presence of infection caused a disassociation of the results because of increased temperature in the affected area; v) the impairment of sympathetic nervous system activity, particularly its inappropriate or compensatory overactivity, was reflected in lower thermographic recordings, indicating selective reduction in skin versus muscular blood flow " (Robins & Bernstein, 1970).

Several criticisms may be made of this study. Half the patients were diabetics who are prone to peripheral and autonomic neuropathy. No assessment of a neuropathic state is mentioned. They say that sympathetic hyperactivity or vasospasm may be demonstrated by the warming response and increased blood flow in the feet consequent on immersing the hands in warm water. This is wrongly called " reactive hyperemia ". It is not. It is the normal reflex vasodilatation brought about by indirect heating (Gibbon & Landis, 1932; Bader & Macht, 1940; Martinez & Visscher, 1945; Barcroft et al., 1947; Randall et al., 1948).

They refer to digital plethysmography as measuring

muscle blood flow, yet there is no muscle in a digit beyond the plethysmographic cuff. Furthermore they say that "...the presence of neurogenic tone will reduce the skin temperature despite, or as a compensation for, increased muscular blood flow." But these measurements were made at rest so there was no demand for muscle blood flow to rise above resting values.

When quoting 'normal' values for skin temperatures of hands and fingers, feet and toes, they omit to mention the environmental temperature which is vital. Clark and Edholm (1985) demonstrated that skin surface temperature is markedly dependent on the temperature of the environment, with quite different patterns of distribution shown with increasing temperature.

Finally, a useful observation was that superficial inflammation will produce a local temperature rise on thermography that is not paralleled by an increase in blood flow measured by plethysmography.

Some difficulties of thermographic interpretation: The introduction of colour thermography.

When examining 16 cases of aortic coarctation and 16 cases of arterial occlusive disease of the lower limb, Siltanen and his colleagues (1971) found that there was a correlation between the development of collateral arterial channels shown angiographically, particularly near the skin, and increased thermal emission shown by thermography. They felt this departure from normal thermographic patterns might help to pin-point significant

arterial occlusions.

During the same year Hackett (1971) showed that areas of skin loss or ulceration in burned patients always had a lower temperature than the surrounding intact skin due to evaporative heat loss. This knowledge was not new (Lawson et al ., 1961; Mladic, 1966). At this time Hackett began using a Polaroid camera and a series of colour filters to show different isotherms on one photograph. He pointed out that, though more expensive, it was a quicker system to use and easier to read.

By the following year colour thermography was regarded as part of the armoury in the investigation of peripheral vascular disease. At this stage it consisted of an eight colour isotherm photograph and although easier to read, it had no greater resolution than the earlier continuous grey-scale pictures. Even so, the vascular surgeon was urged to interpret thermograms "...with caution and skill" (Lippmann et al, 1972).

Comparative prospective studies were vital to establish the place of thermography and Soulen et al (1972) performed thermography in addition to Doppler ultrasound examinations in 300 patients with peripheral vascular disease referred to them for angiography. Unlike Buwalda (1969) they felt that the mottled or blotchy appearance of the thighs in some subjects was a function of their build, being only found in heavier limbs. Unfortunately, they did not say at what temperature they kept the " draft-free, constant-temperature room " in which they made their measurements. They emphasised the normally cold

thermographic appearance of the knee which may be reversed when a superficial femoral or popliteal artery occlusion leads to development of collateral channels around the knee.

Problems arose when the disease was diffuse and multiple sites of stenosis or occlusion produced a variable collateral supply. Proximal blockage could conceal additional more distal occlusion, only unmasked after proximal surgery. Inflammation could also give the impression of adequate perfusion in an area which angiography showed to be grossly ischaemic (Soulén et al., 1972).

Thermography, angiography and Doppler ultrasound; comparison of techniques.

Thermography may be of value in the follow-up of post-operative graft patency. These same authors acknowledged that Doppler ultrasound was more accurate in determining graft patency, but felt that thermography gave an indication of tissue perfusion. Thus, if insonation of the graft confirmed its patency but the thermogram did not show increased heat, the " long-term graft patency and viability of the limb is poor " (Soulén et al., 1972). When this happened arteriography sometimes showed a distal anastomotic stricture which could be revised. Their conclusion was that thermography had a greater role to play in the post-operative evaluation of patients with arterial disease but that the Doppler ultrasound probe was more versatile.

In an attempt to try and avoid arteriography completely, McLoughlin and Rawsthorne (1973) compared the results of 52 patients with peripheral vascular disease who had undergone both angiography and thermography. The results were assessed by three independent observers and only agreed in 50% of cases. They concluded that the amount of subcutaneous fat negatively correlated with the diagnostic accuracy of thermography and that the technique was a poor substitute for femoral angiography. Thermography was most reliable only in advanced cases of occlusive vascular disease where there was no collateral circulation.

Their methodology involved actively heating the patient by a radiant heat source to achieve "...a toe-knee temperature as near as possible to 28°C in the ischaemic limb(s) ", then moving the patient to another room at an environmental temperature of 16°C. Thermograms were made every 2 minutes for 40 minutes or until the ischaemic toe temperature fell to 21°C. No explanation is given for this protocol. It is likely that the insulating effect of the subcutaneous fat was enhanced by the absence of an equilibration period before scanning.

Widening use of thermography in the investigation of vascular disorders.

Singh and Motomiya, (1973), in a short paper outlining the application of thermography to peripheral vascular disease, first described a case of arterio-venous fistula shown by thermography as an area of markedly increased

heat compared with the unaffected limb. This is relevant to these studies and will be discussed in detail later.

The literature describing the value of thermography was growing and 1974 saw publications on its use in re-implantation surgery, Dupuytren's contracture, deep venous thrombosis and varicose ulcers, along with further work on the depth of burns (Baudet et al., 1974; Cooke & Pilcher, 1974; Hackett, 1974).

Holm et al (1974) reviewed 12 patients with peripheral vascular disease in whom both pre- and post-operative thermography was performed. Angiography was also undertaken in all before operation. Nine had superficial femoral artery occlusions. As a result, five underwent thrombo-endarterectomy, one a by-pass procedure, one a digital amputation, and two were put onto an exercise programme. In those six who had either thrombo-endarterectomy or by-pass, the increased heat pattern shown around the knee as a result of collateral circulation disappeared post-operatively. This was regarded as a sign of a successful procedure.

The use of temperature measurement in determining the level of amputation in the critically ischaemic lower limb was first described by Lee (1974). He used thermistors and liquid crystal strips. Although he said that the results obtained helped in the decision making, only one case report is cited and the results are not given. However, the principle that thermographic methods might help to determine amputation level in ischaemic disease is one which recurs in later years and forms part of our

study.

Despite the gradual increase in familiarity with the technique, the need for carefully controlled studies was often submerged in the enthusiasm for reporting its use.

1975-1977; Thermographic doldrums - the lean years.

Lovisatti et al (1974) made dogmatic statements about normal thermographic patterns in the lower limb based on 17 male subjects aged 25-30. They then studied 46 patients - ages not given - with "arteriopathy" who had also been examined by "arterial angiography, morphoscillometry and plethysmography." They describe the thermographic changes to be found in these cases. They do not mention the equipment used, the temperature of the environment in which the measurements were carried out, or the experimental method. No comparison is made with the other techniques.

The next two years produced little advance in the evaluation of thermography as a tool in vascular disease although Acciarri repeated other work on the ischaemic limb (1977) with the same conclusions about the difficulty of interpreting thermograms when both limbs are ischaemic. He also evaluated the technique as a means of choosing a surgical approach in late complications of compound leg fractures to avoid operating through skin with a poor blood supply. Provided the skin appeared warm on thermography he concluded it was safe to operate through it even if it was involved by scar tissue (Acciarri et al., 1977). Intra-operative thermography had been

described the year before in an attempt to decide whether median nerve symptoms in the carpal tunnel syndrome were compressive or ischaemic (Talia & Landi, 1976). Although the two aetiologies are not mutually exclusive and are, in fact, likely to co-exist, the implication of the paper is that the thermographic picture enables the surgeon to spot the limits of the required neurolysis.

1978; Renaissance.

Amongst a collection of papers proclaiming the advantages and limitations of thermography in the prediction and diagnosis of deep vein thrombosis (Cooke, 1978; Browse, 1978; Henderson et al., 1978) came a study which re-emphasised the mottled thermographic pattern in normal but fat thighs (Hallböök et al., 1978). This supported the statement made earlier by Soulen and his colleagues (1972), that the blotchy appearance was a function of the build of the patient, being only found in the heavier thighs, and no further reference could be found to support the claim that the pattern was that of skin - as opposed to deep - blood flow (Buwalda, 1969).

The same year, Henderson and Hackett (1978) added to Lee's earlier work (1974) in using thermography to try and determine a safe level of amputation in the ischaemic limb.

They studied 32 potential candidates for amputation before surgery. Patients were examined in a room at 20°C after 15 minutes equilibration. They recommended that a higher level of amputation be chosen when there was

either; i) a greater than 2°C temperature drop from above to below the knee in patients with one leg already amputated, or, ii) the temperature difference between the skin of the anterior, medial and lateral aspects of the legs at the level of the proposed incisions exceeded 2°C. They summarised that thermography successfully altered the intended level of amputation in 5 cases and would have done so in another 5 if their recommendations had been adopted. This was the first mention of specific recommendations following thermographic measurements made under a strict protocol.

Can thermography determine blood flow? Some stricter experimental protocols, and investigation into underlying pathophysiology.

A claim that thermography could give a quantitative estimate of blood flow under carefully controlled environmental conditions was made by Love (1980) who showed a linear correlation between blood flow measured by strain-gauge plethysmography and the ratio of thermographic temperature change. He argued that previous authors (Draper & Boag, 1971) had, for example, explained that the increased heat overlying a breast cancer was conducted to the surface and was due to the increased metabolic activity of the tumour, and so "...neglected the effect of blood perfusion in computation of the skin temperature patterns."

Furthermore, he felt that the increased metabolism stated by Lawson & Chughtai (1963) as occurring in a tumour

was unlikely to account for such a considerable temperature rise. To conclude that skin temperature was a function of tissue blood flow rather than tissue metabolism, (which was acknowledged to play a smaller part), begged the question, which tissues? And did it matter?

Certainly, in the field of plastic surgery and digital re-implantation, a thermographically cold finger associated with absent pulses on Doppler probe insonation was synonymous with failure and a poor outcome with eventual re-amputation of the finger (Bertrand et al., 1980; Lambiris et al., 1980). This was not always due entirely to ischaemia of the skin but of the digital nerves. Thus a hypothermic finger might not be critically ischaemic but would demonstrate cold intolerance, insensitivity and poor mobility, and fared badly. For these cases thermography identified either complete ischaemia or relative ischaemia with skin sparing. This contrasts with Henderson and Hackett's work (1978) referred to earlier, in which they regarded thermography as an indicator of skin perfusion when choosing amputation sites.

Thermography and lower limb amputation: An important study.

Despite the advances in reconstructive surgery, amputation is still a common operation. Recognition of the fact that accurate selection of amputation level before operation is essential to successful rehabilitation

led Spence and his colleagues (1981) to enlarge upon Henderson and Hackett's work (1978). Their study is one of the most comprehensive in the literature and is worth some detailed attention.

Spence's team examined 107 limbs in 104 patients in a prospective blind trial to determine thermographically the optimum site of amputation in ischaemic disease of the lower limb.

Patients were studied in a thermally controlled environment at 20°C, in a recumbent position, after 15 minutes equilibration time with both lower limbs exposed. Using grey-tone thermographic equipment (EMI Thermoscan) they obtained pictures of the anterior aspect of the limbs from groin to toe and corresponding line scans representing the longitudinal thermal gradient (LTG) from above the knee to the dorsum of the foot.

They predicted a distal amputation (part-foot or Symes) would heal if the LTG was "...within the normal limits of $\pm 2^{\circ}\text{C}$ " and when there was medial to lateral symmetry at the ankle and foot. Below knee (BK) amputation was recommended when there was "...a good LTG, absence of excessive knee hyperthermia and medial/lateral temperature symmetry at the BK flap level." If the LTG was greater than 6°C , an above knee (AK) amputation was advised.

They stressed that hyperthermia in the foot dissuaded them from selecting a distal amputation as it was frequently associated with infection. Similarly, if there was extensive hyperthermia of the leg then a BK was " at risk " as in one case where infection was found at

operation at BK level and an AK amputation was performed. All predictions were made without the knowledge of the surgeon who made his own clinical decision.

Of 107 amputations, 33 required revision to a higher level. Eleven patients had delayed healing. BK amputations accounted for 66% of operations and 49 of 69 (71%) achieved healing, though 3 were delayed requiring further local wedge resection. Of these 49, 42 were correctly predicted by thermography (86%). The 7 remaining had been allocated to distal amputation (3 patients) and AK amputation (4 patients, 3 requiring wedge resection).

Twenty patients needed revision of their BK stump, 17 to AK and 3 to through-knee (TK). Two of these 3 had been predicted correctly by thermography, the other had been recommended for AK. Eleven of the 17 who subsequently had AK amputations had been predicted as AK thermographically. Of the 6 that remained, 4 developed stump skin ischaemia and 2 infection.

At the distal amputation level thermography was less accurate. Fourteen of 22 were successful but only 5 had been correctly predicted by thermography. However, all 8 unsuccessful distal amputations had been assessed as requiring BK amputations thermographically.

They emphasised the care required in interpretation of hyperthermic areas, especially in the foot where the rise in temperature may be a combination of infection, ischaemia and tissue necrosis. The post-sympathectomy "hot foot" may be a particular pit-fall. Even so, they

claimed an 80% success rate at AK, TK and BK levels, and 88% if allowing for 5 cases where the limb was amputated above the thermographically predicted level.

This careful study set the challenge for thermographic prediction of amputation level particularly as it was done without reference to any angiographic or other clinical data.

Thermography and skin blood flow: An association is claimed.

In 1984, Spence and Walker addressed the question of whether thermography was a reflection of skin blood flow (Spence & Walker 1984). They used the clearance of the isotope [4-¹²⁵I]iodoantipyrine (IAP) injected subdermally into the legs of 10 patients with peripheral vascular disease. Colour thermograms were made at an ambient temperature of 21°C after 15 minutes exposure of the legs, which were raised and supported 10° above the horizontal. They demonstrated a significant relationship between skin blood flow and specific isotherms. This was the first time such a correlation had been shown.

The implication was important because if the work was reproducible then a truly non-invasive assessment of skin blood flow had been found. The relationship between cutaneous blood flow and healing of skin flaps was already well established (Holloway & Burgess, 1978; Malone et al., 1981) and it was reasonable to suppose that a relationship between skin temperature and skin blood flow might be found as heat flow from the body core to the skin surface

was thought to "...be mainly a convective process determined by blood flow" (Spence & Walker, 1984).

Tissue viability and healing potential: Does thermography compare with other methods of assessment?

At the same time as these data on thermography were being published an increasing literature was developing on the measurement of transcutaneous oxygen tension ($TcpO_2$) as a method of determining tissue viability (Burgess et al., 1982; Franzeck et al., 1982; Dowd et al., 1983; Mustapha et al., 1983; Ratliff et al., 1984). Values of 40 mm Hg or greater, measured 10 cm below the knee, were associated with a good chance of achieving healing in below knee amputations, but Spence et al (1984) pointed out some difficulties in the interpretation of these results. They stated that in ischaemic skin the extraction and utilisation of oxygen from the blood may be considerably altered so that $TcpO_2$ values are not directly related to the underlying tissue pO_2 levels, nor may they even represent local oxygen availability.

In a critical review of the methods of assessing tissue viability they strongly favoured the thermographic technique as being quick, totally undisturbing to the patient as a non-touch examination, and easily reproducible. However, as no single method had been widely accepted and there was no 'gold standard' by which to compare other methods, they felt thermography combined with isotope clearance provided the best hope for the future (Spence et al., 1984).

Temperature gradients and skin blood flow.

In the course of their studies Spence and his colleagues noted that there was a medial to lateral thermal gradient across the calf in addition to the longitudinal gradient down the limb. This was particularly marked just below the knee around the area where skin flaps might be fashioned in a below-knee amputation. This observation supported the work of Haertsch (1981a) who had demonstrated that the axial skin blood supply to the leg below the knee came from vessels accompanying the saphenous and sural nerves. These arteries arose from a plexus just superficial to the deep fascia and not from any perforating arteries arising from the belly of gastrocnemius (Haertsch, 1981b).

These findings provided the basis for Robinson et al (1982) to recommend a departure from the classical long posterior flap used in below-knee amputation, originally suggested by Bickel and Ghormley (1943), re-iterated by Kendrick (1956), and popularised by Burgess and his colleagues in the 1970's (Burgess, 1968; Burgess et al., 1971). Robinson advocated equal skew flaps based antero-medially and postero-laterally so that these superficial axial arteries could be preserved and included.

McCollum et al (1985) felt that Robinson's hypothesis that skin blood flow was reduced over the tibia was not supported thermographically nor on the results of the washout of IAP injected subdermally 3 cm medial and lateral to the anterior tibial border, 10 cm below the tibial tuberosity. McCollum's study, performed on 21

patients with critical ischaemia, led him and his colleagues to recommend a medially skewed posterior flap in an attempt to preserve the branches of the saphenous artery.

Has thermography any advantages over clinical judgement?

Despite the increasing reliance on thermographic techniques to aid and influence clinical management in vascular disorders and other conditions, including identifying perforating cutaneous arteries (Theuvenet et al., 1986), arterio-venous fistulae (Bergqvist & Bornmyr, 1986), and osteomyelitis (Harway, 1986), not all investigators in the field of thermography felt the method contributed significantly. Luk et al (1986) studied 30 unselected patients with peripheral vascular disease in whom 27 amputations were performed. They compared the amputation levels predicted by thermography, as outlined by previous authors (Lovisatti et al., 1975; Ring, 1980), with Doppler ankle/brachial pressure ratios, (Mooney & Wagner, 1977; Wagner, 1981), and the surgeons' clinical assessment. They found that Doppler pressure ratios were of limited value especially in patients with diabetes mellitus. Thermography tended to indicate a higher level of amputation than was found necessary and that the most reliable assessment came from the surgeons' clinical judgment.

Thermographic ratios and ambient temperature: Influence of the environment on data interpretation and clinical

decision making.

Since the work of Spence and his colleagues (Spence et al., 1981; Spence & Walker, 1984; Spence et al., 1984; McCollum et al., 1985), there had been no published work describing attempts to determine amputation level by any new way of interpreting the thermographic data until our unit proposed the concept of a temperature ratio (Stoner et al., 1989). Using the long posterior flap (Burgess et al., 1982) for below knee amputations Stoner et al stated that the ratio of the skin temperature at the sites for the posterior and anterior incisions was a better indicator of outcome than mean calf skin temperature or the temperature at the site of either skin incision taken alone. If the ratio was greater than 0.98, then 90% of wounds healed, either primarily or after a delay (< 6 weeks). Below that point only 50% healed and only half of those by primary intention.

They also observed that if thermography was being used as a means of assessing blood flow in the skin then an ambient temperature of 20°C - used by other workers (Henderson & Hackett, 1978; Spence et al., 1981) - seemed inappropriate because Clark and Edholm (1985) had stated "...skin blood flow assessment requires a temperature of around 25-27°C whereas 21-23°C is more suitable when identifying subcutaneous thermogenic structures." Stoner and his colleagues used an ambient temperature of 26°C.

Variability of skin blood flow at different sites: The need for further investigation.

Other studies in our department have shown in normal subjects that, unlike in the fingers and toes, skin blood flow (measured by laser Doppler flowmetry) in the forearm and calf is unaffected by a change in ambient temperature from 20^o-30^oC.

This is supported by Bini and Wallin's work on the sympathetic nerve supply to the limbs (Bini et al., 1980a,b; Wallin, 1983). They showed that the two different modalities of sympathetic outflow to the limbs - vasoconstrictor and sudomotor - demonstrated marked activity in the glabrous skin of the hands and feet of subjects when they were cooled or heated. This was in marked contrast to the skin of the forearm and calf where little activity was to be found.

If the skin temperature at an ambient temperature of 20^oC is not a reflection of the cutaneous circulation then it is likely to represent heat conducted from the central core of the limb.

This would be at variance with those who consider it to be a reflection of skin perfusion (Draper & Boag, 1971; Henderson & Hackett 1978; Spence et al., 1981; Spence & Walker, 1984; McCollum et al., 1985;) and means that the relationship between skin temperature and the cutaneous circulation has still to be established.

The next chapter outlines the various methods of non-invasive investigation and puts them into a chronological perspective. The methods and techniques used in the course of these studies are explained in detail and reasons for their choice given.

REVIEW OF METHODS USED TO STUDY LIMB BLOOD FLOW.

Necessary information and influencing factors.

The methods of investigation of the ischaemic limb are legion but involve the study of four basic parameters:

1. Total limb blood flow.
2. Cutaneous blood flow.
3. Nutritional state of the limb.
4. Skin temperature.

All of the above may be influenced by external factors such as ambient temperature, the time allowed for equilibration, air speed, humidity, and the amount and nature of clothing worn. These are quite apart from the constraints imposed by the measuring techniques themselves and the reliability of the instruments involved. Furthermore, the subjects' internal environment may also affect the results. Drugs, including nicotine and ethanol, age, fitness, exercise habits and intercurrent disease such as diabetes will all influence the outcome. Similarly local infection, ulceration or gangrene will all affect the interpretation of results.

In each of the four main areas of assessment, several methods have been proposed in the past. These will be outlined and the particular methods used in this study then described in detail with reasons for their selection.

1. Total limb blood flow: methods of assessment.

Some methods of assessment available include:

- i) Calorimetry;
- ii) Plethysmography; - volume displacement of air or water
 - segmental / capacitance
 - gravimetric
 - impedance
 - photoelectric
 - strain-gauge
- iii) Duplex ultrasound scan;
- iv) Magnetic resonance imaging.

i) Calorimetry.

This method employs the Fick principle (Fick, 1870) which maintains that if the concentrations of a substance 'X' in the blood entering and leaving an organ (or limb) are known, and the rate of usage (or production) of the substance 'X' by the organ be likewise known, then the rate of blood flow through that organ can be calculated (Wright, 1982).

In 1911 Stewart, using this method, where the substance 'X' was the heat content of the blood, measured blood flow in the hand. He immersed the hand in an insulated container full of water and measured the heat given off from the hand to the water. Previous calculation had been made of the temperature difference between arterial and venous blood. Fresh cadaver experimentation had determined the specific heat of the hand. But the method had its drawbacks. The assumption that venous blood reflected skin temperature was not valid (Harris & Marvin, 1927; Pickering, 1936), and incomplete insulation of the

water in the calorimeter could result in a variable heat loss or heat gain (Bierman, 1939). The method was developed to measure the blood flow in the extremities (Sheard, 1926) and is of little value when total limb flow is required. Finally, it involves immersion of the part in water which is unacceptable in the presence of ulceration or gangrene. All methods involving immersion of the limb have been discarded as inappropriate to this work.

ii) Plethysmography: theory and types.

This technique is based on enlargement of a limb following venous occlusion. The term was first coined in 1872 (The Shorter Oxford English Dictionary, 1973) although the principle had been elaborated earlier by Glisson in 1622 and Swammerdam in 1737 (cited by Johnson, 1940). Adapting Archimedes' Principle, they placed an organ in a rigid box filled with air or water. Any subsequent swelling of the organ caused displacement of fluid from the box. This swelling might be due to increased blood flow to the organ which could be measured, being equal to the amount of fluid displaced from the box. Although there have been many refinements over the last 50 years, the present procedure is based on the system devised by Schäfer and Moore (1896) and subsequently adapted for the human limb by Brodie and Russell, (1905), and Hewlett and van Zwaluwenburg (1909). In this system, the limb, or a segment of it, is sealed in a rigid jacket so that volume changes in the enclosed part will displace

the fluid in the space between the limb and jacket. These changes are measured by a volume recorder.

To obtain reliable, reproducible measurements of limb blood flow, certain essential principles of the venous occlusion method need to be observed: - i) that the venous occlusion (not affecting arterial inflow) be as complete and instantaneous as possible so that there is an immediate increase in limb volume (Landowne & Katz, 1942); ii) that the part of the limb to be measured is clearly defined; iii) that calculations are made using the initial slope of the curve obtained on the recorder. (Fig 1).

This is essential because the rate of the volume increase indicates the rate of (arterial) blood inflow from which can be determined the limb blood flow below the tourniquet. From Figure 1 it can be seen that after a few seconds this rate of volume increase declines. This is due to several factors. First, that with continuing application of the cuff, capillary and venous pressures rise and finally exceed the pressure of the occluding cuff. This results in an escape of blood through the veins under the cuff. Second, there is a slowing of inflow into the limb distal to the cuff due to increasing resistance in the distended limb. Third, the flattening of the slope after the initial rise represents the capillary filtration curve. The assumption is that the rate of volume increase at the start of the venous occlusion is equal to the rate of unimpeded arterial blood flowing into the limb just before the venous occlusion (Landowne & Katz, 1942).

FIGURE 1.

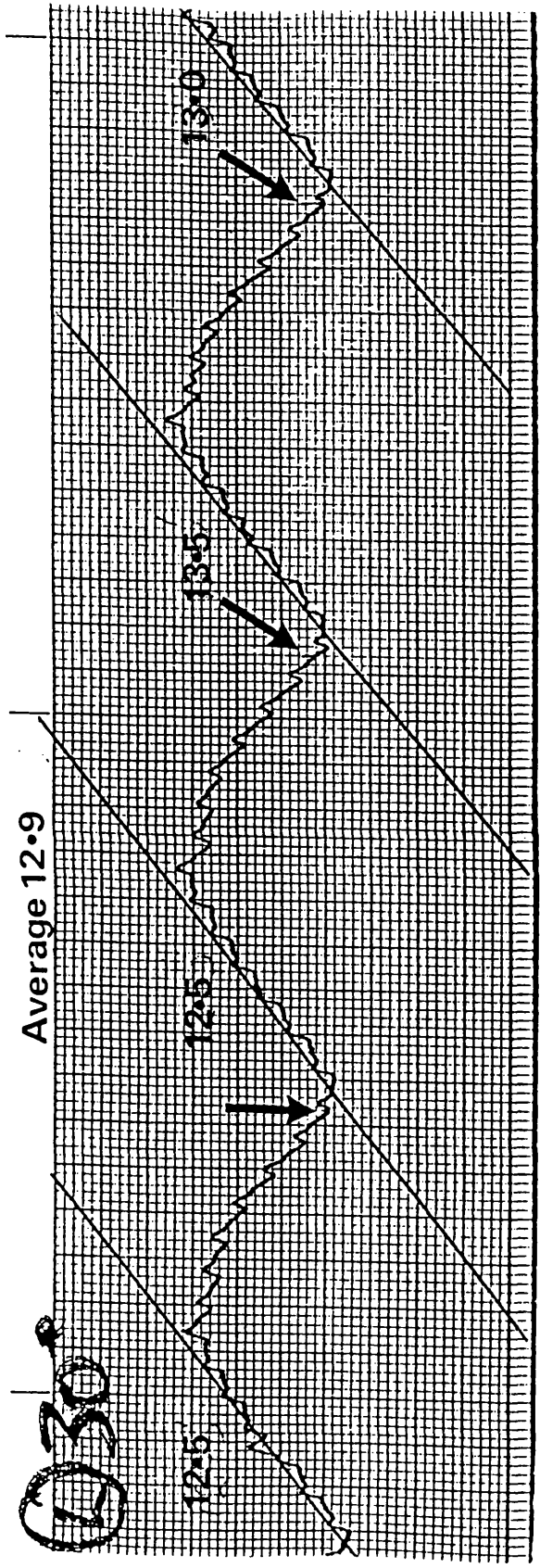
Venous occlusion plethysmograph trace.

The strain-gauge was placed around the greatest circumference of the calf, and the distance measured from the superior border of the patella with the quadriceps femoris muscle relaxed. (See p.108).

The arrows indicate the points of mechanical inflation of the thigh cuff, and the small inflation artifact can be seen as a tiny vertical spike before the trace begins to rise. The cuff was rapidly inflated automatically to 50 mm Hg and held at that pressure for 5 seconds. Swift automatic deflation followed. After a further 5 second interval the cycle was repeated.

The size (gain) control on the SPG 16 unit (Vasculab, Medasonics, California) was x2, the unit was DC coupled for venous recording, the paper speed on the R12B chart recorder (Vasculab, Medasonics, California) was $5\text{mm}\cdot\text{sec}^{-1}$, and the size switch on the R12B unit was set to x1.

A tangent was drawn to the initial rise in the trace (see p.52), and the vertical height measured after 3 seconds. This value appears above the curve of each period of occlusion, and the average height (12.9) noted. Blood flow was calculated from the formula mentioned in the text, page 109.



There are several types of plethysmograph but the volume displacement types (either of air or water) were not suitable for this study due to the nature of the ischaemic limb.

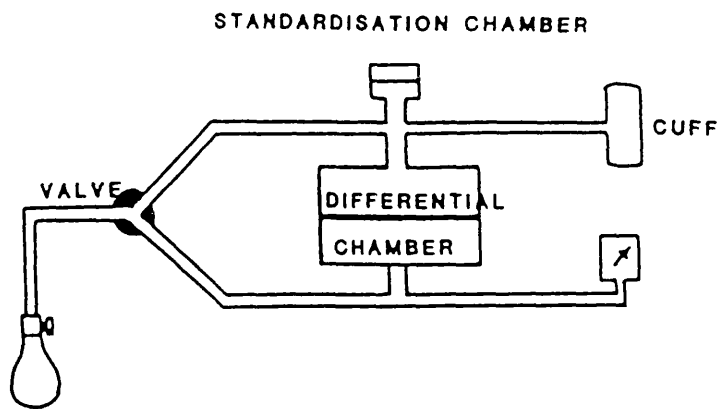
Segmental plethysmography.

When discussing segmental plethysmography, a distinction is usually made between an oscillometer and a segmental plethysmograph. The former records the pulsation of a limb or digit in arbitrary units, and the latter volume changes in millilitres (Woodcock, 1976). The principle of operation of both types, however, is the same, in that air pressure is measured in a cuff which is wrapped around the limb. As the limb swells the pressure in the cuff rises and this can be calibrated in terms of blood flow. The pulsation volume which is recorded by the oscillometer is, however, for our purposes too inaccurate, although it has application in the normal limb under strictly controlled conditions. The volume fluctuations are caused by the phasic inequalities during the cardiac cycle of arterial inflow and venous outflow (Greenfield et al., 1963). A segmental plethysmograph is represented diagrammatically in Figure 2. It is connected to a pneumatic system and the volume change in the limb is derived from the pressure changes over the cardiac cycle transmitted to one side of the diaphragm in the differential chamber (Raines, 1978). The shape of the arterial wave form (whether it is sharply rising or

FIGURE 2.

Pneumatic system of a Segmental Plethysmograph. (After a design by Winsor, 1957).

A cuff is placed around the limb, and the change in air pressure across the diaphragm in the differential chamber is measured following venous occlusion. As the limb swells, the pressure in the cuff rises, and this can be calibrated in terms of blood flow and expressed in millilitres.



'damped' and slowly rising) and the condition of the local vessels both affect the size and form of the fluctuations. So, too, does the position of the limb. Thus, elevating the forearm may treble the pulsation height on the wave form but reduce volume flow, (Holling & Verel, 1957), while in limbs with obstructive arterial disease where the pulse volume may be small, (i.e. the arterial wave form is 'damped'), the resting flow may be within normal limits (Shepherd, 1950). Furthermore, since it involves enclosing the limb, the method was not applicable to our work.

Capacitance plethysmography

Capacitance plethysmography works on the principle that there is a change in capacitance between two electrodes placed on either side of a limb segment due to the swelling of the limb after venous occlusion. Calibration and electrode artifacts may present difficulties; these are mentioned later.

Gravimetric plethysmography

Gravimetric plethysmography is based on the change in weight of a limb being directly proportional to change in limb volume (Smirk, 1933) and has been advocated as a method of obtaining total, as opposed to segmental, blood flow. It has been evaluated in both experimental animal work (Pappenheimer & Soto-Rivera, 1948) and clinical practice in man (Jackson & Matthews, 1977; Humphrey et al., 1980). For man it involves the suspension of both

legs at the ankles in a specially constructed weighing jig. The legs are held at 20° above the horizontal to minimise any venous distension before flow is measured. The elevation also prevents the occlusion cuffs, placed around the thighs, from touching the bed and thus introducing artifacts into the record. The technique is designed to measure blood flow in both legs simultaneously (Humphrey et al., 1980). However, the equipment is bulky and the position uncomfortable for the subject to the extent that some have found it intolerable (Cowell et al., 1979). Furthermore, obtaining successful measurements can be extremely difficult and in one study less than 50% of attempts were successful (L de Cossart & R W Marcuson, unpublished work).

Photoplethysmography

Photoplethysmography relies upon the knowledge that the amount of back-scattered light from illuminated tissue is dependent on the number of red blood cells present in that volume of tissue; i.e. the blood content. In principle, the photoplethysmograph emits infra-red light from a light-emitting diode into the underlying tissue and the back-scattered light is received by an adjacent photodetector. When the signal is filtered and coupled to a DC amplifier, it permits continuous recording of cutaneous blood content in the capillary plexuses (Abramowitz et al., 1979). The technique does not measure absolute flow in terms of volume per unit time, but only changes in blood content, and thus is only of value in the

estimation of relative changes in blood flow. It is also subject to variation in baseline dependent upon the amount of pigment in the skin (Gush et al., 1984); and if venous reflux due to valvular incompetence is present, then unreliable results will be obtained. The method has found considerable clinical application in the investigation of venous incompetence (Abramowitz et al., 1979), and in the monitoring of tissue oxygen saturation (Woodcock, 1984).

Impedance plethysmography

The variation in impedance of a tissue during the cardiac cycle is the foundation of impedance plethysmography. This is due to the changing number of ions brought into the tissue segment by the arterial inflow at a rate which exceeds the venous outflow (Kubicek, 1974). Two techniques have been described; a two and a four electrode technique. When two electrodes are used, they measure both the current and the voltage drop across them. The main disadvantage is that the current distribution in the vicinity of the electrodes is not known and therefore the precise tissue volume through which the current flows is unknown. In the four electrode technique, two electrodes are used to supply a constant current, and two more measure the potential difference between two points on the skin surface. These measurements may be affected by several factors. The major cause of a change in tissue impedance is a change in blood content - which is the underlying assumption of the technique. In the lower limb, van den Berg and Alberts

(1954) felt that absolute flow could not be measured unless the relative components of pulsatile and steady flow were known. However, in 1967, Hill and his colleagues suggested that the whole of impedance plethysmography was based on the measurement of an artifact produced by variable electrode contact (Hill et al., 1967). Later Brown et al went on to show that after filtering out of the impedance changes produced by cardiac action and breathing, which involved a variable contact between the skin surface and the electrode, there was no measurable signal (Brown et al., 1975). Woodcock, however, was prepared to accept that the conductivity and resistivity of the blood depended on the haematocrit and the velocity of the blood (Woodcock, 1984).

These techniques, photoplethysmography and impedance plethysmography, are used without venous occlusion. The latter is used more to measure cardiac output rather than to calculate limb blood flow (Woodcock, 1976).

Strain-gauge plethysmography

Strain-gauge plethysmography was the method employed in these studies and was originally described by Whitney in 1949. It utilises the change in resistance of a metal when it is stretched. This is brought about by the stretching of a fine bore silicone rubber tube filled with mercury and incorporated into a Wheatstone Bridge circuit (Whitney, 1949).

The method has several advantages over previous alternatives. The apparatus in contact with the subject

is small and light and does not involve either immersion of the part or exclusion of it by water or air-filled seals. It is thus suitable for use on patients with peripheral ulceration or gangrene as the gauge is circumferentially applied at mid-calf. Once the gauge has been calibrated, absolute measurements of limb blood flow may be calculated from the records obtained.

Plethysmography is based on enlargement of the limb, and for the purposes of strain-gauge plethysmography it is assumed that there is no change in dimension along the skeletal axis of the limb, and that changes in volume are therefore absorbed in corresponding changes in the transverse sectional area of the limb (Whitney, 1953). The following description of the theory is distilled from Whitney's original paper (1953).

Although the limb is not cylindrical, it can be shown that transverse sectional changes behave geometrically as if it were (Whitney, 1953). At any level of the limb along its axis, the percentage change in volume at that level will be equal to the percentage change of transverse sectional area at that level. Assuming that the shape of the section remains unaltered during expansion or contraction, the percentage change in area of the section will be twice the percentage change of the circumference of the section for small changes of area. The shape of the section remains constant if the measuring device imposes no restraint to the expansion of the deformable tissues, (in this case the calf), and these are truly elastic. Allowing that human limbs approximate to a

circular cross-section, (except at joints), on theoretical grounds fairly accurate volume changes can be derived from observed girth changes. Whitney stated that " the discrepancy between actual and deduced changes was never greater than 2% of the actual change."

A detailed description of the construction of the gauge and its circuitry can be found in Whitney's papers (Whitney, 1949; 1953). In summary, a fine bore silicone rubber tube was filled with mercury; the wall thickness was 0.8 mm and the internal diameter was 0.5 mm. The ends of the tube were closed with tapered copper pins to ensure good electrical contact with the mercury. (These copper pins have since been superseded by molybdenum pins).

Leads from the pins made the gauge one arm of a Wheatstone Bridge circuit. So long as this tube was under slight tension, the change in electrical resistance between the pins was directly proportional to the change in length of the tube (Eagan, 1961; Rushmer, 1955). Little force was required to extend the tube - approximately 15g wt per 1% extension (Greenfield et al., 1963) - but finer, more sensitive gauges are now in use of 0.6 mm external and 0.3 mm internal diameters. These only require a force of 200 mg for a 1% extension (Brugmans et al., 1977). Figure 3 shows the gauge itself (after Whitney, 1953). Brakkee and Vendrik (1966) simplified the calibration by the adjusting screw. The refinement of electrocardiographic triggering of the venous occlusion interval was added by Barendsen et al (1971), but it was not required for this work.

FIGURE 3.

Diagram of Whitney's Mercury-in-Silastic Strain-Gauge.

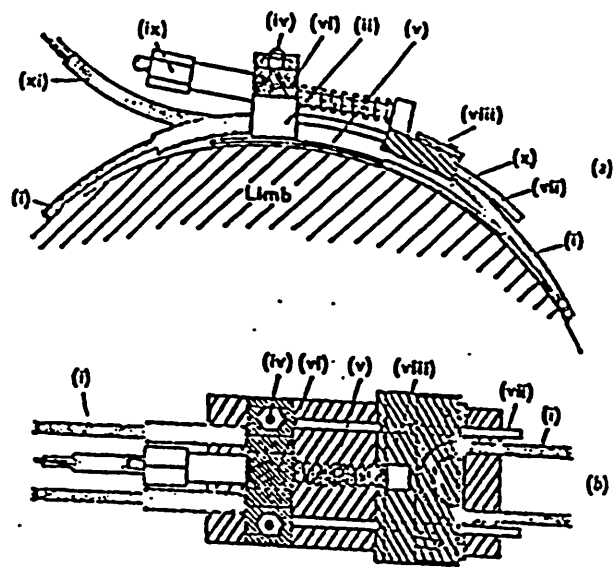
(After Whitney, 1953).

Constructional details of two-strand mercury-in-silastic rubber strain-gauge.

(a) Upper diagram; lateral view of gauge mounting, viewed along the axis of a limb to which the gauge is applied.

(b) Lower diagram; plan view of gauge mounting.

The plug in each end of the mercury -filled gauge (i) is secured in a hole bored in the terminal block (ii) by means of a set screw (iii). The two terminal blocks are each secured to the curved celluloid base (v) by means of a countersunk screw (iv), the ends of the screw protruding above the blocks providing attachments for the Perspex bridge (vi). Each block also carries a curved guide rail (vii) for the sliding Perspex block (viii). A semicircular groove in (viii) accommodates the looped end of the gauge rubber, the rubber being kept in the groove by means of the hinged flap. The adjustment screw has a hinged attachment to the sliding block and passes through the Perspex bridge, any backlash of the adjusting nut (ix) being absorbed by the compression spring mounted on the screw between the bridge and the sliding block. The copper winding for thermal compensation (x) is mounted on the celluloid base, and the three electrical leads from the winding and the two terminal blocks are taken from the gauge by the three-core flexible lead (xi).



The electrical resistance of mercury has an appreciable temperature co-efficient which is important when measurements are to be made at different ambient temperatures. This problem had been solved by a coil of copper wire mounted on the Perspex gauge. This copper coil is subject to the same temperature changes as the mercury filling the gauge; as the remainder of the circuitry has a low thermal co-efficient, changes in the gauge resistance due to temperature changes are compensated by equivalent changes in the resistance of the copper wire (Whitney, 1953).

Later in our studies, as a result of problems with old equipment which was no longer repairable, the mercury-in-silastic strain gauge was replaced with a gallium-indium alloy in silicone tubing (Vasculab, Medasonics, California). This alloy is a liquid above 16°C, and is attached to a Velcro strap which is placed around the limb in the same way as the Whitney gauge. Its cable is connected to one input channel of the amplifier which in turn is connected to a chart recorder. (See Fig 1). Any increase in the volume of the limb or digit will stretch the strain gauge. The electrical path through the conductive alloy in the gauge is therefore made longer and thinner and as a result causes an increase in the electrical resistance of the gauge. The percentage increase in this electrical resistance is mathematically equal to the percentage increase in the volume of the limb around which the strain-gauge is placed.

iii) Duplex Ultrasound Scanning.

In this system a pulsed, range-gated Doppler flowmeter is combined with a B-mode real-time scanner. A single transducer acts as both transmitter and receiver, and during the interval between pulses the transducer receives the scattered signal from the moving blood cells. By means of a gated receiver, the transducer can accept signals from any point across the vessel lumen (Woodcock, 1976). From measurement of the width of the blood vessel and the velocity of the blood, volume flow in the insonated vessel can be calculated (Fish, 1975; Coghlan & Taylor, 1976). One disadvantage of the system is that the distance from the skin to the vessel being imaged can give rise to distortion and ambiguity of the signal received. This is because the pulse repetition frequency is related to the maximum distance of the target from the transducer and the velocity of ultrasound in the tissues (Woodcock, 1979; 1984). Thus, the ultrasound pulse must be allowed to travel to the target vessel and return to the transducer before the next pulse is emitted. If this does not occur, the out-going pulse will collide with the returning pulse and an ambiguous or distorted signal will result.

Although the technique is of value in the surveillance of graft patency in the limb when the graft is relatively superficially placed in the tissues - as in femoro-popliteal or femoro-distal grafts - (Grigg, 1988), it is of little value in the initial assessment of the ischaemic limb as, with the exception of the femoral artery at the

groin, the major arteries are too deeply placed for clear signals to be obtained. This puts limitations on the evaluation of flow in deeper vessels. Newer equipment is now becoming available which may overcome this problem.

iv) Magnetic Resonance Imaging.

Atomic nuclei have three main characteristics which allow them to be influenced by a magnetic field - a net positive charge, a spin, and an associated magnetic moment. When placed in a unidirectional magnetic field, the nuclei experience torque in the applied field, and their axes of spin rotate about the direction of that applied field like miniature bar magnets. If a coil is then placed around the part under investigation and a current induced at 90° to the original field in a pulsed fashion, the nuclei will be tipped away from alignment with the steady radiofrequency field. This movement can be detected, and when two fields are placed around blood vessels, a difference is seen in the signal amplitude when the flow velocity changes (Morse & Singer, 1970). By using ECG gated time sequences of the images obtained, relative blood flow changes over the cardiac cycle can be assessed. When used in conjunction with the flow graph system of blood velocity estimation described by Singer (1981), quantitative blood flow measurements can be made (Woodcock, 1984). This apparatus, however, is very costly and was not available.

2. Skin Perfusion and Cutaneous Blood Flow.

While measurement of total limb blood flow may give information on the blood supply available to the tissues of the limb as a whole, it gives no indication of relative perfusion of different tissues within that limb. Relative ischaemia of the calf muscle, especially after exercise, will give rise to the clinical condition of claudication, while hypoperfusion of the skin and subcutaneous tissues may present as rest pain, ulceration or gangrene. When a leg has to be amputated because of irrecoverable ischaemic disease, Sarmiento and others found that the skin flaps would necrose and the amputation fail if the skin was not adequately perfused. This was true even when cut muscle at the same level appeared to show good bleeding (Burgess et al., 1971; Sarmiento et al., 1979). So there is a need to know how the total limb flow is distributed, both at rest and when the circulation is stressed either by exercise or change in ambient temperature.

In clinical practice, an assessment of skin blood flow is often guessed at by simple palpation of the limb and feeling the degree of warmth, on the assumption that skin temperature is indicative of the state of the cutaneous circulation. However, studies in our unit have shown that the relationship between skin blood flow and skin temperature is a complex one and in no way linear (Stoner et al., 1990).

Selective investigation of the cutaneous microcirculation has, until recently, been performed by clearance or washout techniques of radio-isotopes. Since 1972 the development of the laser Doppler technique

has allowed another method to be evaluated (Riva et al., 1972). The same year Holstein described a method of estimating cutaneous blood flow by what he termed the " skin perfusion pressure " (Holstein, 1973). This could be determined by either an isotope clearance or photoplethysmographic technique.

i) Isotope Clearance:

In 1948 Kety first described the clearance or washout of radioactive sodium (^{24}Na) from muscle tissue by the blood stream (Kety, 1948). Problems arose because removal of the sodium ion from the tissues was limited by diffusion, namely that corresponding to passage across the capillary membrane, and so the rate of washout of radioactive sodium could not provide a quantitative measure of blood flow. When the freely diffusible radio-isotopes of the inert gases Krypton and Xenon became available, this was no longer an impediment to the technique (Braithwaite et al., 1951; Lassen, 1964). Further progress was made when Sejrsen (1971) demonstrated that the epicutaneous application of ^{133}Xe achieved results that agreed well with those obtained by its subcutaneous injection. A small amount of the gas was introduced by syringe and needle underneath a 1.5 cm diameter plastic membrane held on the skin by an adhesive ring. The gas then diffused into the skin and subcutaneous tissues, and the clearance was measured by an external gamma radiation counter. The curve obtained provides an estimate of tissue blood flow. Sejrsen had noted previously (1969) that during the washout process

^{133}Xe accumulated in the subcutaneous tissues, so he performed a series of experiments to investigate this. His aim was to separate the components of the skin and subcutaneous tissues to see if it were possible to estimate the flow through cutaneous tissue only. Tissue was excised from human subjects at various times after ^{133}Xe had been applied either intracutaneously or epicutaneously. Following microdissection and radioautography of thin sections of this tissue, he showed a uniform distribution of ^{133}Xe within the cutaneous tissue at all times. Commenting on Sejrnsen's work, Gush et al (1984) felt that if the papillary loops were presumed to play an active part in the clearance of ^{133}Xe from the skin, then it might have been expected that the radioautograms would demonstrate clearance from the most superficial tissues of the dermis first, but this was not observed. They went on to say that transport of isotope from the counting area will be a function of both convection, (in cutaneous venous blood), and diffusion. But as ^{133}Xe is freely diffusible, it will be cleared effectively only by vessels with swift flow actually leaving the depot, i.e. arterioles and venules, and not capillaries in which there is equivalent flow in all directions (Gush et al., 1984). Other constraints of the technique are firstly that the solvent capacity of the tissue and blood change with temperature; secondly, skin loss or ulceration affects the loss of xenon from the skin surface by 30-40 fold, (normal loss is around 1-2%); and thirdly, that it is an exceptionally time-consuming

exercise, taking up to 2 hours to obtain a clearance curve from one site alone (Sejrsen, 1969; 1971).

ii) Skin Perfusion Pressure. (SPP).

This means of assessing cutaneous blood flow is based on the measurement of pressure in a blood pressure cuff required to prevent washout of an isotope or a signal on photoplethysmography (PPG). The PPG technique is faster and less invasive than the isotope technique, and some authors claim to use SPP - measured by PPG - routinely as their method of determining the level of amputation (Holstein et al., 1980; Stockel et al., 1982; Holstein & Hansen, 1988). However, as both methods involved encasing the limb in a plastic bag, and the isotope was given by intra-dermal injection, neither method was suitable for our studies.

iii) Laser Doppler Flowmetry.

When laser light from a helium-neon laser of 632.8 nm wavelength in vacuum illuminates skin tissue, it is diffusely scattered. This is brought about by the effect of the tissue refraction index on the incident light beam. It has been shown that the penetration depth of this laser light in skin is around 1 mm (Stern et al., 1977; Nilsson et al., 1980; Bonner & Nossal, 1981). For tissue with a low or moderate volume fraction of red cells, the greater part of the light beam is scattered in static tissue structures and remains unshifted in frequency. However, some light is scattered by moving red blood cells and

undergoes a frequency shift according to the Doppler effect. The Doppler frequency shifts depend on blood velocity and on the scattering geometry such that the Doppler shift is minimal when the light scattering blood cell travels perpendicularly to a photon that it scatters, and is maximal when their directions are parallel. Tissue blood volume also affects the degree of multiple scattering (Gush et al., 1984). The capillary loops are mainly oriented perpendicularly to the skin surface with the underlying venous and arteriolar plexuses parallel to the surface (Spalteholz, 1893; Petersen, 1935; Horstmann, 1964; Sparks, 1978). This results in a frequency shift of $4.4 \text{ kHz mm}\cdot\text{sec}^{-1}$ of red cell velocity at a vacuum wavelength of light of 632.8 nm and a tissue refractive index of 1.4. Information about the blood flow in the skin is contained mainly in the alternating portion of the photodetector output signal once it has been processed further (Tenland, 1982). For tissue with a low or moderate red cell fraction, the relative proportion of light which has undergone Doppler shift is approximately in linear relationship with the volume fraction of moving red cells in the tissue, and the mean Doppler frequency is linearly related to the average red cell absolute velocity. But in highly perfused tissues such as a dilated finger-tip, there is a more complex relationship between red cell flux and the Doppler signal, (Nilsson et al., 1980), not least because of the relative density of arterio-venous anastomoses described by Grant and Bland (1931). These are found in abundance in the fingers and

toes, palms and soles, and areas on the face and ears (Ryan, 1973). They are part of a thermoregulatory control mechanism and modify the blood flow through the capillary loops (Johnson et al., 1986). In this way they exert an influence on laser Doppler blood flow measurements (Englehart & Kristensen, 1983).

In 1975, Stern first used a laser Doppler technique to assess skin blood flow. He used a 15 mW powered helium-neon laser and analysed the frequency of the back-scattered light from the skin passing through a pin-hole and detected by a photomultiplier. He observed the changes in width of the frequency spectrum related to blood flow in the finger-tip after release of an arterial occlusion cuff, and after the ingestion of alcohol (Stern, 1975). Since then numerous studies have been performed to investigate the microcirculation of the skin and other tissues, and comparisons made with the xenon washout technique (Holloway & Watkins, 1977; Stern et al., 1977; Watkins & Holloway, 1978; Damber et al., 1982; Duteil et al., 1985; del Guercio et al., 1986). The drawbacks of the xenon washout technique have already been described, and in the present study skin microcirculatory flow was assessed by a helium-neon laser Doppler technique.

3. Tissue Nutrition.

Although it is important to assess blood flow to the skin because of its positive correlation with healing of amputation wounds (Burgess et al., 1971; Sarmiento et al., 1979), it would appear that flow by itself gives little

indication of the state of tissue nutrition. Early work by McEwan and Ledingham (1971), using strain-gauge plethysmography and blood gas analysis of samples taken from foot veins, attempted to correlate regional blood flow and tissue oxygenation derived from mathematical formulae based on an assumed arterial oxygen tension. These studies were performed on clinically ischaemic feet in 13 patients and compared with 17 control subjects. Despite the presence of rest pain, ischaemic ulceration or local gangrene, they did not demonstrate any evidence of " overall regional ischaemia ". Indeed, they showed a consistently increased resting total blood flow in the ischaemic feet. Nor could they find any tissue anoxia to explain the aetiology of the chronic nutritional skin changes in the apparently ischaemic feet. They concluded that " the physiological effectiveness of a regional blood flow ultimately depends on its ability to perfuse the tissues, and...that ischaemic or anoxic nutritional skin lesions develop in the presence of localised tissue perfusion failure and not from any overall regional blood flow insufficiency."

The development of transcutaneous gas tension measurement.

So it seemed that a more sensitive indicator of cutaneous perfusion was needed. In the two years that followed, two separate groups in Germany described the use of transcutaneous oxygen tension (T_{cpO_2}) measurement as it was found to approximate closely to arterial pO_2 (PaO_2) when a heated Clark electrode was placed on the skin of a

neonate (Eberhard et al., 1972; Huch et al., 1973).

Oxygen exchange across the skin was first observed by von Gerlach in 1851 when he analysed the composition of the gas bubbles which formed beneath the shellac applied to the shaved skin of horses, dogs, and man (cited by Rithalia, 1989). One hundred years later, Baumberger and Goodfriend (1951) reported the measurement of the 'PaO₂' through intact human skin. This was achieved by determining the pO₂ of a buffered phosphate solution in which a finger had been immersed and allowed to equilibrate. It was not until 1956 however, that Leland Clark produced his polarographic oxygen electrode. It had, in fact, been built two years earlier, and made transcutaneous pO₂ measurements a practical proposition (Clark, 1956). But it was not until the 1970's that Eberhard (1972) and Huch (1973) with their co-workers independently demonstrated that stable skin surface pO₂ values could be obtained if the electrode was heated to produce local hyperaemia.

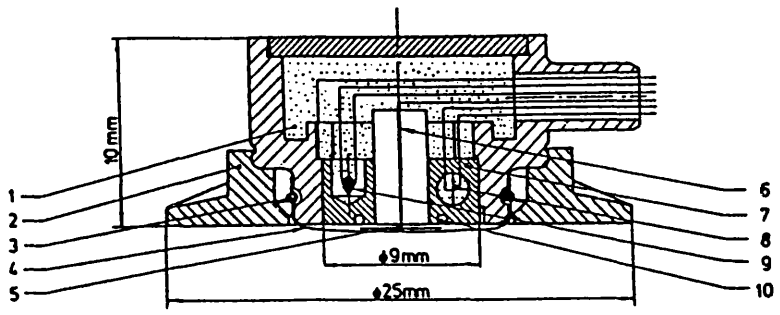
Today's probes for T_{cp}O₂ measurements consist of three parts; i) a Clark-type polarographic electrode with a platinum cathode and a ring-shaped silver/silver chloride anode; ii) a heating element to produce hyperaemia of cutaneous capillaries; iii) a thermistor, linked to a control circuit to keep the electrode at a fixed temperature, usually 44°C. The current then produced by the electrochemical reduction of oxygen at the surface of the cathode ($O_2 + 2H_2O + 4e^- \rightarrow 4OH^-$) is proportional to the partial pressure of oxygen (Tremper, 1984). (Fig 4).

FIGURE 4.

The Clark-type Polarographic Electrode.

This is a schematic cross-section. The electrode is calibrated, and heated to 44°C before each application to the skin.

lc - PO₂ electrode



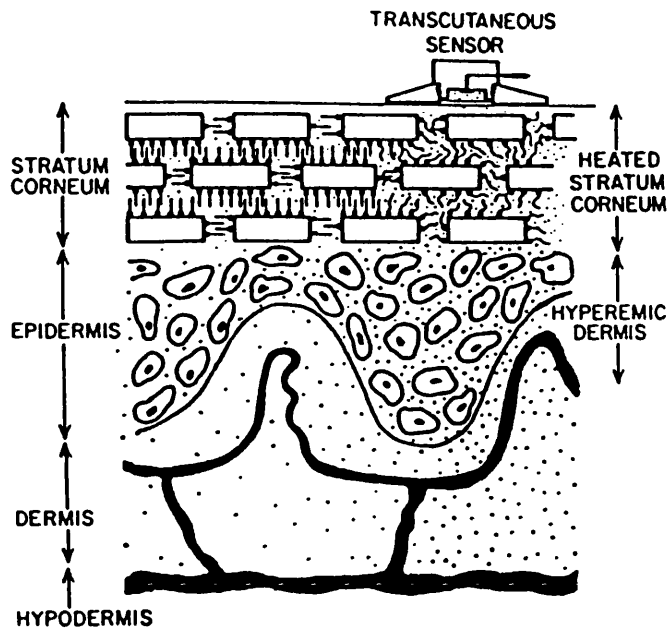
- | | |
|----------------------|-------------------------|
| 1: Epoxy resin | 6: Platinum cathode |
| 2: Retaining ring | 7: Silver anode |
| 3: O-ring | 8: Heating element |
| 4: Teflon membrane | 9: NTC resistor |
| 5: Cuprophane spacer | 10: Electrolyte chamber |

The reason for heating the electrode is to facilitate diffusion of oxygen through the stratum corneum of the skin . This, the most superficial layer, is composed of keratin filaments in a matrix of lipid and non-fibrous protein, forming a very effective barrier to diffusion by virtue of its compressed, interdigitated, regular crystalline structure (Tremper, 1984). So effective is this barrier that the diffusion constants for water and oxygen are in the range of $5 \times 10^{10} \text{ cm}^2 \cdot \text{sec}^{-1}$ and $2 \times 10^8 \text{ cm}^2 \cdot \text{sec}^{-1}$ respectively, which is similar to that of a gas through solid metal foil (Shaw & Messer 1930; Scheuplein & Blank, 1971). If this layer is removed, there is a vast increase in gas exchange (Tolle et al., 1982). This phenomenon was explained by van Duzee (1975) who studied the structure of the stratum corneum at increasing temperatures. He noted a reversible change from the regular crystalline structure to a random architectural appearance at temperatures above 41°C . When the temperature was lowered, the regular crystalline structure reappeared. He concluded that the lipid component of the stratum corneum was melting at approximately 41°C . This transition from solid to liquid phase is thought to increase the diffusion constant and allow gases to diffuse through the stratum corneum 100 - 1,000 times faster. Thus, the heated transcutaneous sensor 'melts' a diffusion window to the living tissue beneath (van Duzee, 1975). (Fig 5).

FIGURE 5.

Schematic cross-section of the Clark-type electrode on the skin. (After Tremper, 1979).

The heated (44°C) transcutaneous sensor 'melts' a diffusion window through the skin to the tissues beneath. The irregular structure of the stratum corneum beneath the electrode represents the melted lipid. The dots represent oxygen.



Transcutaneous oxygen tension measurement can produce useful data for the clinician.

The most significant determinant of $TcpO_2$ measurements on the skin of ischaemic limbs is the local arterial perfusion pressure, although other factors such as skin thickness, electrode oxygen consumption and membrane type - polypropylene or teflon - along with local oedema can all influence the $TcpO_2$ readings (van Urk & Feenstra, 1988). That poor peripheral perfusion pressure results in a large gradient between PaO_2 and $TcpO_2$ can be shown not only in those with ischaemic limbs but also in the critically ill with poor cardiac performance (Rooth et al., 1976; Tremper, 1984). $TcpO_2$ monitors have also been used in the assessment of trauma cases in the emergency department, and low $TcpO_2$ values have been shown to predict hypovolaemia even in the presence of normal blood pressure (Waxman et al., 1983). Our interest in $TcpO_2$ measurement lies in determining to what extent it reflects regional perfusion and tissue nutrition, for many authors have used $TcpO_2$ values both to determine amputation levels and to assess the effectiveness of by-pass grafts (Matson et al., 1980a,b; Mustapha et al., 1983; Hauser & Shoemaker, 1983; Ratliff et al., 1984; Rhodes & Skudder, 1986).

Hauser and Shoemaker (1983) suggested that the ratio of limb to trunk $TcpO_2$ might be a more reliable reflection of local limb oxygen supply as it was independent of variations in systemic oxygen delivery. This was termed the 'regional perfusion index', and although these

workers and others (Katsamouris et al., 1984) found the test to be highly specific and reproducible - even as a means of grading intermittent claudication - more recent studies have not been able to achieve similar results (Holdich et al., 1986). Rhodes & Skudder, (1986) felt that there was no need to map the chest value unless there was concern that the " machines are drifting or the patient is hypoxic at rest." Neither situation applied in our studies.

Magnetic Resonance Spectroscopy is a recent development which is still being evaluated, but may prove to be useful in recognising irreversible limb ischaemia.

Where $TcpO_2$ measurements give information on the amount of oxygen available to the skin, they cannot be any more than a crude guide to tissue survival or viability. The degree and rate of metabolism may alter, and chronic ischaemia is likely to affect the working of cells. Angquist and Sjöström (1980) have shown there is an increase in the number of mitochondria in ischaemic muscle cells such that the maximum use is made of the low concentration of available oxygen. Others have been able to demonstrate cellular damage as a result of chronic ischaemia, leading to a gradual loss of the structural proteins and enzymes essential for function (Teräväinen & Mäkitie 1977; Clyne et al., 1985). It is in this area of assessing cellular function that the technique of Magnetic Resonance Spectroscopy is being used to determine tissue viability.

The principle is the same as described for Magnetic Resonance Imaging, but in this situation the [³¹P]phosphorus nucleus is under investigation. The shift in alignment of the nuclei which occurs when the pulsed secondary magnetic field is applied results in radio-frequency electromagnetic wave signals leaving the molecule. From the particular characteristics of the returning signal, it can be determined whether the phosphorus is in phosphocreatine, ATP or inorganic phosphate (Hands, 1988). Although still a research tool, studies with the technique in the ischaemic limb have shown a rise in the inorganic phosphorus to phosphocreatine ratio associated with a gradual reduction in the returning signal as muscle necrosis sets in (Hands, 1988).

4. Skin Temperature Measurement.

The assessment of skin temperature as an indicator of health or disease in a part of the body has been in practice since at least the time of Hippocrates who lived around 400 BC. He is alleged to have applied wet mud to the skin of his patients and pronounced the area that dried first to be the site of disease (cited in Winsor & Bendezu, 1964). Even today it is common for a clinician to run his hand over the surface of the body to determine if, in his opinion, there may be any underlying inflammatory process present, based on his subjective impression of heat in a localised area. What is not clear however, is the way these data should be interpreted

by the clinician and what assumptions may be made about the underlying presence or absence of pathology. For example, in vascular surgery, decisions as to whether or not a limb is viable may be based on the impression of tactile warmth. But without objective and comparative measurement, wrong conclusions may be drawn.

Measurement of cutaneous temperature has thus been of interest to physicians and surgeons for centuries.

In 1821 Sir Humphrey Davy discovered that the resistance of a metal changes with temperature. This finding was exploited by Sir William Siemens who, in 1871, using platinum as the sensor, developed the electrical resistance thermometer. The platinum resistance thermometer was perfected by Hugh Longbourne Callendar and others, and is the most stable and accurate thermometer available.

At the same time that Sir Humphrey Davy was making his discovery, Thomas Johann Seebeck in Germany observed that an electric current is generated when two dissimilar metals in contact are held at two different temperatures (1822). Thermistor thermometers developed from the first discovery, and thermocouple thermometers from the second. Both are capable of providing excellent accurate and reproducible spot temperature measurements. But no more than that.

The discovery of 'infra-red' rays.

It was the observations made by Sir William Herschel (1800) when passing sunlight through a prism that led the

way to modern thermography. His discovery allowed the temperature of whole limbs, or even the whole body at a time to be assessed, and not just point temperatures. This meant that any individual spot temperature could then be interpreted in the context of the entire limb or body. Herschel discovered that if sunlight was passed through a prism to display the spectrum of visible light in its separate colours, and a thermometer bulb placed into each of the coloured bands in turn, the temperature would rise as the red end of the spectrum was reached. More importantly, he noted that the temperature continued to rise when the thermometer was placed beyond the visible red end of the spectrum. He concluded that the sun had rays which were invisible to the naked eye, and which had heating properties greater than those of visible light, and resided beyond the red end of the spectrum. He called them 'infra-red' rays.

The first 'thermographs'.

His son, Sir John Herschel, continued his father's research. He investigated ways of making visible these 'infra-red' rays. He covered strips of paper with lamp black and soaked them in alcohol. When infra-red rays were focussed on these strips, the alcohol evaporated more rapidly from the parts which received the stronger radiation and so appeared lighter in colour. Sir John called these pictures 'thermographs' (Herschel, 1840).

It was not until the 1950's however, that medical thermography had its beginnings. By this time the

equipment had developed so that an infra-red detector was housed in a floor-mounted camera.

The physics of infra-red imaging.

It is worth outlining some of the physics involved in heat transfer and how the technique of thermography is related to the electro-magnetic energy spectrum, so that an understanding of the method may make interpretation of the results obtained more meaningful.

Although in modern hospitals it is the practice to use clinical thermometers which measure body temperature in degrees Celsius, (named after the Swedish astronomer in 1742), for the purposes of the following discussion the Kelvin scale will be used.

" Heat radiation is the term for the energy exchanged between any two bodies in the universe that have a difference in their temperature " (Clark & Edholm, 1985). The Stefan-Boltzmann law further states that " a solid body heated to a temperature above absolute zero will radiate energy in the form of electromagnetic waves at a rate proportional to the fourth power of the temperature ($^{\circ}\text{K}$) " (Poole, 1976).

Thus: $E = eC_1T^4$ where E is the radiant power of a black body having an absolute temperature T; e is the emissivity of the surface; C_1 is Stefan's constant ($= 5.7 \times 10^{-8} \text{ W/m}^2/\text{K}^4$); and T is the absolute temperature in degrees Kelvin.

A black body is an object which absorbs all radiation that impinges on it of any wavelength. In fact, 'black'

is a misnomer, explained by Kirchoff's Law which states that a body capable of absorbing all radiation of any wavelength is equally capable of emitting radiation of any wavelength. The spectral distribution of radiation from a black body is dependent on the absolute temperature of the body. (Fig 6).

Examples of 3 different spectral distributions of radiating bodies are shown in Figure 6, and similarly in Table 1 are some examples of the relationship between temperature and maximum wavelength (w_{Max}). From these it can be seen that radiation from the human body has a maximum wavelength of 9.3 microns.

Within the electro-magnetic energy spectrum as a whole, the infra-red band is sandwiched between visible light and radio waves. The infra-red band itself is also subdivided, and the various regions named according to their proximity to visible light. (Fig 7).

Although human emission comes from the far infra-red waveband, the detectors used to measure these emissions utilise the 3-5 nm or middle infra-red band.

Infra-red detectors.

Detectors can be divided broadly into two groups; those that are non-selective, and respond to radiation over the whole wavelength region, and those that are selective, responding only to a limited spectral range. For these studies, where a limited range of radiation energy was being explored, the non-selective group were inappropriate. Examples of the selective detectors

FIGURE 6.

The Spectral Distribution of Radiating Bodies.

The spectral distribution of radiating bodies is dependent on the absolute temperature of that body.

From this graph it can be seen that radiation from the human body has a maximum wavelength of 9.3 microns (or 9300 nanometers).

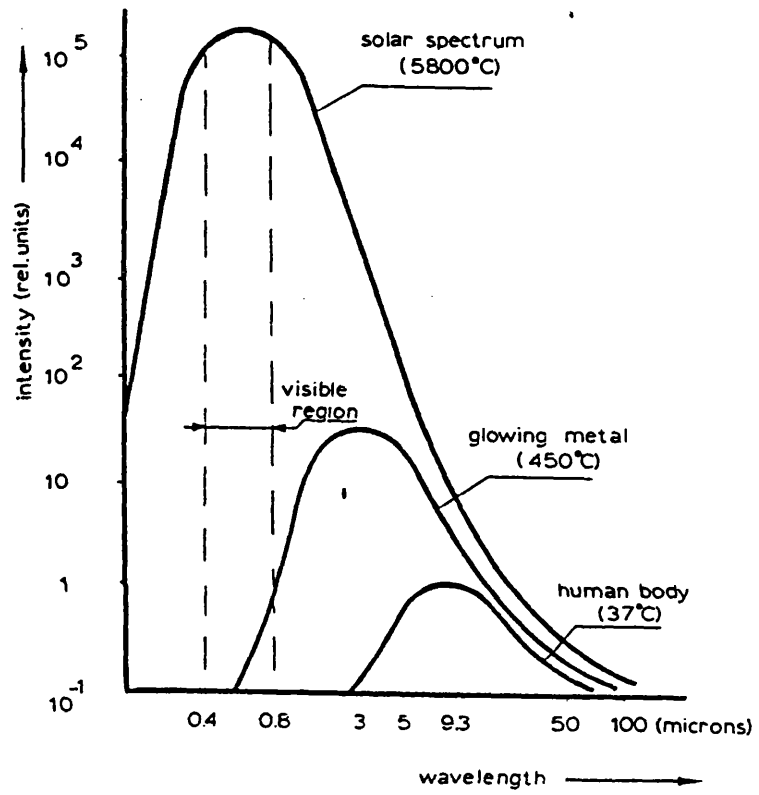


TABLE 1. Sources of Radiant Heat.

<u>Object</u>	<u>Temp. °C</u>	<u>Abs. temp. °K</u>	<u>w Max (μ)</u>
Sun	5800	6073	0.5
Glowing metal	450	723	3.9
Boiling water	100	373	7.8
Human body	37	310	9.3
Melting ice	0	273	10.7
Liquid nitrogen	-196	77	36.1

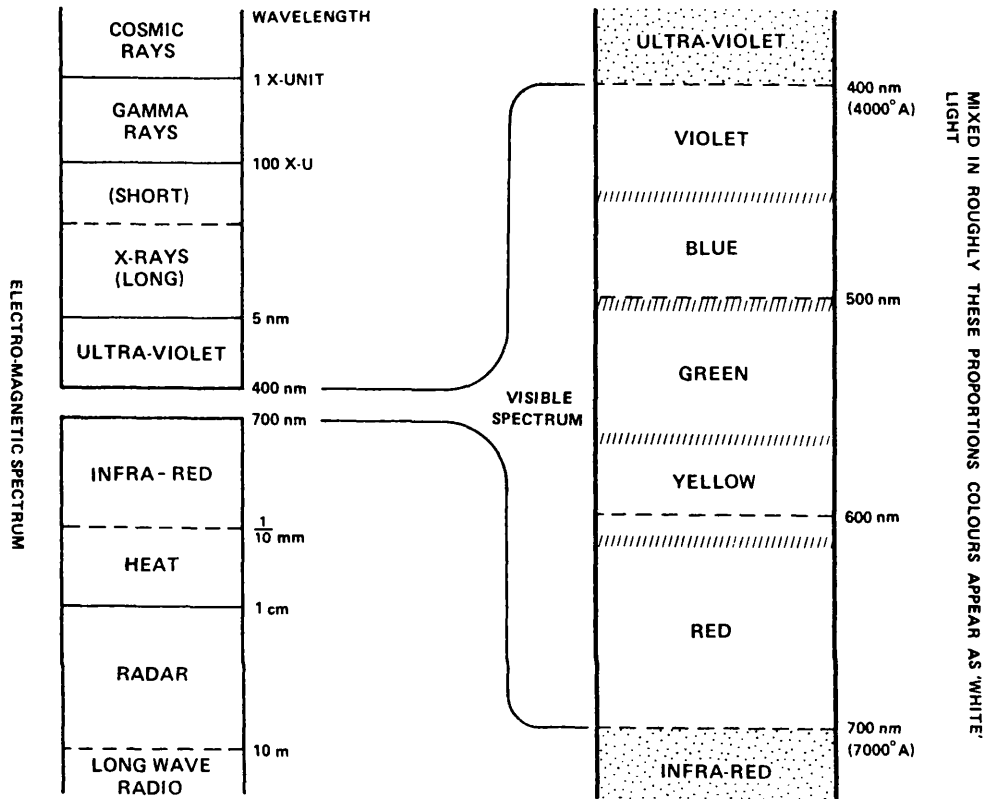
FIGURE 7.

The Infra-red Spectrum within the electromagnetic spectrum.

The position of the infra-red band within whole electro-magnetic spectrum can be seen from the diagram. The infra-red band itself is further subdivided into near (800-3000 nm), middle (3000-6000 nm), far (6000-15000 nm), and extreme (15000-50000 nm) infra-red bands.

Although human emission comes from the far infra-red band, around 9000 nm (9 microns), the detectors used to measure these emissions utilise the middle infra-red band.

[1 millimeter \equiv 1,000 microns \equiv 1,000,000 nanometers]



include the photoelectric devices which work on the principle of photo-conductivity, photo-emission, or the photovoltaic effect. These devices have the advantage of not only being selective over a particular wavelength range, but also of having a rapid response time. This means that they react swiftly to sudden changes in temperature (Herstel, 1969). The responsivity, or signal-to-noise ratio is also at its best in this group of detectors (Poole, 1976).

The detector in our equipment was an indium antimonide semi-conductor, kept cool by liquid nitrogen at -196°C to improve the signal-to-noise ratio. Figure 8 shows its place in relation to other infra-red detectors. It was housed in a camera which was mounted on a mobile stand upon which it could be moved up and down.

The effect of the environment on infra-red emission.

For thermograms to be interpreted without introducing inadvertent bias it is essential that there is a well controlled thermal environment. This means that the ambient temperature, humidity, air speed, and amount of clothing being worn by the subject need to be rigorously controlled.

If, however, the subject being studied is not effectively a 'black body', the spectral emissivity is less than 1.0, and part of the radiation from the walls of the environment is reflected by the surface of the subject being studied. This could lead to erroneous readings of the thermographic images. Hardy (1934) showed

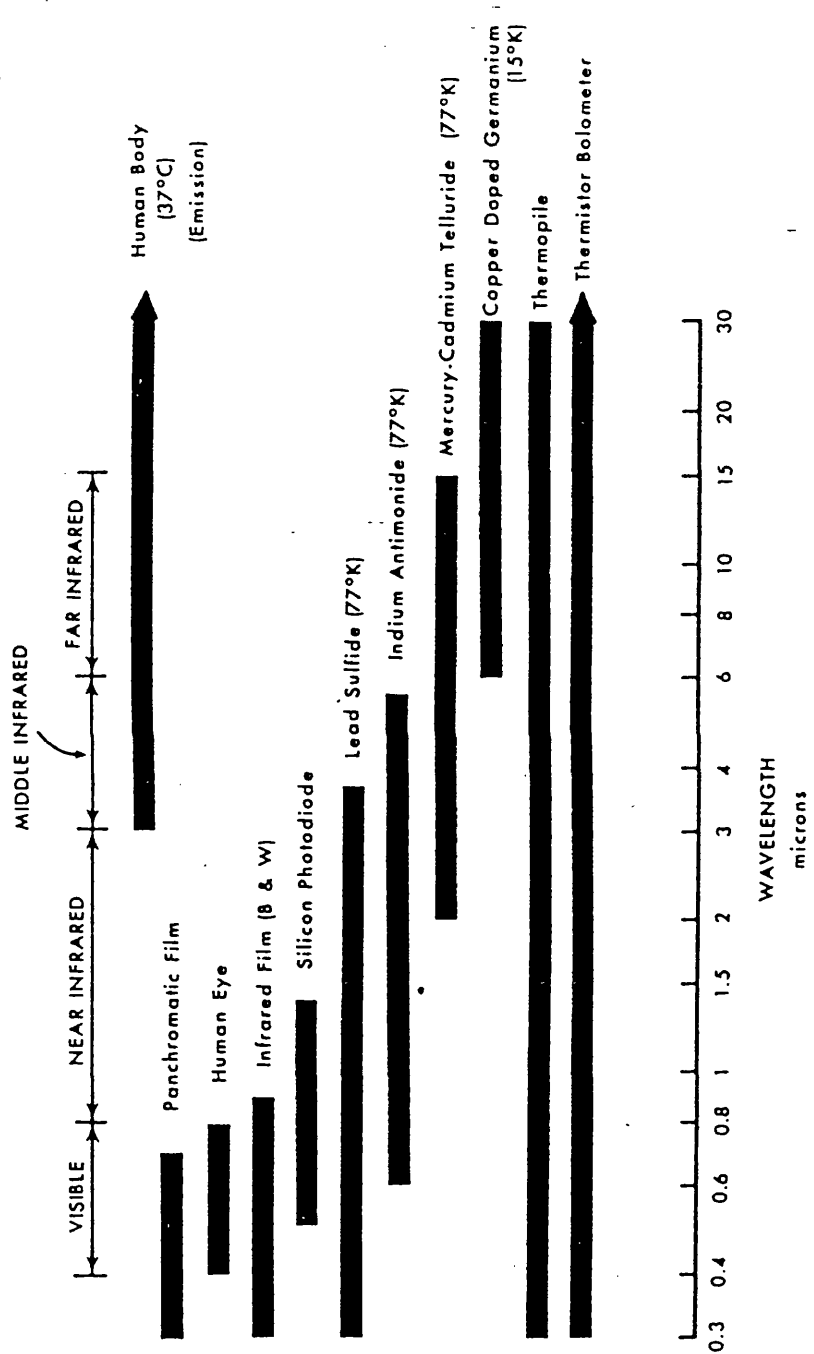
FIGURE 8.

The spectral range for various infra-red detectors.

(After Poole, 1976).

The detector used in our work was an indium-antimonide semi-conductor, cooled by liquid nitrogen at -196°C .

(Fifth from bottom in diagram).



there was no significant difference between the spectral emissivity of black and white skin. He went on to demonstrate that the emissivity of skin is 0.989 ± 0.01 and was, in fact, very close to the perfect black body radiator (Hardy, 1939). Steketee (1979) conducted a series of experiments from which he concluded that even when the walls of a measuring room are covered with aluminium foil, there is no influence on the radiation of non-black surfaces with ambient temperatures between 25°C and 50°C . Other authors (Gros et al., 1969) had recommended making corrections on the readings of radiation thermometers for the emissivity of the environment, but this is now thought unnecessary. Nor is it necessary to cover the walls with black paint or black curtains. Of more importance is the avoidance of strong radiation sources such as incandescent lamps, but even then the effect is relatively small. The greatest effect is brought about by increasing the number of people surrounding the object, as this raises the whole ambient temperature (Steketee, 1973).

How should skin temperature be interpreted clinically?

Enthusiastic use has been made of skin temperature measurement in many clinical areas but agreement is lacking on what this represents. It is by no means clear even at what ambient temperature these measurements should be made. Indeed, it would appear that the optimal ambient temperature for measurement depends on the objective of the study. Clark and Edholm (1985) stated that "...the

room temperature is chosen in relation to the clinical or physiological features being observed. For example, skin blood flow assessment requires temperatures of around 25-27°C, whereas 21-23°C is more suitable when identifying subcutaneous thermogenic structures." This statement has been challenged by Stoner and his colleagues who found that altering the ambient temperature from 20° - 30°C did not result in an increase in calf or forearm skin blood flow measured by reflectance plethysmography and a laser Doppler technique, although there was a increase in skin blood flow in the fingers, palms and toes (H B Stoner, unpublished work). What, then, is being measured? It was in order to try to answer this question that infra-red thermography was used in parallel with other non-invasive methods of assessing perfusion of the lower limb.

The effect of physiological stress on the circulation.

The circulatory and nutritional requirements of the body depend on factors which are not static, so there need to be regulatory mechanisms whereby these changing demands may be met. It is clear that the blood flow of the leg muscles at rest is not as great as when they are exercised. In the same way it is apparent that skin blood flow will increase in order to enhance heat loss from the body at high ambient temperatures.

These parameters may be studied in healthy volunteers and the trend of results anticipated. In the ischaemic limb, by contrast, the responses are less predictable and there is thus a need to subject those under study to a

form of physiological stress to determine what changes occur in total limb flow, skin blood flow, tissue nutrition and skin temperature. By finding what may be achievable in terms of alteration of flow in these ischaemic subjects, it may be possible to predict which patients are likely to benefit from revascularisation procedures or sympathectomy, and in those with end-stage ischaemia, at what level an amputation might heal without complications.

In order to perform these stress tests it was necessary to appreciate from the outset that many subjects with ischaemic limbs would not be able to tolerate any form of exercise testing, although those that could had their resting and post-exercise ankle Doppler pressures measured routinely before surgery. For this reason, in the ischaemic group where exercise testing was not possible, stress was applied by raising the ambient temperature of the measuring room from 20°C to 30°C, with measurements taken at both temperatures. This raising of the ambient temperature has the effect of removing the resting sympathetic tone on skin blood vessels (Bini et al., 1980a,b; Wright, 1982). At normal room temperature (around 26°C) the skin vessels are subjected to little sympathetic vasoconstrictor discharge limiting the flow through them. Until recently, the classical view was that there was no active neurally driven vasodilatation of these vessels, although it had been suspected (Thauer, 1965), but Brengleman (1986) stated that "...in humans, thermoregulatory control of skin blood flow largely

derives from internal and surface temperatures and is implemented through two separate categories of sympathetic neurons, one adrenergic, the other with an as-yet-unidentified transmitter. These, when activated, cause vasoconstriction and vasodilation, respectively " (Johnson et al., 1986). Fox and Edholm (1963) had shown earlier that there were large increases in skin blood flow in hyperthermic (42°C) human subjects. They concluded that although the transmitter was unknown, the effect was brought about by active sympathetic vasodilation. The elusive nature of the neurotransmitter perhaps explains in part why investigators in this field of research have been reluctant to accept the theory of sympathetic vasodilator nervous control of skin blood vessels.

The aim of raising the ambient temperature was to increase the need for heat loss and to see if this might be effected by increased skin blood flow. It should be pointed out that it appears the thermoregulatory role of the cutaneous circulation is confined to those areas richly supplied with the arterio-venous anastomoses described by Grant and Bland (1931). These are abundant in the flexor surface of the hands and fingers, feet and toes, but are scarce elsewhere in the body except in some areas of the nose and ears. Although their existence had been described by Sucquet in 1862 (cited by Grant & Bland, 1931) many years before Grant and Bland's classic description (1931), their role and mode of action in thermoregulation have been the subject of much debate (Aschoff & Wever, 1959; Thauer, 1965; Sparks, 1978).

This will be discussed later.

For control subjects, exercise was a reasonable way of increasing limb blood flow, though it was recognised that the method whereby an increase in limb blood flow was achieved was different to that when the ambient temperature was raised.

A full description of the protocols, equipment and techniques follows in the next chapter.

CONTROL SUBJECTS, PATIENTS, PROTOCOLS, EQUIPMENT &
TECHNIQUES.

Brief summary of Control and Patient groups.

Control subjects formed 3 groups. A group of young (under 40 yr) volunteers in whom exercise stress testing was carried out (Exercise Controls); a group in which all had a peripheral arterio-venous fistula (A-V Fistula group), and finally an older group of subjects (all over 40 yr) who acted as controls for those with severe peripheral vascular disease (PVD Controls). These groups will be discussed in more detail later.

The patients under study were all under the care of one vascular surgeon. There were two groups, those with intermittent claudication (Claudicant group) and those with more severe peripheral vascular disease, most of whom had 'critical' ischaemia as defined below (PVD Patients). Critical ischaemia (Bell et al., 1982) was defined in 1981 at the International Vascular Symposium as:

1. Pain in the foot at rest which is persistent, severe and requires repeated analgesia for at least 4 weeks;
2. Ultrasonic, systolic ankle blood pressure lower than 40 mm Hg;
3. Ultrasonic, systolic ankle blood pressure lower than 60 mm Hg in the presence of superficial tissue necrosis of the foot or digital gangrene involving the base of the phalanx;
4. Diabetics should be excluded from an ideal clinical

study.

The claudicants were all referred for examination from the outpatient clinic, and the other group were in-patients being assessed for limb salvage surgery or amputation.

Full clinical data on all these control groups and patients may be found in Tables 2, 6, 8, 11 and 12, and in the Results chapter.

Diabetics were excluded from all patient groups. The rationale for this is that they represent a different subset of patients both in terms of presentation and the results of revascularisation (Wolfe, 1988). It is well known that local amputation may be effective without concurrent arterial surgery and that the neuropathy in many diabetics serves only to confuse interpretation of the results of surgery as it alters the response to infection and healing.

Ankle Doppler pressures and the ankle/brachial pressure index (ABPI).

All patients with critical ischaemia underwent routine angiography and segmental Doppler pressure measurements in addition to the extra tests required by our studies. Many authors over the years have placed considerable reliance on Doppler pressure measurements in the assessment of the ischaemic limb (Strandness 1966; Yao & Bergan, 1974; Ouriel & Zarins, 1982; Corter, 1982; Greenhalgh, 1988) since the original description for its use by Satomura (1959). However, measurement of ankle Doppler systolic pressure has its drawbacks. Pressure

measurements must be taken in both the dorsalis pedis and the posterior tibial artery and the higher value taken as the reading. Even so, this does not allow for patients in whom the peroneal artery has the highest pressure (and which is not always insonated) so that inappropriate patients may be included with those having critical ischaemia (Wolfe, 1988).

The ratio of the ankle to brachial systolic pressure - (the ankle/brachial pressure index or ABPI) - has been felt by some to give a more valid representation of the degree of ischaemia. Ouriel and Zarins (1982) thought the ABPI of more value in the less severely diseased limb, and an absolute pressure measurement more relevant once the limb had become critically ischaemic. Others felt the opposite to be true and that the ABPI was most helpful in patients with rest pain where a reliable prediction of response to sympathectomy was being sought (Yao & Bergan, 1973; Collins et al., 1981; Walker & Johnson, 1980).

The reasons for the lack of agreement on the place and value of ankle blood pressure measurements and the ABPI are that artifacts are quite frequent and are potentially serious. This is particularly so where calcification of the distal tibial arteries results in high cuff pressures being required to obliterate the pulse. This produces a falsely high pressure reading. On occasion the vessels at the ankle may be so rigid as to be incompressible. Then no reading can be obtained (Lazarus et al., 1978; Bernstein, 1986).

Despite these potential pitfalls, Doppler ankle

pressures and the ABPI have been routinely used in the assessment of the ischaemic limb in this department for the last 10 years.

The exercise bicycle.

Where appropriate, stress testing on an exercise bicycle has been performed in patients with peripheral vascular disease (de Cossart et al., 1982), and the drop in ankle pressure and recovery time charted.

Standardised order of investigation.

The exercise controls and the claudicants were subjected to the same series of tests which took place in the same order in an environmentally controlled room. Similarly, the PVD control group and PVD patients underwent the same tests in the same order. Those patients with peripheral A-V fistulae were examined under the same conditions as the exercise groups. Angiography, where appropriate, and Doppler pressure measurements were performed on a separate occasion and never immediately before our study period.

Environmental control.

Within the environmentally controlled room, air movement and heat loss from the room were kept to a minimum by a double air-lock access door and no open ventilation within the room. As few people as possible were present to avoid unnecessary movement in creating air currents and to prevent alteration in ambient temperature

especially at low levels around 20°C. The temperature of the room was kept to within 1°C of target by wall-mounted convector heater/refrigerator fans.

Humidity was controlled by motor driven humidifiers housed within the same wall unit and was kept between 45-55%. It is important not to allow the atmosphere to become too humid as evaporative loss from the skin would become inhibited as the room approached saturated vapour pressure.

These motors and fans produced air currents. Air speed over the patient was estimated using a hot-wire anemometer, and found to be constant at 0.5 m.sec⁻¹.

Clothing was also taken into account, and for our studies it was standardised to a shirt, pyjama jacket, or nightdress lifted to the waist, and underpants. The assessment of clothing is important as it establishes the insulation value of any particular combination of clothes. This 'insulation value' has been defined as the 'Clo' unit, and was devised by Gagge, Burton and Bazett in 1941. One Clo unit is equivalent to the insulation required to keep a seated subject comfortable at an air temperature of 21°C in an air movement of 0.1m.sec⁻¹. An ordinary suit with shirt and underwear will provide this insulation, and 1 Clo may be expressed as 0.155°C.m²/W. Thus in our studies, the clothing allowed to the subjects did not exceed 0.5 Clo (Clark & Edholm, 1985).

Of the methods whereby the body loses heat, namely convection, conduction, radiation and evaporation, all but conduction have been addressed to some degree by the

manipulation of the environment within the measuring room. To what extent conductive heat loss may play a part is discussed later.

Examination protocol.

i) Removal of clothing to underwear plus nightdress, pyjama jacket or shirt.

ii) Exposure at 20°C in a thermally controlled environment for 15 minutes seated on a couch with the legs either horizontal, and supported at the ankles, or slightly flexed at the knees so that the calves were not resting on the couch. The body and head were supported at 45 degrees.

iii) Venous occlusion strain-gauge plethysmography was performed, left leg before the right, irrespective of the side of the symptoms.

iv) Laser Doppler measurements were made on the skin over the medial head of gastrocnemius, the mid-lateral skin of the calf and the pulp of the hallux.

v) Infra-red thermograms were taken of the medial and lateral sides of each leg and foot with the hip and knee slightly flexed to keep the calf proud of the couch, the heel resting on a polystyrene block.

vi) Thermograms were taken of the soles of the feet.

The temperature of the room was then raised to 30°C over 30 minutes and there was a further 15 minute exposure period once this temperature had been reached. All the observations iii)-vi), were repeated. The patient was then allowed to dress and was returned to the ward.

Transcutaneous oxygen tension was usually measured on the ward the following day, at the same sites marked for the laser Doppler measurements except for the toe pulp (q.v.).

The patients with critical ischaemia were studied once only, before amputation or a final limb salvage procedure. The success of the revascularisation or primary healing of the amputation wound was recorded. Delayed healing was defined as healing by secondary intention after wound breakdown without the need for further surgery. Failed healing of an amputation was when surgical revision to a higher level was needed within 6 weeks of the original procedure.

Equipment and technique.

i) Venous occlusion strain-gauge plethysmography.

Initially, the instrument used was a Lectromed 2582 (Lectromed, Letchworth Garden City) mercury-in-silastic strain gauge. It was placed around the greatest circumference of the calf, and the distance measured from the superior border of the patella with the quadriceps femoris muscle relaxed. A mark was made on the skin at this point with a felt-tip pen, and the circumference of the calf measured. The same distance down the leg was used for the opposite limb and again the girth of the calf measured. The strain gauge was connected to a hot-wire recorder (MX 212, Lectromed) through a coupling unit and DC preamplifier (Units 2583 and 3559, Lectromed). The preamplifier was set to a gain of 12, and a range of 0.25

mV. The gauge was used as described by Whitney (1953), having been calibrated on a rigid cylinder and allowed to equilibrate to room temperature for 30 minutes in accordance with the manufacturers instructions. Blood flow was calculated from the formula -

$$\text{Flow} = \frac{200 \times h \times \text{time base}}{B \times C}$$

where h = average slope of the curve; time base (at a paper speed of 5mm/sec) = 20; B = deflection constant of the silastic loop after calibration; C = circumference of the limb (in millimeters). Flow is expressed in ml.(100 ml tissue)⁻¹.min⁻¹.

A 20 cm wide sphygmomanometer cuff (Accoson, Cossor and Son Ltd., London) was placed above the knee and bandaged firmly in place with a 15 cm wide crepe bandage in order to transmit the inflation of the cuff immediately to producing pressure around the thigh, and not simply to expansion of the cuff away from the leg. In this way venous occlusion would be as instantaneous as possible. The leg was supported at 20° above the horizontal by a padded wedge under the ankle so that the gauge did not touch the couch. Cuff inflation was achieved by connecting it to a timed pump set to a pressure of 50 mm Hg (Sealelectro Ltd., Portsmouth). The pump was set to produce a timed sequence of alternating 5 second periods of inflation and deflation. A rapid return to zero pressure (baseline) was assisted by removal of a Spencer Wells artery forceps from the outlet tube of the cuff. This was re-applied just before the next inflation. Five

complete cycles of inflation and deflation were usually sufficient to obtain adequate traces from which to calculate blood flow.

When irremediable problems arose with both faulty pre-amplifiers and the mercury-in-silastic loops, the equipment was replaced. A gallium-indium alloy in silastic rubber (SG33, Vasculab, Medasonics, California) was used in place of the mercury loops, coupled to an SPG16 Strain Gauge Plethysmograph system amplifier controller (Vasculab, Medasonics, California). This in turn was connected to a two-channel chart recorder (R12B, Vasculab, Medasonics, California). Calibration was performed automatically by pressing the 1% auto-calibration button. The size ('gain') knob was set to x2, and the system run on DC current for venous occlusion. The gallium-indium loop was Velcro mounted and positioned on the limb as the mercury loop had been. The equation for calculating the blood flow was the same but the value obtained was divided by 2 to allow for the gain control increase. The thigh cuff was also replaced with a 24 cm x 122.5 cm contoured cuff, bladder size 22 x 69.5 cm, (CC22, Hokanson, Washington). This cuff has firm Velcro fastening, obviating the need for crepe bandage support, and wide bore tubing allowing rapid inflation and deflation, so that the Spencer Wells forceps were no longer needed. The same mechanical inflation pump was used.

ii) Laser Doppler Measurement.

The Periflux PF3 (Perimed, Sweden) instrument was used.

This is a 2 mW helium-neon laser producing red light (wavelength 632.8 nm) from an unheated probe. The area of skin illuminated by the probe is a "...semisphere of about 1mm radius, its centre just in front of the measuring head" (Perimed Instruction Manual 1986). The probe was held in contact with the skin by its plastic collar, maintained in position by double-sided adhesive rings. For measurements of the hallux pulp, a technician held the probe stationary as the adhesive rings were difficult to apply reliably in this position. The returning signal was analysed by the instrument and displayed as a voltage on a flat-bed recorder. The paper was calibrated in arbitrary 'perfusion units', and the paper speed was 10 cm/min. The machine was zeroed before measuring each limb. The paper was allowed to run until the signal had settled to a steady value or was oscillating about an average value.

iii) Thermography.

Skin temperature was measured by infra-red thermography using an indium-antimonide detector in an Agema Thermovision Camera 680 (Agema, Leighton Buzzard, U.K.). The image was digitalised by an Agema Thermovision Oscar, stored on a Digidata Tape Recorder and displayed on a Microvitec VDU. Analysis of the image was made by an Apple II computer (program by Dr R Salisbury) and a permanent record made of the image by a Canon colour printer. The apparatus was calibrated using as a black body at 28°C, an Agema Model 23 Temperature Reference Source. Towards the end of the experiments the Agema

camera was replaced by a new Inframetrics 600 M camera (Boston, Massachusetts). This also used an indium-antimonide detector, cooled by liquid nitrogen, but had the advantages of continuous recording onto videotape, a wider temperature range (up to 500 degrees Celsius), and more accurate temperature measurement (to 0.01°C , instead of 0.1°C).

At an ambient temperature of 20°C thermographs were taken of the medial and lateral sides of each calf, and of the soles of the feet including the toes. These images were analysed by the computer and average skin temperatures obtained for the shaded areas as shown by the diagrams (Figs 9 & 10). The area of the knee was excluded as it characteristically shows a cold anterior aspect due to the subcutaneous patella and a warmer posterior aspect because of the underlying popliteal artery. If this area were to be included in those with peripheral vascular disease and occluded superficial femoral or popliteal arteries, the resultant collateral circulation around the knee could produce an unusually warm appearance and elevate the average medial or lateral T_{sk} .

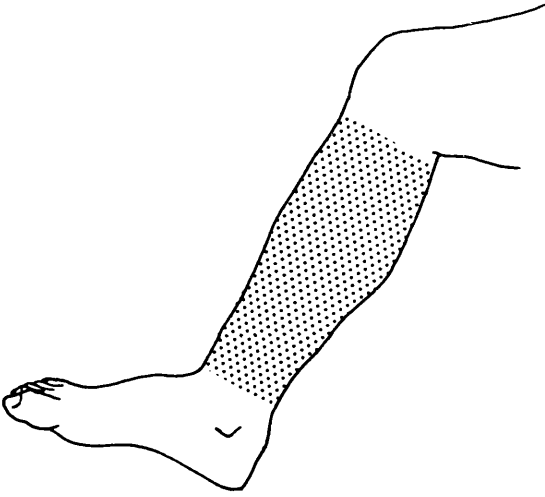
The heel pad was also excluded because the extreme skin thickness of the heel skin is so much greater than the skin of the rest of the sole, toes and leg that the relative significance of T_{sk} in terms of skin or deeper blood flow would be difficult to determine.

In addition to the areas outlined in Figures 9, 10 & 11, an upper anterior and lower posterior box was marked out medially and laterally, and its temperature measured.

FIGURES 9 & 10.

Diagrams of medial and lateral sides of the calf.

The shaded areas represent the skin surfaces which were analysed by the computer, and from which the average calf temperature was calculated.



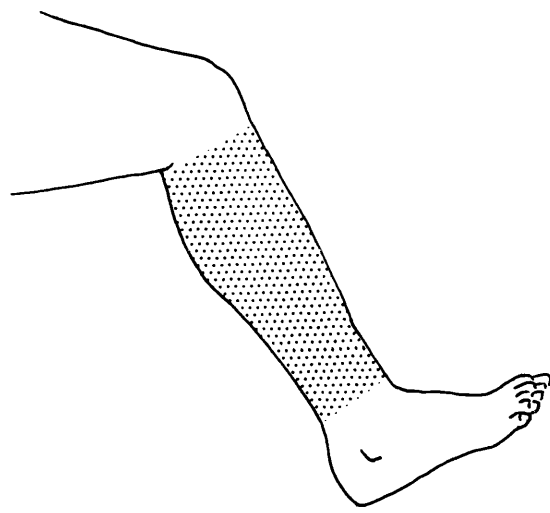
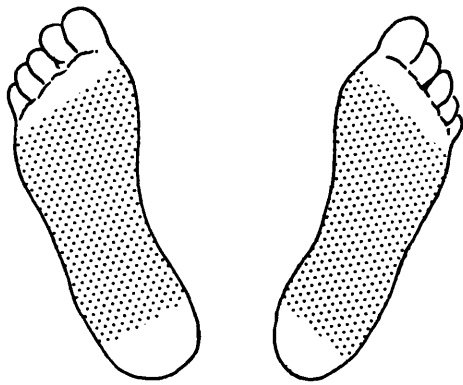


FIGURE 11.

Diagram of the soles of the feet.

The shaded area represents the skin surface which was analysed by the computer, and from which the sole temperature was calculated.



The average of the medial and lateral upper anterior boxes was calculated as it was for the lower posterior boxes and the result expressed as Posterior : Anterior or P/A ratio (Fig 12).

The upper and lower boxes were chosen as the positions at which the skin flaps would be cut in a Burgess-type below-knee amputation and the P/A ratio has been shown to be significant in forecasting primary healing (Stoner et al., 1989).

iv) Transcutaneous gas tension measurements.

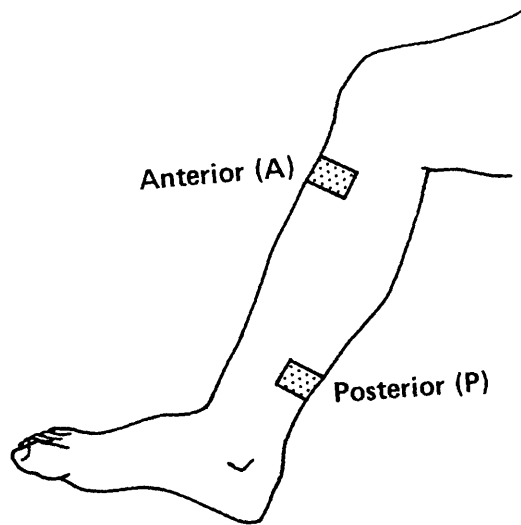
These measurements were performed on the ward using the TCM3 (Radiometer, Copenhagen) instrument. The Clark-type electrode has already been described and was attached, after membranizing and calibration as described in the User's Handbook, to the patient by means of an adhesive fixation ring. Three to 5 drops of S44416 Contact Liquid were placed on the skin in the well of the fixation ring before mounting the electrode on the patient. The sites of measurement were identical to those used for the laser Doppler probe, except that the instep was used instead of the pulp of the hallux because the fixation ring stuck more firmly there. The electrode was re-calibrated at a temperature of 44°C between each site of measurement, in accordance with the makers' instructions.

The transcutaneous oxygen measurements were made on patients either the day before or the day after the other investigations because of the time-consuming nature of the test, and the limit of patient compliance. In control

FIGURE 12.

Diagram of the postero-inferior and antero-superior
'boxes' used to calculate the P/A ratio.

These boxes were analysed on both sides of the calf and the temperature values averaged.



groups, the transcutaneous gas tension measurements were performed after all the other tests had been completed in case the heated electrode might be thought to influence either the laser Doppler or thermographic results. This possibility was, in fact, investigated, and though it was found in control subjects that the skin blood flow (as measured by laser Doppler) directly under the electrode remained elevated immediately after its removal, the values rapidly fell to pre-placement levels within 10 min. Skin blood flow within 1 cm of the transcutaneous oxygen electrode was unaffected throughout the 20 min application of the probe. Thermography could also identify the site where the heated probe had been applied by an increased skin temperature, but this lasted for less than 10 min, after which time the site was no longer discernible thermographically.

Control groups: details of examination.

As mentioned earlier, these fell into 3 categories -

- i) Exercise control group;
- ii) Arterio-venous fistula group;
- iii) Peripheral Vascular Disease Control group.

Exercise Controls.

The first group were under 40 yr and were studied at an environmental temperature of 20°C. Strain-gauge plethysmography and laser Doppler flowmetry were performed with the subject at rest, semi-recumbent on a couch with the legs horizontal and supported proud of the couch at

the ankle. Thermographic images were then taken with the subject standing. Anterior and posterior views of the legs from mid-thigh to ankle were recorded. On a raised platform 15 cm high, with only the toes and forefoot on the platform, the subject performed toe-raises at a rate of one per second for 30 seconds followed by 15 seconds rest. This cycle was repeated 5 times. Thermography was repeated immediately after the last exercise sequence and the subject returned to the couch. Strain-gauge plethysmography and laser Doppler flowmetry were performed as swiftly as possible. Further thermographic images were taken at 15 and 30 minutes after stopping exercise.

This method of generating heat within the limb was chosen as it has been shown that resting muscle blood flow can increase on exercise from $3 \text{ ml. (100 ml tissue)}^{-1} \cdot \text{min}^{-1}$ to $50-70 \text{ ml. (100 ml tissue)}^{-1} \cdot \text{min}^{-1}$ (Barcroft, 1963; Folkow & Neil 1971; Wright, 1982).

A change in limb flow was measured by strain-gauge plethysmography and any effect on the cutaneous circulation estimated by laser Doppler flowmetry. In this way the contribution of deep (muscle) flow and skin blood flow to the change in thermographic picture could be determined.

Arterio-venous fistula group.

The second group consisted of subjects with a surgically constructed arterio-venous fistula at the wrist. This was a modified Brescia fistula (Brescia et al., 1966). All were patients with chronic renal failure

and the operation had been performed to provide access for haemodialysis. One subject included with this group presented with an apparently spontaneous appearance of an arterio-venous fistula in the sole of her foot. She was otherwise healthy.

These subjects were studied at rest in an ambient temperature of 20°C. Strain-gauge plethysmography, laser Doppler flowmetry and thermography was performed on both forearms in similar fashion to the lower limb groups, with care being taken to make no skin flow measurements over the fistula site. Skin-fold thickness was measured over brachio-radialis 4 fingers' breadths below the elbow crease, and the mid-triceps.

This group was selected to see what happened to skin blood flow in a situation where there was a known increase of total limb flow, and where the limb affected was both palpably and thermographically warmer than its opposite member.

Peripheral vascular disease (PVD) controls.

The final group of peripheral vascular disease controls was studied in exactly the same way as the patient groups; first with the ambient temperature at 20°C, and then at 30°C. The aim was to provide a control group of similar age to the patient groups (40-70 yr) having no cardiovascular symptoms, on no medication, and not diabetic. In this way it was hoped that the full effect of environmental stress testing on diseased and healthy individuals might be noted, along with a clear indication

of the value of the various forms of investigative techniques.

Statistical analysis of data.

Advice on the statistical examination of data has been obtained from Dr R Barton of the North Western Injury Research Centre, University of Manchester.

Where possible, non-parametric statistics have been applied. All 'p' values quoted are derived from Wilcoxon's signed rank test for paired data, and Wilcoxon's rank sum test (Mann-Whitney U test) for unpaired data.

When a regression line has been drawn by the method of least squares, using parametric statistical analysis, the correlation has been examined using Kendall's rank correlation test, and 'p' obtained from the 'z' value given.

Ms S Hollis of the Department of Computation and Statistics, Manchester University Medical School, has given specific advice on the construction of a curve for Figure 20.

RESULTS.

Observations on Control subjects.

The initial observations were made on a group of apparently healthy volunteers on no medication and all over 40 yr. The age range was from 42-70 yr, (median 48 yr). The minimum age of 40 yr was chosen in an attempt to try and age-match the group with patients suffering from peripheral vascular disease who were studied in later groups. (Table 2).

The Influence of Ambient Temperature.

The effect of raising the ambient temperature (T_a) from 20°C to 30°C was noted on the thermographic appearances of the calf and foot and the results are described below.

Effect of ambient temperature on Skin Temperature (T_{sk}).

The skin temperature of the leg was studied thermographically at two environmental temperatures, 20°C and 30°C, in a group of 8 control subjects. (Appx 1).

Attention was paid to the appearance of the leg below the knee as it was anticipated that in the ischaemic limb the most significant changes would be in that region.

At an ambient temperature (T_a) of 20°C the thermographic images in all subjects showed that the medial side of the calf was cooler than the lateral side. The skin temperature (T_{sk}) on the medial side varied between 24.1°C and 30.5°C (median 27.7°C), and on the lateral side between 25.1°C and 31.2°C, (median 28.8°C). The

TABLE 2. Data from PVD Control Subjects.

No	Age	Sex	Brachial Pr. Ankle Pressure (mm Hg)				ABPI	
			(mm Hg)	R leg	L leg	R leg	L leg	
1	42	M	110	135	135	1.2	1.2	
2	51	M	150	155	150	1.03	1.0	
3	45	M	120	150	150	1.25	1.25	
4	44	M	155	185	185	1.19	1.19	
5	57	F	-	-	-	-	-	
6	70	M	140	160	170	1.14	1.2	
7	42	F	115	145	145	1.26	1.26	
8	51	M	125	140	135	1.12	1.08	

Age range: 42-70 yr, median 48 yr.

Brachial BP range: 110-155 mm Hg, median 125 mm Hg.

Ankle BP range: 135-185 mm Hg, median 150 mm Hg.

[7.5 mm Hg \equiv 1 kPa]

difference was significant ($p < 0.01$). The T_{sk} of the calf was higher nearer the knee than at the ankle but the fall in T_{sk} down the leg did not show a steady drop. The warmest part of the calf was found at the junction of the upper and middle third, corresponding with the skin overlying the greatest bulk of the calf muscle. From that point there was a fairly rapid and constant fall in T_{sk} to the malleoli. The coolest area of the skin overlay the subcutaneous border of the tibia in its upper two thirds, and the Achilles tendon or anterior ankle tendons at the level of the malleoli. The skin over these distal areas was consistently cooler than that over the malleoli.

The lateral aspect of the calf was always warmer than the medial, and the hottest area was centred posterolaterally away from the axis of the limb. (Fig 13). On the medial side the hottest area of skin was off-set from the central axis of the limb and was found posteromedially, but the area was less well defined on this side of the calf, and the isotherms often appeared irregular.

Previous work in this department (Stoner et al., 1989) had suggested that when the skin temperature of the upper anterior and lower posterior boxes was measured, the P/A ratio (see pp.47 & 118) would give a better picture of the disease state than the mean calf temperature. This had proved particularly relevant in those with ischaemic disease but control values had not been recorded. When the T_{sk} in the upper anterior and lower posterior boxes was measured in Stoner's study, the P/A ratio was found to lie between 0.95 and 1.04 (median 0.995).

FIGURE 13.

Thermograms of PVD Control subject's legs. Medial and lateral surfaces, at an ambient temperature of 20°C.
Subject number 3. (Note the isotherm temperature scale).

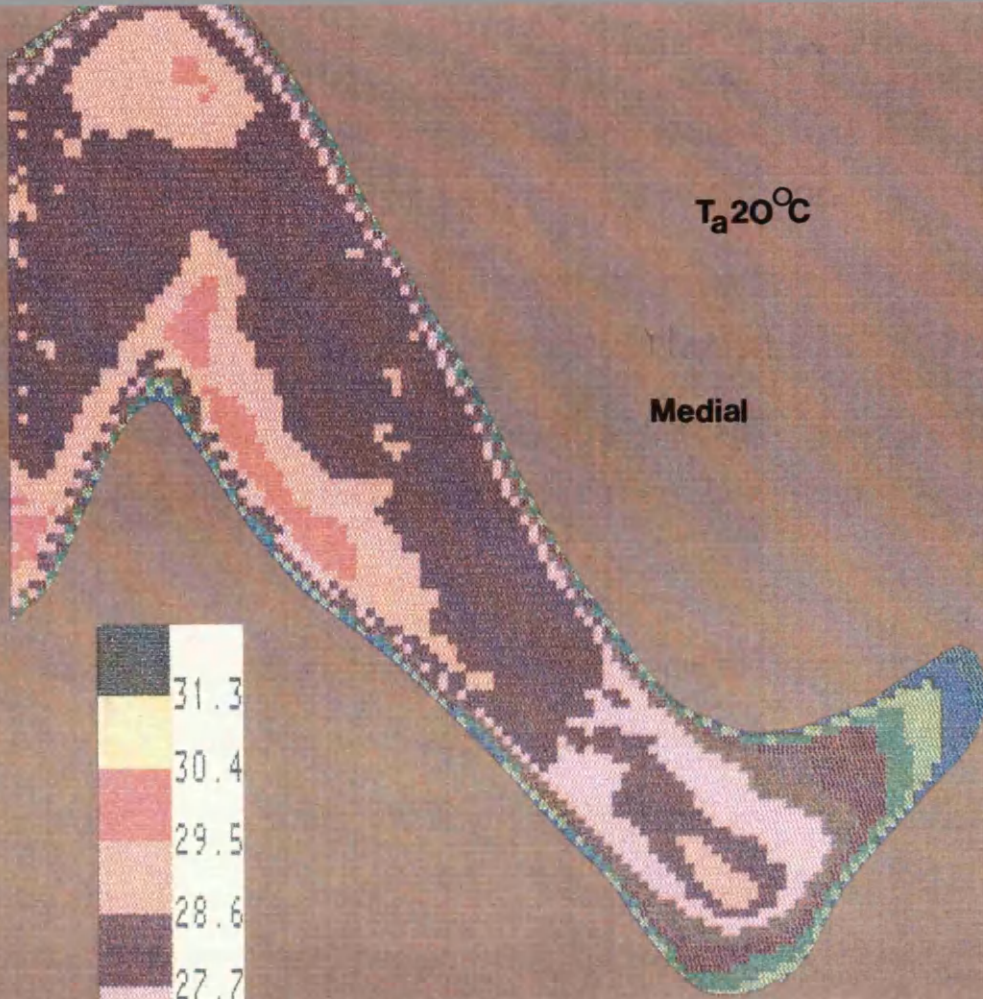
The lateral surface is warmer than the medial. The warmest part of the calf can be seen to lie around the junction of the upper and middle third. The coolest area of skin overlies the subcutaneous border of the tibia in its upper two thirds and the Achilles tendon or anterior ankle tendons at the level of the malleoli. The skin over these distal areas is cooler than that over the malleoli.

The medial surface of the calf can be seen to be cooler than the lateral, but again the hottest area is centered around the junction of the upper and middle third of the calf postero-laterally.

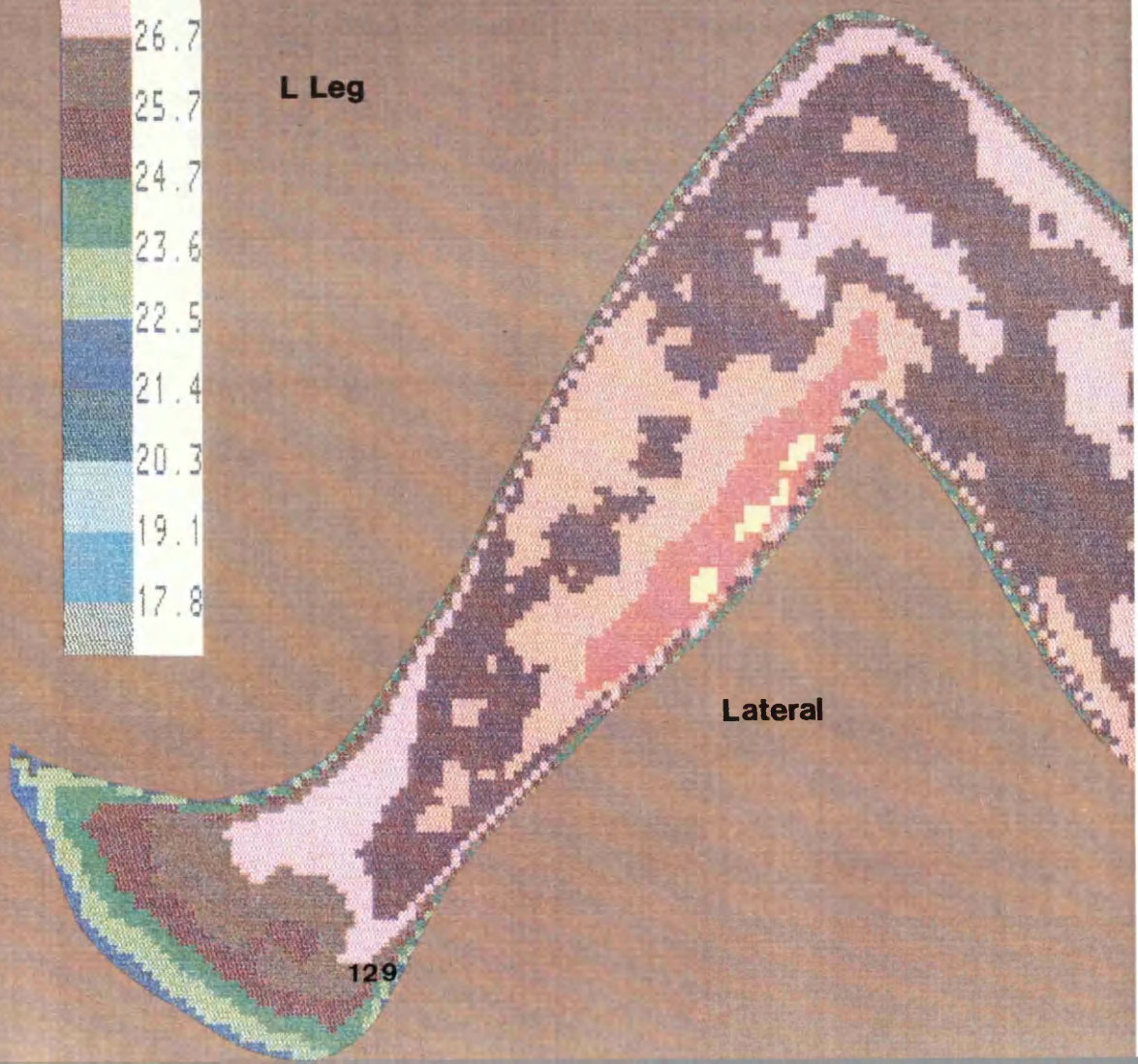
The isotherms are less well defined here than on the lateral side of the calf, and rather irregular.

$T_a 20^{\circ}\text{C}$

Medial



L Leg



Lateral

Returning to the studies for this thesis, examination of thermograms of the feet revealed a more distinct, repeated and recognisable pattern which was reminiscent of a pair of butterfly wings when both feet were viewed from beneath (Fig 14). The T_{sk} on the instep of each foot fell in a series of concentric rings to the base of the toes and heels. These concentric rings often continued on into the toes. The heels were usually warmer than the toe pulps, being around the same temperature as the isothermic ring found over the ball of the foot. The T_{sk} on the lateral side of the foot was always lower than on the medial side, and frequently a cool crescent was observed running down from the little toe to about mid-foot on the lateral border.

The sole temperatures (median 23.1°C , range 21.2°C - 31.4°C), were always higher than the hallux pulp temperatures (see Appendix 1), (median 19.9°C , range 17.6°C - 29.4°C). This difference was statistically significant ($p < 0.01$).

When the T_a was increased to 30°C , the thermographic appearances of the limbs altered (Fig 15). In general T_{sk} was increased, with broader and warmer isotherms reaching down to include the malleoli. Cool skin was only seen in the feet. The highest T_{sk} of the calf was still the postero-lateral surface, but there was a more widespread increase in mid to upper calf skin temperature so that the obvious hot spots seen at T_a 20°C were less well defined.

Although the skin on the lateral aspect of the calf was usually warmer than on the medial side, T_{sk} ranging

FIGURE 14.

Thermograms of PVD Control subject's feet (soles). Views of plantar surfaces taken at an ambient temperatures (T_a) of 20° and 30°C . Same subject as Fig 13. (Note the isotherm temperature scale).

The 'butterfly-wing' patterning is obvious at T_a 20°C , though less distinct at T_a 30°C .

The heels are warmer than the toe pulps, and about the same temperature as the ball of the foot.

The cool lateral crescent can be seen running down from the little toe to mid-foot on the lateral border.

The sole temperatures, as a group, were significantly higher than the toe pulp temperatures ($p < 0.01$).

At T_a 30°C there is a uniform increase in T_{sk} in the soles of the feet. The butterfly-wing patterning is still present, though less distinct as there are fewer isotherms.

Note that the pulps of the toes become increasingly cool from medial to lateral (hallux to little toe).

The cooler crescent, which ran down the lateral border of the foot clearly at T_a 20°C , is not so easy to see at T_a 30°C .

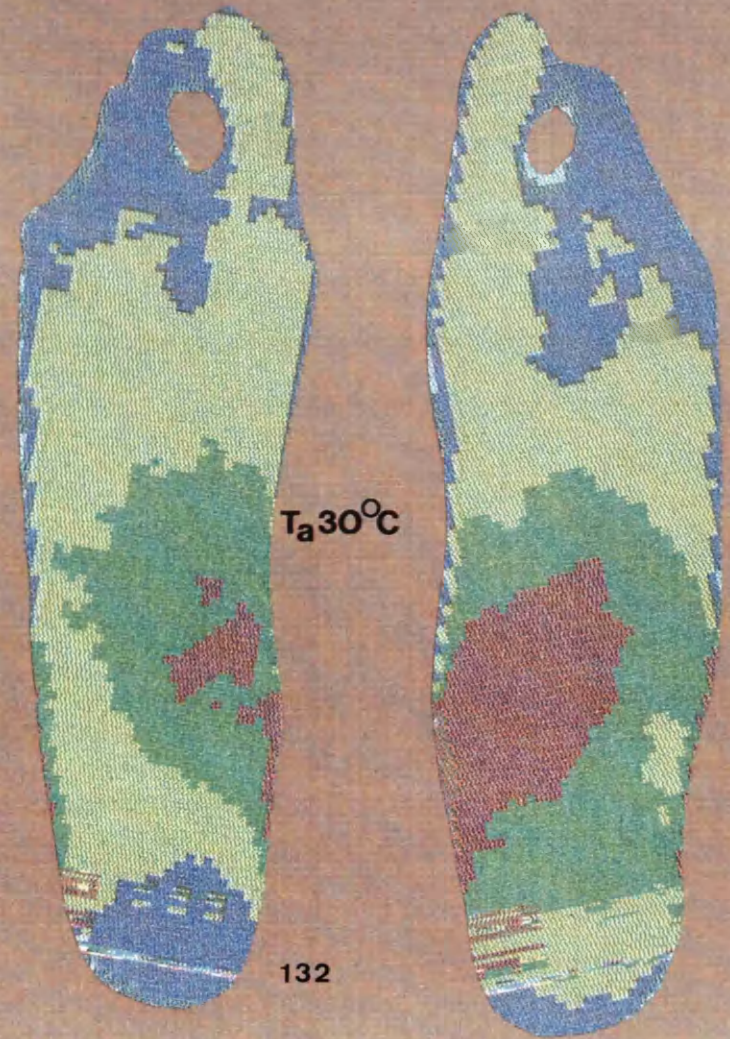


FIGURE 15.

Thermograms of PVD Control subject's legs. Medial and lateral aspects, made at an ambient temperature of 30°C.

Same subject as Figs 12 & 13.

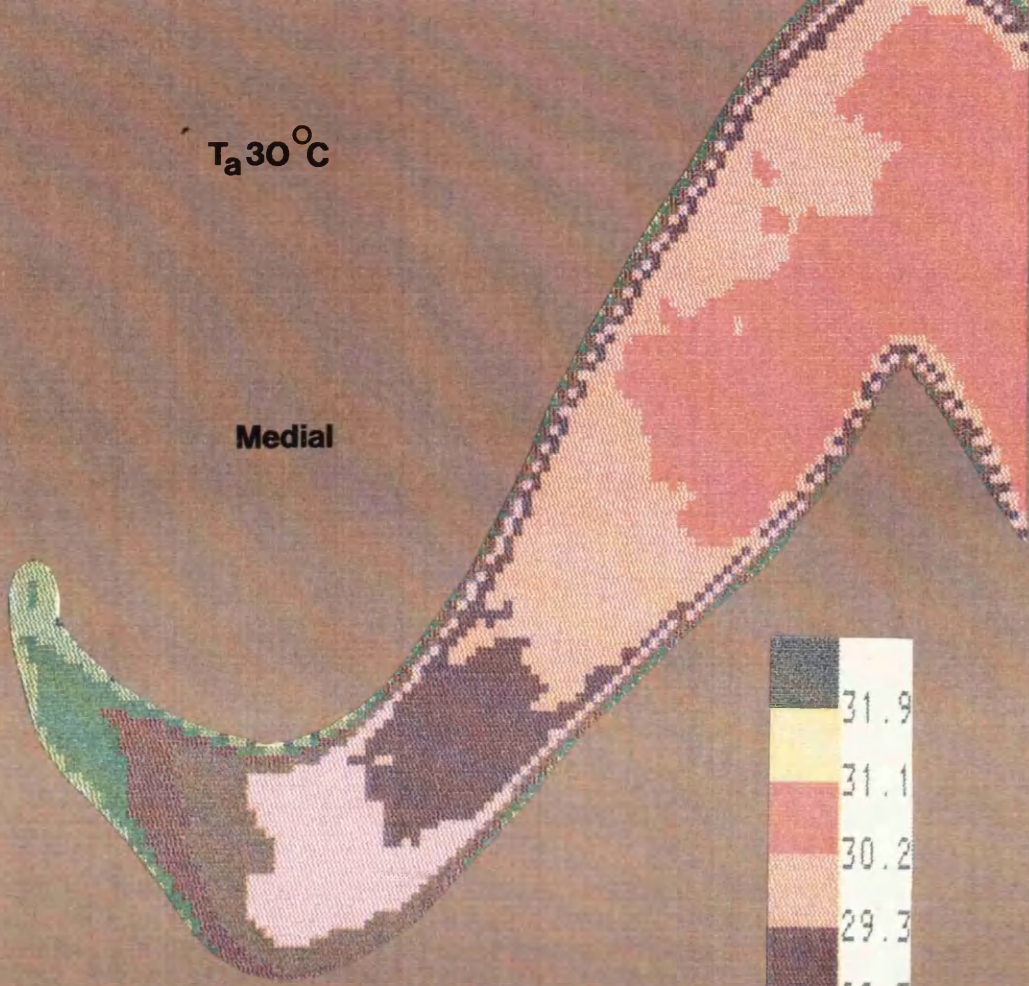
Note that the medial side is still cooler than the lateral, but the difference is not so striking. The cool subcutaneous border of the tibia is not so obvious.

On the lateral surface the isotherms are broader and warmer than at T_a 20°C, and now reach down to include the malleoli. Only the feet are cool.

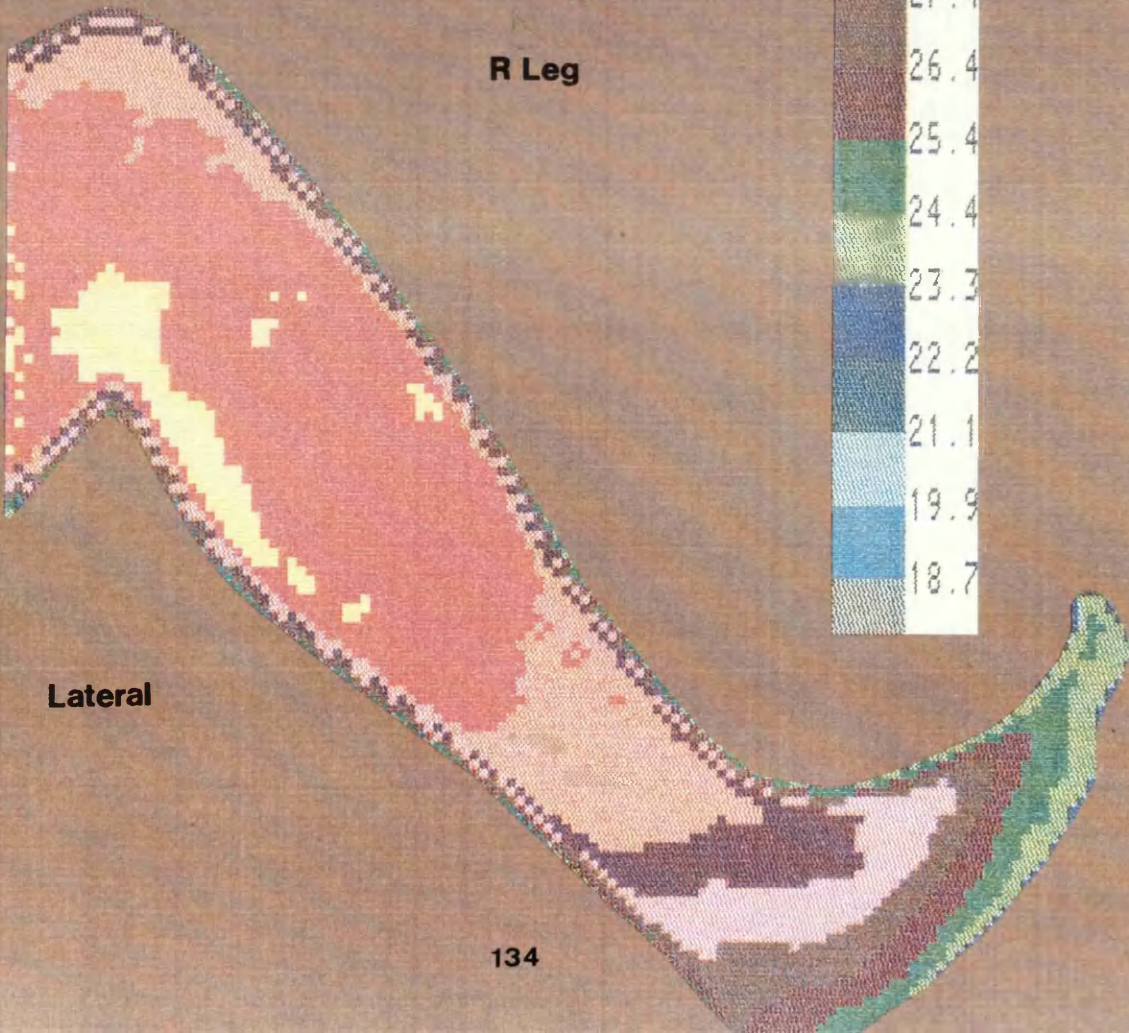
The well-defined 'hot spot' seen in the postero-lateral calf at T_a 20°C is less distinct although the highest T_{sk} is still in that area.

$T_a 30^\circ\text{C}$

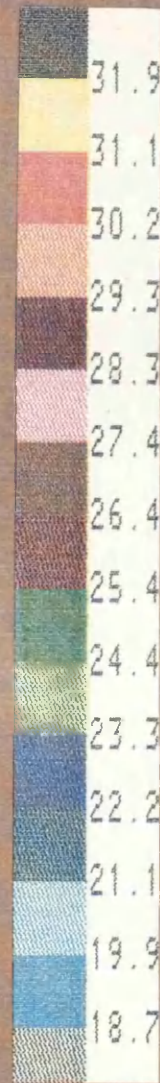
Medial



R Leg



Lateral



between 28.0°C and 31.7°C (median 31.2°C) laterally, and between 28.1°C and 32.4°C (median 29.6°C) medially, this was not always so and the cooler subcutaneous border of the tibia was not so obvious. The difference in T_{sk} between medial and lateral sides of the calf was no longer statistically significant. The P/A ratios at T_a 30°C ranged between 0.94 and 1.00 (median 0.98). Although only slightly less than that at T_a 20°C (median 0.995), the difference was statistically significant ($p < 0.01$). (Table 3).

In the soles the increased T_{sk} was of a uniform distribution, and although the butterfly-wing patterning was still present, it was less clear than before as there were fewer isotherms (Fig 13).

The hallux pulp T_{sk} was warmer than that of the lateral toes which were increasingly cool from medial to lateral. The cool lateral crescent seen at T_a 20°C was less apparent at T_a 30°C.

In all three areas - calf, sole and hallux, there were highly significant increases in T_{sk} on raising the T_a from 20°C to 30°C ($p < 0.001$). (Fig 16). However, the increase in T_{sk} of the hallux pulp was greater than that found in the sole ($p < 0.01$), and very much greater than that in the calf ($p < 0.001$). A significant negative correlation was found between the initial T_{sk} of both calf and hallux ($r = -0.7$ and $p < 0.01$ in each case) and the size of the subsequent increase in T_{sk} at the higher T_a of 30°C.

Throughout the literature, and as recently as 1988, (Clark et al., 1988), the assumption has been made that

TABLE 3. PVD controls - P/A ratios at T_a 20° and 30°C

No	Age/Sex	Right leg		Left leg	
		(Ambient temp.) 20°C	30°C	20°C	30°C
1	42/M	0.96	0.96	0.96	0.95
2	51/M	0.99	0.96	1.00	0.98
3	45/M	0.98	0.97	1.00	0.98
4	44/M	1.00	0.96	0.98	0.96
5	57/F	0.99	0.99	1.00	0.98
6	70/M	1.00	0.99	0.98	0.97
7	42/F	1.00	1.00	1.00	1.00
8	51/M	1.00	1.00	0.99	1.00

P/A Ratios at 20°C: Range 0.96-1.00, median 0.995

at 30°C: Range 0.95-1.00, median 0.985

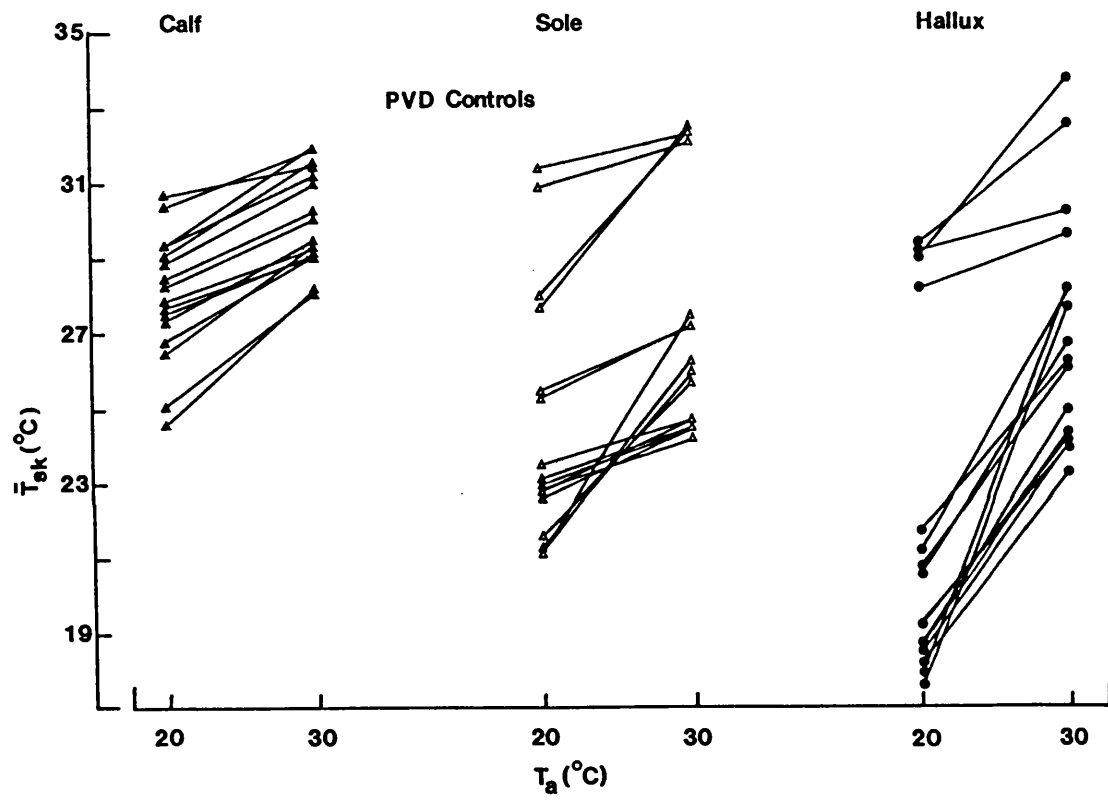
Significance: $p < 0.01$

FIGURE 16.

Graph of mean skin temperature against ambient temperature in Control subjects. Calf, sole and hallux values are shown.

All 3 areas - calf, sole and hallux - show statistically significant increases in T_{sk} following a rise in T_a from 20°C to 30°C ($p < 0.001$).

The increase in T_{sk} in the hallux pulp was greater than that in the sole ($p < 0.01$), and very much greater than that in the calf ($p < 0.001$).



skin temperature was related to skin blood flow, so our next investigation at each ambient temperature was to measure skin blood flow (SkBF) using a laser Doppler technique.

Effect of ambient temperature on Skin Blood Flow (SkBF).

At T_a 20°C the range of SkBF (Appx 2) was the same over the medial head of gastrocnemius and in the mid-lateral calf position, (2.5-11.5 perfusion units [PU]). The medians differed slightly, (5.0 PU on the medial side and 5.5 PU on the lateral), but the difference was not significant. There was no statistical difference in the values found for the same sites in the two legs, and all calf values on both legs were essentially the same for any one subject.

Skin blood flow in the pulp of the hallux showed a considerably larger range in values than either of the calf sites, (4.0-40.0 PU; median 10.8 PU). This difference was statistically significant ($p < 0.01$).

When the T_a was raised to 30°C the calf SkBF increased a little in both legs. The rise just failed to achieve statistical significance on the lateral side but it did on the medial side ($p < 0.02$). The range for medial calf SkBF was 4.5-14.5 PU (median 6.8 PU), and for the lateral calf, 4.5-15.0 PU (median 5.8 PU). Both legs behaved in the same way.

All subjects, with one exception, showed a rise in SkBF in the pulp of the hallux at T_a 30°C. The range had risen to between 9.0 and 67.0 PU, with a median value of 20.0

PU, ($p < 0.001$). (Fig 17).

Thus, although the rise in SkBF on the medial calf from a median of 5.0 PU to a median of 6.8 PU was statistically significant, it was not a big enough rise to make it significantly different from the lateral calf at T_a 30°C where the change had only been from 5.5 PU to 5.8 PU (median values). Even so, the hallux pulp at both ambient temperatures showed a significantly higher SkBF when it was compared to either the medial or lateral side of the calf ($p < 0.01$). Figure 18 shows a typical SkBF trace. At this stage, therefore, we were able to test the assumption that skin temperature was a function of skin blood flow.

c) Relationship between skin temperature and skin blood flow.

No significant relationship was found between T_{sk} and SkBF of the calf (Fig 19) but there was an association between T_{sk} of the hallux and its skin blood flow ($r = 0.39$, $p < 0.05$). (Fig 20).

In the calf and the hallux there was a negative relationship between the initial T_{sk} at T_a 20°C and the size of the increase in T_{sk} after raising the T_a to 30°C. Thus, the lower the initial T_{sk} , the greater the subsequent rise when T_a was raised. The same held true for SkBF in the hallux (see Fig 17) but not in the calf. (Fig 21).

These results suggested that although T_{sk} and SkBF were related in the foot (and hand, as had been shown before by

FIGURE 17.

Graph showing the change in hallux skin blood flow (SkBF) with rise in ambient temperature (T_a) in both PVD Controls and those with severe peripheral vascular disease (PVD Patients).

There is a highly significant rise in hallux SkBF in Controls ($p < 0.001$). This is in contrast to PVD Patients' 'good' feet, which show a smaller rise ($p < 0.01$), and PVD Patients' 'bad' feet, which show no statistically significant rise in SkBF.

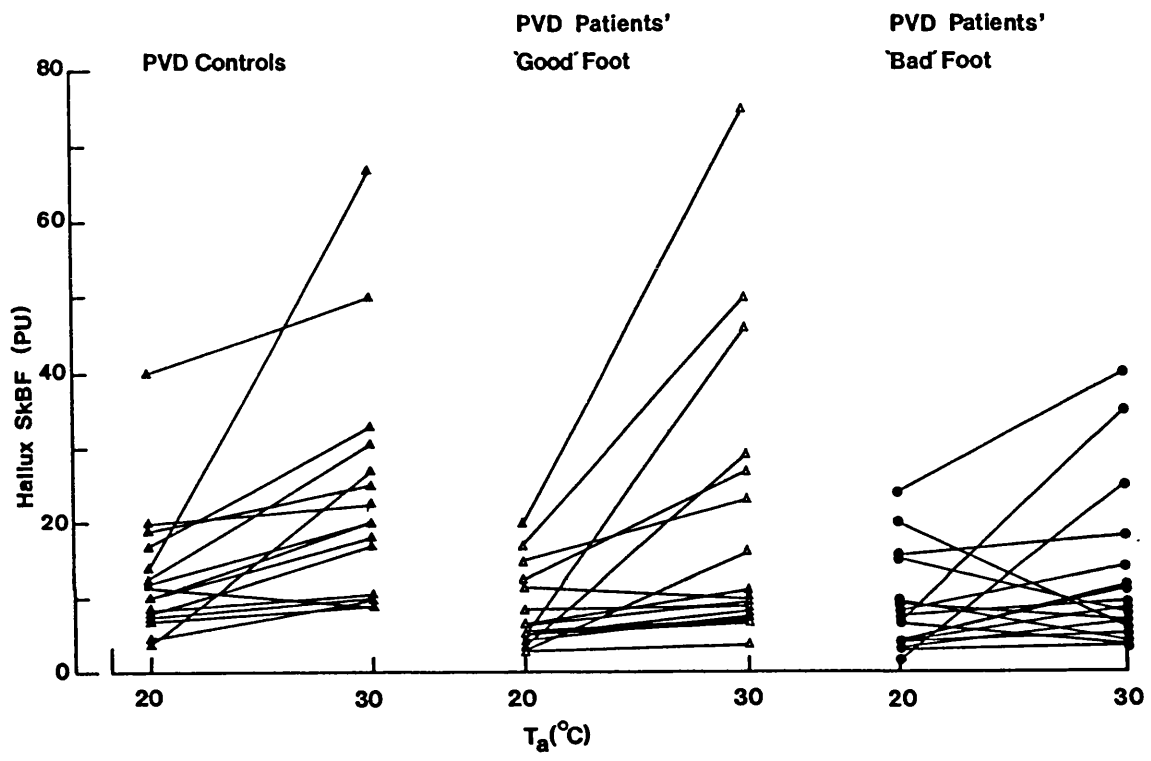


FIGURE 18.

Trace of skin blood flow (SkBF) made by a laser Doppler technique in a PVD Control subject at both T_a 20°C and T_a 30°C. Subject number 8.

The trace reads from left to right.

LM = Left Medial calf site, over the medial head of gastrocnemius.

LL = Left Lateral calf site, made mid-way down the calf on the lateral side.

LH = Left Hallux pulp site.

RM, RL and RH refer to the equivalent sites of measurement on the Right leg.

The scale is in arbitrary Perfusion Units (PU).

The vertical lines represent the movement of the pen recorder when the paper was stationary, and the gaps between recording traces are where the instrument was zeroed before each measurement.

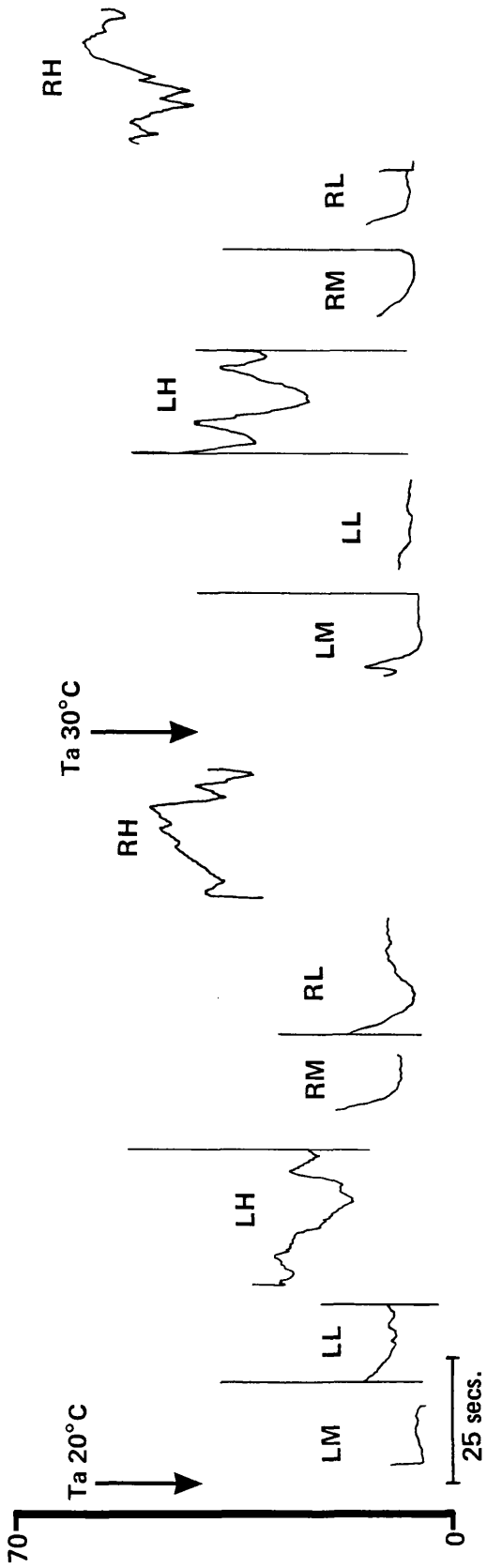


FIGURE 19.

Graph of SkBF v T_{sk} Calf in PVD Control subjects.

No statistically significant relationship could be found between these two variables.

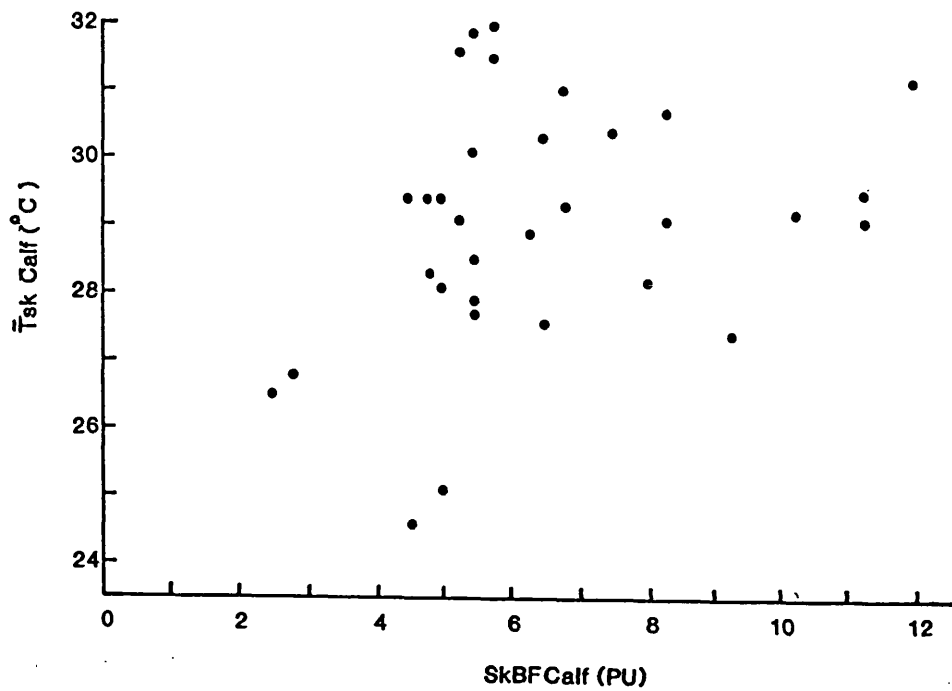


FIGURE 20.

Graph of S_kBF v T_{sk} Hallux in PVD Control subjects.

There is a relationship between skin blood flow and skin temperature in the hallux when all values at both ambient temperatures are plotted ($r=0.39$, $p<0.05$).

A straight line and a curve were fitted to the observed points, allowing for error in both variables.

Straight line: - $temp = a + b \cdot flow$

Curve: - $temp = A(1 - \exp(-k(flow - c)))$

For the straight line, the parameter estimates (standard errors) were;

$$a = 3.97 (1.35)$$

$$b = 0.191 (0.060)$$

$$RSS = 3169.52$$

For the curve;

$$A = 12.7 (2.44)$$

$$k = 0.084 (0.054)$$

$$c = 3.25 (5.52)$$

$$RSS = 1424.2$$

Comparing the residual sums of squares (RSS) indicates that the curve gives a considerably better fit to the data than a simple straight line. However, due to the high variability in the sample the exact values of k and c cannot be determined, as is evident from their large standard errors. So it appears that a curve would describe the relationship between temperature and blood flow but it is not possible from this set of data to determine the precise curve.

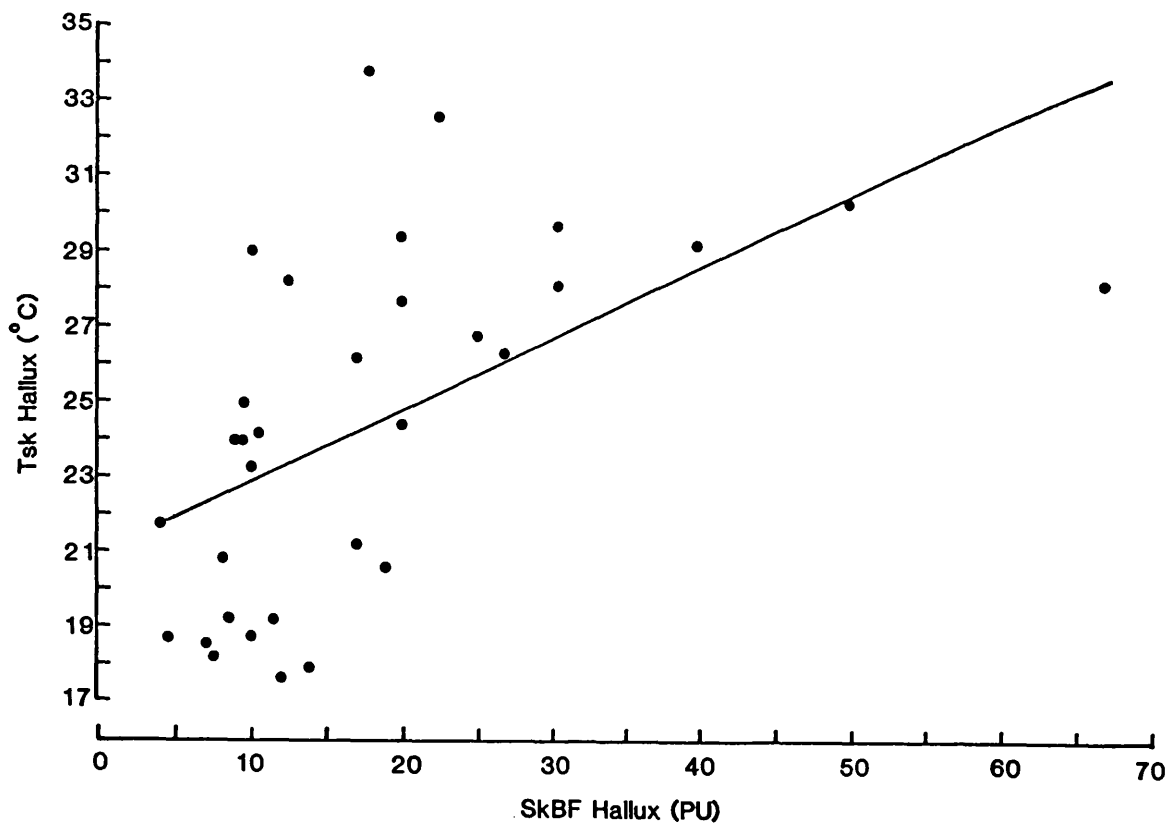
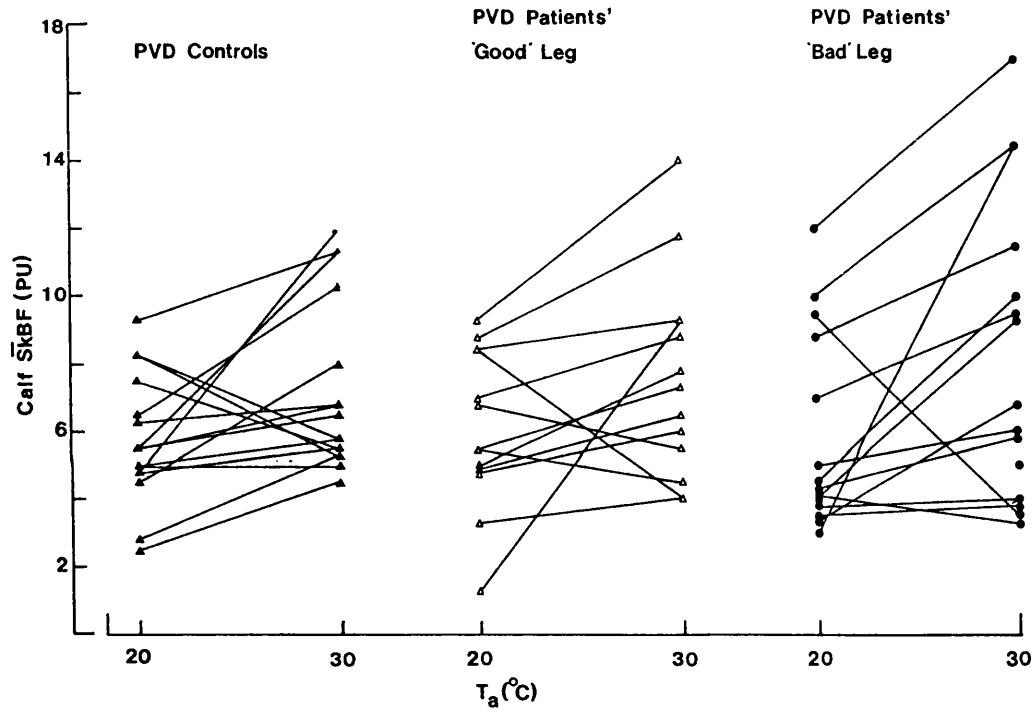


FIGURE 21.

Graph showing the change in mean calf SkBF with rise in T_a in PVD Controls and PVD Patients.

Although there are changes in SkBF, they are not statistically significant in any group, nor are there significant differences between the three groups. Furthermore, it can be seen that not all changes are in the same direction.



work in this unit; Stoner et al., 1989), the rise in T_{sk} of the calf could not be accounted for by a rise in calf SkBF. The hypothesis that deep or core limb blood flow was responsible for skin temperature over the calf or forearm by outward conduction of heat was therefore raised and examined further in two groups of subjects in whom core limb blood flow was known to be increased. The first group was made up of normal subjects, all under 40yr, who underwent an exercise programme to increase deep limb blood flow. (Analysis of mean calf skin temperature in this sample population showed that it was not skewed and so the group was assumed to have a normal distribution). The second group was an heterogeneous group of patients, all in chronic renal failure, in whom an arterio-venous fistula had been fashioned at one wrist to provide access for haemodialysis. In addition to this second group there was a 26 yr old woman who had been found to have an arterio-venous fistula of unknown aetiology in the sole of her foot.

Observations on the relationship between total blood flow, skin blood flow and skin temperature.

Effect of Exercise in healthy subjects.

At an ambient temperature of 20°C, 6 healthy subjects, 4 men and 2 women, aged 29-38yr, (median 35yr), were exercised as described before, (p.122). The men and women responded similarly and the results are shown in Figure 22 and Tables 4 & 5. Total blood flow (TBF) through the calf was significantly increased, usually

FIGURE 22.

Thermograms of the posterior aspect of the legs of an Exercise Control subject (number 6) Before and After Exercise.

These thermograms were made at an ambient temperature of 20°C. The increase in skin temperature over the whole of the calves can be seen. This occurred without a similar alteration in skin blood flow, although total limb blood flow, measured by venous occlusion plethysmography, was significantly increased.



T_a 20°C



TABLE 4. Resting data from Control Subjects before Exercise test.

<u>No</u>	<u>Age</u>	<u>Sex</u>	<u>Brach Pr.</u>	<u>Ank Pr. (mm Hg)</u>		<u>ABPI</u>	
				<u>(mm Hg)</u>	<u>R leg</u>	<u>L leg</u>	<u>R leg</u>
1	38	M	160	185	180	1.16	1.09
2	34	F	110	125	130	1.14	1.18
3	29	M	135	145	135	1.07	1.00
4	36	M	125	135	140	1.08	1.12
5	33	M	-	-	-	-	-
6	36	F	105	120	110	1.10	1.00

Age range: 29-38 yr, median 35 yr.

Brachial BP range: 105-160 mm Hg, median 125 mm Hg.

Ankle BP range: 100-185 mm Hg, median 135 mm Hg.

ABPI range: 1.00-1.18, median 1.10.

TABLE 5. Effect of Exercise in Control Subjects.

	<u>Before Exercise</u>	<u>After Exercise</u>
	<u>Median (Range)</u>	
<u>Total calf blood flow</u> (ml.(100 ml tissue). ⁻¹ min ⁻¹ .)	3.4 (1.8-8.8)	8.5 (3.4-14.5)*
<u>Calf skin blood flow</u> (PU) 3 sites.	4.9 (3.7-6.0)	5.1 (4.8-5.3)†
<u>Calf temperature</u> (°C).	27.6 (25.5-29.3)	28.8 (25.8-30.6)*

* p<0.03 Wilcoxon matched-pairs signed ranks test

† N.S. (Not significant)

about 3-fold. This was not accompanied by any significant increase in the perfusion of the calf skin. The values for the latter were always similar to the low values found previously. There was, however, a significant increase in the mean temperature of the calf skin. This occurred in all subjects. The maximum temperature was not always reached by the end of the last exercise cycle and in 2 subjects the rise in T_{sk} continued for 15 min. The 'after-exercise' value for T_{sk} in Table 3 is therefore based on the maximum value recorded during the first 15 min after the end of the exercise. No further increases were observed after this point. When all the values were considered together, a significant positive relationship was found between the T_{sk} of the calf and the total blood flow ($p < 0.001$). (Fig 23).

Observations on patients with an A-V fistula.

A further group of people in which the arterial inflow to a limb is increased is in patients with peripheral arterio-venous (A-V) fistulae. In these patients a short circuit between the main arteries and veins of a limb will increase the arterial inflow even when the limb is at rest at ordinary room temperatures. The effect of such an A-V fistula on the surface temperature of a limb was studied in two situations.

Patients with a modified Brescia fistula.

Observations were made on 9 patients, 6 men and 3 women aged between 21 and 76yr, (median 50yr), 8 days to 10

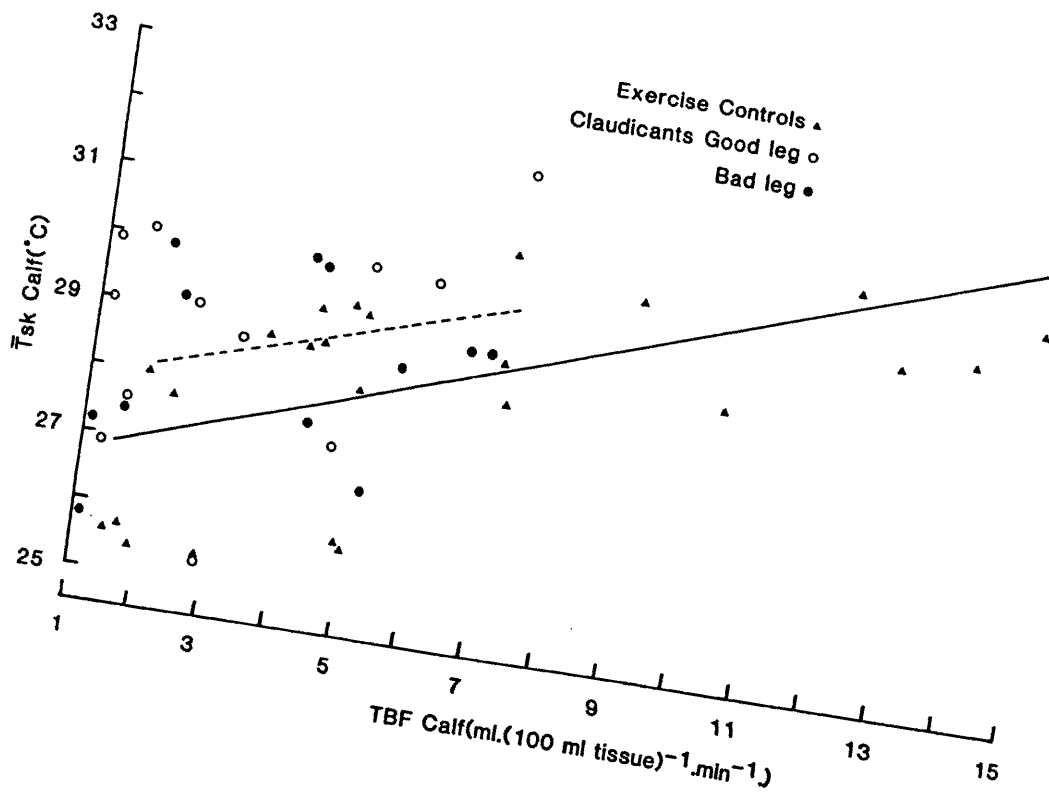
FIGURE 23.

Graph of T_{sk} calf v Total Blood Flow (TBF) calf in Exercise Control subjects and Claudicants.

The continuous line represents the Exercise Control subjects. There is good correlation between calf skin blood flow and total limb blood flow in this group of subjects ($r=0.69$, $p<0.001$).

The interrupted line represents the Claudicant group. There is also a relationship between these two variables in this group although it is not so strong ($r=0.39$, $p<0.05$).

There is a significant elevation between the two slopes ($p<0.02$). This means that for any given calf blood flow, the Claudicant group has a significantly higher calf skin temperature.



months (median 23 days) after the construction of a modified Brescia fistula (Bell & Wood, 1983) at the wrist to provide access to the circulation for haemodialysis. (Table 6).

The surgical construction of a Brescia fistula was followed by a large increase, about 5-fold, in the total blood flow (TBF) through the forearm. (Table 7). The T_{sk} of the forearm on the operated side was significantly elevated (Fig 24), not just around the site of the fistula which was excluded from the calculation of the mean T_{sk} , but proximally where the circumference of the forearm was maximal. The mean SkBF in the forearm was also greater ($p < 0.01$) on the operated side (ratio 1.1-2.5, median 1.3), but the values were always within the range found previously on normal subjects. (We have found that in the normal subject the perfusion of the skin of the two forearms does not differ significantly). However, when looking at the specific sites of skin blood flow measurement and their related skin temperatures, no relationship could be found at any site on either forearm. Nor was any significant difference found in any individual patient between the maximum circumference of the two forearms or in the skinfold thickness at that site.

Patient with an A-V fistula in the foot.

This was a 26yr old woman with an A-V fistula of unknown aetiology in her right foot. The site of this patient's A-V fistula was determined by angiography and is

TABLE 6. Data from Patients with a Brescia fistulae.

<u>No</u>	<u>Age</u>	<u>Sex</u>	<u>Forearm Circum. (mm)</u>		<u>Duration of Fistula</u>
			<u>Normal</u>	<u>Fistula</u>	
1	32	M	244	250	12 days
2	63	F	-	-	8 days
3	32	M	244	250	7 weeks
4	60	F	240	245	24 days
5	64	F	210	215	10 months
6	76	M	245	245	2 weeks
7	40	M	235	260	4.5 months
8	61	M	270	265	23 days
9	21	M	260	260	2 weeks

Age range: 21-76 yr, median 60 yr.

Median duration of fistula, 23 days.

TABLE 7. Effects of Forearm Fistula.

	<u>Normal side</u>	<u>Fistula side</u>
	<u>Median (Range)</u>	
<u>Total forearm flow</u> (ml.(100 ml tissue). ⁻¹ min ⁻¹).	6.3 (1.9-16.3)	22.1 (5.6-31.5)*
<u>Forearm skin blood flow</u> (PU) 3 sites.	6.0 (3.7-15.3)	8.2 (4.2-17.2)†
<u>Forearm skin temperature</u> (°C).	29.6 (26.5-30.7)	31.2 (29.7-32.2)#

* p<0.002 Mann-Whitney 'U' test

† p<0.01 Mann-Whitney 'U' test

0.02>p>0.002 Mann-Whitney 'U' test

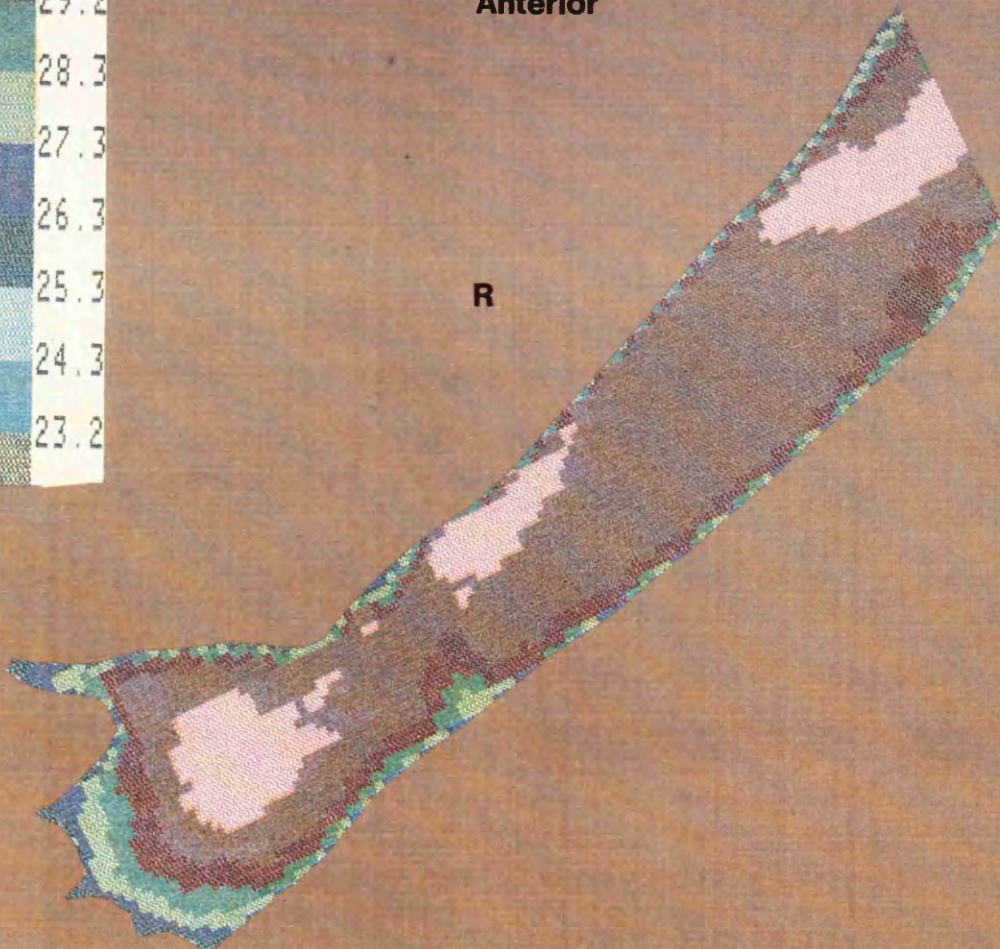
FIGURE 24.

Thermogram of a patient (number 1) with a Brescia fistula at the left wrist. Anterior aspect. Ambient temperature 20°C.

The increased T_{sk} on the side of the fistula can be seen. The area of the fistula itself was excluded from the computer analysis of the skin temperature over the anterior aspect of the forearm. The equivalent area was excluded from the normal opposite arm.



T_a 20°C
Anterior



shown in Figure 25. Lying in the sole of the right foot it was fed by a greatly enlarged tibio-peroneal trunk which did not branch to give a posterior tibial artery until the level of the malleoli, after which the peroneal element rapidly dwindled. From its usual site behind the medial malleolus, the posterior tibial artery then ran forward to provide the main source of inflow to the fistula in the sole.

The total blood flow through the calf on the side of the fistula was greatly increased (Table 8). Skin perfusion over the calf on the affected side was variable and somewhat higher than on the normal side but the values were in the range found in normal subjects. There was a marked increase in the mean T_{sk} of the calf on the affected side (Table 6), and the way in which the temperature was distributed is shown by the isotherms on the anterior and posterior aspects of the legs. (Figs 26a & b). The points relating mean calf T_{sk} and the total calf blood flow in the legs of this patient were close to the regression line relating those variables in the normal subjects undergoing exercise. The calf on the affected side was slightly larger at its maximum circumference (340 v 330 mm).

These observations supported the hypothesis that T_{sk} of the calf and forearm was a function of the deep arterial inflow to the limb rather than its skin perfusion. It was felt, therefore, that if this were so, then in subjects where there was known to be a limited or reduced arterial inflow to the calf - as in those with peripheral vascular

FIGURE 25.

A tracing of the angiogram of the patient who had an arterio-venous fistula in the sole of the right foot.

An enlarged tibio-peroneal trunk (a) can be seen running down to the level of the malleoli from where the posterior tibial artery arises. The peroneal element then dwindles. From behind the medial malleolus, the posterior tibial artery runs forward into the sole to provide the main arterial inflow to the fistula (b).

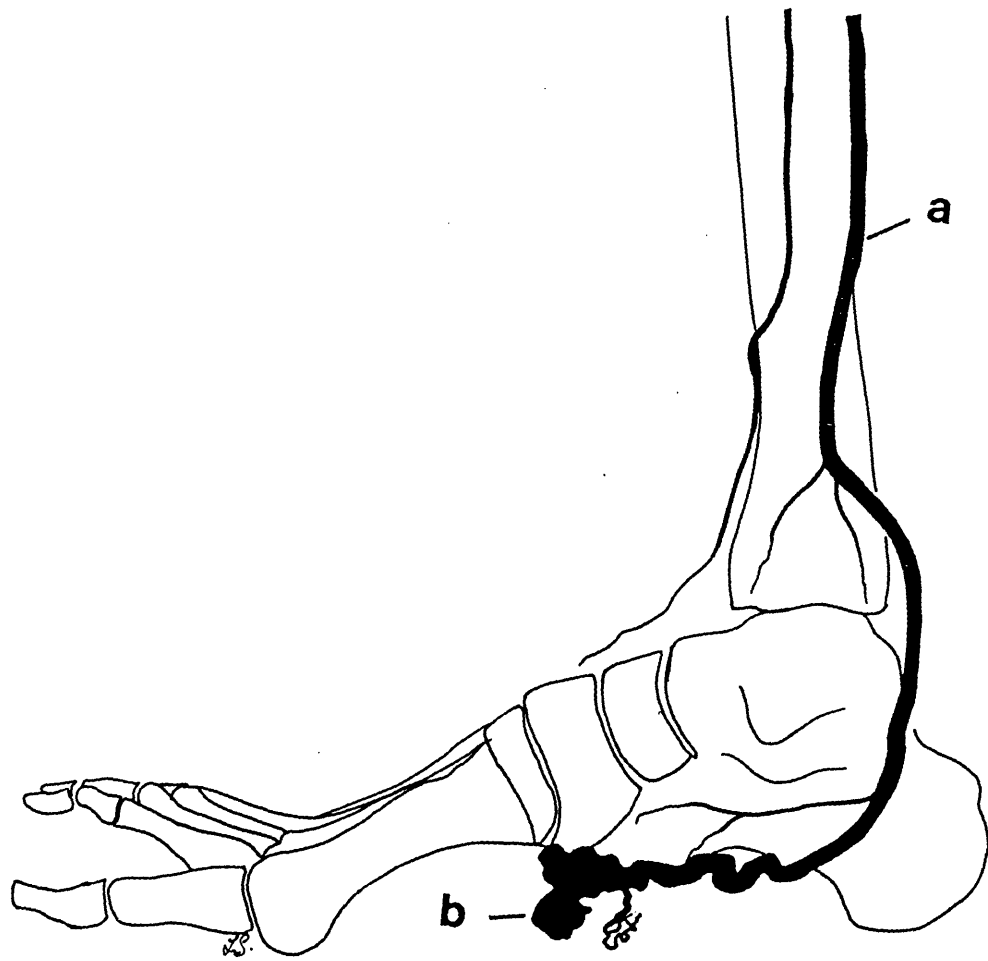


TABLE 8. Effect of an A-V fistula in the foot.

	<u>Normal side</u>	<u>Fistula side</u>
<u>Total calf blood flow</u> (ml. (100 ml tissue). ⁻¹ min ⁻¹).	2.7	10.6
<u>Mean calf skin blood flow</u> (PU) 3 sites.	2.8	4.3
<u>Mean calf skin temperature</u> (°C).	28.9	30.4

FIGURE 26a.

Thermograms of patient with an arterio-venous fistula in the sole of the right foot. Anterior and posterior aspects of the legs are shown at an ambient temperature of 20°C.

The increased in T_{sk} can be seen to extend all the way up the calf and into the thigh. The points relating mean calf skin temperature and the total calf blood flow in the legs of this patient lie close to the regression line relating those variables in Exercise Control subjects.

R



Post

L



T_a 20 °C

L



Ant

R



FIGURE 26b.

Thermograms of the feet in patient with an arterio-venous fistula in the sole of the right foot. Plantar aspect, and at T_a 20°C.

The sole of the right foot can be seen to have a very much hotter skin temperature than that of the left foot.

The area of maximal heat overlies the area corresponding with the site of the fistula demonstrated angiographically.

Plantar Surface
 T_a 20°C



disease - this reduced limb core perfusion might be reflected in the surface temperature of that calf.

With this in mind we studied 2 groups of patients with peripheral vascular disease of differing severity; those suffering from intermittent claudication, and those with more advanced disease.

Observations on patients with Peripheral Vascular Disease.

In each of these groups the initial investigations of ankle systolic blood pressure and ankle/brachial pressure index (ABPI) were performed and their results compared with the over-40 yr control group. It was recognised that the spectrum of peripheral vascular disease does not lend itself easily to natural divisions between patients, but that a gradual progression of severity might allow an individual patient to have intermittent claudication in one leg with the early development of rest pain in the opposite limb. As the patients presented, the predominant symptom dictated into which group they were placed.

Comparisons were then made between the ankle pressures and ABPIs of all three groups - controls, claudicants and those with more severe peripheral vascular disease, usually critical ischaemia. This latter group was designated the 'PVD Patient' group, in order to differentiate it from the 'Claudicant' group.

Observations on ABPI and Ankle Pressure differences between all 3 groups; Claudicants, PVD Controls and PVD Patients.

Patients suffering from Intermittent Claudication.

This group was made up of 4 men and 2 women, aged 60-81 yr, (median 70.5 yr). (Table 9). Claudicating leg pain prevented further walking on level ground between 50-300 yards. Four of the patients had bilateral symptoms but in each case one leg hurt considerably more than the other and was deemed the 'bad' leg.

The median ankle pressure on the predominantly symptomatic side was 90 mm Hg, (range 75-100 mm Hg), and on the 'good' or less symptomatic side the median ankle systolic pressure was 135 mm Hg, (range 75-170 mm Hg). This was a statistically significant difference ($p < 0.01$) and was reflected in similar significant differences in the ankle/brachial pressure index (ABPI). On the 'bad' side the ABPI range was 0.53-0.65, (median 0.56), and on the 'good' side the range was 0.58-1.08 (median 0.91), $p < 0.01$. It was in these examinations that the most convincing separation of the 3 groups occurred.

Comparison between groups.

The claudicants had significantly lower ABPIs than the PVD control group ($p < 0.001$) as did both 'good' and 'bad' legs of the PVD patients and at the same level of significance. However, comparison of the claudicants' and PVD patients' 'good' legs revealed no significant difference in ABPI. Differences were found between ABPIs in claudicants and PVD patients' 'bad' legs, where the claudicants' values were significantly higher ($p < 0.02$), and between 'good' and 'bad' legs in the PVD patient group

TABLE 9. Data from Patients with Intermittent Claudication.

No	Age	Sex	Brachial BP	Ankle BP (mm Hg)		ABPI		Exercise completed
			(mm Hg)	'Good'	'Bad'	'Good'	'Bad'	
1	60	M	140	130	75	0.93	0.54	2.5
2	61	F	190	170	100	0.89	0.53	1.5
3	73	M	175	120	95	0.69	0.54	5
4	68	M	165	170	95	1.03	0.58	5
5	81	F	130	140	85	1.08	0.65	4.5
6	78	M	130	75	75	0.58	0.58	4

('Good' and 'Bad' refer to the leg in which the lesser or greater symptoms were experienced.

'Exercise completed' refers to the number of cycles of toe-raises managed).

Age range: 60-81 yr, median 70.5 yr.

Brachial BP range: 130-190 mm Hg, median 153 mm Hg.

Ankle BP range ('Good' leg): 75-170 mm Hg, median 135 mm Hg.

Ankle BP range ('Bad' leg): 75-100 mm Hg, median 90 mm Hg.

ABPI range ('Good' leg): 0.58-1.08, median 0.91.

ABPI range ('Bad' leg): 0.53-0.65, median 0.56.

Ankle and ABPI values were significantly different between 'good' and 'bad' legs, $p < 0.01$.

as was expected ($p < 0.05$).

When examining the systolic ankle pressures of each of these groups, similar results emerged. The claudicants showed a small but significantly lower ankle pressure in their 'bad' legs compared with PVD patients' 'good' legs ($p < 0.05$), where no significant difference had been found in ABPI. Controls did not show any difference in ankle pressure from claudicants' 'good' legs, nor did the claudicants' 'bad' legs show any difference between either the 'good' or 'bad' leg of the PVD patients. However, it was thought likely that this was due to the small numbers as the PVD patients' 'good' legs were found to be significantly higher than their 'bad' legs ($p < 0.05$). Highly significant differences in ankle pressure were shown between controls and claudicants' 'bad' legs, as well as between controls and both legs of the PVD patient group ($p < 0.001$). Similarly, claudicants' 'good' legs' ankle pressures differed significantly, both from their 'bad' legs and the PVD patients' 'good' legs ($p < 0.05$), and even more so from the PVD patients' 'bad' legs ($p < 0.01$).

In the PVD patients, ankle systolic blood pressures in the symptomatic leg ranged between 20-160 mm Hg, (median 40 mm Hg). (Table 10). In the 'good' or less symptomatic leg, the ankle pressure range was 30-165 mm Hg, (median 95 mm Hg). This was statistically different ($p < 0.01$). As expected, the ABPI values showed a similar significant difference between the 'good' and 'bad' legs. In the 'bad' leg the range was 0.13-1.10 (median 0.28), and in the 'good' leg the range fell between 0.28-1.14 (median

TABLE 10. Data from Patients with Severe Peripheral Vascular Disease.

No	Age	Sex	Brach Pr. (mm Hg)	Ank Pr. (mm Hg)		ABPI		Rest Pain	Gangrene (wet/dry)
				'Good'	'Bad'	'Good'	'Bad'		
1	64	M	185	amp	25	N/A	0.13	+	+ (wet)
2	66	M	130	75	40	0.58	0.30	+	+ (wet)
3	49	M	145	75	30	0.52	0.21	+	-
4	88	F	230	-	-	-	-	+	+ (dry)
5	58	M	105	30	20	0.28	0.14	+	+ (both)
6	59	M	145	45	30	0.31	0.14	+	+ (dry)
7	69	M	185	110	30	0.59	0.16	+	-
8	57	M	145	165	160	1.14	1.10	-	-
9	50	M	110	95	25	0.86	0.23	+	-
10	73	M	160	70	40	0.44	0.25	+	+ (wet)
11	74	M	145	60	25	0.34	0.17	+	+ (dry)
12	57	M	160	115	105	0.72	0.50	-	-
13	57	M	145	140	105	0.96	0.72	-	-
14	49	M	145	145	160	1.00	1.10	-	-
15	64	F	170	105	80	0.62	0.44	+	+ (wet)
16	33	F	115	120	115	1.04	1.00	-	-
17	80	F	140	55	55	0.39	0.39	+	+ (wet)

('Good' and 'Bad' indicate the same as in Table 11).

Age range: 33-88 yr, median 59 yr.

Brachial Pressure range: 105-230 mm Hg, median 145 mm Hg.

Ankle Pressure range ('Good' leg): 30-165 mm Hg, median 95 mm Hg.

Ankle Pressure range ('Bad' leg): 20-160 mm Hg, median 40 mm Hg.

ABPI range ('Good' leg): 0.28-1.14, median 0.59.

ABPI range ('Bad' leg): 0.13-1.10, median 0.28.

0.59), ($p < 0.01$). These last results, dependent upon systolic blood pressure measurements taken with a Doppler probe, are not unexpected but need to be viewed with caution. One man required a part-foot amputation for gangrene despite patent posterior tibial and dorsalis pedis arteries. He was excluded from here as both these arteries were incompressible.

Exercise and calf skin temperature.

Each of these subjects was exercised in the same way as the control exercise group although only 2 managed all 5 cycles of exercise. This they did despite claudication pain towards the end of the exercise.

Except for one, these patients showed a fall in ankle systolic pressure after exercise (Table 11) in both legs, and all patients with one exception showed an increase in total blood flow (TBF) after exercise (Table 12). The exception was the same patient in each instance and although his 'bad' leg behaved in the same way as all the others, his 'good' leg showed a small rise in ankle systolic pressure after exercise (130 to 135 mm Hg), accompanied by a similar small fall in total calf blood flow 1.7 to 1.2 ml.(100 ml tissue)⁻¹.min⁻¹. Calf skin temperature rose in both legs after exercise in all patients except two. One showed a drop in calf T_{sk} from 29.2°C to 29.0°C despite a rise in TBF on that side from 2.3 to 6.6 ml.(100ml tissue)⁻¹.min⁻¹. In the other, T_{sk} fell 0.2°C along with a fall in TBF of 0.5 ml.(100ml tissue)⁻¹.min⁻¹. (Table 13).

TABLE 11. Effect of exercise on ankle blood pressure in patients with intermittent claudication.

No	Age	Ankle BP Before		Ankle BP After		Cycles completed
		'Good'	'Bad'	'Good'	'Bad'	
1	60	130	75	135	70	2.5
2	61	170	100	85	40	1.5
3	73	120	95	75	65	5
4	68	170	95	160	35	5
5	81	140	85	40	50	4.5
6	78	75	75	50	40	4

Range: 75-170 75-100 40-160 35-70 mm Hg

Median: 135 mm Hg, 90 mm Hg, 80 mm Hg, 45 mm Hg

TABLE 12. Effect of exercise on calf total blood flow (TBF) in Claudicants.

Total Calf Blood Flow. (ml.(100 ml tissue)⁻¹.min⁻¹).

No	Before Exercise		After Exercise		Change in TBF	
	'Good'	'Bad'	'Good'	'Bad'	'Good'	'Bad'
1	1.7	2.0	1.2	4.3	-0.5	2.3
2	1.6	1.1	3.2	5.6	1.6	4.5
3	2.5	2.3	5.0	6.6	2.5	4.3
4	1.2	1.6	7.2	4.1	6.0	2.5
5	2.9	1.1	4.7	4.3	1.8	3.2
6	1.3	5.2	6.0	6.9	4.7	1.7

TABLE 13. Effect of exercise on mean calf skin temperature in Claudicants ($^{\circ}\text{C}$).

No	Before Exercise		After Exercise		Change in T_{sk}	
	'Good'	'Bad'	'Good'	'Bad'	'Good'	'Bad'
1	30.1	29.9	29.9	29.9	-0.2	0.0
2	27.6	27.2	28.7	28.6	1.1	1.4
3	29.1	29.2	30.0	29.0	0.9	-0.2
4	29.0	27.4	31.7	30.0	2.7	2.6
5	25.3	25.8	27.3	27.6	2.0	1.8
6	26.9	26.7	29.9	29.0	3.0	2.3

Since neither leg was normal in those suffering from intermittent claudication and no statistical difference could be demonstrated between them, when considered as a group of diseased limbs, some comparisons could be made with the exercise controls. With the exceptions already mentioned, all legs showed a small rise in TBF after exercise even though only 2 patients managed to complete all 5 cycles.

Because of the variable amount of exercise performed by individual patients within the claudicant group, no statistical analysis was made of the group, nor was it compared with the exercise control group. However, because a relationship had been found between calf T_{sk} and TBF in the exercise control group, the same variables were plotted for the claudicants.

Exercise and total limb blood flow (TBF): a relationship between T_{sk} and TBF.

A similar, though weaker, correlation was found ($r=0.39$; $n=12$; $p<0.05$), but it was noted that the regression line was not only parallel to , but significantly higher than that of the controls ($p<0.02$), (Fig 23). This meant that for any given total blood flow, the skin temperature was significantly higher in the claudicant group.

Apart from this, the claudicants' legs behaved in the same way as the exercise control group. The possible reasons why the relatively ischaemic limb should have a significantly higher calf T_{sk} for any given TBF are

discussed in the next chapter.

Initial calf T_{sk} and its increase after exercise.

The negative relationship found between the increase in T_{sk} and the initial T_{sk} of the calf, demonstrated in the control group, was found to hold true for the claudicants as well, but the same was not true for total blood flow to the calf.

Thus, in a relatively ischaemic limb, because of a limited ability to increase TBF, a similar lack of increase in T_{sk} was seen. With this in mind we went on to study a group of patients with severe peripheral vascular disease, the majority of whom had limbs which were critically ischaemic.

Observations on patients with severe peripheral vascular disease (PVD). (Table 10).

Because of the severity of their disease these patients could not be exercised as those with intermittent claudication had been, so the stress applied to the circulation was restricted to raising the ambient temperature from 20°C to 30°C. This had been shown to increase calf T_{sk} and $SkBF$ in the pulp of the hallux in the control group, and therefore by inference, the TBF through the limb. We elected to study a group with severe ischaemia to see if they were able to increase their peripheral circulation in any way in response to physiological stress. There were 17 patients, 13 men and 4 women, aged 33-88 yr (median 59 yr). Many had bilateral

disease demonstrated angiographically but their symptoms were predominately unilateral. 12 of the group had true Critical Ischaemia as defined before.

Of the 12 patients with critical ischaemia, 9 had frank gangrene in the toe, foot or leg. In 5 this was wet and in 3, dry gangrene. One patient had a mixture of both wet and dry gangrene. All but 2 of those with gangrene had an ankle systolic pressure of 40 mm Hg or less, and an ABPI less than 0.30. The 2 exceptions had ankle pressures of 55 mm Hg and 80 mm Hg, with ABPIs of 0.39 and 0.44 respectively. All 12 critically ischaemic patients complained of rest pain.

As with the PVD control group, the initial examination was to study the effect of raising the ambient temperature on the skin temperature of the limb.

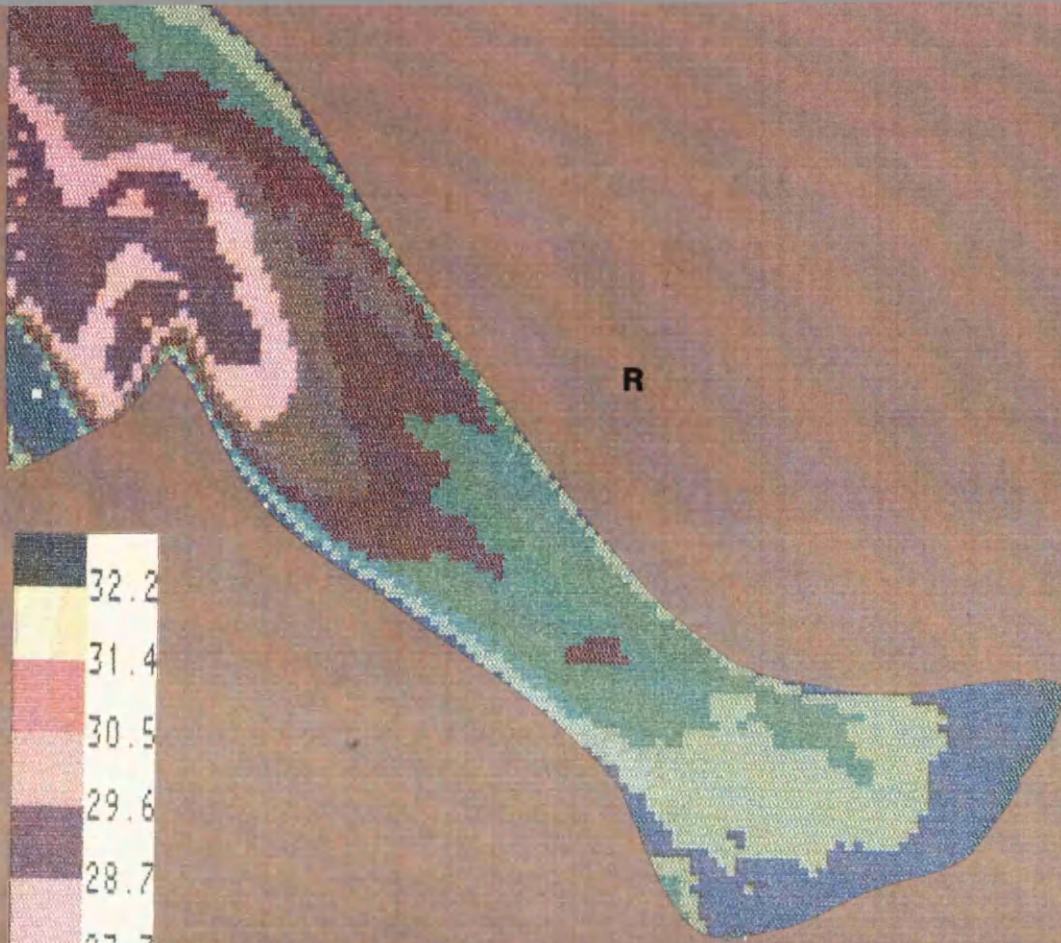
Effect of ambient temperature (T_a) on skin temperature (T_{sk}).

Examination of thermograms of these subjects at a T_a of either 20°C or 30°C showed the lack of any consistent pattern of skin temperature, (Figs 27-31). In general, the appearance of the warm area in the skin over the mid-posterior calf found in the control group was lost, as was the graduated and regular reduction in skin temperature normally found towards the ankle. Instead, in the PVD patients, there was a more blotchy or patchy appearance on thermography. This was often seen bilaterally, making identification of the symptomatic leg by thermographic means alone unreliable. Furthermore, the presence of

FIGURE 27a.

Thermograms of PVD patient (number 5) with gangrene of the Right foot. Lateral surface of calves. T_a 20°C.

The right calf appears cooler than the left in the distal third, which might be expected, but the foot on the affected side is warmer than the opposite (left). This increased warmth appears to be confined to the dorsum of the right foot - see Fig 27c.

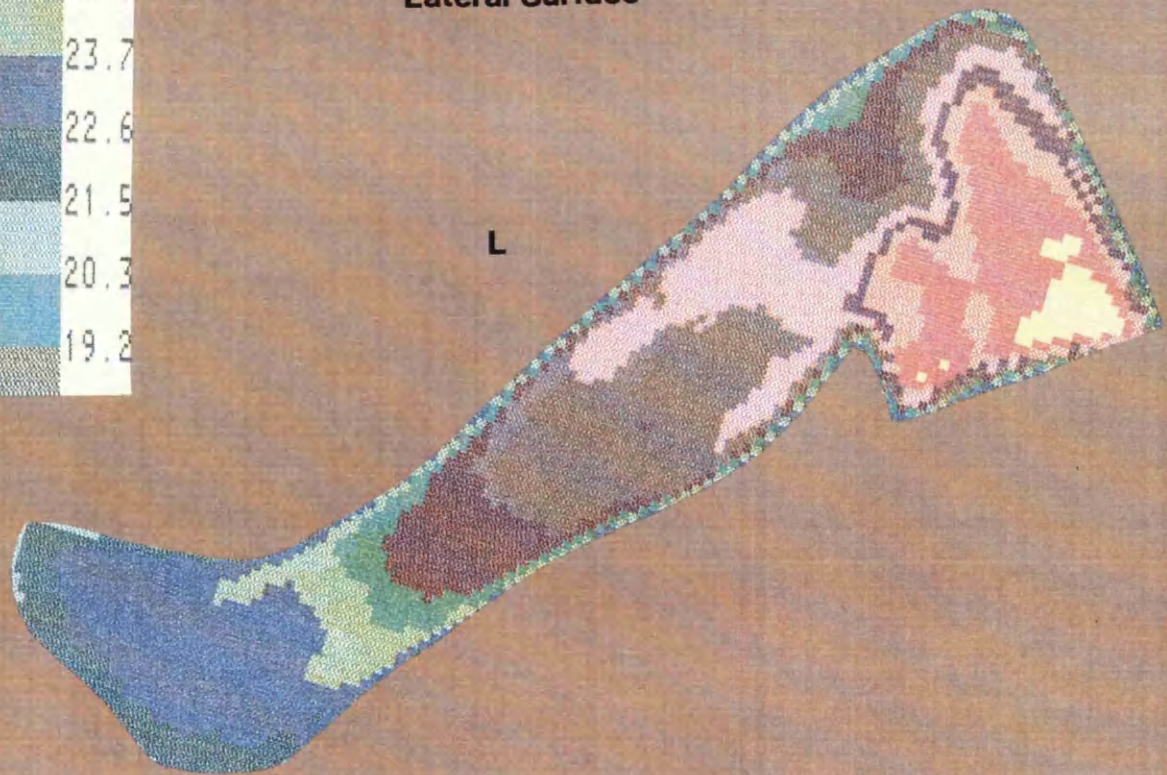


R



$T_a 20^{\circ}\text{C}$

Lateral Surface

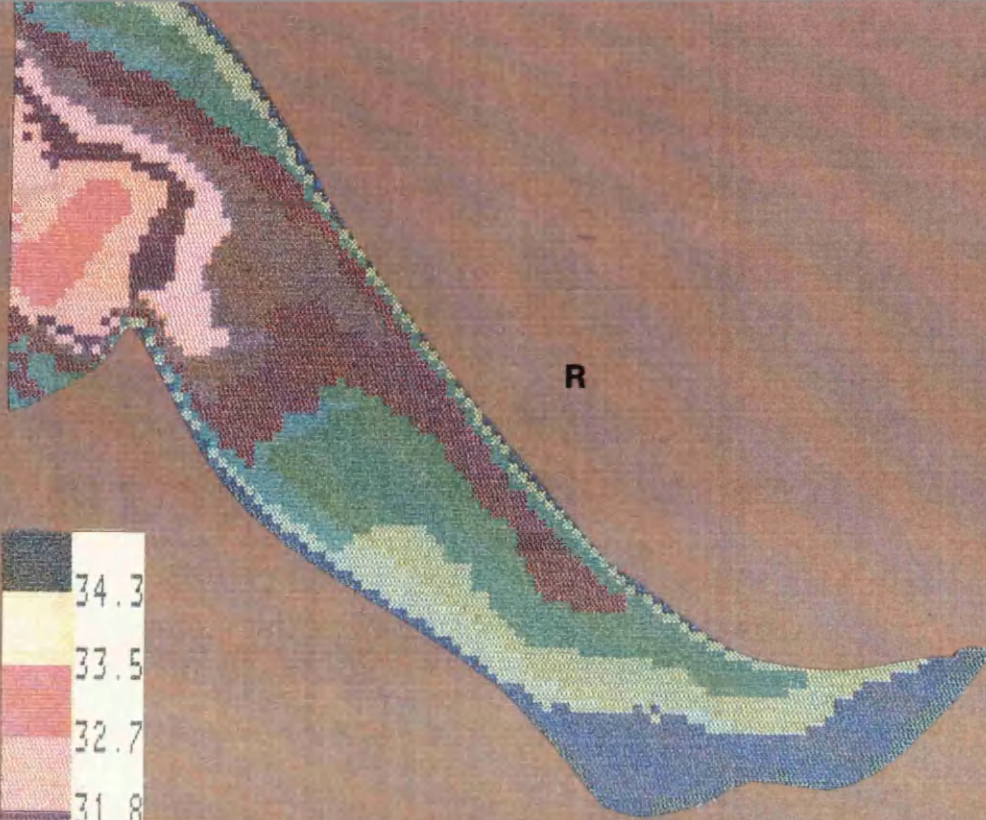


L

FIGURE 27b.

Thermograms of PVD patient with gangrene of the Right foot. Lateral surface of calves. T_a 30°C. (Same patient as Fig 27a).

At the higher ambient temperature, the cooler appearance of the posterior calf on the right is more marked, and may reflect the distribution of the run-off vessels distal to a more proximal arterial occlusion. Note that the right foot is still warmer than the left.

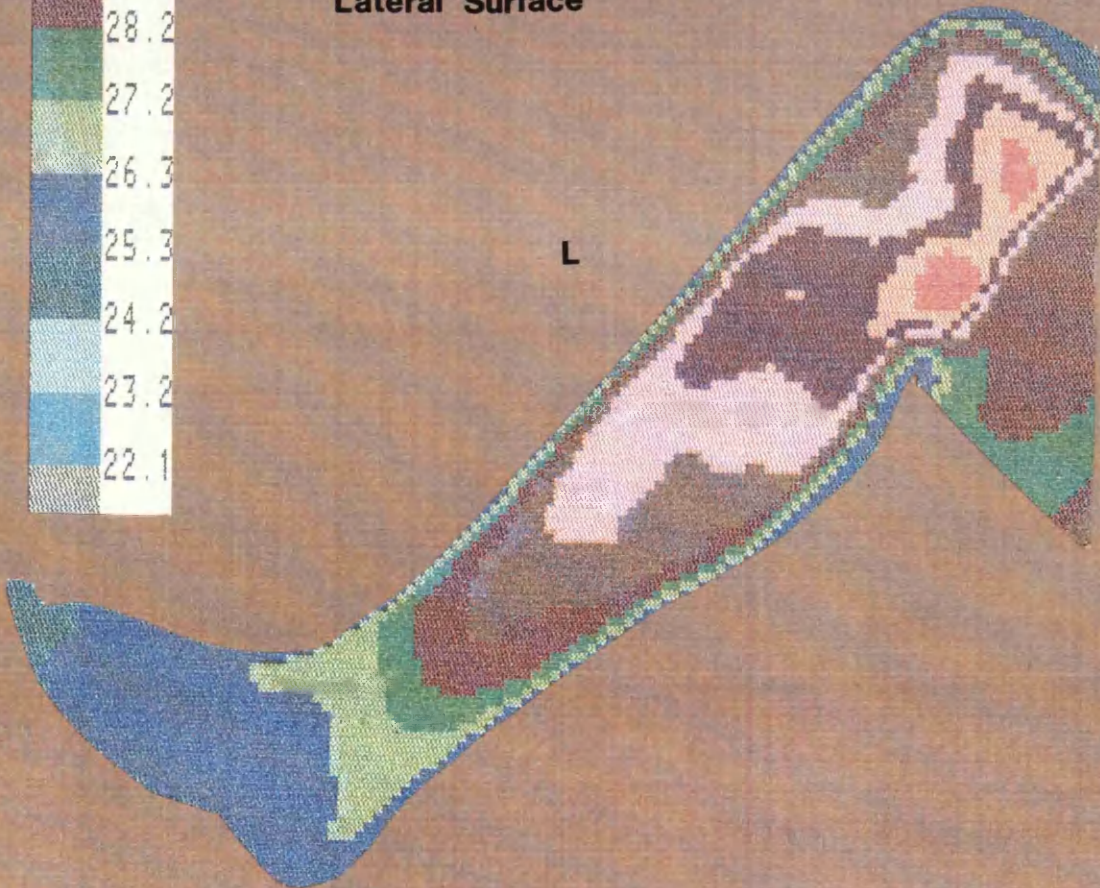


R



$T_a 30^\circ\text{C}$

Lateral Surface



L

FIGURE 27c.

Thermograms of PVD patient's feet at both T_a 20° and 30°C. Plantar surface. Gangrene present in Right foot. (Same patient as Figs 27a & b).

The lateral two toes had wet and blistering gangrene. The increased evaporative heat loss which resulted is responsible for the 'thermographic amputation' of these toes. The remaining toes were affected by dry gangrene only.

At both ambient temperatures the 'butterfly-wing' appearance observed in normal controls (Fig 14) has disappeared. It has been replaced at T_a 20°C by an indistinct stacking of isotherms, gradually becoming cooler from heel to toe, although a slightly warmer instep is seen on the affected side. (See also Fig 28c). At T_a 30°C there is an almost complete lack of any isotherm pattern on the right, and very little is left on the opposite side. It is interesting to note that in these plantar views the gangrenous foot is clearly colder than the opposite limb. This is in contradistinction to the dorsal surface of the foot which appeared warmer than the unaffected side. (See Figs 27a & b).



$T_a 20^\circ\text{C}$



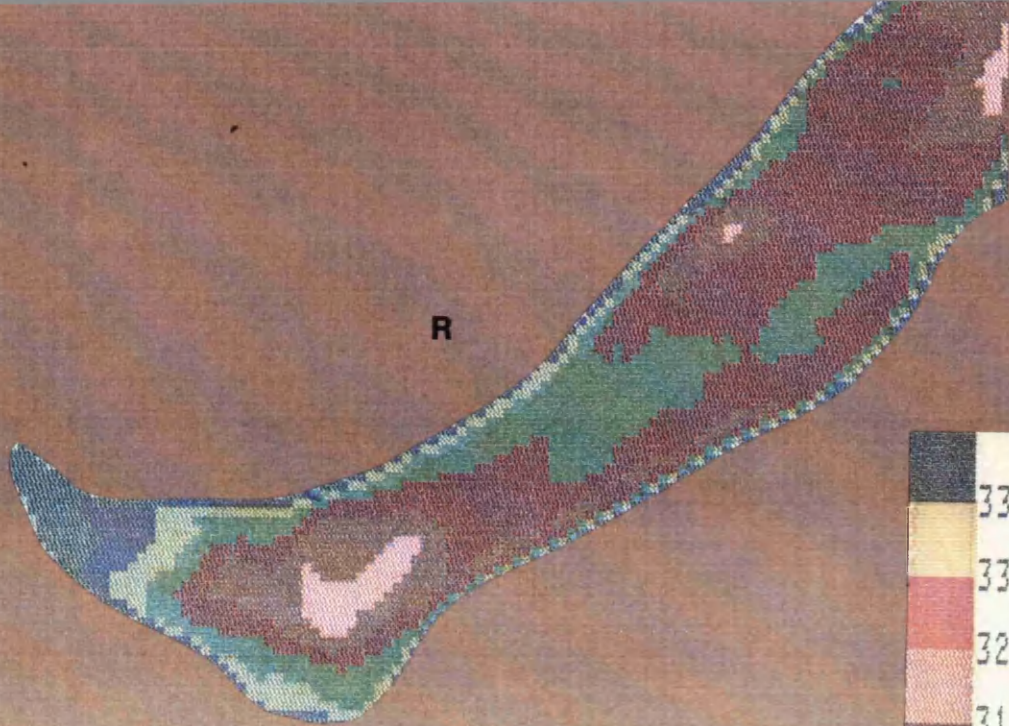
$T_a 30^\circ\text{C}$



FIGURE 28a.

Thermograms of PVD patient (number 11) with dry gangrene in the Right 2nd toe. Medial surface of calves. T_a 20°C .

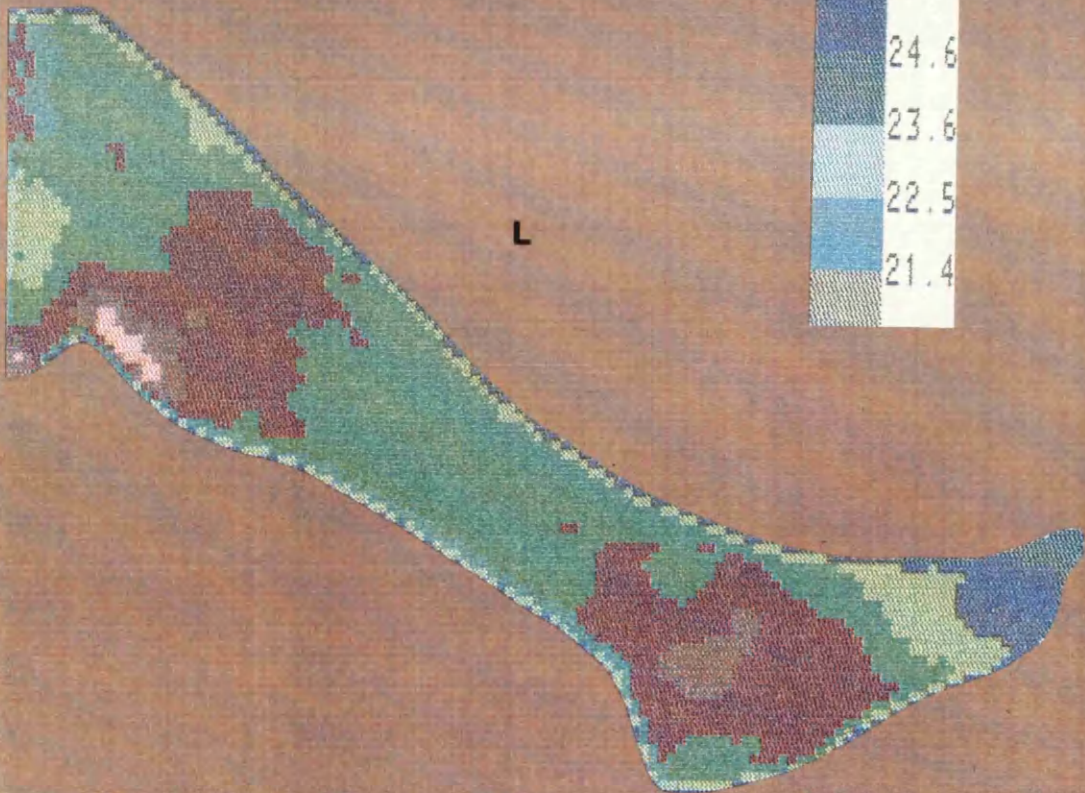
Unlike the patient in Fig 27, the limb affected by gangrene here is warmer than the opposite member, this being so even on the medial side which, in normal individuals, is usually cooler. Even so, the absence of any recognisable pattern is striking, and the haphazard arrangement of the isotherms in both limbs make it hard to determine which is the diseased limb. Clinically, there was little difference in the degree of severity of disease between patients in Figs 27 & 28.



R

$T_a 20^{\circ}\text{C}$

Medial Surface



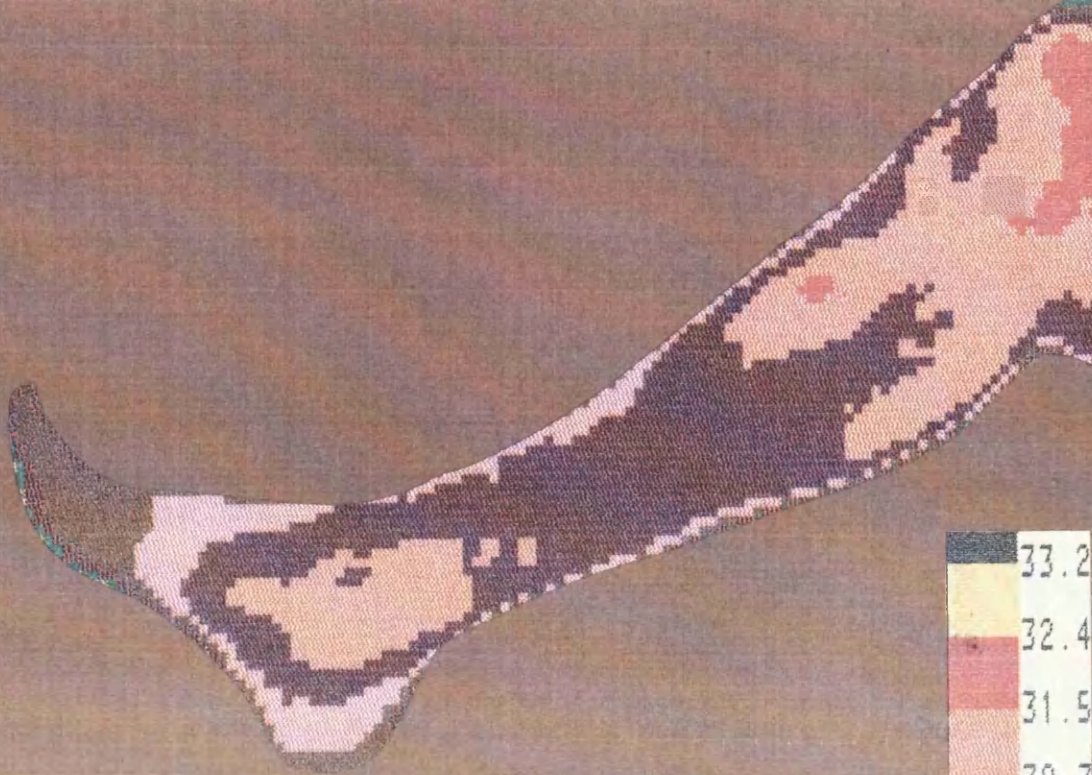
L

FIGURE 28b.

Thermograms of PVD patient with dry gangrene in the Right 2nd toe. Medial surface. T_a 30°C. (Same patient as Fig 28a).

The limb affected with gangrene (upper thermogram) is again seen to be warmer than the opposite side. At this ambient temperature the difference in skin temperature is even more obvious than at T_a 20°C.

The warmest area in the ischaemic limb is found around the knee, and might suggest the appearance of collateral circulation. This was not always borne out by angiographic studies. In the normal limb, the anterior of the knee is cooler than its posterior aspect, as is shown in the lower thermogram. (See also Figs 13 & 15).



T_a 30°C

Medial Surface

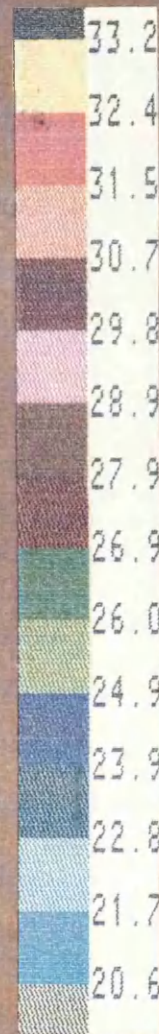


FIGURE 28c.

Thermograms of PVD patient's feet at both T_a 20° and 30°C. Plantar surface. Dry gangrene is present in the Right 2nd toe. (Same patient as Figs 28a & b).

Here the gangrenous foot at T_a 20°C (upper left thermogram) has slightly warmer toes than the unaffected foot. This is the opposite situation to the patient in Fig 27c, where the gangrenous foot showed a cooler plantar surface, as might be expected. There is the remains of the 'butterfly-wing' pattern of isotherms on the soles at the lower ambient temperature, but when T_a is raised to 30°C, no trace of it can be seen. In addition, it is not possible to distinguish between the affected and unaffected foot at the higher ambient temperature.



$T_a 20^\circ\text{C}$



$T_a 30^\circ\text{C}$



FIGURE 29.

Thermograms of PVD patient's feet at both T_a 20° and 30°C. Plantar surface. Dry gangrene is present in left 4th toe. Patient number 6.

This patient had marked oedema of his left foot and ankle in addition to his gangrenous toe. It is obvious that the affected foot is considerably warmer than the opposite side at both ambient temperatures. There was no evidence of osteomyelitis on X-ray examination of the foot, nor was there any overt infection in the foot. A possible explanation for the increased skin temperature seen on the affected side is the increased thermal conductivity of oedema fluid (which is essentially water) over fat and muscle. (See text, pp.245 & 250).

The normal 'butterfly-wing' pattern is lost in these thermograms also.



T_a 20°C



T_a 30°C

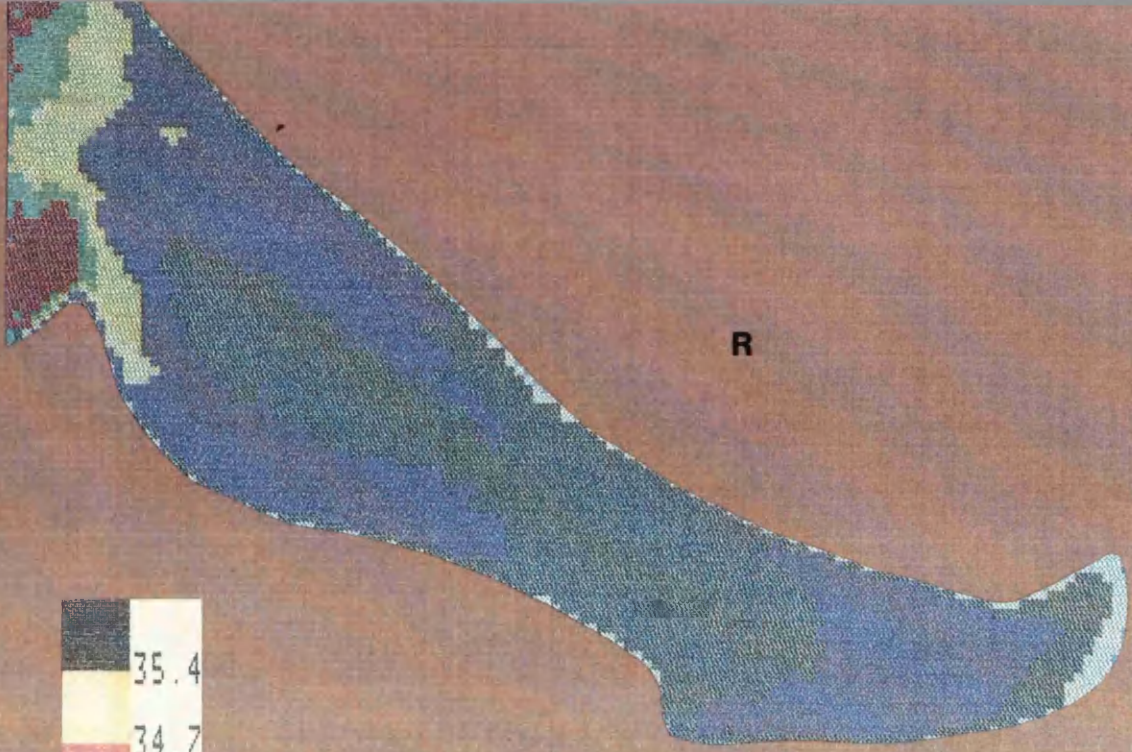
FIGURE 30a.

Thermograms of PVD patient (number 4) with dry gangrene of the left 4th and 5th toes. Lateral surface of legs. T_a 20°C.

These thermograms clearly show the confusion that may arise if skin temperature is used as an indicator of skin perfusion in the calf.

It is the left leg (lower thermogram) which is critically ischaemic, with dry gangrene present in two toes, although the right seems, thermographically, considerably worse. Popliteal pulses were present on both sides, but no pulses were palpable distally.

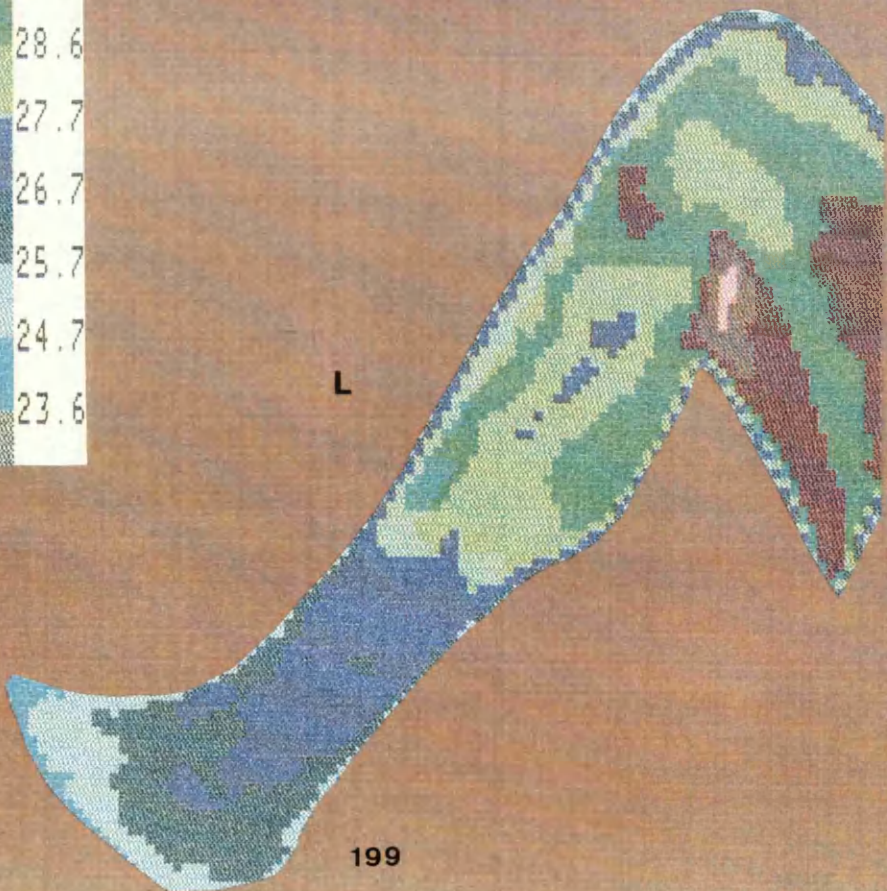
If the degree of ischaemia had reached a point where there had been an accumulation of lactate and inorganic phosphate in the affected limb, then vasodilatation on that side with reflex vasoconstriction on the opposite side might account for these appearances. (See text, page 258).



R



Ta 20°C Laterals



L

FIGURE 30b.

Thermograms of PVD patient with dry gangrene of the left 4th and 5th toes. Lateral surface of legs. T_a 30°C. (Same patient as Fig 30a).

Note, as in Fig 30a, that the critically ischaemic left leg (lower thermogram) is considerably warmer than the clinically asymptomatic right leg.

Whether the sharp skin temperature drop just below the knee joint in the right leg is indicative of vasoconstriction is not certain.

The appearances of the left leg are not unlike some normal control subjects, despite the presence of gangrene in the foot.



R



T_a 30°C Laterals



L

FIGURE 31.

Thermograms of PVD patient (number 15) with mixed wet and dry gangrene of the left foot. Plantar surface of both feet. T_a at both 20° and 30°C.

(Note that these thermograms were made using the Inframetrics 600 M thermal imaging camera during its trial period in our unit).

The lateral three toes of the left foot have been amputated and the wound remains unhealed. The hallux and second toe show the changes of dry gangrene.

The striking appearance of the crowded isotherms, particularly noticeable at T_a 20°C, resembles the irregular stacking of geological strata in rock.

It is still present, though less pronounced, at T_a 30°C.

It is more marked at both ambient temperatures in the affected foot.



Ta 20°C



Ta 30°C



gangrene could not be deduced from study of the thermograms, as in some cases the T_{sk} of the affected side was warmer than the opposite side, and in others it was cooler. Wet gangrene could produce the appearance of 'thermographic amputation' due to the increased heat loss by evaporation (Fig 27c). It might also be expected to be frankly infected, rather than the leathery mummification characteristic of dry gangrene. If the wet gangrene was infected, the associated surrounding inflammation might well give rise to a warmer thermographic appearance on the affected side. There seemed to be no trend in the changes found after raising the T_a to 30°C. Both limbs showed an increase in T_{sk} , but the change did not differ significantly between the two legs.

The anterior aspect of the knee, usually cooler than the posterior aspect in the control group, appeared warm in the PVD patients. Initially this was felt likely to represent superficial collateral circulation resulting from occlusion of the superficial femoral artery, as had been shown by other workers (Lovisatti et al., 1975; Acciarri, 1977; Spence et al., 1981), but later study of the relevant angiograms did not always confirm this.

In the lower part of the leg, towards the ankle, where controls usually showed the skin over the malleoli to be warmer than that over the anterior or posterior ankle tendons, the PVD group of patients showed no such tendency. The isotherms were fewer, larger and less regular. In cases where there was a lack of thermographic definition around the ankle and lower leg, it was often

found to occur in patients who had a lot of peripheral oedema in the lower limbs. (Fig 29).

When the antero-superior and postero-inferior boxes (see Fig 12) were examined on the calf thermograms and the P/A ratios calculated (Appx 3), no difference was found between 'good' and 'bad' legs at T_a 20°C nor was there any statistically significant difference between 'good' and 'bad' legs at T_a 30°C. However, when the T_a was raised from 20°C to 30°C there was a small but statistically significant fall in P/A ratio in both the PVD patients' 'bad' leg from a median of 0.99 to 0.98, and in the control group from a median of 0.99 to 0.975, ($p < 0.01$). No significant change occurred in the P/A ratio of the PVD patients' 'good' leg despite a small alteration in the range, (0.97-1.00 at T_a 20°C and 0.95-1.00 at T_a 30°C), the median remained unaltered at 0.98.

Observations on medial to lateral calf skin temperature gradients.

The medial to lateral rise in temperature gradient seen in the control group was not observed in the PVD patients' 'bad' legs at either ambient temperature, nor was it seen in their 'good' legs at T_a 20°C. The lateral side of the calf was significantly warmer than the medial only at T_a 30°C and in the patients' 'good' legs ($p < 0.05$). There was no difference in the rise in calf T_{sk} between 'good' and 'bad' legs, nor was there any difference between the two legs. As expected therefore, when calf skin temperatures were averaged, no difference was found between 'good' and

'bad' legs at either ambient temperature.

However, there were statistically significant increases in both 'good' and 'bad' legs' calf skin temperatures when the ambient temperature was raised, ($p < 0.01$), as had been found in the PVD control group, although the rise in T_{sk} was greater in the latter group, $p < 0.001$. (Fig 15 & Appx 4).

Comparison of T_{sk} changes between calf, sole and hallux.

The increases in T_{sk} of the calf in the PVD patients were not as large as the increments observed in the T_{sk} of the hallux of both legs ($p < 0.01$). Although the T_{sk} of the hallux rose significantly in both feet between the two ambient temperatures no statistical difference between the values for 'good' and 'bad' feet could be detected. (Figs 32 & 33).

When the thermograms of the soles of the feet were studied, the butterfly-wing patterning seen in the control group was found to be missing from most patients. It was replaced by crowded isotherms of reducing temperature peripherally, which resembled the irregular stacking of geological strata in rock. (Fig 31). The soles of the feet showed no difference in their skin temperature between 'good' and 'bad' legs at either T_a despite the presence of frank gangrene in 9 of the 17 patients. Furthermore, both feet had statistically significant increases in T_{sk} of the sole with rising T_a ($p < 0.01$), although there was no difference in the size of the increase between the two feet. This was in contrast to

FIGURE 32.

Graph showing mean calf T_{sk} changes with rise in T_a in PVD Patients. Comparison of 'good' and 'bad' legs.

There is a significant rise in both legs ($p < 0.01$), as there is in the Control group (Fig 16), but there is no significant difference between 'good' and 'bad' legs.

The rise in calf T_{sk} is significantly less than in the hallux in PVD Patients ($p < 0.01$). (See Fig 33).

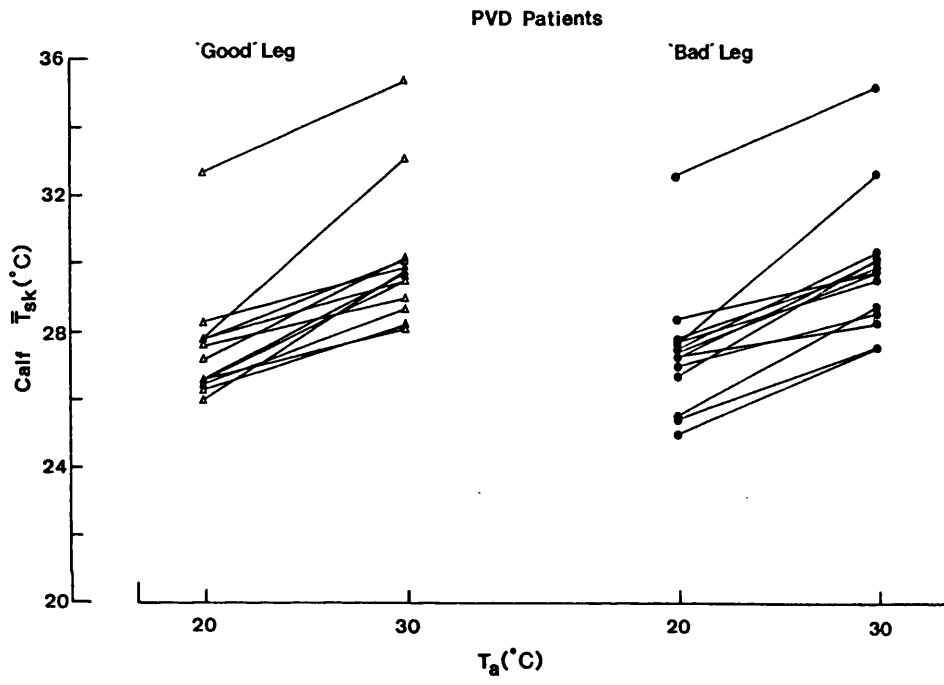
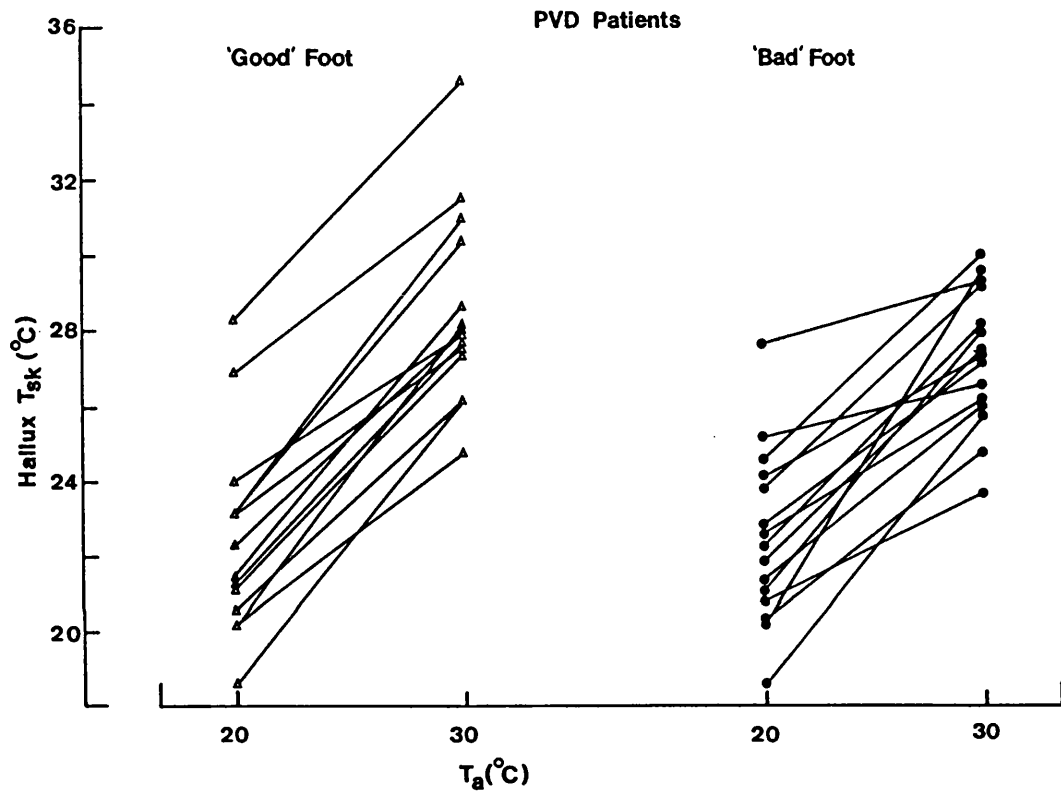


FIGURE 33.

Graph to show the change in hallux T_{sk} following rise in T_a in PVD Patients.

There is a statistically significant rise in T_{sk} in the halluces of both 'good' and 'bad' feet ($p < 0.01$), but it is a significantly smaller rise in the patients' 'bad' foot ($p < 0.05$).

Because the median value for the change in hallux T_{sk} in the Control group (5.25°C) lay between that of the Patients' 'good' halluces (6.3°C), and the value for Patients' 'bad' halluces (4.6°C), no statistical difference was found between the three groups.



the T_{sk} of the hallux pulp on the 'bad' leg where there was a significantly smaller rise in T_{sk} with changing T_a when compared with the T_{sk} of the hallux pulp on the 'good' leg ($p < 0.05$). Interestingly, when compared with the change in hallux pulp skin temperature in the control group (Fig 16), no statistically significant difference could be found between this group and either 'good' or 'bad' leg of the PVD patients (Fig 33). This was because the median value for the change in hallux T_{sk} in controls (5.25°C) lay between that of patients' 'bad' halluces (4.6°C) and 'good' halluces (6.3°C).

Whether the altered pattern of T_{sk} was mirrored by a change in behaviour of skin perfusion was then studied.

Effect of ambient temperature on skin blood flow (SkBF).

When skin blood flow was measured by laser Doppler as described before, (see page 110), no difference was found in the values between 'good' and 'bad' legs at any of the 3 sites of measurement. (Appx 5). This was true at both ambient temperatures (Fig 21). However, when different sites on an individual leg were compared with each other, small but significant differences were found although these were never great enough to produce statistically significant differences between the two legs. At T_a 20°C there were no differences in SkBF between medial calf, lateral calf or the pulp of the hallux in the patients' 'good' leg, but when the T_a was raised to 30°C a small but significant increase was noted in SkBF of the hallux over the SkBF of both sides of the calf ($p < 0.05$). The opposite

effect was seen in the patients' 'bad' leg. At the initial T_a of 20°C a similar small and just significantly higher SkBF was found in the hallux when compared with the lateral side of the calf ($p < 0.05$), but no differences in SkBF at the 3 sites were demonstrated at the higher ambient temperature of 30°C .

Skin blood flow changes at separate sites at T_a 30°C .

All 3 sites in patients' 'good' legs showed statistically significant increases in SkBF when measured individually, and the ambient temperature was raised from 20°C to 30°C , although the medial and lateral calf sites had less marked increases in SkBF ($p < 0.05$) than did the SkBF of the hallux ($p < 0.01$). In patients' 'bad' legs similar increases in SkBF were seen on the medial side of the calf ($p < 0.05$), but the changes were somewhat greater on the lateral side ($p < 0.01$). In contrast to the 'good' legs, the SkBF of the hallux on the 'bad' legs did not alter significantly when the ambient temperature was raised. When calf SkBF values were averaged, statistically significant differences disappeared.

Comparison with PVD Control group SkBF changes.

When these results were compared with the control group, the most striking feature following the stimulus of raising T_a from 20°C to 30°C was that the most significant increase in SkBF was in the hallux of control subjects ($p < 0.001$), which was mirrored by patients' 'good' legs though this was not as big an increase ($p < 0.01$). No detectable rise was found at all in the hallux

SkBF of patients' 'bad' legs. Calf skin blood flow did change, but not significantly in any group; the control group and patients' 'bad' legs showing an increase on the lateral side, and the patients' 'good' legs on the medial side. In no group was a correlation found between the size of increase in SkBF at any measured site and the initial SkBF measured at the same site at $T_a 20^{\circ}\text{C}$.

When comparison was made between groups of individual SkBF values at each site and at each ambient temperature, no difference was found in the SkBF of the calf at either T_a for any group. However, in the hallux at an ambient temperature of 20°C , the control group showed significantly greater values for SkBF than both patients' 'good' legs and 'bad' legs ($p < 0.05$). When T_a was raised to 30°C , the difference between the control group and patients' 'good' legs was no longer significant but a greater difference was noted between the control group and patients' 'bad' legs ($p < 0.01$). There was no significant difference between the SkBF in the hallux of patients' 'good' and 'bad' legs at either ambient temperature.

Relationship between SkBF and T_{sk} :

The correlation found in the control group between SkBF and T_{sk} of the hallux was lost in the PVD patient group in both legs, and similarly the negative correlation between the initial T_{sk} and the size of the increase of T_{sk} , present in both calf and hallux in controls, was no longer found in either of the patient groups' legs.

Observations on Transcutaneous Oxygen ($TcpO_2$) and Carbon

Dioxide (T_{cp}CO₂) tensions.

In both the control group and those with severe peripheral vascular disease, transcutaneous oxygen and carbon dioxide tension measurements were made. (See page 118). The values for the control group can be seen in Table 14 and those for the patients' 'good' and 'bad' legs in Tables 15 and 16. Example traces can be seen in Figures 34 and 35.

In the control subjects no difference was found between the T_{cp}O₂ values obtained over either the medial or lateral sides of the calf, but both these sites showed significantly higher values than at the instep ($p < 0.01$).

Carbon dioxide tension values behaved in the same way so that there was no difference between medial and lateral calf sites but a small though significant drop occurred between both these sites and the instep ($p < 0.05$).

The patient group showed differences too, not only from the control group but also between 'good' and 'bad' legs. In the 'good' leg no differences could be found in T_{cp}O₂ at any of the 3 sites, but there was a difference in T_{cp}CO₂ values on each side of the calf and the instep, the instep being the lower value in each case. The differences were significant on the medial side ($p < 0.02$), and on the lateral side ($p < 0.05$). When looking at the symptomatic or 'bad' leg, no differences could be found in either T_{cp}O₂ or T_{cp}CO₂ values at any site of measurement.

Comparison of groups.

Comparison of groups revealed a significantly higher

TABLE 14. Transcutaneous Oxygen and Carbon Dioxide tension results in PVD

Control Subjects. (7.5 mm Hg \equiv 1 kPa).

No	<u>OXYGEN</u> (mm Hg)			<u>CARBON DIOXIDE</u>		
	<u>Medial</u>	<u>Lateral</u>	<u>Instep</u>	<u>Medial</u>	<u>Lateral</u>	<u>Instep</u>
1	77	63	39	33	37	31
	76	82	57	38	30	24
2	-	-	-	-	-	-
3	65	76	58	33	32	28
	60	75	62	33	31	28
4	71	64	41	35	38	32
	72	71	64	41	34	31
5	61	52	56	29	29	30
	54	60	50	29	38	31
6	54	50	55	44	43	44
	58	49	52	42	42	41
7	59	64	54	32	35	34
	60	63	61	36	33	34
8	63	65	37	38	33	38
	66	65	60	35	36	33

Oxygen tension ranges:

Medial calf; 54-77 mm Hg, median 62 mm Hg.

Lateral calf; 49-82 mm Hg, median 64 mm Hg.

Instep; 37-64 mm Hg, median 55.5 mm Hg.

Carbon dioxide tension ranges:

Medial calf; 29-44 mm Hg, median 35 mm Hg.

Lateral calf; 29-43 mm Hg, median 34.5 mm Hg.

Instep; 24-44 mm Hg, median 31.5 mm Hg.

TABLE 15. Transcutaneous Oxygen and Carbon Dioxide tension results in PVD Patients' 'Good' legs.

No	OXYGEN (mm Hg)			CARBON DIOXIDE		
	Medial	Lateral	Instep	Medial	Lateral	Instep
1	Patient had had limb removed for gangrene previously					
2	64	54	38	34	35	29
3	54	40	64	48	50	43
4	46	44	55	35	35	27
5	29	40	49	48	43	31
6	64	49	42	35	40	>75
7	45	22	20	51	50	41
8	75	-	52	30	-	27
9	36	24	-	44	48	-
10	14	5	16	>48	>42	>40
11	41	67	57	38	41	36
12	69	59	70	38	36	29
13	60	89	61	28	29	25
14	59	77	52	37	33	31
15	42	39	48	36	36	31
16	61	63	58	34	36	35
17	73	67	55	33	31	32

Oxygen tension ranges:

Medial calf; 14-75 mm Hg, median 57 mm Hg.

Lateral calf; 5-89 mm Hg, median 49 mm Hg.

Instep; 16-70 mm Hg, median 52 mm Hg.

Carbon dioxide tension ranges:

Medial calf; 28-51 mm Hg, median 36 mm Hg.

Lateral calf; 29-50 mm Hg, median 36 mm Hg.

TABLE 16. Transcutaneous Oxygen and Carbon Dioxide tension results in PVD Patients' 'Bad' legs.

No	OXYGEN (mm Hg)			CARBON DIOXIDE		
	Medial	Lateral	Instep	Medial	Lateral	Instep
1	49	23	7	37	39	72
2	1	-	-	89	-	-
3	34	44	58	50	53	38
4	62	66	47	33	32	41
5	5	3	20	52	112	110
6	46	44	34	48	40	>96
7	67	-	32	28	-	30
8	33	7	-	46	>62	-
9	4	6	12	>60	>48	71
10	43	22	21	43	45	53
11	62	67	66	39	35	31
12	64	70	60	28	29	23
13	58	67	58	34	32	20
14	28	53	64	48	40	48
15	43	8	23	49	54	>100
16	70	72	50	36	32	35
17	60	57	32	30	34	37

Oxygen tension ranges:

Medial calf; 1-70 mm Hg, median 47.5 mm Hg.

Lateral calf; 3-72 mm Hg, median 44 mm Hg.

Instep; 7-66 mm Hg, median 34 mm Hg.

Carbon dioxide tension ranges:

Medial calf; 28-89 mm Hg, median 41 mm Hg.

Lateral calf; 29-112 mm Hg, median 40 mm Hg.

FIGURE 34.

Transcutaneous gas tension tracing in PVD Control
subject (number 8). Medial calf site.

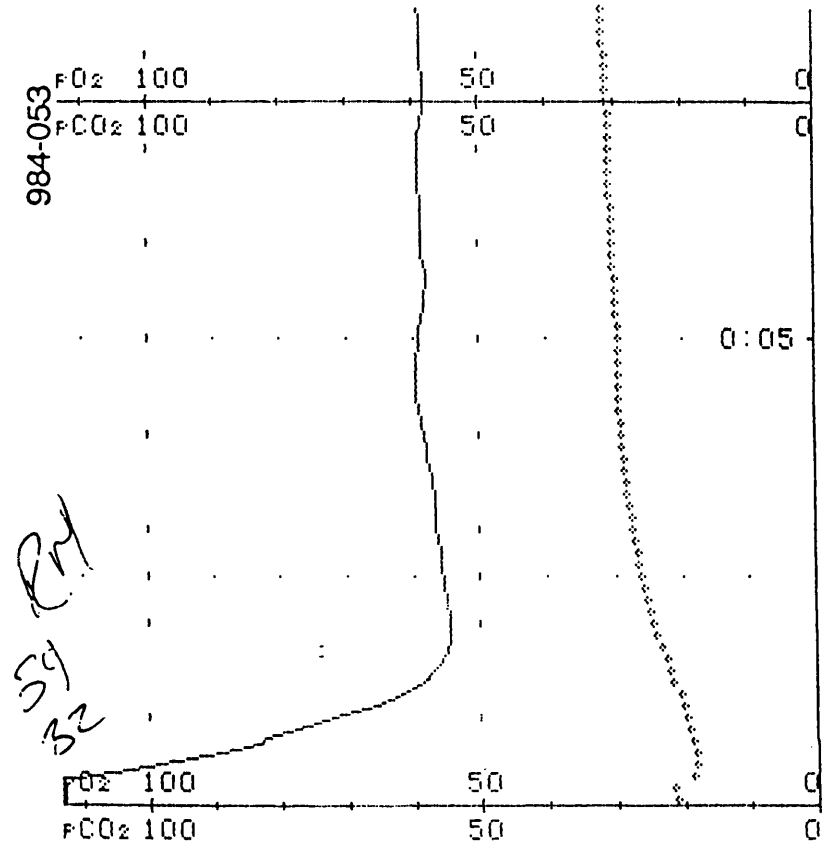
The trace is read from the bottom upwards. Calibration is performed before each application of the electrode to the skin. The time scale in minutes is marked on the right hand vertical axis. The oxygen trace is the left hand linear marking, and the carbon dioxide trace is dotted.

Following the application of the electrode, the oxygen tension can be seen to fall rapidly because air was excluded from the site of application by the inclusion of the contact liquid. Gradual equilibration to a steady state then follows over a period of about 7.5 min. The final values are marked on the linear scale at the top of the trace. For this trace, the oxygen value is just less than 60 mm Hg, and the carbon dioxide value is about 30 mm Hg.

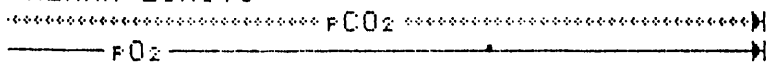
F_{CO2} 200 100 0

F_{O2} 200 100 0

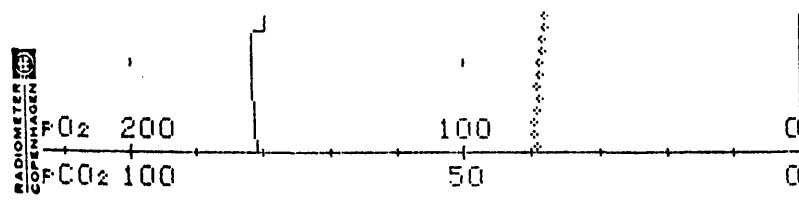
x, y = 2.5 min.



ALARM LIMITS:



READY



CALIBRATION

CALIBRATION VALUES:

F_{O2}: 159 mmHg, F_{CO2}: 38 mmHg

SITE TIME SETTING: 4:00

F_{CO2} CORRECTION: F_{CO2}/1.40 - 5 mmHg

ELECTRODE TEMPERATURE: 44.0°C

FIGURE 35.

Transcutaneous gas tension measurements obtained from a PVD patient (number 17) suffering from critical ischaemia. Medial calf site.

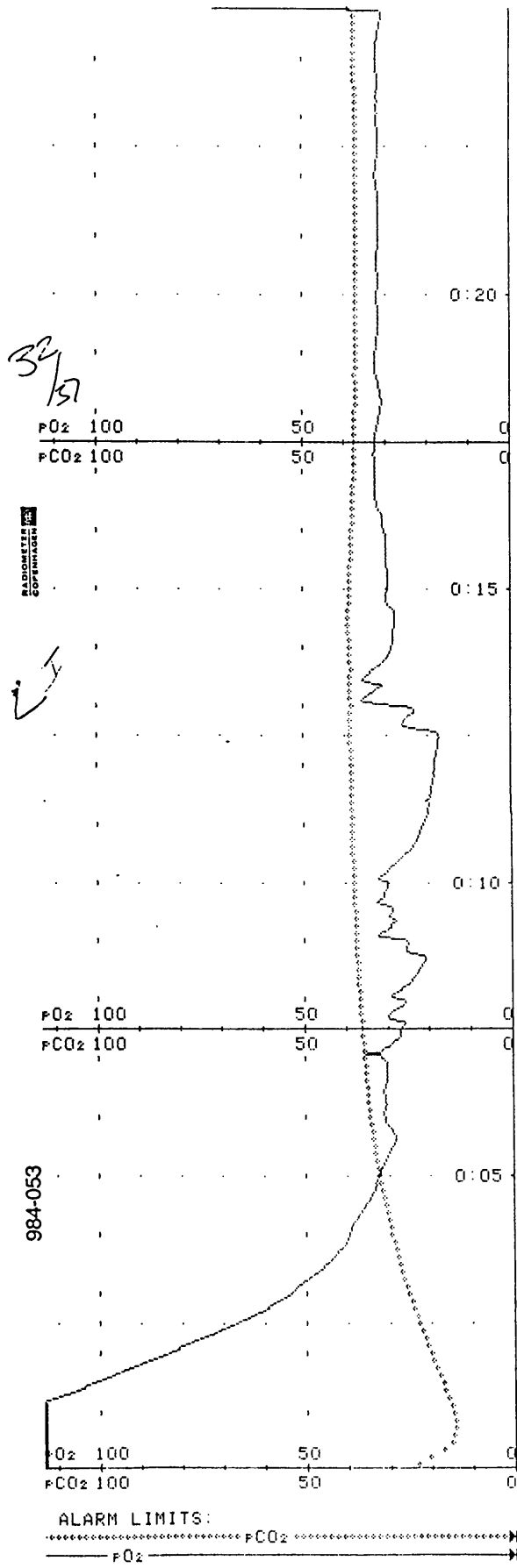
(This tracing has been photo-reduced to enable it to fit on the page).

As in Figure 34, the same conditions of calibration and application of the electrode applied. The trace is read in the same way.

In this patient the less rapid response and overswing of the oxygen and carbon dioxide can be seen. The two gas tensions have inverted their normal positions, although were the oxygen to have reached the carbon dioxide values seen here, it would still be critically low.

The time taken to achieve a steady state on the trace is 17.5 min, which is 10 min longer than in the control trace. (Fig 34).

The final values lie between 30-40 mm Hg for both oxygen and carbon dioxide, with the CO₂ having the slightly higher value. This is clearly abnormal.



READY

TcpO₂ value over the medial head of gastrocnemius in the control group than was found in either the patients' 'good' legs (p<0.05) or the patients' 'bad' legs (p<0.01). The same was true for the control group when the mid-lateral calf site was studied (p<0.05) but there was no statistically significant difference between groups in the oxygen values obtained at the instep.

However, when transcutaneous carbon dioxide results were analysed, the patients' 'bad' legs showed a consistent and significantly higher level of TcpCO₂ at the instep only when compared with the control group legs (p<0.05).

Relationship between transcutaneous gases, T_{sk} and SkBF.

No correlation could be found between transcutaneous oxygen tension and either skin blood flow or skin temperature at an ambient temperature of 30°C at any of the 3 sites of measurement. This was true for all groups. The comparison was made at T_a 30°C to approximate as closely as possible to the transcutaneous gas electrode temperature of 44°C.

Appendix 6 presents the TcpO₂ and TcpCO₂ values and eventual outcome of each of the patients in the PVD group. Only 3 underwent below-knee amputation and 2 had delayed healing. One of these had a medial calf TcpO₂ value of less than 35 mm Hg. The other patient, though considerably older, had a TcpO₂ tension of 60 mm Hg which suggested that the stump should have healed.

Assessment of patency, perfusion, and viability do not

go hand in hand. Discussion of their inter-relationship as a result of these studies follows.

Introduction: Skin temperature in context.

Non-invasive assessment of the ischaemic limb developed from the realisation that while the combination of clinical examination and contrast angiography enabled the clinician to form an impression of the degree of ischaemia, and provided him with an anatomical map, by defining the distribution of the diseased vessels, it gave no indication of the pathophysiology or functional aspects of the condition.

Clearly there was a need for some form of clinical testing which could be used to complement the surgeon's clinical skills without risk or upset to the patient, which would not only provide a baseline but could be used for repeated measurements in follow-up, forewarn of sudden deterioration, aid in making a prognosis and assist in making the correct decision when surgical management was required.

The Introduction and Review of Methods (Chapters 1 & 2) have described the development of some of these non-invasive techniques, several of which have been used in these studies. One method which seemed to hold promise was the use of infra-red thermography since skin surface temperature was assumed to reflect skin blood flow. Clearly, the cutaneous circulation must be supported by the deep arterial inflow to the limb, without which the nutritional integrity of the limb would be compromised. As the surface temperature of the skin was thought to be related to skin blood flow, the logical

assumption was that the skin temperature must therefore be an indicator of the nutritional integrity of the limb.

However, scientific evidence for this assumption was lacking and the argument seemed based on the common sense premise that if animal or human tissue is warm to the touch, it is likely to be supported by a circulation, and is therefore alive and viable. This is not always so.

In a warm environment inanimate objects will eventually achieve the temperature of that environment. Animate objects have methods of thermoregulating their internal environment to ensure adequate heat loss to prevent hyperthermia. Furthermore, it is known that following death by asphyxia the body temperature can rise for some hours in tissue supported by no circulation at all in an ambient temperature cooler than the body itself (Simpson, 1978).

Objective of study.

Despite the lack of a sound scientific basis for using the surface temperature of a limb as a means of assessing its circulation, ever more complex and expensive techniques and machinery have been used in the field of thermography. These were developed mainly for use in industry, and the medical applications of thermography have been realised following appreciation of the benefits of its use in industry. Thermography is only an accurate but expensive way of measuring skin temperature. What skin temperature means in terms of physiology has to be determined, and investigation into the scientific basis of how the technique might be used in clinical practice has

formed the bulk of this work.

Factors determining skin temperature: Radiation, Convection and Evaporation.

Some appreciation of the methods of heat exchange is necessary for an understanding of the mechanisms involved in the different situations described in these studies.

Human skin has a radiation emissivity approximately equal to 1 so that it behaves as if it were a black body. This means it can absorb all radiation of any wavelength and is capable of emission of radiation of any wavelength. The spectral distribution of radiation from human skin is dependent on the absolute temperature, and the radiative heat exchange is dependent on the difference in temperature between skin and the environment.

Similarly, convective heat loss from the skin is dependent on the temperature gradient between skin and air. In all our examinations the 'wind-chill' factor was calculated and the air speed was constant at $0.5 \text{ m}\cdot\text{sec}^{-1}$ over the couch or when the subject was exercising in front of the air-conditioning unit. At an ambient temperature (T_a) of 20°C this produced a corrected effective temperature of 19°C , and at T_a 30°C a corrected effective temperature of 29.5°C (Ellis et al., 1972).

The body will still lose heat by evaporation despite the absence of active sweating. At rest these losses are negligible within the T_a range 20 - 30°C . Water is lost by diffusion through the calf skin and at T_a 20°C is estimated to be fairly constant at 6 - $10\text{g}/\text{m}^2\cdot\text{hr}^{-1}$. Once

active sweating has started above T_a 30°C there is more variation within the range $15\text{-}35\text{g}/\text{m}^2\cdot\text{hr}^{-1}$, but calf skin tends towards the lower end of this range (Childs, 1989).

The humidity of the thermally controlled room in which these studies were carried out varied between 45-55%. At these levels the minimal evaporative skin losses would not have been inhibited by saturated vapour pressure.

The concept of body 'core' and heat conduction.

The concept of a central, warm body 'core', responsible for maintaining the vital body organs at or near a constant temperature, is important in understanding the mechanisms of heat loss to the environment by conduction through the body tissues or 'shell' surrounding this 'core'. Heat conduction is the process of thermal energy transfer from molecule to molecule within a substance, (solid, liquid or gas), where those molecules are in contact with one another. In this way, thermal energy or heat is brought to the skin surface from the warm central body core, and at the skin/air interface heat is then transferred to the environment by convective air movement. As such, conduction is the first mechanism involved in the initiation of convective heat transfer at the skin/air interface.

Thermal conductivity

The amount of heat that flows through any substance is dependent on the area involved (A), and heat per unit time (Q), and is expressed by Fourier's Law as $Q=kA(T_1-T_2)/b$,

where b is the thickness involved, and T_1 and T_2 represent a change in temperature across a substance of thermal conductivity k . (Fig 36). The thermal conductivity (k) varies between substances and is expressed as $W/m.^{\circ}C$. Table 17 shows the thermal conductivity for various substances and body tissues.

These body tissues, skin, fat and muscle, form the shell surrounding the core. The size of the core changes depending on the metabolic activity of the body and the amount of heat being lost at the skin surface. The thickness of the shell will also change in reciprocal fashion. This has been represented graphically and can be seen in Figure 37 (Fox, 1974).

Comparison of thermographic findings with other reported work.

Despite the extensive use of thermography in the last 25 yr there have been few detailed descriptions of the thermographic images obtained in the normal lower limb. This was probably because to start with all thermographic pictures were black and white or 'grey-tone' photographs, colour thermography not being commercially developed until the late 1970s. The descriptions, with some notable exceptions, (Spence, 1981; 1984; Clark et al., 1988), tended to be brief and rely on the actual temperature gradient measured down the limb and not on the appearance and distribution of temperature isotherms. Gradients of $2-6^{\circ}C$ from groin to toe have been regarded as normal by some authors (Holm et al., 1974), $2-4^{\circ}C$ from knee to ankle

FIGURE 36.

Diagram to explain the principle of Thermal Conductivity.

The diagram shows how Fourier's Law of Thermal Conductivity is derived.

The amount of heat that flows through any substance is dependent on the area involved (A), and heat per unit time (Q), and is expressed by Fourier's Law as $Q = kA(T_1 - T_2)/b$, where 'b' is the thickness involved, and T_1 and T_2 represent a change in temperature across a substance of thermal conductivity 'k'. The thermal conductivity (k) varies between substances and is expressed as W/m.^{°C}. Table 17 shows the thermal conductivity for various substances and body tissues.

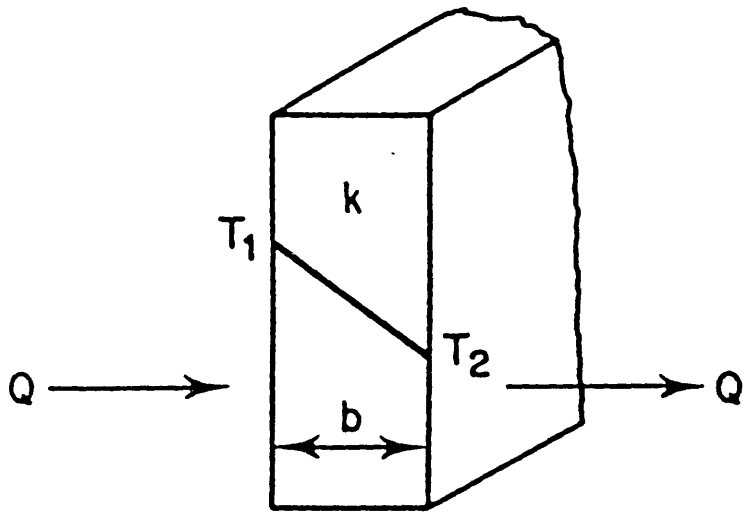


TABLE 17. Thermal Conductivity of some relevant substances.

<u>Material</u>	<u>Thermal Conductivity</u> <u>(W.m⁻¹.°C⁻¹.)</u>
Water	0.59
Air	0.025
Muscle	0.39
Fat	0.2

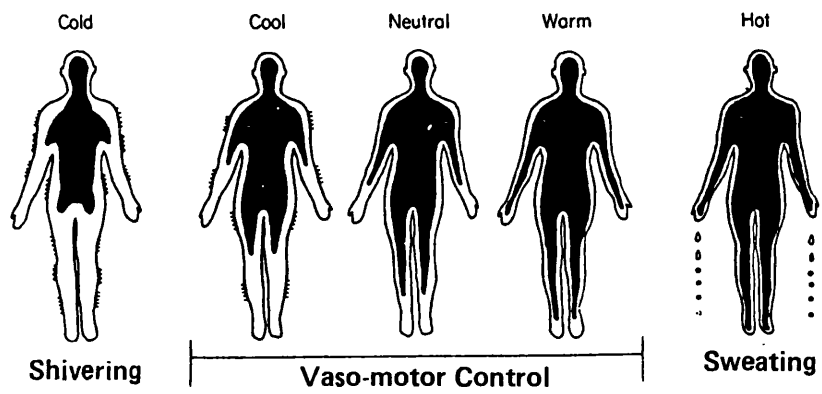
FIGURE 37.

The concept of a body 'core' and 'shell'. (After Clark & Edholm, 1985).

The diagram illustrates the role played by ambient temperature on the body's control of thermoregulation.

In cool, neutral and warm conditions, temperature regulation is under vasomotor control.

In cold conditions, shivering thermogenesis provides a defence against the cold, and in hot conditions, sweating is necessary in order to protect against the danger of overheating.



by others (Lovisatti et al., 1974), and $<2^{\circ}\text{C}$ from above to below knee by others (Henderson & Hackett, 1978). The majority of authors describe the 'grey-tone' thermograms as showing a gradual decrease in temperature distally with asymmetry present when an ischaemic leg appears cooler. The warm appearance around the knee associated with superficial collateral circulation has already been mentioned. Spence and his colleagues, using an injected isotope washout technique of [4- ^{125}I] iodoantipyrine, described the relationship between skin blood flow measured by this technique to thermographic skin temperature measurement (Spence et al., 1984). They found a highly significant relationship between skin blood flow and skin temperature at different isotherms in the calf. This was not our experience and indeed it has been shown that skin temperature can change without changes in skin blood flow, and blood flow can change without changes in skin temperature (Thauer, 1965).

Reported studies on regional skin blood flow have tended to use isotope washout techniques and are thus not comparable to our work using a laser Doppler technique.

Regional variation in sympathetic vasoconstrictor nerves

Earlier studies in this department examined the possible relationship between skin blood flow and skin temperature (Stoner et al., unpublished work). We discovered that in the ambient temperature range $20\text{-}30^{\circ}\text{C}$ there was no association between skin temperature and the perfusion of the skin of the calf or forearm, whereas in the foot and hand there was a positive correlation. This could be explained by a

reduction in activity of the rich, sympathetic vasoconstrictor nerve supply in the glabrous skin of acral regions, not found in the more proximal part of the limb (Edholm et al., 1956; 1957; Rowell, 1977; Sparks, 1978; Bini et al., 1980 a & b). Bini and his colleagues showed a reduction in sympathetic vasoconstrictor nerve impulses within the median and peroneal nerves as ambient temperature rose from 23°C to 30°C. Above 35°C sympathetic sudomotor activity was noted which increased in frequency as profuse sweating started at T_a 40°C to 45°C (Bini et al., 1980 a & b). At this ambient temperature the mechanism of active sympathetic vasodilatation has been also claimed to be in effect, (Barcroft & Edholm, 1943; Fox & Edholm, 1963; Johnson et al., 1986), though it still seems uncertain whether the effect noticed is due to actual sympathetic vasodilator neurones (Lundberg et al., 1989) or the release of bradykinin-like polypeptides from sweat gland activity (Fox & Hilton, 1958).

Our studies did not proceed above an ambient temperature of 30°C, and so stayed (at T_a 30°C) within the thermoneutral zone of approximately 28-32°C (Clark & Edholm, 1985). There was no visible sweating at T_a 30°C and as the subjects were not exposed to auditory or mental stimuli, humoral factors and active sympathetic vasodilatation could be excluded.

'Steady states' are not achieved in either skin blood flow or skin temperature: The concept of 'Vasomotion'.

Our studies have shown that in the pulp of the hallux in normal subjects, as T_a rises so SkBF at that site

increases. This did not occur in the calf. The laser Doppler technique used in these experiments has been evaluated by Tenland and other workers (Tenland, 1982; Nilsson, 1984; Gush et al., 1984) and is well accepted. There is a rhythmic and cyclical variation in skin blood flow demonstrable by laser Doppler flowmetry, and this is known as 'vasomotion'. The phenomenon of vasomotion has been well described in both normal individuals and more recently in patients suffering from peripheral vascular disease (Seifert et al., 1988). However, unlike Seifert and his colleagues, our interest was in mean levels of skin blood flow, expressed as arbitrary perfusion units (PU), and the gain was kept deliberately low on the Periflux laser Doppler (Perimed, Sweden) to eliminate as far as possible the natural oscillations of vasomotion. Furthermore, we used an unheated probe throughout our experiments whereas Seifert et al used a probe temperature of 32°C. It is obviously important, therefore, to determine exactly what variables are to be examined in order to derive the maximum benefit from the equipment and methodology used.

The effect of 'equilibration' time.

Similarly, with something as dynamic as skin temperature, the idea of an 'equilibration' time is probably inappropriate.

A 15 min exposure time was allowed in all subjects before any measurements were made. This was in keeping with other workers (Delius et al., 1972; Normell & Wallin,

1974; Khan et al., 1988). Even so, in an experiment to determine the effect of prolonged exposure we found that skin temperature in the limbs dropped towards the ambient temperature over extended exposure periods up to 45 min at T_a 20°C in control subjects before the onset of shivering thermogenesis. The drop in T_{sk} was most noticeable in the fingers and toes where a fall in T_{sk} of 6.0 or 7.0°C was recorded. In one subject the T_{sk} of the hallux fell below the ambient temperature. The T_{sk} of the forearm and calf fell more slowly in 2 control subjects (aged 39 and 70 yr) over the whole period of the experiment, where a third subject (aged 20 yr) showed a fall initially in forearm and calf for the first quarter to half an hour, followed by recovery to pre-exposure T_{sk} , and rebound to warmer than initial T_{sk} at both sites by 45 min. His finger and toe temperatures fell in the same way as the 2 older controls. Barcroft and Edholm (1946) also found a continuing fall in limb temperatures during 2 hr exposure to T_a 18.5°C.

The phenomenon of skin temperature 'cycling', described by Clark and Goff (1979), has shown that subtle temperature changes are occurring over the whole body even when at rest in a thermally controlled environment. Although the greatest temperature changes occurred in the sensitive skin of the hands and face, over a 4 hr period no area of the body was unaffected. As the body is always responding to change - endocrine, metabolic and diurnal, (as well as environmental), it is misleading to speak of 'equilibration' to ambient temperature. Another factor in

our choice of exposure time was that in patients with critical ischaemia and rest pain, 15 min was as much as they could tolerate.

The relationship between T_{sk} and SkBF in the calf and hallux of control subjects.

We established that the skin temperature of the hallux and its skin blood flow were related, but that this was not the case with calf T_{sk} and SkBF. Therefore, the temperature of the calf skin must be a result of heat conducted away from the warm central core of the limb to the surface. This was a reflection of the amount of warm arterial blood entering the limb by the major vessels, (although slightly cooled by counter-current flow in the adjacent venae comitantes), and was thus a reflection of its deep perfusion. It should be remembered that there is a reduction in heat loss at higher T_a as the temperature gradient is smaller. This finding is central to the core of our argument that no assumption can be made about the state of the cutaneous circulation of the calf from its skin temperature.

Methods of increasing limb perfusion; Exercise and A-V fistula.

Resting muscle blood flow in man is estimated to be around 2-5 ml/100g min⁻¹. Maximal exercise may increase this value to 50-75 ml/100g min⁻¹ (Barcroft, 1963; Folkow & Neil, 1971). Accepting that our resting flow values were not exclusively muscle blood flow figures, our

results were of the same order of magnitude having a median of $3.4 \text{ ml. (100 ml tissue)}^{-1} \text{ min}^{-1}$. Although exercise in our studies was not designed to be maximal, a nearly 3-fold increase in TBF was observed.

Similarly, our values for total blood flow in the forearm containing a peripheral A-V fistula were lower than some (Hurwich, 1969) though in line with others (Herron & Wallace, 1971; Bussell et al., 1971). Comparison of values of this sort are not always easy to make as different techniques of measuring blood flow have been used between studies, resulting in expression of flow rates in different units. In addition, the actual configuration of the arterio-venous anastomosis (end-to-end; end-to-side) is known to affect the flow through it (Bell & Wood, 1983).

Whichever method is used for increasing total limb blood flow the effect of expanding the limb core should be the same. In exercise, the increased metabolic activity opened up the arterial bed in the calf muscle, and the A-V fistula provided a peripheral short circuit of a major artery and vein, by-passing the capillary bed.

The aim of investigating the expansion of the warm core of the limb by one of these methods was to test the hypothesis that, in a situation where total limb perfusion was known to be increased by a measurable amount, there was no relationship between skin blood flow and skin temperature of the limb, either forearm or calf. This had been found in control subjects at rest by varying ambient temperature and was then achieved in exercise controls and

those patients with peripheral A-V fistulae.

The relationship between T_{sk} , SkBF and TBF in Exercise controls and subjects with an A-V fistula.

A relationship was found between calf T_{sk} and calf TBF both in exercise control subjects and in the one patient with an idiopathic A-V fistula in the foot. In all, there was a generalised and measurable increase in limb blood flow without a concurrent rise in calf SkBF following exercise in that control group. However, there was a small but statistically significant elevation in calf SkBF, when compared with the normal side, in the patient with the A-V fistula in her foot, as there was in the affected forearm SkBF of patients with a Brescia fistula at the wrist. The reason for this was obscure but might be due to the increased blood content in dilated cutaneous capillaries as a result of increased venous pressure on the side of the fistula (R Gush, 1989, personal communication).

However, despite the small increase in SkBF in the affected limb it is important to emphasise that, unlike in the glabrous skin of the hands and feet, no local relationship to T_{sk} or TBF of the forearm or calf could be demonstrated. This increase in SkBF in the calf or forearm of patients with peripheral A-V fistulae merits further investigation. It may represent an adaptive phenomenon whereby the body attempts to get rid of excess heat by dilating capillaries not usually involved in major heat exchange in temperate environmental conditions. It

may be a purely mechanical result of the increase in venous pressure already mentioned. Perhaps because of the high pressure, distended veins are more prone to minute leakage of blood cells which, once in the tissues, set up a low-grade, sub-clinical inflammatory process and so the increased SkBF seen in the affected limb is a result of the humoral mediators of inflammation.

How might the information provided by thermography be applied to the assessment of the ischaemic limb?

It should be remembered that in the ambient temperature range employed in these studies, a T_a of 20°C is a cold stimulus and a T_a of 30°C is sufficient to place the subject in the thermoneutral zone without complicating heat loss by sweating which occurs usually above T_a 35°C . The patterns of heat loss will alter with changing ambient temperature as the thermal gradient between skin and air temperature alters.

If, then, the size of the central core is determined by the circulation of warm blood within that core and thus the rate of conductive heat loss from that warm blood via the skin to the environment, it would seem that the measurement of skin temperature could be applied to patients with peripheral vascular disease to assess the flow through the shell or tissues of the limbs.

Clearly, little would be gained by examining the patients at an ambient temperature of 20°C as the core would have contracted and the shell thickened in response to the cold stimulus. However, if the environmental

temperature were to be raised to 30°C, then the expansion of the warm central core should give an indication of the perfusion possible in these ischaemic limbs.

The reduction in temperature gradient between skin and air would tend to minimise radiation and convective heat losses from the skin.

Nonetheless, information would be obtained from the degree of reactivity or response to a warm stimulus to the body as shown by the ability of the ischaemic limb to increase the size of its core by increasing deep perfusion.

The Claudicant group: Were they a representative sample?

The patients suffering from intermittent claudication in our studies would appear to be a rather more severely affected and elderly group than those found in other studies. Greenhalgh (1988) stated that " if the pressure index is lower than 0.9, the exercise test is certainly not indicated...". Our patients had a median ABPI value in the 'good' leg of 0.91 and in the 'bad' leg of 0.56. Even so, only 2 of the 6 failed to manage at least 4 of the 5 cycles of calf-raising exercise. Seifert et al (1988) studied 2 groups of claudicants of differing severity. Those patients who had a pain-free walking distance of more than 200 m had a median age of 56 yr, mean systolic ankle pressure of 119.6 ± 24.4 mm Hg and mean ABPI of 0.81 ± 0.1. Their severe claudicants had a median age of 72 yr, mean systolic ankle pressure of 89.4 ± 17.7 mm Hg, and a mean ABPI of 0.62 ± 0.2. It is not

clear from their data whether these pressure values are of both legs taken together and averaged, or of the worse side taken alone. In either event, our group (median age 70.5 yr, and median systolic ankle pressure of the 'bad' leg 90 mm Hg, and a median ABPI on the same side of 0.56) would seem to match Seifert and his colleagues' group of severe claudicants.

As exercise testing in patients with intermittent claudication in reported work is usually performed with treadmill or bicycle ergometer, our method of calf-raising could not be compared with other series. In one reported series of patients subjected to exercise testing in which calf blood flow was measured, resting flow was around $2.7 \text{ ml. (100 ml)}^{-1} \cdot \text{min}^{-1}$, rising to nearly $20 \text{ ml. (100 ml)}^{-1} \cdot \text{min}^{-1}$ after 3 min 2 sec of treadmill exercise (Strandness & Sumner, 1969). Our group of claudicants were more severely ischaemic than this, (median resting blood flow in our patients was $1.8 \text{ ml. (100 ml tissue)}^{-1} \cdot \text{min}$), and they would not have tolerated 3 min of continuous treadmill exercise.

Claudicants v Exercise Controls: Relationship between T_{sk} and TBF.

Not only could the core be expanded by raising the ambient temperature to simulate a tropical environment, but the effect of muscular exercise produced an increase in muscle blood flow as shown in exercise controls. This in turn increased heat conduction to the skin. As mentioned before, problems arose in those with

intermittent claudication in that most were unable to fulfil the full exercise programme and therefore could not be compared statistically with the control group.

Nonetheless, as a relationship between calf T_{sk} and calf TBF had been found in controls, it was not unreasonable to hope that this might also be true for the claudicant group. As described in the previous chapter (Results) the correlation was weaker in these patients, but the most striking feature was that the regression line was parallel to and above that of the exercise control group. Furthermore, it was a statistically significant elevation. This meant that the rise in calf T_{sk} in claudicants obeyed the same rules as controls, in that for any given rise in TBF, the rise in T_{sk} was the same as that found in controls. But for any given calf blood flow the calf skin temperature was significantly higher than in controls. The reasons for this are not clear.

There may be an alteration in the physical geometry of the limb with peripheral vascular disease. Wasting of the calf muscle, atrophy of the subcutaneous tissues and peripheral oedema (more often found in those with critical ischaemia), may all be features of the ischaemic limb. This could result in warmer skin in the claudicants than in the controls by two methods. Firstly, if the muscle were atrophied then the circulating warm core blood be nearer the surface of the limb, so reducing the amount of tissue through which heat needed to be conducted. Atrophy of subcutaneous tissues would enhance this effect. Secondly, atrophy of the fat in association with the

increased tissue water present in peripheral oedema would raise the thermal conductivity of the tissues approximately 3-fold as can be seen from Table 17.

The finding of a relatively warmer leg in claudicants for any given blood flow warrants further investigation. Starting with simple anthropomorphic measurements and perhaps proceeding to include magnetic resonance imaging, the composition of the ischaemic limb when compared with controls might be determined.

The results of calf TBF and T_{sk} found in exercise controls and the claudicant group indicated that though a relationship between these two variables existed in both groups, it was still important to be able to view the whole leg and foot on the thermogram.

The thermographic image suggested the possibility of further underlying and unexplained pathology which would otherwise have been missed. Because of the patchy and irregular nature of the thermograms in those patients with peripheral vascular disease, isolated spot temperature measurements of the skin of the calf could easily have missed the areas of maximum temperature. If this had occurred, the observation that claudicants had a definitely higher calf skin temperature than controls (for any given blood flow) would have been overlooked.

Can thermography assess the Critically Ischaemic limb?

In attempting to determine whether thermography could assist in the investigation of the severely ischaemic limb, we examined a group of patients admitted to the ward

under the care of one vascular surgeon.

The majority were suffering from rest pain, often in association with gangrene. It should be stressed that this was a very heterogeneous group which was not standardised in any way, made up of those patients presenting for study in the time available. No predictions could be made from a group of this size because the numbers were too small. Even so, there were lessons to be learned from their examination.

As mentioned before, there have been only limited descriptions of the actual thermographic patterns found in the critically ischaemic limb, the majority of reports emphasising the large thermal gradient found on the affected side. However, Spence and his colleagues (1984) and Clark et al (1988) have made findings which are supported by our work.

Spence and co-workers (Spence et al., 1984; Spence & Walker, 1984) noted that there was not only a longitudinal thermal gradient but often also a transverse thermal gradient. In his work, the medial side of the calf was always warmer than the lateral side. Our findings were opposite to these in that we found the lateral side of the calf warmer than the medial. However, the thermograms in Spence's work were anterior and posterior projections, which tend to throw the posterior calf muscle bulk into more prominence medially. Our thermograms were medial and lateral projections, allowing a less angled view of the posterior calf muscles.

Although mention is made of elevation of the legs by

10° (Spence & Walker, 1984), no mention is made as to whether the calf was in contact with the couch. This could make a difference. The couch would act as a thermal insulator, and give rise to falsely high thermographic recordings.

Clark and his colleagues (1988) described the " bland and unstructured thermal pattern... " that "...is typical of that found in ischaemic limbs." Our findings are in complete agreement with this statement.

At what ambient temperature should thermography be carried out?

There is considerable variability in the range of environmental temperatures in which the examinations are carried out. Clark & Edholm (1985) have stated that skin blood flow assessment " requires temperatures of around 25-27°C whereas 21-23°C is more suitable when identifying subcutaneous thermogenic structures." Our studies throw doubt on this statement and suggest that this assumption be reconsidered. In the past thermography has been performed over a wide range of different ambient temperatures, and sometimes no reference has been made to environmental temperature; 23°C (Winsor, 1968), 18.5°C (Holm et al., 1974), no mention at all (Lovisatti et al., 1974; Henderson & Hackett, 1978), 20°C (Spence et al., 1981), 21°C (Spence & Walker, 1984), no mention (Harway, 1986), 27°C (Clark et al., 1988), 26°C (Stoner et al., 1989). This lack of standardisation led Stoner and his colleagues to question the optimum ambient temperature for

thermographic examination (Stoner et al., 1987). The reasons for our choice of environmental temperatures of 20°C and 30°C have already been discussed.

Thermographic variability in critical ischaemia: Some diagnostic pitfalls.

The variability of the thermograms and absence of any recognisable pattern in patients with peripheral vascular disease becomes more of a problem with increasing severity of disease. Although it might appear that if a limb is gradually becoming progressively more ischaemic to the point where there is obvious gangrene, then its' skin temperature should fall correspondingly. Some of the reasons why this should not be so have been considered already. However, more variables may influence the thermographic appearance of the critically ischaemic limb.

In our group of severely affected PVD patients, 12 of 17 had unremitting rest pain and it was neither ethical nor humane to exercise them. They barely coped, in a semi-recumbent position, with the amount of time required for the examination resting with the legs elevated and supported at the ankle. Several had marked peripheral oedema and most had been either bed or chair-bound for many weeks.

Not much could be inferred from observation of their thermograms at T_a 20°C, although usually one limb was obviously warmer than the other, but when the T_a was raised to 30°C, the leg which showed the lesser change in T_{sk} was usually the one in which the worse disease was

found. Because of the greater severity and greater age of these patients, they were also prone to more associated pathology which could affect the appearance of their limbs on thermography as described below.

It has been stated before that the warm knee is often assumed in the arteriopath to represent superficial collateral circulation as a result of major arterial occlusion. However, it may equally be caused by underlying inflammation of the knee joint. One of our patients had both a superficial femoral artery occlusion with the development of collaterals around the knee, and active painful osteo-arthritis of that joint. It could not be deduced from the thermogram which pathological state was more responsible for the warm thermographic image of his knee.

Gangrene of the foot may often be associated with underlying infection of the soft tissues, and even bone. This may occur without obvious signs of inflammation or suppuration and result in a paradoxically warm foot (and sometimes calf) on thermography.

Similarly, as most of these patients are elderly, virtually immobile and often smokers, their likelihood of having or developing a deep venous thrombosis is high. Such a condition is well known to produce a warm image on thermography (Browse, 1978; Cooke, 1978; Thomas et al., 1989).

When conditions of both subclinical infection and deep venous thrombosis co-exist, it is not hard to understand the difficulties that may arise in interpretation of the

thermographic image.

The problem of peripheral oedema, mentioned before, may not always result in a warmer appearance of the limb on thermography when compared to a non-oedematous limb. Although the thermal coefficient of water is considerably higher than that of subcutaneous fat, (0.59 v 0.2), it might be expected that the limb would appear warmer. But this does not allow for the depth of the oedematous tissue. This may be so great that it will distance the deep arterial inflow in the core of the limb so far from the skin surface that the resultant thermogram appears cooler than the non-oedematous or less oedematous side. Even if both limbs are equally affected by peripheral oedema, the reduced inflow to the critically ischaemic limb will result in a similar, cooler thermographic image.

These difficulties in interpretation of the variable thermographic images explain why identification of the affected leg, and the extent and nature of the pathology within it cannot be determined by thermography alone.

Even if there was no increase in flow at all within a limb when the ambient temperature was raised, thermography of the limb would still show some change in temperature because of the reduced thermal gradient between the limb T_{sk} and ambient air. This would mean that the limb lost heat less readily and so would appear warmer thermographically.

Is no flow better than too little?

Work on cerebral blood flow at very low flow states has

suggested that the damage sustained by the brain is less if ischaemia is complete - provided it is not over-prolonged - than if a trickle of blood is present (Hossman & Kleihues, 1973; Siesjö, 1984). Clearly, the concern in both the ischaemic limb and the ischaemic brain is the ability of the tissue to use the oxygen delivered to metabolise the energy substrates available. As the oxygen supply to the brain is reduced there is a progressive failure of function with loss of electrical activity, followed by ion-pump failure and ending with complete disintegration of energy metabolism (Stoner & Cremer, 1985). Concentrations of phosphocreatine and ATP fall, as does the pH, and lactate concentration rises. The ion-pump failure results in tissue and cellular oedema, particularly marked in the astrocytes. As these events occur under extreme conditions, it might be thought that cell survival could be improved if some flow could be maintained, rather than none at all. However, Hossman and Kleihues (1973) showed that this was not always so and suggested that the brain might suffer less damage with no flow than with very low flow. More recently, Siesjö (1984) stated (regarding cerebral perfusion,) that provided the "...blood glucose and tissue lactic acid concentrations do not rise unduly a small residual perfusion during ischemia improves recovery " but "...if hyperglycemia develops, a trickle of flow may be detrimental."

If the tissue has the capacity for anaerobic metabolism the changes may be minimal initially until the lactate

concentration has reached a critical level. This level will vary between tissues throughout the body, and the ability of any particular tissue to metabolise lactate.

The question arises as to whether similar biochemical disorders may not be prelude to cellular disintegration in the ischaemic limb, and that once flow has dropped below a critical level then the development or spread of gangrene is inevitable. Definite cellular changes have been documented in ischaemic muscle. Fibres atrophy and capillaries become more numerous to aid diffusion of oxygen into the cell (Hammersten et al., 1980; Henriksson et al., 1980; Clyne et al., 1982). Within the cell there is an increase in muscle mitochondria (Angquist & Sjöström, 1980) to make the most use of the low oxygen concentrations available. However, not all the changes are beneficial.

Chronic ischaemia can lead to cellular damage with gradual loss of the structural proteins and enzymes responsible for cell function (Teräväinen & Mäkitie, 1977; Clyne et al., 1985). These changes may not, therefore, always be advantageous and there would seem to be no direct relationship between local blood supply and cell metabolism. This is a field in which further work is being performed and the relationship between inorganic ^{31}P and ATP concentrations in ischaemic muscle is being studied using Magnetic Resonance Spectroscopy (Hands et al., 1986; Hands, 1988).

Estimation of the severity of disease.

Having established that skin temperature changes would

be expected even if no flow changes occurred when the ambient temperature was raised, it follows that if flow into the limb did increase with rising T_a , then a greater rise in skin temperature would occur.

In the severely affected ischaemic limbs of our PVD patient group, where total blood flow had not been measured, and the relationship between SkBF and T_{sk} in the hallux had been lost, it seemed that the arterial inflow was so precarious, in that no apparent change occurred with raising T_a , that no assessment of core blood flow could be made by study of calf temperature alone.

It would be useful to determine, in a larger group of critically ischaemic patients, if there was an absolute mean calf temperature value above which survival of the limb was possible, and below which amputation was the only option. As mentioned previously, studies reported in the literature do not discuss absolute temperatures but concentrate on the size of the gradient down the leg as the criterion upon which to make a surgical decision. The concept of absolute skin temperatures in determining viability could form the basis for further work.

When considering absolute levels it should be emphasised that only by standardising environmental conditions will useful results be obtained. Similarly, the attempt to find an absolute level for the P/A ratio which will delineate between viable and non-viable tissue also needs to be subjected to the same environmental conditions of examination.

Because no statement could be made about core perfusion

in the severely ischaemic limb, the ability of thermography to assess any increase in flow would rest on examination of the size of the change in calf T_{sk} between T_a 20°C and 30°C. However, no difference could be found in the size of the change in T_{sk} of the calf between controls and either 'good' or 'bad' PVD patients' legs. But there was an indication that the PVD patient group were behaving differently than the controls other than just in the disordered appearance of their thermograms.

Comparison of T_{sk} in PVD Patients and Controls.

The negative relationship found in controls between the initial calf T_{sk} and the size of the subsequent rise in calf T_{sk} was lost in PVD patients' legs, both 'good' and 'bad'. Thus, in controls, the cooler the starting calf T_{sk} , the greater the rise when T_a was raised to 30°C. This supports the argument that the greater the rise in T_{sk} , the larger the capacity for the warm, central core to expand into the limb. In this way a measure of the sensitivity and ability of the circulation to respond to an atraumatic physiological stress could be assessed.

It is interesting to note that although this negative relationship was lost in PVD patients in the calf, it was still present in the hallux. When the change in hallux skin temperature was compared between controls and PVD patients' halluces, no statistically significant difference was found. This was not surprising because the controls' mean (5.4°C) fell between the mean for the PVD patients' 'good' halluces (6.1°C) and 'bad' halluces

(4.8°C). However, the difference between the means of the patients' 'good' and 'bad' halluces was statistically significant ($p < 0.05$). This indicated that there was a lack of response to a rise in ambient temperature in the hallux T_{sk} of the critically ischaemic leg. Furthermore, this lack of response was in that part of the limb shown previously in normal subjects to be the most susceptible to changes in ambient temperature.

Comparison of SkBF in PVD Patients and Controls.

The sensitivity and ability of the hallux to alter its SkBF in response to a thermal challenge was also examined and once more differences between groups were found.

In the cool environment of 20°C there were significant differences between each of the patients' halluces' SkBF and control values ($p < 0.02$). But when the ambient temperature was raised to 30°C the difference between the critically ischaemic hallux and its less affected partner became apparent by comparison with the controls. All 3 groups showed a rise in SkBF in the hallux. The control group and patients' 'good' halluces almost doubling their SkBF; controls' median value rose from 12.25 to 23.75 PU, (a rise of 93.8%), and patients' 'good' hallux median value rose from 5.5 to 10 PU (81.8%). Patients' 'bad' halluces rose only from a median of 6.5 to 8.5 PU (30.8%).

Although the actual range and median values between 'good' and 'bad' halluces in the patient group were not significantly different from each other at either T_a , the ability of the 'bad' hallux to respond to a thermal

challenge was severely impaired.

Can use be made of these findings?

The sensitivity of the hallux skin blood flow might be used as a test of sympathetic activity in the limb as this site has been shown to be richly supplied with vasoconstrictor sympathetic nerves. This might allow the non-invasive pre-operative prediction of the response to sympathectomy to be assessed. If the hallux SkBF showed no significant rise on raising T_a to 30°C when compared to the opposite side, this would suggest that despite the removal of the sympathetic vasoconstrictor tone, the circulation was incapable of expanding into the limb. If there was a rise in SkBF of the hallux following T_a rise to 30°C , then the chances of a successful result following sympathectomy would be greater.

This work could be extended to test for autonomic neuropathy in patients with diabetes mellitus.

Study of Diabetics.

The usual clinical investigation of patients with diabetes mellitus to test for autonomic and peripheral neuropathy has included testing vibration sense and ankle reflexes for peripheral neuropathy, and Valsalva, deep breathing and tilt table tests for autonomic function. Recently, the re-warming response of the foot T_{sk} to cooling followed by indirect heating has been studied (Sundkvist et al., 1984) in diabetics both with and without one or both forms of neuropathy. They noted a

marked delay in toe temperature increase after cooling followed by indirect heating in diabetics of short duration (5-19 yr, mean 11 yr) with autonomic neuropathy.

Our observations of an impaired response of hallux T_{sk} and $SkBF$ to rise following a thermal challenge might be used in the investigation of autonomic neuropathy in patients with diabetes mellitus.

It would be valuable to study a group of diabetics with peripheral vascular disease to see if their thermographic isotherm distribution showed any characteristic pattern. Stoner et al (1989) and Clark and co-workers (1988) have described thermograms in such patients with an obvious horizontal banded appearance which is in contrast to those seen in any of our groups of subjects, from which diabetic patients were excluded. It is in the diabetic population with peripheral vascular disease that reliable methods of assessing limb integrity and viability are so greatly needed. Ankle pressures are notoriously unreliable (Wolfe, 1988) due to the propensity for the peripheral arteries to calcify, and transcutaneous gases are also prone to erroneous interpretation (Deane et al., 1988).

Thermal challenge and the P/A ratio.

The limited ability of the ischaemic limb to react to a rise in T_a by increasing its perfusion might be reflected in more than one way by the P/A ratio.

The limb that was primarily affected by an ischaemic foot, i.e. with reasonable flow to the knee but poor run-off, might be expected to show a significant drop in P/A

ratio at the higher ambient temperature. This would reflect a response by the core to expand into the proximal calf, unaccompanied by an increase in distal perfusion. Hence there would be a drop in P/A ratio from T_a 20°C to 30°C. If, however, the majority of the limb were compromised by, for example, an external iliac occlusion and a poor circulation through the profunda femoris, then the P/A ratio might change little between the two ambient temperatures. This would be the result of an inability to expand the core significantly in any part of the limb, so leaving the P/A ratio essentially unchanged.

In fact, both the PVD patients' 'bad' legs and controls' P/A ratios did drop slightly between the two ambient temperatures, but patients' 'good' legs remained unchanged. Although an explanation for these findings could be put forward as to why the PVD patients' 'good' legs did not alter their P/A ratios, it is not so obvious why the controls did.

With a rise in ambient temperature there would be a peripheral vasodilatation and an increase in cardiac output. If the severely ischaemic ('bad') limb could not respond by increasing its perfusion sufficiently to fill the enlarged vascular bed, there would be an increased production of anaerobic metabolites, inorganic phosphate and lactate which would produce a reflex vasoconstriction in the opposite limb, at the same time causing vasodilatation on the ischaemic side (Barnes & Trueta, 1942; Stoner & Threlfall, 1954; Fox & Hilton, 1958). In this way there would be no significant increase in

perfusion in the PVD patients' 'good' legs with a rise in ambient temperature, (although they would theoretically and angiographically be capable of such an increase), and hence no significant change in P/A ratio. However, if this had been the mechanism involved we would not have expected to see the observed fall in P/A ratio in PVD patients' 'bad' legs. Clearly, more work could be done to clarify this.

Prediction of healing in the ischaemic limb: Problems of patient selection and test variability.

Recognising the difficulties of thermographic interpretation in the ischaemic limb, Stoner and his colleagues (1989) in this unit examined 37 patients with end-stage ischaemia in 39 limbs. They performed thermography at an ambient temperature of 26°C, which is at the lower end of the thermoneutral zone, and concluded that if below-knee amputation had been restricted to those patients with a P/A ratio of more than 0.98, the rate of failure to achieve primary healing would have fallen from 28% to 10%. Even so, in their series 50% of patients with a P/A ratio of less than 0.98 eventually healed without surgical revision.

The problem of overlap is one common to the clinical setting. Ratliff and his colleagues (1984) found similar overlap when using transcutaneous oxygen tension to predict successful primary healing in a below-knee amputation.

They found that all those with a pre-operative $TcpO_2$

above 35 mm Hg healed, (measured over the medial head of gastrocnemius), and that all those who failed had a value below 35 mm Hg. But 17 of 24 below-knee amputations healed despite having a $TcpO_2$ value of less than 35 mm Hg.

A problem associated with both these studies is that patients with diabetes mellitus were included. 43% of patients were diabetic in Stoner's study, and 39% in Ratliff's.

Diabetics have additional pathology which is known to affect blood vessels, peripheral and autonomic nerves and transcutaneous gas tension measurements (Sundkvist et al., 1984; Wolfe, 1988; Deane et al., 1988). The last would appear to be a relatively recent finding and not widely reported in the literature. Deane and co-workers found two types of abnormal response when measuring transcutaneous gases.

The first was a type of plateau phenomenon, where the $TcpO_2$ appeared to stabilise and then rose to a higher level where it again appeared to stabilise. This process could be repeated over periods of up to 45 min, (which in their study was the maximum period of patient compliance), at which time the $TcpO_2$ might have risen to within normal limits. When this pattern was observed, no finally stable level was reached.

The second variation was that of continual oscillation. Again no stable level was ever achieved, and wide oscillation of values occurred continuously, of up to 7.5 mm Hg, typically over a 5 min cycle around an apparent mean level. The authors attributed this second response

pattern to some form of underlying vasomotor instability. However, 70% of diabetic patients do not exhibit either of these responses and behave in the same way as non-diabetic patients.

There is difficulty then in interpretation of Ratliff's data (1984) as 39% of patients in his series were diabetic and $TcpO_2$ readings were taken at 20 min in each case. If some of these patients had exhibited the plateau phenomenon, then their eventual $TcpO_2$ might have been within the normal range and this might explain why 17 of 24 below-knee amputations in patients with $TcpO_2$ values (apparently) below 35 mm Hg healed.

More recent studies have suggested that resting $TcpO_2$ values are unreliable because even in ischaemic limbs with transcutaneous oxygen tensions of zero, amputation stumps have been found to heal (McCollum et al., 1986; Slagsvold et al., 1989). Attempts to increase the sensitivity of the test have included breathing 100% oxygen and measuring the rate of $TcpO_2$ response in the ischaemic limb (McCollum et al., 1986), the application of an arterial touniquet for 3 min to the ischaemic limb, and measuring the time to begin recovery along with the speed of recovery towards pre-occlusion $TcpO_2$ values (Slagsvold et al., 1989). Neither method has been universally accepted.

Furthermore, there are variations between the commercially available measuring instruments in their physical characteristics, such as the membrane thickness and electrode oxygen consumption, which may result in different response times being recorded, depending on the

type of electrode used (van Urk & Feenstra, 1988).

Transcutaneous oxygen tension and gangrene.

Transcutaneous gas tension measurements cannot be viewed as absolute figures of oxygen supply to the tissues, but as a resultant of the balance between supply to the tissues and oxygen demand of those tissues. Added to this is another variable, that of oxygen utilisation, which is known to alter in ischaemic tissue as discussed before.

In a moderately ischaemic limb the oxygen supplied to it may just satisfy that limb's requirement and ability to utilise it; consequently the transcutaneous pO_2 may be low. However, if the limb is severely ischaemic, the $TcpO_2$ over an area of frank gangrene may be unexpectedly high because dead tissue cannot use the oxygen available to it from underlying viable tissues.

Ulceration and T_{sk} .

It has been noticed in our studies and by Clark and his colleagues (1988) that areas of frank ulceration of the skin are invariably 'cold' on thermographic appearance. This does not necessarily mean (as he implies) that there is a limited ability to heal because of poor perfusion. The 'cold' appearance is due to the greatly increased heat loss by evaporation from the damp surface of the ulcer and in no way represents the vascularity of the ulcer base. Indeed, work on burns has shown that even when there is an eschar overlying the area of skin loss, the increased

evaporative loss is not reduced. (H B Stoner, 1989, personal communication).

Some work has been done to eliminate these evaporative losses by covering the ulcer base with 'cling-film' (P Shakespeare, 1989, personal communication), whereupon the radiant heat loss from the ulcer may then be seen and give a clearer indication of underlying tissue perfusion. Much could be learned from further studies of this kind.

Ulcerated ischaemic limbs condemned to amputation might be rerieved. The ulcer which still remained 'cold' thermographically when covered with an impermeable membrane such as 'cling-film', might warrant a more aggressive therapeutic approach.

Thus, the spectrum of disease severity and occasional apparent paradoxes found in the results of clinical investigations would indicate that no single method of assessment is likely to provide a definitive answer regarding the ability of the ischaemic limb to heal.

Conclusion.

The prime aim of this work has been to provide a sound, scientific physiological basis for understanding thermography as it relates skin temperature to blood flow. This has been achieved. The second aim has been to see how these observations may alter in patients with different degrees of peripheral vascular disease. However, it is clear that in patients with ischaemic limbs the alterations from normal are many and complex such that no reliable conclusions can be drawn.

It would seem reasonable therefore, that the following

statements and recommendations could be made:

1. Thermography has been demonstrated in these studies to be of value in assessing skin blood flow of the fingers and toes. Thus, the method could be useful in the investigation of the autonomic neuropathy associated with diabetes mellitus and other sympathetic dystrophies, and predict the response to surgical sympathectomy.

2. Thermography has a role in monitoring the patency of arterio-venous shunts in patients on haemodialysis, and possibly also in assessing the efficacy of embolisation of arterio-venous fistulae.

3. Thermography has a useful part to play in the investigation of vasospastic conditions, such as Raynaud's Disease, and in objective assessment of the response to different forms of therapy.

4. Thermography remains essentially a research tool but may still prove of value in specialised burns and plastics units to estimate the depth of burn and potential for ulcer healing.

5. Full thermographic assessment is both expensive and time-consuming. It is unlikely at the present time to either replace or complement more conventional methods of investigation of the ischaemic limb and its routine use in vascular units in District General Hospitals cannot be recommended.

APPENDICES

Appendix 1. PVD controls - Skin temperature (°C).

No	Age/Sex	Site	Right leg		Left leg	
			(Ambient temp.) 20°C	30°C	20°C	30°C
1	42/M	Medial calf	27.3	29.0	27.4	29.5
		Lateral calf	27.9	29.3	27.4	29.5
		Hallux	18.7	25.0	18.7	24.4
		Sole	23.0	24.5	22.8	24.7
2	51/M	Medial calf	25.6	28.6	26.6	28.8
		Lateral calf	27.4	30.1	27.0	29.4
		Hallux	17.9	28.2	17.6	27.7
		Sole	21.6	25.7	21.3	26.0
3	45/M	Medial calf	27.8	29.6	28.3	30.2
		Lateral calf	28.8	30.5	28.7	30.3
		Hallux	19.2	24.2	19.2	24.0
		Sole	22.9	24.2	23.1	24.5
4	44/M	Medial calf	26.9	28.7	27.5	29.0
		Lateral calf	28.9	29.8	27.8	29.1
		Hallux	18.2	23.3	18.5	24.0
		Sole	22.6	24.5	23.5	24.7
5	57/F	Medial calf	24.1	28.1	24.8	28.1
		Lateral calf	25.1	28.3	25.4	28.0
		Hallux	21.2	28.1	20.6	26.8
		Sole	21.2	27.5	21.2	26.3
6	70/M	Medial calf	28.9	31.1	28.8	30.9
		Lateral calf	29.8	31.2	29.0	31.0
		Hallux	21.7	26.3	20.8	26.2
		Sole	25.5	27.2	25.3	27.7

7	42/F	Medial calf	28.9	32.1	29.5	32.3
		Lateral calf	29.3	31.1	29.2	31.7
		Hallux	29.0	33.8	29.4	32.6
		Sole	28.0	32.4	27.7	32.5
8	51/M	Medial calf	30.2	31.7	30.5	32.4
		Lateral calf	31.2	31.2	30.3	31.3
		Hallux	29.2	30.3	28.2	29.7
		Sole	31.4	32.3	30.9	32.1

Appendix 2. PVD controls - Skin blood flow. Perfusion Units (PU).

No	Age/Sex	Site	Right leg		Left leg	
			(Ambient temp.)	20°C	30°C	20°C
1	42/M	Medial calf	9.0	14.5	11.5	10.0
		Lateral calf	4.0	6.0	7.0	12.0
		Hallux	4.5	9.5	10.0	20.0
2	51/M	Medial calf	2.5	4.5	3.0	5.0
		Lateral calf	2.5	4.5	2.5	5.5
		Hallux	14.0	67.0	12.0	20.0
3	45/M	Medial calf	5.0	6.5	6.0	8.0
		Lateral calf	4.5	4.5	5.0	5.0
		Hallux	8.5	10.5	11.5	9.0
4	44/M	Medial calf	6.0	8.0	5.0	7.5
		Lateral calf	5.0	5.5	6.0	15.0
		Hallux	7.5	10.0	7.0	9.5
5	57/F	Medial calf	4.5	6.0	4.0	5.0
		Lateral calf	4.5	10.0	6.0	5.0
		Hallux	17.0	33.0	19.0	25.0
6	70/M	Medial calf	5.0	11.5	5.0	6.5
		Lateral calf	4.5	12.5	7.5	7.0
		Hallux	4.0	27.0	8.0	17.0
7	42/F	Medial calf	5.0	5.0	4.0	6.5
		Lateral calf	11.5	5.5	6.0	5.0
		Hallux	10.0	18.0	20.0	22.5
8	51/M	Medial calf	8.5	5.5	5.5	5.0
		Lateral calf	8.0	6.0	9.5	6.0
		Hallux	40.0	50.0	12.5	30.5

Appendix 3. P/A ratio related to outcome in PVD Patients.

('Bad' leg only).

No	Age/Sex	P/A at T _a 20°C	P/A at T _a 30°C	Procedure	Outcome
1	64/M	0.99	0.98	AKA	1 ^o healing
2	66/M	-	-	AKA	1 ^o healing
3	49/M	-	-	Bypass	Patent at 5/12
4	88/F	0.98	0.99	No op.	Died in hosp.
5	58/M	0.95	0.93	AKA	Died in hosp.
6	59/M	0.97	0.98	Bypass	Patent at 1 yr.
7	68/M	0.99	0.98	BKA	1 ^o healing
8	57/M	1.00	0.98	No op.	ISQ
9	50/M	0.99	0.97	Bypass	DNA in OPD
10	73/M	1.01	0.99	Bypass	Patent at 5/12
11	74/M	0.99	0.99	Bypass	Patent at 3/12
12	57/M	0.98	0.96	ABG	Patent at 6/12
13	57/M	0.99	0.99	No op.	ISQ
14	49/M	0.99	0.96	No op.	ISQ
15	64/F	1.00	0.98	BKA	Delayed healing
16	33/F	-	-	Angioplasty	ISQ
17	80/F	1.00	0.98	BKA	Delayed healing

Appendix 4. Thermographic data (T_{sk}) from PVD Patients ($^{\circ}\text{C}$).

No	Age/Sex	Site	'Good' leg		'Bad' leg	
			20 $^{\circ}\text{C}$	30 $^{\circ}\text{C}$	20 $^{\circ}\text{C}$	30 $^{\circ}\text{C}$
		(Ambient temp.)				
1	64/M	Medial calf	amputated B/K		27.2	28.4
		Lateral calf	-	-	27.3	28.2
		Hallux	-	-	25.2	26.6
		Sole	-	-	-	-
2	66/M	-				
3	49/M	-				
4	88/F	Medial calf	26.6	28.0	27.4	29.2
		Lateral calf	26.6	28.2	27.9	30.0
		Hallux	23.1	27.6	22.6	26.2
		Sole	26.2	27.5	25.2	27.2
5	58/M	Medial calf	26.1	29.0	24.1	27.1
		Lateral calf	27.0	29.9	25.9	28.1
		Hallux	20.2	24.8	20.3	24.8
		Sole	22.8	24.9	21.9	24.1
6	59/M	Medial calf	27.4	28.8	28.2	29.6
		Lateral calf	27.7	29.2	28.5	30.0
		Hallux	21.5	28.7	23.8	29.2
		Sole	25.0	27.8	27.0	29.6
7	68/M	Medial calf	28.2	29.8	27.7	29.6
		Lateral calf	28.4	29.9	27.9	30.2
		Hallux	23.2	31.0	21.4	26.0
		Sole	26.6	31.1	23.8	26.4
8	57/M	Medial calf	27.0	28.5	25.2	27.8
		Lateral calf	25.6	27.9	25.5	27.4
		Hallux	20.6	26.2	20.8	25.7

		Sole	24.8	27.0	23.3	26.2
9	50/M	Medial calf	27.7	29.4	26.2	30.2
		Lateral calf	27.8	29.5	27.1	30.2
		Hallux	23.2	30.4	22.9	27.2
		Sole	-	-	-	-
10	73/M	Medial calf	26.9	30.0	27.8	30.8
		Lateral calf	27.4	30.3	27.2	30.1
		Hallux	21.3	27.7	21.9	27.5
		Sole	27.0	29.9	26.8	29.1
11	74/M	Medial calf	26.6	29.5	27.1	30.3
		Lateral calf	26.5	29.9	27.4	29.9
		Hallux	22.3	28.0	24.2	27.4
		Sole	25.5	28.4	25.6	28.6
12	57/M	Medial calf	27.9	30.1	27.0	29.6
		Lateral calf	27.6	30.1	27.7	29.9
		Hallux	21.1	27.4	21.1	28.0
		Sole	25.3	27.5	24.7	27.1
13	57/M	Medial calf	26.2	28.4	26.5	28.3
		Lateral calf	26.8	28.9	27.4	28.8
		Hallux	20.1	28.2	20.2	29.6
		Sole	23.3	27.4	23.3	27.3
14	49/M	Medial calf	25.3	28.9	25.2	28.5
		Lateral calf	26.6	29.4	25.7	29.1
		Hallux	18.6	26.2	18.6	25.8
		Sole	22.1	25.5	22.0	25.8
15	64/F	-				
16	33/F	-				
17	80/F	Medial calf	26.8	32.3	27.5	32.4
		Lateral calf	28.8	33.8	27.9	32.9

Hallux	26.9	31.5	24.6	30.0
Sole	29.5	32.6	28.9	31.1

Appendix 5. Skin Blood Flow data from PVD Patients. (PU).

No	Age/Sex	Site	'Good' leg		'Bad' leg	
			(Ambient temp.)	20°C	30°C	20°C
1	64/M	Medial calf	amputated B/K		5.0	3.0
		Lateral calf	-	-	3.2	3.6
		Hallux	-	-	2.8	3.6
2	66/M	-				
3	49/M	-				
4	88/F	Medial calf	7.0	7.0	10.0	3.2
		Lateral calf	10.0	1.0	9.0	4.0
		Hallux	6.5	11.0	9.5	4.0
5	58/M	Medial calf	5.3	9.0	4.5	12.5
		Lateral calf	4.5	4.0	4.5	7.5
		Hallux	5.5	6.5	4.0	8.5
6	59/M	Medial calf	7.0	4.0	4.5	3.5
		Lateral calf	4.0	5.0	3.0	4.5
		Hallux	4.5	7.5	4.0	5.0
7	68/M	Medial calf	9.0	7.0	10.5	14.0
		Lateral calf	8.0	11.5	9.5	15.0
		Hallux	8.5	9.0	7.5	9.5
8	57/M	Medial calf	10.5	17.0	7.5	11.0
		Lateral calf	12.5	22.0	10.0	12.0
		Hallux	17.0	50.0	24.0	40.0
9	50/M	Medial calf	9.0	12.0	4.5	10.0
		Lateral calf	8.5	11.5	3.5	8.5
		Hallux	5.0	46.0	4.0	11.5
10	73/M	Medial calf	1.0	11.0	5.0	15.0
		Lateral calf	1.5	8.0	1.0	14.0

		Hallux	3.0	16.0	1.5	25.0
11	74/M	Medial calf	11.5	17.0	13.0	17.0
		Lateral calf	8.0	11.0	11.0	17.0
		Hallux	11.5	10.0	15.5	18.0
12	57/M	Medial calf	7.0	9.5	5.0	6.0
		Lateral calf	7.0	8.0	5.0	6.0
		Hallux	20.0	75.0	6.5	35.0
13	57/M	Medial calf	5.5	9.0	4.5	6.0
		Lateral calf	5.0	5.5	4.0	5.5
		Hallux	6.5	9.5	8.0	14.0
14	49/M	Medial calf	3.5	4.0	3.5	5.5
		Lateral calf	3.0	4.0	3.5	2.0
		Hallux	3.0	3.5	3.0	6.5
15	64/F	-				
16	33/F	Medial calf	6.5	7.0	4.5	6.5
		Lateral calf	3.0	5.0	2.0	7.0
		Hallux	5.0	7.0	4.0	11.0
17	80/M	Medial calf	8.0	5.0	7.0	8.5
		Lateral calf	5.5	6.0	7.0	10.5
		Hallux	5.0	8.0	6.5	3.5

Appendix 6. Relationship of Transcutaneous Oxygen and Carbon Dioxide
tension results with outcome in PVD Patients' 'Bad' legs.

<u>No</u>	<u>Age/Sex</u>	<u>Oxygen</u>	<u>Carbon Dioxide</u>	<u>Outcome</u>
		<u>(medial calf site; mm Hg)</u>		
1	64/M	49	37	AKA 1 ^o healing
2	66/M	1	89	AKA 1 ^o healing
3	49/M	34	50	Bypass graft
4	88/F	62	33	No op. Died in hosp.
5	58/M	5	52	AKA Died in hosp.
6	59/M	46	48	Bypass graft
7	68/M	43	49	BKA 1 ^o healing
8	57/M	67	28	No op. ISQ
9	50/M	33	46	Bypass graft
10	73/M	4	>60	Bypass graft
11	74/M	43	43	Bypass graft
12	57/M	62	39	Bypass graft
13	57/M	64	28	No op. ISQ
14	49/M	58	34	No op. ISQ
15	64/F	28	48	BKA Delayed healing
16	33/F	70	36	Angioplasty ISQ
17	80/F	60	30	BKA Delayed healing

Appendix 7. Table of investigations performed on PVD Patients.

<u>No</u>	<u>Age/Sex</u>	<u>Ankle BP</u>	<u>ABPI</u>	<u>Thermoq.</u>	<u>TBF</u>	<u>SkBF</u>	<u>TcpO₂</u>
1	64/M	+	+	+	-	+	+
2	66/M	+	+	-	-	-	+
3	49/M	+	+	-	-	-	+
4	88/F	-	-	+	-	+	+
5	58/M	+	+	+	-	+	+
6	59/M	+	+	+	-	+	+
7	68/M	+	+	+	+	+	+
8	57/M	+	+	+	-	+	+
9	50/M	+	+	+	-	+	+
10	73/M	+	+	+	+	+	+
11	74/M	+	+	+	+	+	+
12	57/M	+	+	+	+	+	+
13	57/M	+	+	+	+	+	+
14	49/M	+	+	+	+	+	+
15	64/F	+	+	+	-	+	+
16	33/F	+	+	-	+	+	+
17	80/F	+	+	+	+	+	+

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Relationships between skin temperature and perfusion in the arm and leg

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Summary. Relationships between skin temperature (T_{sk}) and perfusion have been studied to provide a basis for the use of T_{sk} in the non-invasive assessment of limb circulation in peripheral vascular disease.

Raising the ambient temperature (T_a) from 20 to 30°C increased the perfusion of the glabrous skin of the hands and feet without changing that of the skin of the forearm or calf. On a fractional basis the response in the hand and foot was the same. T_{sk} was higher in the arms than the legs and in the proximal than distal parts of the limbs. A fall in T_{sk} was often seen when T_a rose from 20 to 25°C and was attributed to counter-current cooling. Subsequently T_{sk} rose even in regions where there was no increase in skin perfusion. T_{sk} can only be related to its perfusion in the fingers, palm and toes. Forearm T_{sk} was related to the perfusion of the digits. This relationship implies a link with the arterial inflow to the limb which determines the size of its thermal core. Heat conduction from the core seemed important for the skin of areas like the forearm and calf where the constant, low perfusion limited the amount of heat which could be transported to it directly by the blood.

The importance of conduction was supported by studies, at T_a 20°C, on subjects during calf muscle exercise and on patients with arterio-venous fistulae. Here an increase in the arterial inflow to the limb was associated with a rise in T_{sk} of the forearm/calf unrelated to the perfusion of its skin.

Key words: A-V fistula, exercise, limb bloodflow, skin blood flow, skin temperature.

Introduction

Skin temperature (T_{sk}) has been used to decide the level of a limb amputation for peripheral vascular disease and to predict its outcome (Spence *et al.*, 1981; Stoner *et al.*, 1989). If thermography is to be used more widely in the non-invasive,

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problems have been extensively studied (see reviews by Hertzman, 1959; Roddie, 1983; Rowell, 1983; Johnson, 1986; Thauer, 1966) much remains obscure. To this end we have studied T_{sk} in the arm and leg when the blood flow to these parts has been altered by ambient temperature (T_a), exercise and arterio-venous fistulae.

Methods

The effect of changes in T_a was studied in 12 healthy Caucasian subjects (six men, six women) not receiving any medication and without symptoms of peripheral vascular disease. The men were aged between 21 and 69 years (median 30 years) and the women between 21 and 36 years (median 30 years). They were studied during the first three (winter) months of the year and all the subjects normally resided in the UK. The effect of exercise was studied in six similar subjects, four men and two women aged between 29 and 38 years (median 34 years).

Observations were made on nine patients with arterio-venous fistulae in the forearm. These were six male and three females, aged between 21 and 76 years (median 50 years), in whom a modified Brescia fistula (Bell & Wood, 1983) had been constructed at the wrist 8 days to 10 months (median 23 days) previously to provide access for haemodialysis. In addition, an otherwise healthy 26-year-old woman with an arterio-venous fistula of unknown aetiology in the sole of her right foot was also examined.

PHYSIOLOGICAL TECHNIQUES

Skin temperature (T_{sk}) was measured by infrared thermography using an Agema Thermovision Camera 680 (Agema, Leighton Buzzard, UK) as before (Stoner *et al.*, 1989).

The perfusion of the microcirculation of the skin was studied with a Periflux PF3 Laser Perfusion Monitor (Perimed, Sweden). This instrument uses an helium-neon laser (632.8 nm; 2 mW). The probe is held in an unheated plastic holder attached to the skin to provide a constant geometry. The apparatus has been described by Tenland (1982). The returning signal is analysed by the instrument and presented as a voltage which was recorded and used as an arbitrary 'Perfusion Unit'. In some subjects skin perfusion was also assessed, in arbitrary units, by reflectance pulse plethysmography using the PH77 head of a PPG13 Photoplethysmograph (Medasonics, California, USA).

Total blood flow in the forearm and calf was measured with a mercury-in-silastic strain-gauge venous occlusion plethysmograph (Witney, 1953), the pressure changes being recorded on an Ormed recorder (Lectromed, UK).

Skin-fold thickness was measured with Harpenden callipers (British Indicators Ltd, St. Albans, UK).

All tests were carried out in a temperature controlled room. Dry-bulb air temperature (T_a) was measured with two mercury-in-glass thermometers at different positions in the room and care was taken to maintain T_a within 1°C of the target value. Relative humidity varied between 34 and 46%. Informed consent to the tests was obtained from all the subjects and patients and the work was approved by the Salford Health Authority Ethical Committee.

(1) For the studies on the effect of changing T_a the subjects wore a minimal amount of clothing (men, underpants; women, beachwear) and lay semi-recumbent on a couch. The hallux was between 20 and 30 cm below the axilla. After 15 min exposure to T_a 20°C thermograms were recorded from the anterior and posterior surfaces of the forearm, hand and digits and from the medial and lateral surfaces of the leg and foot of the same side. The thermograms were stored and subsequently analysed. Skin perfusion was then assessed by the laser-Doppler technique on the pulps of all five fingers, the palm and dorsum of the hand and at three sites on the forearm. This was followed by measurements on the pulps of the hallux and second toe, the medial and dorso-lateral parts of the foot and at three sites on the calf. The measurements on the upper limb were made with the forearm at the level of the heart. The position of the holders was marked so that subsequent measurements could be made at the same sites. In the 'Results' mean values are shown for the digits, forearm and calf since the separate values in these three areas did not differ significantly (Friedman's two-way analysis of variance of the data from 12 subjects at three T_a s).

These measurements were completed in 20–25 min. The T_a was then raised to 25°C. This took 10 min. After 15 min at 25°C all the observations were repeated during a period of 20–25 min. T_a was then raised to 30°C during the next 10–15 min and then, after a further 15 min, a final set of observations was recorded. The whole experiment lasted about 150 min.

(2) The effect of calf muscle exercise was studied at T_a 20°C. After 15 min exposure of both legs in a semi-recumbent posture the total calf blood flow and the perfusion of the calf skin (expressed as the mean of the values at three sites) was measured. Thermograms of the legs were then taken in the standing position. The subject then carried out 30 ankle raises at 1 s⁻¹. This was followed by a 15-s rest after which the sequence was repeated until five cycles had been completed. Thermography, with measurements of skin perfusion and total calf blood flow, was repeated immediately and further thermograms were taken at 15 and 30 min.

(3) Arterio-venous fistulae were studied at T_a 20°C. For those at the wrist the patient was seated with both arms exposed. After 15 min the total forearm blood flow and the perfusion of the forearm skin (expressed as the mean of the values at three sites) was recorded in both forearms supported at the level of the heart. Thermograms of both arms were then taken. In the patient with the arterio-venous fistula in the foot thermograms were taken and total calf blood flow and skin perfusion measured in both legs after 15 min exposure to T_a 20°C.

where possible the results have been expressed as the median and range and comparisons have been made by non-parametric methods (Siegel, 1956).

Results

EFFECT OF ENVIRONMENTAL TEMPERATURE ON SKIN TEMPERATURE

At all the T_a studied the distal parts of the upper and lower limbs were cooler than the proximal parts and, in this particular group, T_{sk} was generally higher in men than women.

For the anterior surface of the digits the response to an increase in T_a depended on the T_{sk} at T_a 20°C (Fig. 1). In those with a relatively high T_{sk} at T_a 20°C, T_{sk} increased or remained about the same, when T_a rose from 20 to 25°C. When T_{sk} was low at T_a 20°C, T_{sk} fell, or remained about the same, during this change in T_a . Subsequently, when T_a was raised from 25 to 30°C T_{sk} rose in all. Similar changes occurred in the temperature of the skin on the posterior surface of the digits except that more subjects (8/12) showed an increase when T_a rose from 20 to 25°C.

Changes of this type were also seen in the skin of the palm (Fig. 1) and dorsum of the hand. The two surfaces of the forearm behaved similarly and the pattern of the change in the anterior surface is illustrated in Fig. 1. All the subjects showed an increase when

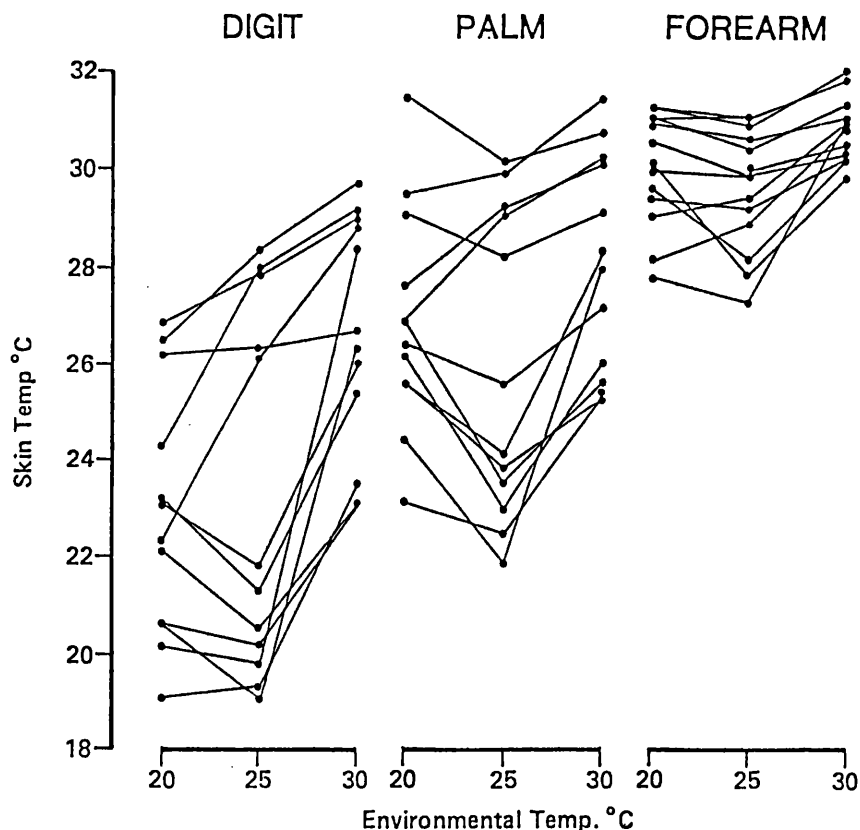


Fig. 1. Skin temperatures at T_a 20, 25 and 30°C for anterior surface of digits, palm and anterior surface of the forearm. Each line refers to a separate subject.

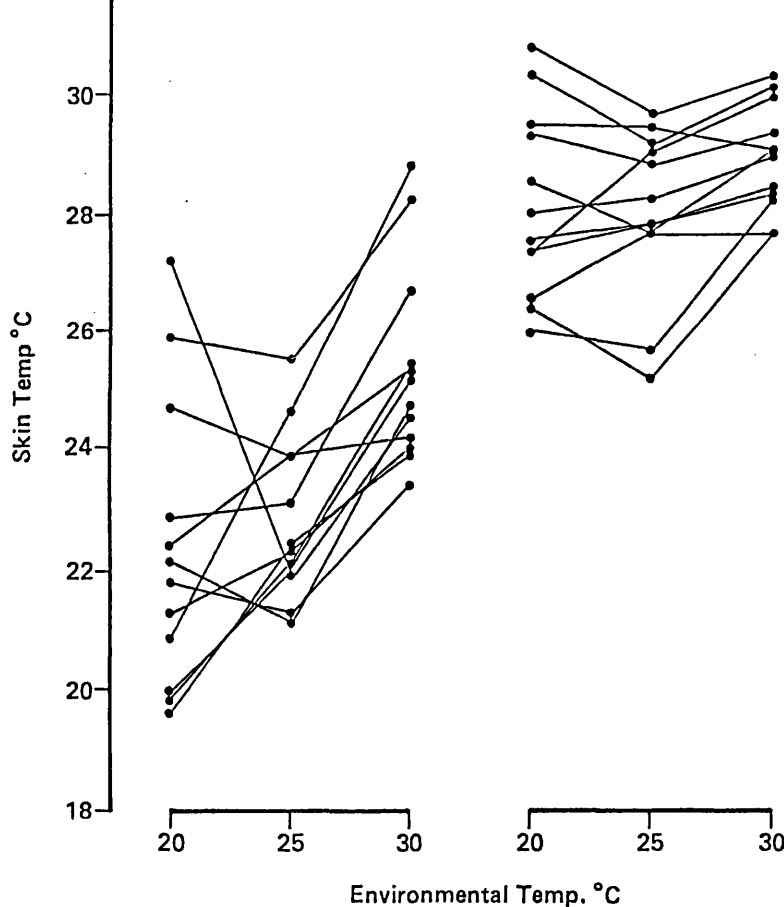


Fig. 2. Skin temperatures at T_a 20, 25 and 30°C for hallux and medial surface of calf. Each line refers to a separate subject.

T_a rose from 25 to 30°C and at the time of measurement forearm T_{sk} exceeded the initial value in 10 of the 12 subjects.

Skin temperatures were lower in the lower limb but a similar pattern was seen with the main changes occurring in the distal parts, so that the temperature gradient down the limb decreased as T_a increased (Fig. 2). The pattern of the changes in the hallux and calf as T_a rose from 20, through 25, to 30°C resembled that for the fingers and forearm. The same pattern was also seen in the temperature of the medial and dorsolateral surfaces of the foot during this sequence of changes in T_a .

EFFECT OF ENVIRONMENTAL TEMPERATURE ON SKIN PERFUSION

(1) *Laser-Doppler Flowmetry* (Figs 3 and 4). The direction of the response was the same in the different subjects although there were individual variations in its size, especially in the upper limb. There were no discernible differences in the responses of the male and female subjects.

In all subjects the perfusion of the digits at T_a 30°C was significantly greater than at 25 and 20°C and in nine of the 12 subjects this increase began between 20 and 25°C.

the hand tended to decrease with the rise in T_a but the change was not significant. The perfusion of the forearm skin did not change consistently with the alteration in T_a (Friedman's two-way analysis of variance).

The perfusion of the pulps of the hallux and second toe was significantly ($P < 0.006$ and $P < 0.003$ respectively) greater at 30°C than at the lower T_a s, the increase starting when T_a rose above 25°C . The same was true for the skin of the medial part of the foot although the increase was much smaller. No significant change occurred in the perfusion of the skin of the dorso-lateral part of the foot or of the skin of the calf.

Thus, the skin circulation in comparable regions of the upper and lower limbs responded similarly when T_a was raised from 20 to 30°C . Although the absolute increase in the perfusion of the skin of the thumb was significantly greater ($P < 0.001$, two-tailed sign test) than of the hallux, as was that of the palm vs. the medial surface

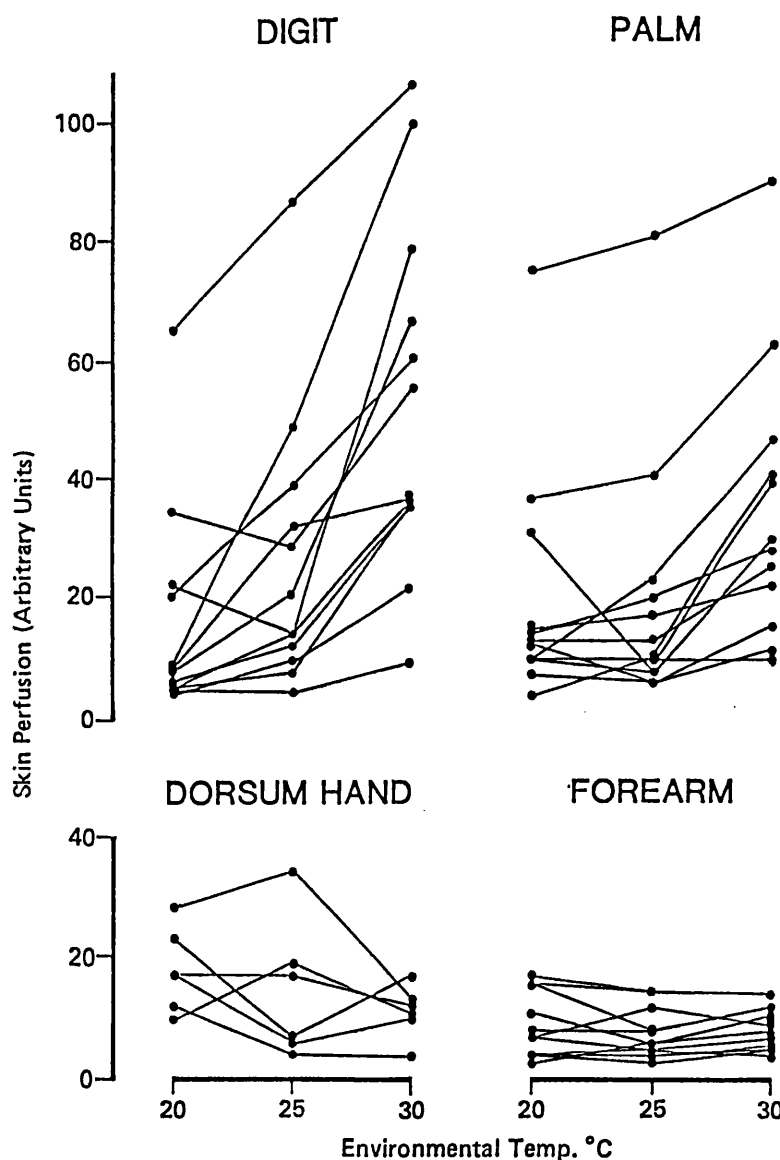


Fig. 3. Skin perfusion at T_a 20, 25 and 30°C in digits, palm, dorsum of hand and forearm. Each line refers to a separate subject.

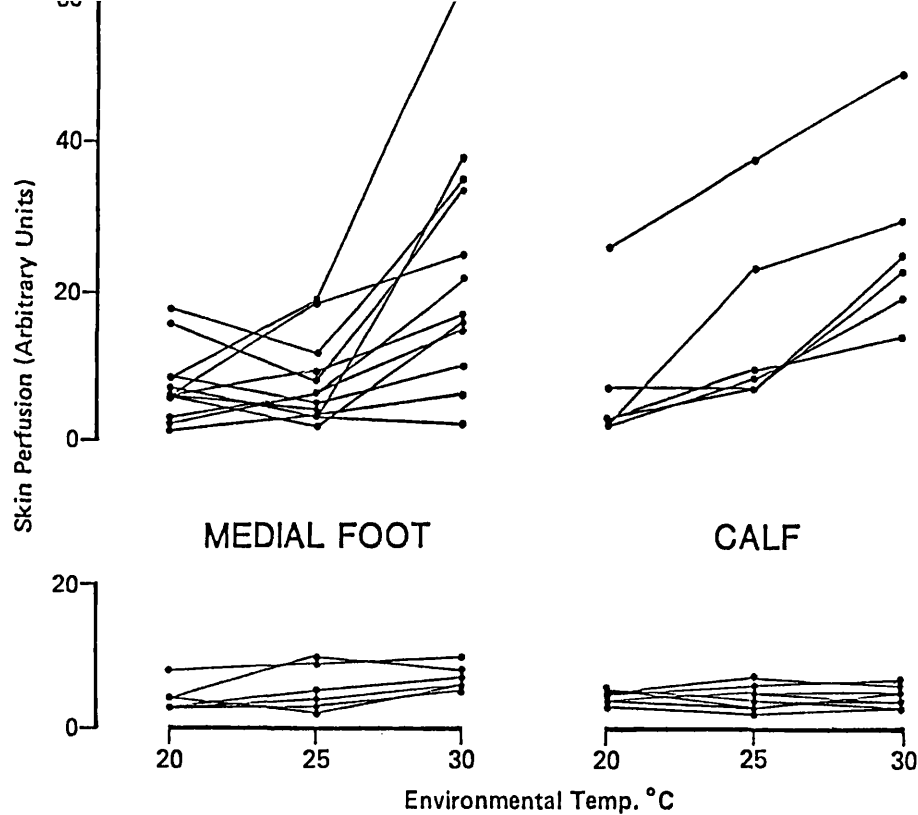


Fig. 4. Skin perfusion at T_a 20, 25 and 30°C in hallux, second toe, medial surface of foot and calf. Each line refers to a separate subject.

of the foot, the fractional changes in these pairs of skin regions were not significantly different (Wilcoxon's matched pairs signed-ranks test, Mann-Whitney U -test). The same was found when the fractional changes in the perfusion of the pulps of the digits (mean) and of the index finger were compared with those in the hallux and second toe respectively.

(2) *Photoplethysmography* (Fig. 5). Simultaneous measurements of the circulation in the skin of the forearm and finger pulp were made in four subjects. This technique also showed that when T_a rose from 20 to 30°C there was an increase in the perfusion of the finger pulp without change in that of the skin of the forearm. The elimination of the flow through the hand by inflating a cuff around the wrist had no effect on the recording from the forearm.

RELATIONSHIP BETWEEN SKIN TEMPERATURE AND PERFUSION MEASURED BY LASER-DOPPLER FLOWMETRY

Relationships were sought between T_{sk} and perfusion in the anterior surface of the digits, the palm, the anterior surface of the forearm, the hallux, the dorsolateral region of the foot and the lateral surface of the calf by Spearman's rank correlation method. Significant relationships over the range of ambient temperatures used were found only

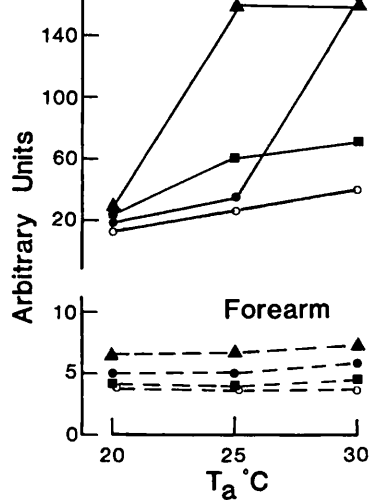


Fig. 5. Skin perfusion measured by photoplethysmography in the pulp of the middle finger and the anterior surface of the forearm at T_a 20, 25 and 30°C in four subjects. Each subject indicated by a different symbol.

in the digits ($r_s = 0.730$, $P < 0.001$, 36 pairs), palm ($r_s = 0.838$; $P < 0.001$, 36 pairs) and hallux ($r_s = 0.363$, $P < 0.05$, 36 pairs). Considering the data at individual T_a s it was found that the relationship between T_{sk} and flow in the hallux was best at T_a 30°C ($r_s = 0.657$, $P < 0.05$, 12 pairs). In the digits significant relationships were found at T_a 20 and 30°C ($r_s = 0.669$ and 0.0651 respectively, $P < 0.05$, 12 pairs) but not at 25°C.

The values of T_{sk} for the anterior and posterior surfaces of the forearm were averaged to give a mean T_{sk} for the forearm and this was found to be significantly related to the perfusion of the pulps of the digits ($r_s = 0.500$, $P < 0.01$, 36 pairs). It was not possible to show a similar relationship in the leg where the spread of values was very much less.

EFFECT OF MUSCULAR EXERCISE (Table 1)

The response to exercise was similar in the men and women and the group has been considered as a whole. The total blood flow through the calf rose about three-fold but this was not accompanied by any significant increase in the perfusion of the calf skin. The values for the latter were always similar to the low values found above. There was, however, a significant increase in the mean temperature of the calf skin in all the subjects. The maximum temperature was not always reached by the end of the last exercise cycle. In two subjects the rise in T_{sk} continued for 15 min. The 'after-exercise' value of T_{sk} in Table 1 is therefore based on the maximum value recorded during the first 15 min after the end of the exercise. No further increases were observed after this point. When all the values were considered together a significant positive relationship was found between the T_{sk} of the calf and the total calf blood flow (Spearman's rank correlation method, $r_s = 0.753$, $P < 0.001$, 24 pairs).

	Before exercise	After exercise
Total calf blood flow (ml [100 ml tissue] ⁻¹ min ⁻¹)	3.4 (1.8–8.8)	8.5 (3.4–14.5)*
Calf skin perfusion (perfusion units)	4.9 (3.7–6.0)	5.1 (4.8–5.3)†
Calf skin temperature (°C)	27.6 (25.5–29.3)	28.8 (25.8–30.6)*

Values are shown as median and range.

* $P < 0.01$, Wilcoxon matched pairs signed-rank test.

†Not significant.

EFFECT OF A FOREARM FISTULA (Table 2)

After the construction of a Brescia fistula the total blood flow through the forearm increased about five-fold. The T_{sk} of the forearm on the operated side was significantly elevated, not just around the site of the fistula, which was excluded from the calculation of the mean T_{sk} , but proximally where the circumference of the forearm was maximal. The skin perfusion in the forearm was also greater ($P < 0.01$) on the operated side (ratio 1.1–2.5; median 1.3) but the values were always within the range found above in normal subjects. In normal subjects the perfusion of the skin of the two forearms does not differ significantly. There was no relationship between T_{sk} and perfusion at the three sites used for the measurement of the latter in either forearm. In an individual patient there was no significant difference between the maximum circumference of the two forearms or in the skin-fold thickness at that site.

Table 2. The total blood flow, the mean skin perfusion and the mean skin temperature of the forearm in nine patients with a Brescia fistula at the wrist

	Normal side	Fistula side
Total forearm blood flow (ml [100 ml tissue] ⁻¹ min ⁻¹)	6.3 (1.9–16.3)	22.1 (5.6–31.5)*
Forearm skin perfusion (perfusion units)	6.0 (3.7–15.3)	8.2 (4.2–17.2)*
Forearm skin temperature (°C)	29.6 (26.5–30.7)	31.2 (29.7–32.2)*

The values are shown as the median and range.

* $P < 0.01$, Wilcoxon matched pairs signed-rank test.

EFFECT OF A FISTULA IN THE FOOT

The site of this patient's arterio-venous fistula was revealed by angiography (Fig. 6). Lying in the sole of the right foot it was fed by a greatly enlarged tibio-peroneal trunk which did not branch to give a posterior tibial artery until the level of the malleoli,

fistula. The total blood flow through the calf on this side was greatly increased (Table 3). Skin perfusion over the calf on the affected side was variable and somewhat higher than on the normal side but the values were in the normal range for this T_a . There was a marked increase in the mean T_{sk} of the calf on the affected side (Table 3) and the temperature distribution is shown by the isotherms on the posterior aspects of the legs (Fig. 7). The points relating mean calf T_{sk} and total calf blood flow in the legs of this patient were close to the regression line relating these variables in the normal subjects undergoing exercise. The calf on the abnormal side was slightly larger at its maximum circumference (340 vs. 330 mm).

Table 3. The effect of the arterio-venous fistula in the foot, shown in Fig. 6, on the total blood flow through the calf, the calf skin perfusion and the mean calf skin temperature

	Normal side	Fistula side
Total calf blood flow (ml [100 ml tissue] ⁻¹ min ⁻¹)	2.7	10.6
Mean calf skin perfusion (perfusion units)	2.8	4.3
Mean calf skin temperature (°C)	28.9	30.4

Discussion

The results of this type of investigation are very dependent on the techniques employed and the protocol followed. Some of the variability in the control subjects could possibly have been decreased by standardizing their nutritional status and the

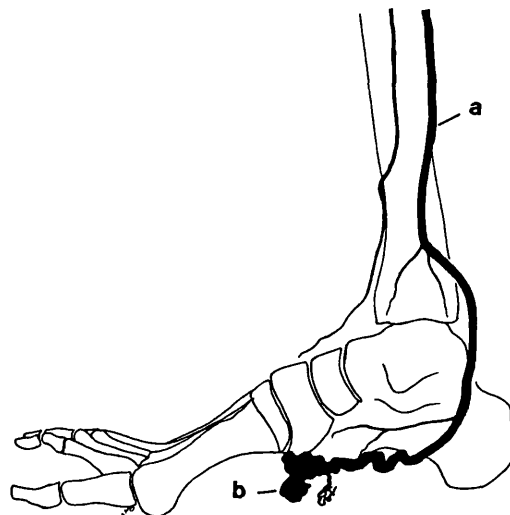


Fig. 6. Tracing of the angiogram of the patient's right foot to show a lateral view of the arterio-venous fistula. a, tibio-peroneal artery; b, arterio-venous fistula.

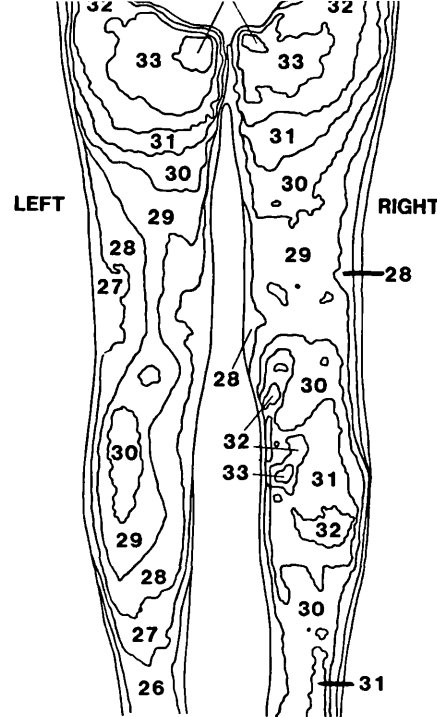


Fig. 7. Tracings of thermograms of posterior aspects of the legs of the patient with an arterio-venous fistula in the right foot to show the contours of areas of different skin temperature. The numbers show the mean skin temperature ($^{\circ}\text{C}$) of the area to the nearest degree.

time of day for the tests. As one of our aims was to devise procedures for testing elderly patients with advanced peripheral vascular disease this was not practicable. This aim also led us to choose a semi-recumbent rather than recumbent posture and the short equilibration periods. The 15-min exposure period before starting the tests should have been long enough to eliminate the short-lived effects of minor disturbances (Delius *et al.*, 1972; Normell & Wallin, 1974) and to allow for equilibration of the nervous responses (Khan *et al.*, 1988). However, 15 min may not be long enough for thermal equilibrium although this is the usual period of exposure before thermography in patients with peripheral vascular disease (Henderson & Hackett, 1978; Spence & Walker, 1984; Stoner *et al.*, 1989) and in our experience is as long as such patients will tolerate, particularly at T_a 20°C . We have found, like Barcroft & Edholm (1946), that prolonged exposure to T_a 20°C leads to a continuing fall in limb temperature. It is doubtful whether real stability is ever achieved as the body is always responding to change, both internal and external, often in a cyclical fashion (Clark & Edholm, 1985).

While infrared thermography provides us with a good way of measuring T_{sk} there is no absolute way of measuring the blood flow through an area of human skin. The available techniques give relative measures, expressed in arbitrary units, and are not strictly comparable since they reflect different aspects of the perfusion. We have used two methods; mainly laser-Doppler flowmetry which has many clinical advantages,

of blood in a rather larger block of skin. In our subjects the two methods showed the same pattern of response to changes in T_a . This was confirmed in recent work (unpublished observations) in which the two methods were compared simultaneously on the finger pulps of the same subject.

Our results, like those of Bini *et al.* (1980a, b), showed that raising T_a from 20 to 30°C led to an increase in the perfusion of the glabrous skin of the hands and feet without significant change in that of the forearm and calf. By using a temperature change which did not provoke sweating (Bini *et al.*, 1980a) the effects can be attributed to a reduction in the sympathetic vasoconstrictor outflow to the skin. These vasoconstrictor nerves are distributed mainly to the distal parts of the limb and the blood flow to the muscles is not altered in this response (Shepherd, 1963; Thauer, 1966). Bini *et al.* (1980b) showed that bursts of sympathetic vasoconstrictor nerve activity occurred synchronously in the median and peroneal nerves and, on a fractional basis, we found no significant difference in the vascular responses in the hands and feet, although the perfusion of the latter was less. This accords with the work of Hassan *et al.* (1986) which showed that the local mechanisms reducing skin perfusion in the dependent limb are overcome by the thermoregulatory release of sympathetic vasoconstrictor tone.

Clinicians often link skin temperature with its perfusion but our results suggest that for unblemished skin this can only be done with confidence at certain sites—digits, palm and toes. In the forearm and calf T_{sk} varied independently of skin perfusion.

In our experiments on T_a change the skin of the proximal parts of the limbs was always warmer than that of the periphery. Returning venous blood from cold fingers and toes would, therefore, tend to cool the proximal parts by countercurrent cooling of the incoming blood (Bernard, 1876; Bazett *et al.*, 1948a, b). This effect was most clearly seen in the digits and palm when T_a rose from 20 to 25°C and perfusion of the cold digits began to increase. The separate nature of the skin perfusion of the fingers and forearm was shown by the lack of change in the photoplethysmographic record from the latter when the circulation through the hand was occluded at the wrist. Since the perfusion of the skin of the forearm and calf is persistently low little heat will be transported to it directly by the blood. With the rise in T_a part of the increase in the T_{sk} of the forearm and calf will be due to reduced radiation and convection losses from the surface because of the lower temperature gradient between the skin and the environment. However, the significant relationship between T_{sk} of the forearm and the perfusion of the digits, i.e. with the amount of blood passing through the forearm to the hand, indicates the importance of conduction from the thermal core which will be expanded by the rise in T_a (Fox, 1974). This change in the thermal core was shown indirectly by Saltin *et al.* (1968) who recorded an increase in the temperature of inactive muscle when T_a was raised from 20 to 30°C.

The interaction between the loss of heat from the surface by convection and radiation and its conduction to the surface from the thermal core heated by the arterial

of heat transported directly to the skin by the blood is small, was borne out when the size of the thermal core was increased under constant environmental conditions. This occurred when the blood flow into the limb was increased by exercise or by peripheral arterio-venous fistulae. The increased venous return from the exercising muscles of the calf would not have affected the skin over them and the blood passing through the fistulae returned immediately via the large superficial veins.

In all these situations an increase in total limb blood flow was associated with a raised T_{sk} of the forearm or calf. In those undergoing exercise there was no significant change in the perfusion of the skin itself but there was a positive relationship between the total blood flow through the calf and the temperature of the overlying skin. It is unlikely that the heat generated in the muscle by the amount of exercise used would have made a significant contribution to the effect (Clark & Edholm, 1985). In the patient with the arterio-venous fistula in the foot, where the calf was hotter on the affected side at rest, the relationship between T_{sk} calf and total calf blood flow was similar to that in the exercise subjects.

In the fistula patients skin perfusion was raised in the forearm/calf of the affected side. This increase was never outside the normal range at T_a 20°C and was small in comparison with the changes in those parts of the limbs where a relationship between T_{sk} and perfusion has been demonstrated. There was no local relationship between skin perfusion and temperature at the sites studied in the calf or forearm. The reason for the higher perfusion of the skin in these parts of the limb with a fistula is not known.

Our results show that the size of the thermal core, which depends on the arterial inflow to the limb, is important for the T_{sk} of the forearm and calf. By showing the different relationships between T_{sk} and blood flow in different parts of the limbs these results may help in the interpretation of T_{sk} measurements in patients with peripheral vascular disease (e.g. Stoner *et al.*, 1989). Such measurements, and the changes which can be produced by physiological stimuli, may be useful in the non-invasive pre-operative assessment of these patients.

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