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# Thermal Control of Blood Flow Through Capillaries and Arteriovenous Anastomoses in Skin of Sheep

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**Abstract.** Using radioactive microsphere and electromagnetic techniques, hindleg vascular responses were studied in 38 conscious, chronically prepared sheep subjected to either exposure to a warm environment, and/or local warming of the hypothalamus, spinal cord, forelegs or hindlegs. The total proportion of cardiac output passing through AVA's was increased by all treatments. AVA flow in hindleg skin was increased but capillary flow was unchanged by warming the hypothalamus, spinal cord or forelegs. AVA flow was unchanged but capillary flow was increased by warming the ambient air or the hindlegs alone. Equivalent cooling treatments resulted in AVA and capillary flow changes converse to warming.

It is concluded that, in sheep, blood flow through cutaneous AVA's is controlled by specific thermoregulatory reflexes, whereas capillary flow is the target of local temperature effects. A significant role for the direction of the thermal gradient across the skin is implicated.

**Key words:** Skin blood flow – Arteriovenous anastomoses – Thermoregulation – Heat stress – Cold stress – Microspheres.

## Introduction

The existence of arteriovenous anastomoses (AVA's) in many tissues, particularly skin, has been well documented, mainly through histological studies. The general concept of AVA's opening during "heat stress" and closing during "cold stress" is widely accepted, but the thermoregulatory role of blood flow through AVA's as distinct from the capillary network in skin has been principally the subject of speculation (Kerslake, 1972; Hales, 1974a).

Employing modern radioactive microsphere techniques, marked increases in the total proportion of the cardiac output passing through AVA's during exposure to hot environments have been demonstrated in sheep and dogs (Hales, 1971, 1973a, b; Hales and Dampney, 1975); cold exposure caused a marked decrease (Hales et al., 1976a). However, these studies provided no information on the site of patent AVA's or on control mechanisms. Further, measurements of skin temperature and capillary blood flow during localized warming of the spinal cord (Hales and Iriki, 1975) or hypothalamus (Hales et al., 1977) led to the conclusion that under these conditions there was significant AVA blood flow in skin. Subsequently, thermal stimulation of the central nervous system, and exposure to warm or cool environments were found to have differential influences on the partition of skin blood flow between capillaries and AVA's (Hales et al., 1975b; Hales and Iriki, 1977). Ingram and Legge (1971) reported that total skin blood flow in the pig's tail can be changed by similar magnitudes by manipulating temperature of the hypothalamus, spinal cord, distal skin, or the skin area directly, however, heat-induced vasodilatation in the baboon's leg appears to be mainly due to drives from deep body temperature-sensitive mechanisms (Proppe et al., 1976). The present study assesses the influences of central nervous system temperatures, superficial body temperatures, indirect and direct thermal effects on blood flow through AVA's and capillaries in hindleg skin of the sheep.

## Methods

*Animals.* Conscious Merino wethers 2–3 years old, weighing 22–36 kg and having a fleece depth of 15–45 mm were used. They were

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trained to stand quietly held by a yoke in a climatic room, and were adapted to laboratory conditions including experimental treatments.

All techniques are as described in detail elsewhere (Hales, 1974b; Hales et al., 1978a).

*Surgical Preparations.* During about one hour's general anaesthesia (Halothane) in all animals, at least 24 h before beginning experimental observations catheters were established in both femoral arteries, via the supreme genicular artery, the pulmonary artery, and an external jugular vein. In 10 animals the left cardiac ventricle was catheterized. Stainless steel hypothalamic thermodes (Hales et al., 1977) and polyethylene spinal thermodes (Hales and Iriki, 1975) were implanted about 14 days before experimentation; 7 animals had only hypothalamic, 12 only spinal and 3 both hypothalamic and spinal thermodes. Electromagnetic cuff-type blood flow probes and occluders for zeroing the probe were implanted on the femoral arteries of 14 animals 5–10 days before experimentation (see later methods for technical details). No major blood vessels were ligated.

*Blood Flow (Microspheres).* Radioactive microspheres (3 M Co., St. Paul, Minnesota) of nominally 15 μm diameter (actually within the range of mean ± S.D. = 13.3 ± 1.0 to 15.0 ± 1.9 μm) and labelled with $^{141}$Ce, $^{51}$Cr, $^{85}$Sr, or $^{46}$Sc were used essentially as previously described (Hales, 1974b, 1978a). That is, for measuring *cardiac output (C.O.), skin capillary blood flow and the percentage of C.O. passing through AVA's*, the dose of microspheres was injected into the left ventricle and blood was sampled from a femoral artery and the pulmonary artery during and for approximately 60 s following injection of the dose. To obtain the values for skin capillary blood flow, the animal was ultimately killed and skin samples removed for gamma assay; the skin samples were 80 × 30 mm centred on the outer surface of the metatarsal segment of the leg, and all subcutaneous fat and connective tissue was removed.

*Percentage of hindleg blood flow passing through AVA's* is calculated from cardiac output as measured by injecting a small dose of microspheres into a jugular vein and sampling from the pulmonary artery and the escape of microspheres through leg microvasculature – approximately $5 \times 10^6$ microspheres was injected into the femoral artery and blood was sampled from the pulmonary artery. A full description of this technique and its validation have been presented (Hales et al., 1978a).

*Blood Flow (Electromagnetic).* Electromagnetic blood flow transducers (Model E-2 or SL-E, in vivo Metric Systems, Redwood Valley, California) were used in conjunction with a flow meter (Type SFMB-1-28, EMI, Sydney). The transducer zero was checked frequently by stopping arterial flow using an inflatable occluder. At least 8 days after transducer implantation, observations were made over a 2–8 day period. Finally, with the animal anaesthetized, the undisturbed transducer was calibrated by timed collection from the femoral via a large catheter inserted several cm downstream.

*Blood Pressure.* Arterial pressure was monitored via one of the femoral catheters and a strain gauge transducer (Bell and Howell Model 4-422-0002).

*Blood Gases.* The $P_{O_2}$, $P_{CO_2}$ and pH of arterial blood samples were measured directly using electrodes (BMS 3 Mk II, Radiometer, Copenhagen) at 38°C and corrected to the animal's deep body temperature.

*Temperatures* were monitored to within 0.05°C using 38 swg copper-constantan thermocouples. *Body core* temperatures were measured by inserting thermocouples into the guide tubes in the hypothalamus ($T_{hy}$) and spinal canal ($T_{sc}$) of appropriately prepared animals, and by means of a thermocouple fixed at the tip of a plastic probe inserted 10 cm into the rectum ($T_{re}$) of all animals. *Skin surface* temperatures were measured by gluing thermocouples onto the mid-dorsal surface of each ear, outer surface of each foreleg and hindleg about two-thirds way down the metacarpus and metatarsus respectively, and the midside of the body.

*Experimental Procedure.* Experiments have been carried out over a 3 year period, covering all seasons. Animals were housed indoors for at least 6 weeks prior to experimentation and during this period ambient dry bulb temperature ($T_{db}$) varied between about 8°C and 35°C. About 20 h before commencing a period of experimental observations, each individual animal was placed in the climatic room with conditions approximating thermoneutrality. Skin surface temperatures of the six extremities were taken as an index of cutaneous vasomotor state. Before taking experimental data ambient $T_{db}$ was adjusted so that hindleg skin temperatures indicated a tendency towards the constricted state before a heat treatment, or the dilated state before a cold treatment; $T_{db} \simeq 18$°C (range 10–24°C) and $T_{wb} \simeq 11$°C (range 7–19°C). When skin and body core temperatures, heart rate, blood pressure, respiratory frequency and femoral flow (when available) indicated that the animal was in a steady state (usually after 1–5 h), control measurements were taken: in all animals, a measurement of cardiac output was immediately followed by the partition of flow in one of the femoral arteries between AVA's and capillaries; in approximately half of the animals (see Results) an arteriel blood sample was then drawn (for gas analyses) and measures of skin capillary blood flow rate, cardiac output, and the proportion of cardiac output passing through AVA's were taken. This procedure was repeated when hindleg skin temperature indicated a vasomotor response during one of the following treatments.

*The experimental treatments* employed were: *A. Heat:* (a) Exposure to a *warm environment* ($T_{db} = 40$°C, $T_{wb} = 26$°C) until a new equilibrium state was established (approximately 1 h while the room was heating plus 1 h with temperatures steady). (b) *Heating the hypothalamus* or (c) *the spinal cord* to a recorded temperature of approximately 42°C by perfusing the thermodes with water at 44°C. (d) *Heating the forelegs* or (e) *the hindlegs* by standing in a water bath at 44°C.

*B. Cold:* (a) Exposure to a *cool environment* ($T_{db} = 5$°C, $T_{wb} = 3$°C) until a new equilibrium was established (approximately 1.5 h while the room was cooling plus 1 h with temperatures steady). (b) *Cooling the hypothalamus* or (c) the *spinal cord* to a recorded temperature of approximately 30°C by perfusing the thermodes with water at 26°C. (d) *Cooling the forelegs* or (e) the *hindlegs* by standing in an iced water bath.

For treatments (b), (c) and (d) of both A and B, measurements began immediately hindleg skin temperature showed a rapid increase or decrease, and took about 4 min when only cardiac output and leg AVA/capillary partition were measured, or 5.5 min when capillary blood flow and the proportion of cardiac output passing through AVA's was also measured. This meant a total duration of thermal stimulation of approximately 5–6.5 min for treatments (b) and (c), or 20–40 min for treatment (d). With treatment (e), measurements on the hindlegs were begun when foreleg skin temperature rapidly increased or decreased (20–40 min).

## Results

Data basic to the blood flow measurements are given in Tables 1 and 2. Figures illustrating the typical time course of changes have been published previously (Hales and Iriki, 1975; Hales et al., 1977). All treatments were accompanied by changes in leg skin temperature indicative of changes in skin blood flow. There was no statistically significant change in body core temperature, other than that of a site being purposely

**Table 1.** Effects on body temperatures and cardiorespiratory functions, of exposure to a warm environment or of warming the hypothalamus, spinal cord, forelegs or hindlegs. Mean ± S.E. for the number ($n$) of conscious sheep shown. "Control" is under thermoneutral conditions, and "heat" is during the treatment, as detailed in the text

| | Environment | | Hypothalamus | | Spinal cord | | Forelegs | | Hindlegs | |
|---|---|---|---|---|---|---|---|---|---|---|
| | control | heat | control | heat | control | heat | control | heat | control | heat |
| $n$ | 13 | 13 | 11 | 11 | 10 | 10 | 6 | 6 | 4 | 4 |
| Rectal temp. (°C) | 39.6 ± 0.1 | 39.8 ± 0.2 | 39.2 ± 0.1 | 39.0 ± 0.1 | 39.7 ± 0.2 | 39.3 ± 0.1* | 39.5 ± 0.1 | 39.9 ± 0.2 | 39.6 ± 0.2 | 39.7 ± 0.2 |
| Hypothalamic temp. (°C) | 39.6 ± 0.2 | 39.5 ± 0.2 | 39.4 ± 0.2 | 42.7 ± 0.3** | 39.8 ± 0.1 | 39.3 ± 0.1* | 39.5 ± 0.1 | 39.4 ± 0.1 | | |
| Leg skin temp. (°C)[a] | 28.1 ± 2.1 | 38.9 ± 1.0* | 27.5 ± 3.0 | 33.6 ± 0.8* | 28.4 ± 1.9 | 34.5 ± 0.6* | 30.0 ± 1.5 | 33.2 ± 1.0* | 26.3 ± 1.5 | 43.6 ± 0.2** |
| Heart rate (beats $min^{-1}$) | 91 ± 14 | 100 ± 15 | 84 ± 9.0 | 106 ± 9.9* | 102 ± 9.0 | 110 ± 10 | 105 ± 11 | 135 ± 12** | 76 ± 6.1 | 99 ± 11* |
| Mean art. press. (mmHg) | 96 ± 4.2 | 97 ± 5.3 | 95 ± 1.9 | 91 ± 1.7 | 92 ± 5.0 | 102 ± 7.2 | 97 ± 2.2 | 98 ± 2.4 | 88 ± 2.1 | 92 ± 1.9 |
| Cardiac output ($l\,min^{-1}$) | 3.25 ± 0.60 | 3.15 ± 0.27 | 2.95 ± 0.39 | 3.02 ± 0.26 | 3.21 ± 0.41 | 3.33 ± 0.26 | 3.69 ± 0.44 | 3.28 ± 0.20 | 3.04 ± 0.27 | 3.00 ± 0.29 |
| TPR[b] ($mmHg\,l^{-1}\,min^{-1}$) | 31.2 ± 2.1 | 32.5 ± 1.9 | 35.2 ± 6.0 | 32.5 ± 3.5 | 34.1 ± 2.5 | 31.9 ± 1.9 | 35.4 ± 3.2 | 31.5 ± 2.1 | 29.1 ± 3.5 | 31.5 ± 3.3 |
| Resp. frequency (breaths $min^{-1}$) | 29 ± 8 | 135 ± 20** | 35 ± 7 | 104 ± 30* | 39 ± 8 | 142 ± 25*** | 21 ± 1 | 50 ± 6* | 35 ± 10 | 114 ± 24* |
| $P_{CO_2}$ (mmHg) | 39 ± 1.0 | 38 ± 0.8 | 34 ± 2.0 | 33 ± 3.1 | 38 ± 1.8 | 36 ± 2.2 | 34 ± 1.4 | 34 ± 1.1 | 34 ± 0.9 | 33 ± 0.8 |
| $P_{O_2}$ (mmHg) | 100 ± 5.4 | 98 ± 6.0 | 96 ± 2.1 | 99 ± 3.5 | 99 ± 3.8 | 102 ± 4.5 | 97 ± 3.3 | 94 ± 4.0 | 97 ± 3.9 | 96 ± 2.2 |
| pH | 7.49 ± 0.03 | 7.51 ± 0.02 | 7.52 ± 0.01 | 7.51 ± 0.02 | 7.50 ± 0.02 | 7.56 ± 0.01 | 7.52 ± 0.02 | 7.54 ± 0.02 | 7.52 ± 0.01 | 7.51 ± 0.01 |

Student's paired '$t$' test: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

[a] The hindleg under observation

[b] Total peripheral resistance

**Table 2.** As for Table 1, but cold treatments

| | Environment | | Hypothalamus | | Spinal cord | | Forelegs | | Hindlegs | |
|---|---|---|---|---|---|---|---|---|---|---|
| | control | cold | control | cold | control | cold | control | cold | control | cold |
| *n* | 7 | 7 | 6 | 6 | 5 | 5 | 5 | 5 | 4 | 4 |
| Rectal temp. (°C) | 39.8 ± 0.2 | 39.6 ± 0.2 | 39.8 ± 0.1 | 39.9 ± 0.2 | 39.5 ± 0.2 | 39.6 ± 0.1 | 39.7 ± 0.2 | 40.0 ± 0.2 | 39.4 ± 0.2 | 39.5 ± 0.2 |
| Hypothalamic temp. (°C) | | | 39.7 ± 0.1 | 30.5 ± 0.2*** | 39.4 ± 0.1 | 39.6 ± 0.1 | | | | |
| Leg skin temp. (°C)[a] | 34.0 ± 1.0 | 9.4 ± 0.7*** | 32.7 ± 1.9 | 27.0 ± 1.0* | 33.1 ± 0.9 | 30.2 ± 0.6* | 34.1 ± 0.4 | 31.7 ± 0.3* | 35.3 ± 0.6 | 3.4 ± 0.6*** |
| Heart rate (beats $min^{-1}$) | 98 ± 8 | 155 ± 12** | 95 ± 6 | 130 ± 20* | 97 ± 9 | 100 ± 12 | 84 ± 2 | 157 ± 25* | 78 ± 9 | 118 ± 18 |
| Mean art. press. (mmHg) | 92 ± 3.5 | 92 ± 5.5 | 100 ± 4.2 | 105 ± 3.8 | 90 ± 3.2 | 93 ± 3.7 | 91 ± 4.0 | 99 ± 8.7 | 89 ± 2.0 | 97 ± 3.8 |
| Cardiac output ($l\,min^{-1}$) | 2.72 ± 0.28 | 3.99 ± 0.21* | 3.00 ± 0.08 | 4.22 ± 0.49* | 3.23 ± 0.30 | 3.94 ± 0.32 | 3.93 ± 0.49 | 5.07 ± 0.63 | 2.68 ± 0.39 | 3.79 ± 0.97 |
| TPR[b] ($mmHg\,l^{-1}\,min^{-1}$) | 37.5 ± 2.3 | 26.9 ± 1.5 | 33.6 ± 2.0 | 30.2 ± 3.2 | 29.4 ± 1.9 | 34.7 ± 3.1 | 23.6 ± 2.0 | 20.0 ± 3.3 | 35.1 ± 4.5 | 29.4 ± 5.3 |
| Resp. frequency (breaths $min^{-1}$) | 29 ± 5 | 20 ± 2 | 27 ± 3 | 23 ± 2 | 29 ± 5 | 19 ± 3 | 28 ± 3 | 23 ± 1 | 30 ± 6 | 16 ± 1* |
| $P_{CO_2}$ (mmHg) | 35 ± 0.9 | 35 ± 1.1 | 34 ± 1.0 | 35 ± 0.9 | 36 ± 0.6 | 34 ± 1.0 | 34 ± 0.4 | 36 ± 0.8 | 34 ± 1.3 | 35 ± 1.3 |
| $P_{O_2}$ (mmHg) | 97 ± 4.2 | 99 ± 3.1 | 94 ± 3.2 | 91 ± 1.9 | 100 ± 2.0 | 98 ± 2.1 | 99 ± 4.5 | 87 ± 4.8 | 93 ± 1.2 | 91 ± 1.2 |
| pH | 7.49 ± 0.02 | 7.48 ± 0.01 | 7.50 ± 0.01 | 7.49 ± 0.01 | 7.51 ± 0.02 | 7.49 ± 0.02 | 7.53 ± 0.01 | 7.51 ± 0.03 | 7.51 ± 0.01 | 7.49 ± 0.01 |

Student's paired '*t*' test: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

[a] The hindleg under observation

[b] Total peripheral resistance

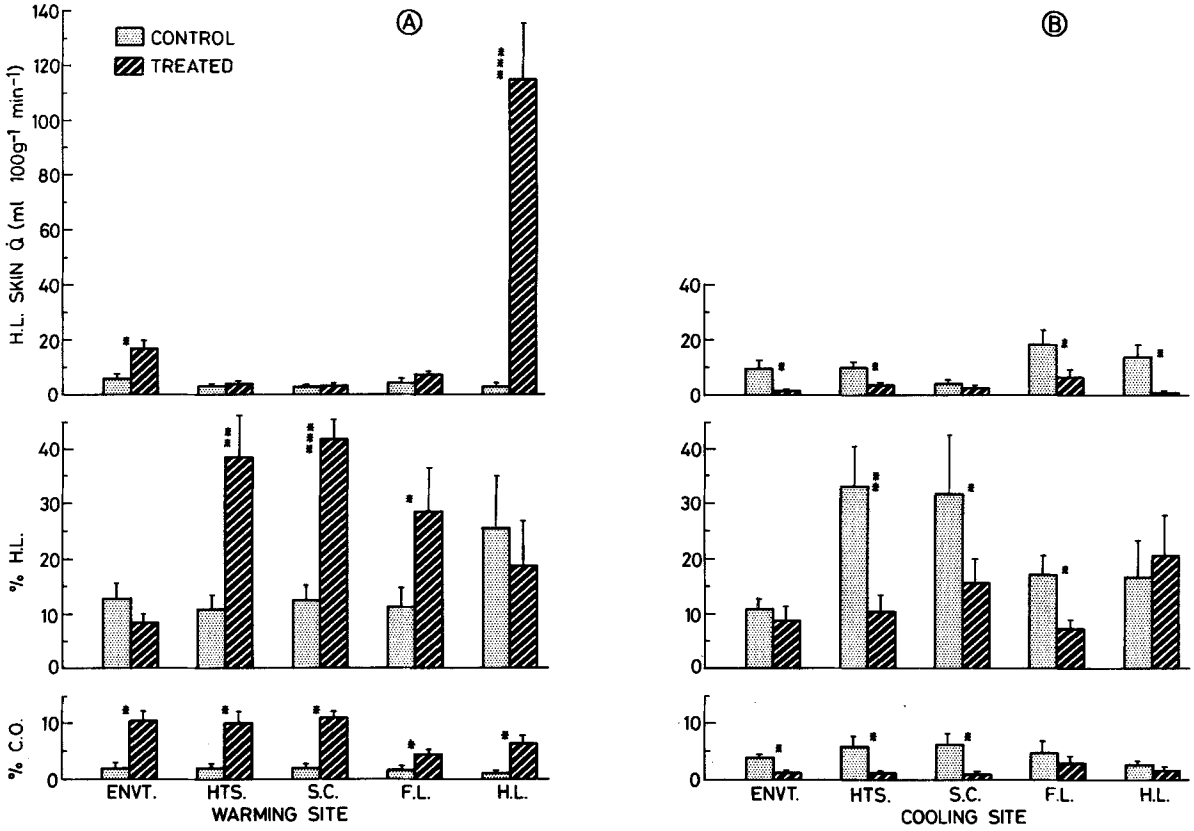


**Fig. 1.** Effects of various heat (**A**) and cold (**B**) treatments on percent cardiac output (% C.O.) and percent hindleg blood flow (% *H.L.*) passing through AVA's and on blood flow rate in hindleg skin (*H.L. Skin* $\dot{Q}$). Exposure to a warm or cool environment (*ENVT.*); warming or cooling the hypothalamus (*HTS.*), spinal cord (*S.C.*), forelegs (*F.L.*) or hindlegs (*H.L.*). Mean ± S.E. is drawn and significance of the effect of the treatment is shown. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

manipulated, with the exception that hypothalamic and rectal temperatures decreased during spinal heating. In 3 of the 13 exposures to a warm environment, body core temperature did increase by up to 0.4° C. Other significant changes were (a) panting elicited by each heat treatment, (b) increased heart rate during exposure to the cold environment, hypothalamic or foreleg cooling or warming, and heating the hindlegs, (c) increased cardiac output during cold exposure or hypothalamic cooling, and (d) decreased respiratory frequency during hindleg cooling.

*Heat* (Fig. 1A). The proportion of cardiac output passing through AVA's increased significantly with all five heat treatments; the proportion of hindleg blood flow passing through AVA's also increased significantly with heating of the hypothalamus, spinal cord or forelegs, however, there was no significant change during exposure to the warm environment or with hindleg heating alone. The converse of this latter situation was seen with capillary blood flow in skin of the hindleg, i.e. no change with the heating of the hypothalamus, spinal cord or forelegs, but a significant increase in the warm environment or with hindleg heating alone. Values for femoral arterial flow measured electromagnetically are shown in Fig. 2A: Total flow increased significantly with hypothalamic or hindleg heating and did not change significantly with the other three treatments. Microsphere partitions of flow between AVA's and capillaries were not invariably made on the same animals as electromagnetic measurements. Therefore the mean values for partition were combined with the mean total femoral flows to provide the values for AVA and capillary flow which are illustrated. AVA flow increased and there was no significant change in capillary flow with hypothalamic, spinal cord or foreleg warming; the converse was the case with hindleg warming, whereas neither AVA nor capillary flow changed significantly during exposure to the warm environment.

*Cold* (Fig. 1B). All five cooling treatments resulted in either a statistically significant decrease in the proportion of cardiac output passing through AVA's, or a small decrease on top of an already low level. The proportion of hindleg blood flow passing through

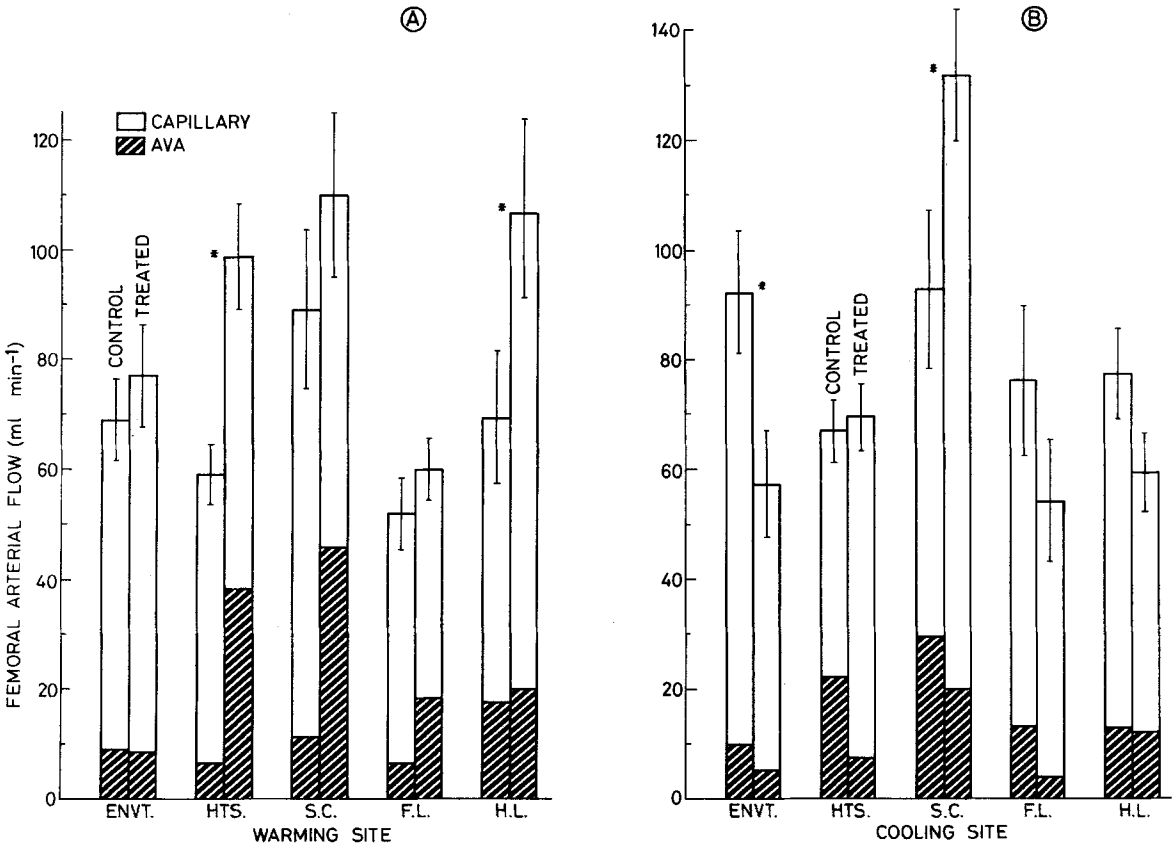


**Fig. 2.** Effects of various heat (**A**) and cold (**B**) treatments on total femoral arterial flow and its partition between AVA's and capillaries. See legend to Fig. 1 for other details

AVA's decreased significantly with cooling of the hypothalamus, spinal cord or forelegs, but did not change significantly with exposure to the cold environment or with hindleg cooling alone. Capillary blood flow in hindleg skin decreased significantly with all cooling treatments excluding the spinal cord; in the latter case, the control level of capillary blood flow was already very low (approximately 4 ml $100\,g^{-1}\,min^{-1}$). Electromagnetic data combined with microsphere values for AVA/capillary partitions as for the heat treatments are presented in Fig. 2B: Both total femoral flow and that passing though capillaries decreased in the cold environment and during hindleg cooling alone; with the latter treatment AVA flow did not change, whereas it decreased in the cold environment. During spinal cord cooling total flow increased because of a marked increase in capillary flow while AVA flow decreased. Neither hypothalamic nor foreleg cooling caused a significant change in total femoral flow, but that passing through AVA's decreased.

## Discussion

Elsewhere (Hales et al., 1978a) we have shown that the techniques used here are adequate for studying thermal control of blood flow through capillaries and AVA's in hindleg skin of sheep. As previously pointed out, it should be borne in mind that use of microspheres means that the differentiation between capillary or nutrient flow and AVA or non-nutrient flow is made on a morphological and not a functional basis.

The importance of skin blood flow in determining body heat transfer is well appreciated, as is control by the interaction of thermal inputs from the body core, local and distant skin temperature (Ingram and Legge, 1971; Proppe et al., 1976; Rowell, 1977). However, precise characteristics of responses at the microvascular level have remained unknown, although a knowledge of this would assume particular importance if, for example, flow through AVA's and capillaries in skin differ significantly in efficacy of heat transfer.

Recently there have been clear demonstrations of marked changes in the total proportion of cardiac output passing through AVA's in the conscious sheep and dog subjected to various thermal stimuli (Hales, 1971, 1973a, b; Hales and Iriki, 1975; Hales and Dampney, 1975; Hales et al., 1976a, 1977). That is, an increase from around 1% up to 10% of the cardiac output with exposure to warm environments or warming the spinal cord or hypothalamus and a decrease

from 1–4% down to <1% with equivalent cold stimuli. These observations have been confirmed in the present study (Figs. 1 and 2) and it would seem reasonable to assume that such changes in flow through AVA's were occurring primarily in tissues concerned with heat exchange. However, the data on leg AVA's (Figs. 1 and 2) does not entirely support this, at least with respect to skin: With environmental warming or cooling there was no significant change in leg AVA flow but capillary blood flow increased or decreased respectively. In contrast, hypothalamic or spinal warming resulted in a mean 3.5-fold increase in leg AVA flow with no significant change in skin capillary flow. The maximum leg AVA flow recorded was 59% with hypothalamic warming and 80% with spinal warming. This is a similar order of magnitude to that which we have recorded during nembutal anaesthesia (Hales et al., 1978a) and might be taken to represent maximal flow through the AVA's. Cooling resulted in equally significant changes in the opposite direction to heating. It therefore seems that, as concluded from a limited number of early experiments (Hales et al., 1975), CNS temperatures strongly influence cutaneous AVA activity with little or no effect on the capillaries and vice versa for superficial body temperatures.

However, the possibility of reflex (or indirect) versus direct influences of thermal stimuli remained an alternative explanation. Therefore temperatures of the forelegs or hindlegs were manipulated: The same effects as obtained with the other treatments were seen with respect to the total proportion of cardiac output passing through AVA's but the hindleg AVA and skin capillary blood flow measurements were most revealing. With foreleg warming, hindleg AVA flow increased markedly whereas skin capillary flow did not alter, as with hypothalamic or spinal warming (Fig. 1). With hindleg warming, i.e., direct warming of the tissue under study, the response was as seen in the warm environment (Fig. 1) – AVA flow did not alter whereas skin capillary flow increased (to levels higher than anything previously recorded). Cooling treatments had the converse effects.

The partition of femoral flow between AVA's and capillaries need not necessarily reflect changes in the absolute levels of flow. Therefore the electromagnetic measurements of total femoral flow were taken and partitioned using the microspheres. As seen in Fig. 2 femoral flow was markedly influenced by certain treatments, however, the data show that there is no need to modify the earlier conclusions based on simple fractional partitioning of the flow. Two portions of this data warrant further comment because at first sight they appear to conflict with the earlier data. First, in the warm environment there was an increase in femoral flow through capillaries (Fig. 2A) which was small relative to the increase in skin capillary blood flow demonstrated by skin sampling (Fig. 1A); this is explicable as the result of decreased muscle capillary blood flow under these conditions (Hales, 1973c) but not with spinal (Hales and Iriki, 1975) or hypothalamic (Hales et al., 1977) heating. Secondly, hypothalamic and spinal cooling elicited a significant increase in femoral flow through capillaries (Fig. 2B) contrasting with the decrease in skin capillary flow seen with direct measurement (Fig. 1B), whereas during cold exposure, femoral flow through capillaries as well as directly measured skin capillary flow decreased; this is explicable if the degree of increase in muscle capillary flow paralleling shivering is sufficient to more than offset the decrease in skin flow with hypothalamic or spinal cooling, but vice versa with environmental cooling.

This work also emphasises that blood flow through AVA's does not increase at the expense of capillary flow under these conditions; many workers have been under the misapprehension that blood would be diverted away from capillaries, to the AVA's (e.g., see discussion by Piiper, 1959).

Our evidence therefore points to blood flow through cutaneous AVA's being the target of specific *reflex* thermoregulatory effects, whereas the *direct* effects of temperature are exerted on capillary flow. It has previously been demonstrated that direct heating will increase and cooling will decrease flow through AVA's in the hindleg of the anaesthetized dog (Bostroem and Schoedel, 1953; Piiper et al., 1954) and there are the numerous classical observations on the rabbit ear (e.g. Grant et al., 1932; Clark, 1938; Sonomoto, 1953; Ferguson and Levinson, 1955). These results seem to conflict with our demonstration of no increase in hindleg AVA flow in the warm environment. However, the ambient temperature employed by the above workers cannot be ascertained from their publications whereas our reported observations were made in an environment of 40° C dry bulb temperature which is slightly above core and well above skin surface temperature. In view of: (a) these different results; (b) earlier observations of graded opening of AVA's with increasing ambient dry bulb temperature after starting with the animal in a 'thermoneutral' environment (Hales, 1973b), and (c) spontaneous oscillations in cutaneous efferent sympathetic activity in 'thermoneutral' conditions (Iriki and Hales, 1976) we suggest that the patency of cutaneous AVA's is sensitive to the direction of the thermal gradient across the skin. In further support of this: (a) with a dry bulb temperature of about 30° C, both leg AVA and capillary flow are increased and (b) when leg AVA's have been opened by spinal warming, the response can be reversed by increasing the leg skin temperature to about 42° C (Hales and Fawcett, unpublished observations). That

is, when skin surface temperature is lower than blood temperature, any of the types of thermal stimulation tested will open AVA's to greatly facilitate heat transfer to the external environment; however, when ambient temperature is such as to provide a thermal gradient for heat flow into the body, the opening of AVA's is inhibited – teleologically this is attractive.

Mean arterial pressure did not change significantly in any of our experiments and therefore the changes in blood flow must be due to changes in local vascular resistance. Many of the above-mentioned studies demonstrated that an intact sympathetic nerve supply is necessary for the AVA's to be closed. Further, when the hypothalamus, spinal cord or a distant area of skin is warmed or cooled, cutaneous efferent sympathetic activity is decreased or increased respectively (Walther et al., 1970; Iriki et al., 1971; Riedel et al., 1972; Ninomiya and Fujita, 1976). Such activity has now been shown to closely parallel changes in activity of the AVA's rather than capillaries (Hales et al., 1976b, 1978b). This whole question of sympathetic control is dealt elsewhere (Hales et al., 1978b); however, it must be noted here that vascular resistance and blood viscosity have been observed to decrease with tissue warming in a hibernator (Kirkebö, 1968) and it is conceivable that some very localized influences of this nature could have been present in our direct-heating experiments. The possible potent influences of changes in $P_{O_2}$, $P_{CO_2}$ and pH can be dismissed because of their stability (Tables 1 and 2), unless there were very localized changes in the direct-heating experiments.

Prime remaining problems must include: (a) control – the precise role of the thermal gradient across the skin, control of resistance vessels other than the AVA's and the neurotransmitter(s) involved; (b) the relative efficacy of blood flow through cutaneous AVA's or capillaries in determining body heat exchange.

The conclusions drawn in this paper rely entirely on sub-primate animal models and must be viewed with extreme caution in relation to man who has few AVA's in most of his skin but nevertheless exhibits extremely large increases in skin blood flow apparently due to an active, neurally-mediated process (see review: Rowell, 1977).

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