J. Physiol. (1960), **153**, *pp.* 232–238
With 1 *text-figure*
Printed in Great Britain

VASOMOTOR FIBRES TO SKIN IN THE UPPER ARM, CALF AND THIGH

By D. A. BLAIR, W. E. GLOVER and I. C. RODDIE
From the Department of Physiology, The Queen's University of Belfast

(*Received* 30 *November* 1959)

Though the responses of the hand and forearm skin blood vessels to body heating and cooling are qualitatively similar there is a difference in the pattern of vasomotor control in the two areas. The blood vessels of the hand are normally subject to a high degree of vasoconstrictor tone even when the subject is comfortably warm. Blocking the nerves to the hand with local anaesthetic normally increases the blood flow through the hand to about 30–40 ml./100 ml./min (Roddie, Shepherd & Whelan, 1957*a*). The very large increase in hand blood flow during body heating seems due entirely to release of vasoconstrictor tone. Despite the evidence for vasodilator fibres to the hands of patients with Raynaud's disease (Lewis & Pickering, 1931), careful investigation has failed to provide any evidence that such fibres are involved in the vasodilatation during body heating in the hands of normal individuals. During body heating the blood flow in the normal hand does not exceed that in the nerve-blocked hand (Warren, Walter, Romano & Stead, 1942; Sarnoff & Simeone, 1947; Arnott & Macfie, 1948; Gaskell, 1956; Roddie, Shepherd & Whelan, 1957*c*) and atropinization of the hand tissues fails to reduce the vasodilatation (Gaskell, 1956; Roddie, Shepherd & Whelan, 1957*b*).

In forearm skin, however, the vessels are not subject to any appreciable vasoconstrictor or vasodilator tone when the subject is comfortably warm. When the cutaneous nerves to the forearm are blocked under these conditions there is little change in flow (Grant & Holling, 1938; Doupe, Cullen & Macaulay, 1943; Edholm, Fox & Macpherson, 1957). If the nerves are blocked when the subject is cold an increase in skin blood flow is observed, indicating the presence of vasoconstrictor fibres (Roddie, Shepherd & Whelan, 1957*d*). The fall in forearm blood flow during body cooling can be prevented by intra-arterial administration of bretylium tosylate, an adrenergic blocking agent (Blair, Glover, Kidd & Roddie, 1959) showing that the vasoconstrictor fibres in forearm skin are adrenergic. The increase in skin blood flow during body heating seems to be due to the activity of cholinergic nerves producing vasodilatation. It does not occur if the

sympathetic nerves to forearm skin are blocked (Grant & Holling, 1938; Doupe *et al.* 1943; Edholm *et al.* 1957; Roddie *et al.* 1957*d*) and it is reduced and delayed by atropinization of the forearm (Roddie *et al.* 1957*b*; Fox & Hilton, 1958). There is now evidence that the skin vasodilatation in the forearm during heating may be due to products of sweat-gland activity rather than to the excitation of specific vasodilator fibres (Fox & Hilton, 1958).

In view of the contrast between the vasomotor innervation of hand and forearm it seemed desirable to study the innervation of skin areas elsewhere in the limbs and the present paper describes some experiments which were designed with this end in view.

METHODS

Nine experiments were performed on six healthy young adults lying recumbent in a comfortably warm room (temperature 21–23° C). Subjects were lightly clad, but covered with a blanket. In any one experiment blood flow was measured bilaterally in either forearm, upper arm, calf or thigh. Forearm blood flow was measured by means of the water-filled plethysmographs described by Greenfield (1954). A larger plethysmograph with a suitably sized sleeve was used to measure flow in the calf and upper arm, and in thinner subjects, the thighs. In all experiments the plethysmograph was maintained at 35° C. During measurements the circulation to the limb distal to the plethysmograph was arrested by a cuff inflated to 200 mm Hg. A collecting cuff was applied just proximal to the plethysmograph. After the subject had rested in the laboratory for about 1 hr, resting blood flows were measured on the two sides. The position of the plethysmograph on the left limb was marked with a skin pencil, and the plethysmograph was then removed from the limb. The positions of the cutaneous nerves supplying the skin area under study were determined by faradic stimulation. The nerves were traced proximally up the limb and blocked by infiltrating 1–2 ml. of 2 % lignocaine containing adrenaline (1:80,000) around each of them. The block was performed as far away as possible from the plethysmograph area. When about 80 % or more of the skin area under study had become anaesthetic, the limb was replaced in its original position in the plethysmograph and the blood flow was again measured bilaterally at intervals until the end of the experiment. The anaesthesia of the skin area was checked at intervals throughout the experiment and, where necessary, further injections of local anaesthetic were made.

The subjects were then cooled for about 40 min. The blanket was removed and the room temperature was allowed to drop to 16–18° C. The subjects' feet (forearm and upper-arm experiments) or hands (calf and thigh experiments) were immersed in water at 17° C. Iced water was sprayed in a current of air from a vacuum cleaner pump over their naked chests and abdomens. Shivering frequently occurred in the first few minutes of cooling but then ceased and the subject was reasonably comfortable during the period in which observations were made.

Indirect heating was then applied. The room temperature was returned to 21–23° C. The subjects were wrapped in blankets and their feet and calves (upper arm and forearm experiments) or hand and forearm (thigh and calf experiments) were placed in stirred water at 44° C. Heating was continued for 40–60 min. This degree of heating usually causes an increase in body temperature of about 1° C and is accompanied by profuse sweating.

RESULTS

Figure 1 illustrates the result of an experiment in which blood flow was simultaneously measured in both forearms. At the beginning of the experiment, when the subject was comfortably warm, the blood flow through each forearm was about 4 ml./100 ml./min. Blocking the cutaneous nerves to the left forearm caused little change in the level of blood flow in either arm. Cooling the body caused a 58 % fall in the blood flow in the normal forearm, but only a 12 % fall on the nerve-blocked side. This is in

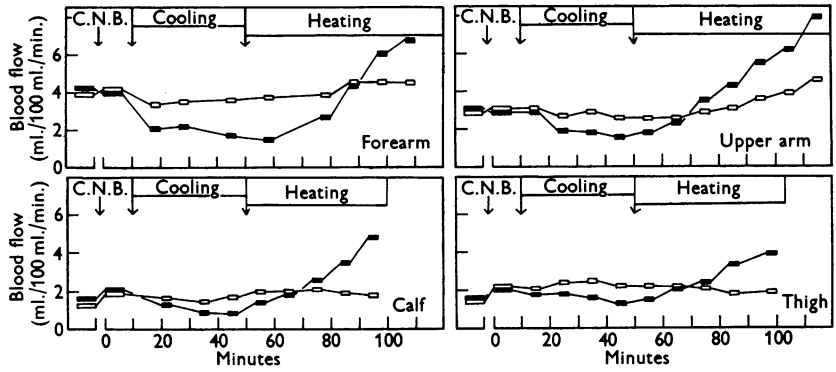

Fig. 1. The effects of body cooling and heating on blood flow in the normal and cutaneous-nerve-blocked forearm, upper arm, calf and thigh: ■ right side; □ left side. C.N.B. = cutaneous nerves on left side blocked with local anaesthetic.

keeping with the conclusion that the blood vessels in forearm skin are innervated with vasoconstrictor fibres which are activated in response to cooling the body (Roddie *et al.* 1957*c*, *d*). Heating the body caused a 93 % increase in blood flow above the resting level in the normally innervated forearm, whereas it only increased by 12 % on the nerve-blocked side. Visible sweating was observed in the normal though not the nerve-blocked forearm. This result confirmed the findings of Edholm *et al.* (1957), which indicated that the vasodilatation in forearm skin during body heating is due to an active vasodilator mechanism mediated through fibres running with the cutaneous nerves.

In four experiments of similar design the vasomotor innervation of the skin of the upper arm was studied (Fig. 1; Table 1). The pattern of result was similar to that found in the forearm. When the subject was comfortably warm, blocking the cutaneous nerves to the upper arm caused little change in blood flow, the average change being a fall of 0·2 ml./100 ml./min. However, when the subject was subsequently cooled, the average fall in blood flow in the nerve-blocked upper arm was only 12 %, whereas in the normal upper arm the average fall was 67 % of the resting level. Nerve block also depressed the vasodilatation during body heating. The

average increase in flow on the nerve-blocked side was 41 % above the resting level, whereas the average increase on the normal side was 79 %. It is likely that the difference would have been greater had the cutaneous nerve block been complete in all instances.

A similar pattern emerged in two experiments on the calf (Fig. 1; Table 1). Though cutaneous nerve block caused a small increase in blood flow (average 0·7 ml./100 ml./min), an increase (average 0·4 ml./100 ml./min) was also seen in the opposite (control) limb. Nerve block did not,

TABLE 1. The effects of body cooling and heating on blood flow in normal (control) limbs and limbs with the cutaneous nerves blocked (test limbs). The figures in the table are average values obtained for blood flow (ml./100 ml./min) during 5 min periods before nerve block, after nerve block, during body cooling and during body heating

		Control limb				Test limb			
Subject	Part studied	Before block of test limb	After block of test limb	During cooling	During heating	Before block of test limb	After block of test limb	During cooling	During heating
W.E.G.	Forearm	4·2	4·0	1·7	6·7	4·0	4·2	3·7	4·7
B.G.	Upper arm	4·2	4·0	0·8	7·0	4·0	3·7	2·7	4·8
L.A.	Upper arm	3·7	4·2	2·0	7·5	3·0	2·5	3·0	4·0
D.A.B.	Upper arm	3·0	2·9	1·4	8·5	3·0	3·0	2·5	4·9
I.C.R.	Upper arm	5·7	5·7	1·3	7·0	3·5	3·7	2·0	4·5
D.A.B.	Calf	3·6	3·6	1·8	6·5	3·6	4·3	3·7	3·0
W.E.G.	Calf	1·7	2·4	1·0	5·0	1·4	2·1	1·7	2·0
I.C.R.	Thigh	2·1	2·7	1·8	3·8	1·8	3·0	2·5	2·8
P.H.	Thigh	1·8	3·0	1·5	3·8	1·8	2·4	2·4	2·0

therefore, greatly alter the level of flow relative to that on the control side. Body cooling caused an average reduction of 53 % in the blood flow in the normal calf but only a 16 % reduction in the nerve-blocked calf. In response to body heating there was a 94 % increase in flow above the resting level on the normal side but there was no increase at all on the nerve-blocked side.

In two experiments on the thigh similar results were obtained (Fig. 1; Table 1). Though cutaneous nerve block resulted in a rise in blood flow, there was a similar increase on the normal side. Cooling the body resulted in an average fall in blood flow of 37 % on the normal side compared with a fall of only 7 % on the nerve-blocked side. Heating the body resulted in an average increase in flow of 36 % on the normal side, whereas the blood flow on the nerve-blocked side showed no increase.

It is clear, therefore, that in the upper arm, calf and thigh as in the forearm, cutaneous nerve block in a comfortably warm subject does not result in any important change in flow relative to that in the control limb. In response to body cooling and heating limb blood flow decreases and increases respectively. These changes in flow are depressed or abolished by blocking the cutaneous nerves to the part.

DISCUSSION

Cutaneous nerve block greatly reduced or abolished the changes in blood flow during body heating and cooling. It follows that the changes which normally occur are brought about by vasomotor nerves in skin. If methods are employed in the forearm which allow simultaneous estimation of skin and muscle blood flow, it can be shown that the increase in forearm blood flow during body heating is confined to the skin. For example, when skin and muscle blood flow in the forearm are simultaneously estimated by Hensel's heated thermocouples (Barcroft, Bock, Hensel & Kitchin, 1955), or by changes in the oxygen saturation of effluent blood from superficial and deep forearm veins (Roddie, Shepherd & Whelan, 1956), skin but not muscle flow increases during body heating. Body heating fails to cause an increase in forearm blood flow when the skin circulation is suppressed by adrenaline iontophoresis (Edholm, Fox & Macpherson, 1956). The present experiments indicate that a similar situation prevails in the upper arm, thigh and calf, and provides further evidence that the 'vasomotor centres' controlling skin vessels can function independently of those controlling muscle vessels.

The pattern of vasomotor control of skin in the upper arm, calf and thigh appears similar to that in the forearm. The finding that cutaneous nerve block caused little change in the blood flow in these areas indicated that the skin vessels were not subjected to any important vasoconstrictor or vasodilator tone when the subject was comfortably warm. Body cooling caused the blood flow on the normal side to fall below that on the nerve-blocked side, indicating the presence of vasoconstrictor fibres. During cooling the blood flow in the forearm, upper arm, calf and thigh fell to about half that of the previous resting level. This degree of reduction in flow has been obtained in the forearm by iontophoresis of adrenaline into the skin (Cooper, Edholm & Mottram, 1955) which has been shown to suppress, completely or almost completely, the cutaneous circulation (Edholm *et al.* 1956). It would appear from the present experiments that the activity of vasoconstrictor fibres in forearm skin can also almost completely suppress the skin circulation.

During body heating the blood flow on the normally innervated side rose substantially above that on the nerve-blocked side. This finding shows that the increase in blood flow that normally occurs is due to an active vasodilator mechanism. Though there is no evidence which definitely excludes the participation of specific vasodilator fibres in this response, it now seems more probable that the vasodilatation is due to release of bradykinin-forming enzyme from the activated sweat glands, and the subsequent formation of bradykinin (a polypeptide with vasodilator

properties) in the subcutaneous tissue space. Bradykinin-forming activity has been demonstrated in sweat collected from the human hand and forearm, and an increase in bradykinin activity occurs in the perfusate of the subcutaneous tissue space of the forearm during body heating (Fox & Hilton, 1958). There is a close analogy between the behaviour of the sweat glands and the salivary glands, where the vasodilatation associated with glandular activity has been shown to be due to release of bradykinin-forming enzyme from the activated gland (Hilton & Lewis, 1956). In certain animal species which lack eccrine sweat glands the skin vasodilatation in response to body heating seems to be due exclusively to release of vasoconstrictor tone (Green, Howard & Kenan, 1956). Finally, emotional sweating which occurs in the hand during stress is frequently accompanied by a vasodilatation (Allwood, Barcroft, Hayes & Hirsjärvi, 1959).

The present experiments indicate that the skin blood vessels of the upper arm, calf and thigh take part in temperature regulation. During body cooling the blood flow through these parts fell due to vasoconstrictor nerve activity, and during body heating it rose due an active vasodilator mechanism. The fact that the blood-flow changes with heating and cooling were of different sizes in different areas does not necessarily imply that there is any quantitative difference in the behaviour of the vasomotor nerves in these areas. It is possible that it is only a reflexion of the varying proportions of skin, muscle and bone in the different parts.

SUMMARY

1. Blood flow was measured bilaterally in the upper arm, calf or thigh of normal subjects by venous occlusion plethysmography.

2. When the subject was comfortably warm, blocking the cutaneous nerves to the experimental side with local anaesthetic caused little change in flow on the experimental side relative to that on the control side. It was concluded that the skin blood vessels in these areas, like those in the forearm, are not subjected to any important vasoconstriction or vasodilator tone under these conditions.

3. When the subject was subsequently cooled, the blood flow on the innervated side fell to a greater extent than on the nerve-blocked side. This result indicates the presence of vasoconstrictor fibres in the skin of the areas studied.

4. When the subjects were heated, the blood flow on the control side rose substantially above that on the nerve-blocked side, indicating that the vasodilatation was due to an active vasodilator mechanism mediated through fibres running with the cutaneous nerves.

REFERENCES

ALLWOOD, M. J., BARCROFT, H., HAYES, J. P. L. A. & HIRSJÄRVI, E. A. (1959). The effect of mental arithmetic on the blood flow through normal, sympathectomized and hyperhidrotic hands. *J. Physiol.* **148**, 108–116.

ARNOTT, W. M. & MACFIE, J. M. (1948). Effect of ulnar nerve block on blood flow in the reflexly vasodilated digit. *J. Physiol.* **107**, 233–238.

BARCROFT, H., BOCK, K. D., HENSEL, H. & KITCHIN, A. H. (1955). Die Muskeldurchblutung des Menschen bei indirecter Erwärmung und Abkühlung. *Pflüg. Arch. ges. Physiol.* **261**, 199–210.

BLAIR, D. A., GLOVER, W. E., KIDD, B. S. L. & RODDIE, I. C. (1959). The effect of bretylium tosylate (Darenthin) on certain vascular reflexes in human limbs. *J. Physiol.* **149**, 74–75*P*.

COOPER, K. E., EDHOLM, O. G. & MOTTRAM, R. F. (1955). The blood flow in skin and muscle of the human forearm. *J. Physiol.* **128**, 258–267.

DOUPE, J., CULLEN, C. H. & MACAULAY, L. J. (1943). Studies in denervation. F. The circulation in the skin in the proximal parts of the limbs. *J. Neurol.* **6**, 129–132.

EDHOLM, O. G., FOX, R. H. & MACPHERSON, R. K. (1956). The effect of body heating on the circulation in skin and muscle. *J. Physiol.* **134**, 612–619.

EDHOLM, O. G., FOX, R. H. & MACPHERSON, R. K. (1957). Vasomotor control of the cutaneous blood vessels in the human forearm. *J. Physiol.* **139**, 455–465.

FOX, R. H. & HILTON, S. M. (1958). Bradykinin formation in human skin as a factor in heat vasodilatation. *J. Physiol.* **142**, 219–232.

GASKELL, P. (1956). Are there sympathetic vasodilator nerves to the vessels of the hands? *J. Physiol.* **131**, 647–656.

GRANT, R T. & HOLLING, H. E. (1938). Further observations on the vascular responses of the human limb to body warming; evidence for sympathetic vasodilator nerves in the normal subject. *Clin. Sci.* **3**, 273–285.

GREEN, H. D., HOWARD, W. B. & KENAN, L. F. (1956). Autonomic control of blood flow in hind paw of the dog. *Amer. J. Physiol.* **187**, 469–472.

GREENFIELD, A. D. M. (1954). A simple water-filled plethysmograph for the hand or forearm with temperature control. *J. Physiol.* **123**, 62–64*P*.

HILTON, S. M. & LEWIS, G. P. (1956). The relationship between glandular activity, bradykinin formation and functional vasodilatation in the submandibular salivary gland. *J. Physiol.* **134**, 471–483.

LEWIS, T. & PICKERING, G. W. (1931). Vasodilatation in the limbs in response to warming the body; with evidence for sympathetic vasodilator nerves in man. *Heart*, **16**, 33–51.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1956). Evidence from venous oxygen saturation measurements that the increase in forearm blood flow during body heating is confined to the skin. *J. Physiol.* **134**, 444–450.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1957*a*). Humoral vasodilatation in the forearm during voluntary hyperventilation. *J. Physiol.* **137**, 80–85.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1957*b*). The contribution of constrictor and dilator nerves to the skin vasodilatation during body heating. *J. Physiol.* **136**, 489–497.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1957*c*). A comparison of the heat elimination from the normal and nerve-blocked finger during body heating. *J. Physiol.* **138**, 445–448.

RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1957*d*). The vasomotor nerve supply to the skin and muscle of the human forearm. *Clin. Sci.* **16**, 67–74.

SARNOFF, S. J. & SIMEONE, F. A. (1947). Vasodilator fibres in human skin. *J. clin. Invest.* **26**, 453–459.

WARREN, J. V., WALTER, C. W., ROMANO, J. & STEAD, E. A. (1942). Blood flow in the hand and forearm after paravertebral block of the sympathetic ganglia. Evidence against sympathetic vasodilator nerves in extremities of man. *J. clin. Invest.* **21**, 665–673.