# THE INTERRELATION OF THERMOREGULATORY AND BARORECEPTOR REFLEXES IN THE CONTROL OF THE BLOOD VESSELS IN THE HUMAN FOREARM

## By R. J. CROSSLEY,\* A. D. M. GREENFIELD,† G. C. PLASSARAS‡ AND DOROTHY STEPHENS§

From the Cardiovascular Research Institute, University of California Medical Center, San Francisco, Cal., U.S.A.

(Received 26 July 1965)

## SUMMARY

1. The interrelation of thermoregulatory and baroreceptor reflexes in the control of the circulation through the forearm has been investigated in eight men.

2. The results are compatible with the current hypotheses that thermoregulatory reflexes employ exclusively blood vessels in the skin, and that baroreceptor vasodilator reflexes excited by transfer of blood from the legs to the trunk employ exclusively blood vessels in the muscles. They are compatible with the hypothesis that baroreceptor vasoconstrictor reflexes excited by transfer of blood from the trunk to the legs employ blood vessels in muscles, but not with the hypothesis that they do so exclusively.

3. The results indicate that when blood is transferred from the trunk to the legs, vasoconstriction over-rides thermoregulatory vasodilatation, presumably in the blood vessels of the skin.

4. The circulation through the skin appears, therefore, to be under baroreceptor as well as thermoregulatory reflex control, and over the short period of time examined, namely 1 min, the baroreceptor control takes precedence.

#### INTRODUCTION

The previous paper (Brown, Goei, Greenfield & Plassaras, 1966) describes the effects, on the pulse rate, arterial pressure and the total forearm circulation, of trapping blood by suction on the legs of recumbent subjects, and then allowing it to return very quickly to the general circulation.

\* Present address: St John's College, Oxford.

‡ Present address: Therepeutic Clinic, School of Medicine, University of Athens, Greece.

§ Present address: The Queen's University of Belfast.

<sup>†</sup> Present address: Department of Physiology, St Mary's Hospital Medical School, London, W. 2

The behaviour of the circulation through the forearm during and after suction has now been examined in cold and hot, as well as in comfortably warm subjects. Heating and cooling the subject are thought to vary the circulation through the skin but not through deeper tissues of the forearm (Edholm, Fox & MacPherson, 1956). In a cold subject, the vessels of the skin are constricted by adrenergic vasoconstrictor nerves. In a hot subject, this activity is abolished, and the vessels of the skin are dilated secondarily to the activity of the cholinergic sudomotor nerves (Roddie, Shepherd & Whelan, 1957*a*; Love & Shanks, 1962). On the other hand, transfer of blood from the legs to the trunk, which can be brought about by passively raising the legs, leads to a reflex vasodilation of the muscle circulation, brought about by a reduction in adrenergic vasoconstrictor activity and no change in the skin circulation (Roddie, Shepherd & Whelan, 1957*b*).

The present experiments are in agreement with these earlier conclusions. They show further that, when blood is transferred from the remainder of the body to the lower limbs, a reflex vasoconstriction is provoked which reduces the circulation through the skin. This vasoconstriction is effective even when the rate of skin blood flow is at a high level in response to the needs of thermoregulation.

#### METHODS

The subjects were healthy men aged 20-46 years. They lay in a room whose temperature could be varied from 15 to 46° C. Provision was made to apply suction of 70 mm Hg below atmospheric pressure to the parts of the body below the iliac crests for periods of 1 min, Suction reached 90% of final value within 3 sec, and on release the pressure dropped 90% of the way towards atmospheric in  $0.5 \sec$  (Brown *et al.* 1966). Recordings were made of the e.c.g. and of the blood flow in one forearm by venous occlusion plethysmography (Greenfield Whitney & Mowbray, 1963) four or more times a minute. The plethysmograph was filled with water at 34° C. In some experiments the subjects were comfortably warm throughout. In others, the room temperature at the start was about 15° C, and the subjects were feeling cold but were not shivering. After several observations had been made, the room was heated, and at the end the subjects were feeling hot and were sweating. The forearm blood flow progressively increased and the effects of suction were observed at several levels of flow. In some experiments arterial pressure was recorded through a needle in the brachial artery using a Statham P. 23 AC pressure tranducer; the system was slightly underdamped and the damped natural frequency as used was better than 10 c/s.

#### RESULTS

Figure 1 shows recordings made in an experiment on R. L. while he was hot. Arterial pressure before suction was 110/70 mm Hg. At the onset of suction it fell to 95/60, but recovered by the 15th sec to 100/70 and by the 30th sec to 105/75, remaining at about this level until the end of suction. The forearm blood flow was about 11 ml./100 ml. per minute before suction, and fell to about  $3 \cdot 5 \text{ml.}/100 \text{ ml.}$  per minute during suction, the lowest reading being  $2 \cdot 6 \text{ ml.}/100 \text{ ml.}$  per minute. Following suction there was the usual overshoot, and the flow reached 15.5 ml./100 ml. per minute. Similar measurements were made in three other experiments on this subject while he was hot, and the changes in arterial pressure were similar whether he was hot or just comfortably warm.



Fig. 1. The effect of exposing the parts between the iliac crests and the feet of a hot recumbent subject to a pressure 70 mm Hg below atmospheric on the forearm blood flow and arterial blood pressure. Subject, R.L.

Figure 2 shows typical records of blood flow from the subject D.Ga., first while he was cold and then while he was hot. While cold the average resting forearm blood flow was  $1\cdot3$  ml./100 ml. per minute. During suction the flow fell to a minimum of  $0\cdot3$ , a fall of  $1\cdot0$ . After suction it rose to a maximum of  $5\cdot6$ , which was  $4\cdot3$  above resting level. While he was hot, the average resting forearm flow was  $10\cdot4$ . During suction the flow fell to a minimum of  $3\cdot1$ , a fall of  $7\cdot3$ . After suction it rose to a maximum of  $18\cdot6$ , which was  $8\cdot2$  above resting level. The minimum and maximum values in Fig. 2 are identified by open circles.

Figure 3 summarizes the results of these and three other such pairs of experiments on D.Ga., together with the results of similar series of experiments on seven other subjects. The abscissa shows the average resting blood flow. The ordinate scale shows the minimum blood flow during suction, and maximum after release, both these quantities being plotted for each experiment. All points would lie on the diagonal line if the experiment caused no change in blood flow. The vertical distance of points below this line indicates the amount by which the minimum blood flow during suction was reduced below resting level. The vertical distance of points

**63**0



Fig. 2. Changes in forearm blood flow brought about by exposing the parts below the iliac crests to a pressure 70 mm Hg below atmospheric while the subject was cold, and later while he was hot. Subject D.Ga.



Fig. 3. Minimum forearm blood flow during exposure of the parts below the iliac crests for 1 min to a pressure 70 mm Hg below atmospheric (points below the diagonals) and maximum blood flow following exposure (points above the diagonals) at various levels of forearm blood flow. For full explanation see text. Observations on eight subjects, identified by their initials.

above this line indicates the amount by which the maximum blood flow after suction was increased above the resting level. The points derived from the experiments on D.Ga. shown in Fig. 2 are identified in Fig. 3 by open circles in the panel labelled D.Ga.

The data in Fig. 3 are based on measurements of minimum flow during suction and maximum flow following suction, ignoring other measurements. A more comprehensive summary, based on all measurements of flow during and after suction, is shown in Fig. 4. To construct



Fig. 4. The difference between the average forearm blood flow responses to suction below the iliac crests when the subjects were hot and when they were cold. For explanation see text. Observations on eight subjects, identified by their initials.

this figure, all the available blood flow curves of the type shown in Fig. 2 from one subject while hot were averaged. The curves for the same subject while cold were similarly averaged. The average cold curve was then subtracted from the average hot curve, and the difference curve entered

in Fig. 4. This was then done for the seven other subjects. Figure 4 therefore shows, for each subject, the increase in flow at all states, before, during and after suction, which can be attributed to the effect of warming up a cold subject.

### DISCUSSION

The observations in Fig. 1 show that in the hot subject no important part of the changes in forearm blood flow during suction is likely to be due to changes in arterial perfusion pressure. The changes in arterial pressure when the subject was cold were very similar to those shown in Fig. 1, and lead to a similar conclusion. Moreover, in the comfortably warm subject, the changes in forearm blood flow during and after suction are almost abolished by blocking the sympathetic adrenergic pathway with bretylium tosylate (Brown *et al.* 1966) and are therefore due mainly to active changes in peripheral resistance, and are not passive changes to altered arterial pressure.

In the experiments in Fig. 2, the difference between the levels of blood flow before suction is attributable to the effects of heating the subject. The evidence of Edholm *et al.* (1956) indicates that the difference is due to increased blood flow through the skin. The reduction in blood flow during suction while the subject was hot (a reduction of  $7\cdot3$  ml./100 ml. per minute) greatly exceeded the reduction while the subject was cold (a reduction of  $1\cdot0$ ), and it was also greater than the total resting flow while cold ( $1\cdot3$ ). Such a reduction while hot indicates that the flow was reduced by suction in the circulation through the skin, in which it had been increased by heating the subject. Had suction influenced the flow only through the tissues other than skin, in which the circulation is unaffected by heating the subject, the reduction in flow during suction would have been equal in the hot and in the cold subject.

In the experiment in Fig. 2, the rise of the peak flow after suction above the previous base-line flow was greater while the subject was hot  $(8\cdot 2 \text{ ml.}/100 \text{ ml.} \text{ per minute})$  than while he was cold  $(4\cdot 3)$ . The difference was not usually so large as this, as may be seen by reference to Figs. 3 and 4.

The data in Fig. 3 summarize the spread of results. Consider first the points below the diagonals, relating to the decreases in blood flow during suction. In all subjects, these points tend to fall farther below the diagonal, indicating a greater reduction in flow, at high levels of resting flow than they do at low levels of resting flow. In the case of three subjects, D.Ga., R.C. and R.P. the points all lie fairly close to the abscissa, indicating that flow was always reduced to a very low level during suction however high the level of resting blood flow.

Let us now consider the points above the diagonal in Fig. 3. These relate to the increase in blood flow after suction, and their vertical distance above the diagonals indicates the size of the increase. In general, for each subject, these points are at much the same vertical distance above the diagonal. The size of the increase in blood flow after suction is largely independent of the resting level of blood flow before suction.

Figure 4 shows, for each subject, the average increase in total forearm blood flow attributable to heating a cold subject, the increase being shown at all stages before, during and after suction. In all eight subjects the increase was less during suction than it was before or afterwards, but the difference was greater in some subjects than in others. In only two subjects (D.Ga. and R.L.) was the increase notably greater immediately after suction than it was before suction; only in these two subjects was the overshoot of flow after suction notably higher above resting level while they were hot than while they were cold.

The general picture, from all these results, is that in the hot, as compared with the cold subject, the fall in forearm blood flow during suction is increased, but the overshoot of forearm blood flow after suction is little changed in size.

As a first hypothesis, let us suppose that in the forearm there are two parallel vascular pathways or sets of vessels. One pathway might be through the skin, the other through the muscles and other tissues. Let us suppose that one pathway is responsive to thermo-regulating reflexes and one to baroreceptor reflexes. Then the effect of heating a cold subject would be to increase the level of blood flow by a constant amount before, during and after suction. The measurements in Figs. 3 and 4 are not in accord with this hypothesis. It is possible, and perhaps likely, that the baroreceptor stimulus is stronger in a hot than it is in a cold subject because blood may be moved more quickly and in greater quantity when the peripheral vessels are dilated than when they are constricted. However, the most such an enhanced stimulus could do would be to stop the flow of blood in the vascular pathway under baroreceptor control. The flow of blood in this pathway must clearly be less than the total resting flow of blood in the limb of a cold subject. This is in turn much less than the reduction in flow of blood in the hot subject during suction. Therefore, an enhanced action in the hot subject on the vascular pathway controlled by baroreceptor reflexes does not explain the observed reduction in flow during suction.

As a second hypothesis, suppose that the vascular pathways of the forearm belong to a single population, and are employed in both thermoregulatory and baroreceptor reflexes, and that the baroreceptor reflexes over-ride the thermoregulatory ones. During suction, the forearm blood flow would be reduced by different amounts, but to much the same level, in cold and in hot subjects. Observations of minimum flow in Fig. 3 would lie along lines parallel to the abscissa. Observations in Fig. 4 would fall to zero during suction. No results conform exactly to this hypothesis, but those on D.Ga. and R.P. come fairly close to doing so.

A third hypothesis is that there are two vascular pathways, one responsive mainly to thermoregulatory reflexes and modestly to baroreceptor reflexes, the other responsive mainly to baroreceptor reflexes and modestly to thermoregulatory reflexes.

A fourth hypothesis is that the vascular pathway responds to both types of reflex stimulation. The dominant reflex may vary with the circumstances. For example, over short periods baroreceptor reflexes may be pre-potent, and over longer periods thermoregulatory reflexes may be pre-potent.

The third and fourth hypotheses predict results intermediate between the first and second hypotheses, and they cannot be distinguished by the present experimental evidence. The results on all subjects fit either of these hypotheses.

There is a strong body of evidence that the thermoregulatory reflexes affect only the vessels of the skin, and not the vessels of the muscle, of the human forearm (Barcroft, Bock, Hensel & Kitchen, 1955; Edholm *et al.* 1956; Roddie, Shepherd & Whelan, 1956). There is also strong evidence that when the legs are raised, and the blood is returned from them to trunk, the reflex increase in blood flow in the forearm is confined to the muscle vessels (Roddie & Shepherd, 1956).

Present observations on the increase in forearm flow following the release of suction on the legs are in agreement with this finding. The increase in flow above base-line level is of a fairly constant size in any one individual, and independent of changes in the resting level of forearm flow brought about by heating or cooling the subject.

The present experiments indicate, however, that the converse is not true. When blood is transferred from the trunk to the legs, the resulting baroreceptor reflex reduces the flow in pathways that are also used for thermoregulation, and are therefore presumably in the skin.

There is no evidence at present to show whether the thermoregulatory and baroreceptor reflexes act on common effector blood vessels, or whether they act on two sets of blood vessels in series.

We wish to thank Dr J. H. Comroe, Jr. for the hospitality of the Cardiovascular Research Institute, Dr Ellen Brown for the hospitality of the Environmental Control Laboratory of the Department of Medicine, and their subjects for their co-operation. The work was supported by United States Public Health Service Grant HE 06285 and the Robert Benjamin Harris Fund allocated by the Committee on Research of the University of California School of Medicine. R. J. Crossley and Dorothy Stephens were Summer Student Research Fellows, A. D. M. Greenfield was a Visiting Professor in the Cardiovascular Research Institute, and G. C. Plassaras was a Research Fellow of the San Francisco Heart Association.

#### REFERENCES

- BARCROFT, H., BOCK, K. D., HENSEL, H. & KITCHEN, A. H. (1955). Die Muskeldurchblutung des Menschen bie Indirecter Erwärmung und Abkühlung. *Pflügers Arch. ges. Physiol.* 261, 199–210.
- BROWN, E., GOEI, J. S., GREENFIELD, A. D. M. & PLASSARAS, G. (1966). Circulatory responses to simulated gravitational shifts of blood in man induced by exposure of the parts below the iliac crests to sub-atmospheric pressure. J. Physiol. 183, 607–627.
- EDHOLM, O. G., FOX, R. H. & MACPHERSON, R. L. (1956). The effect of body heating on the circulation in skin and muscle. J. Physiol. 134, 612-619.
- GREENFIELD, A. D. M., WHITNEY, R. J. & MOWBRAY, J. F. (1963). Methods for the investigation of peripheral blood flow. Br. med. Bull. 19, 101-109.
- LOVE, A. H. G. & SHANKS, R. G. (1962). The relationship between the onset of sweating and vasodilation in the forearm during body heating. J. Physiol. 162, 121-128.
- RODDIE, I. C. & SHEPHERD, J. T. (1956). The reflex nervous control of human skeletal muscle blood vessels. *Clin. Sci.* 15, 433-440.
- 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. (1957a). The contribution of constrictor, and dilator nerves to the skin vasodilation during body heating. J. Physiol. 136, 489–497.
- RODDIE, I. C., SHEPHERD, J. T. & WHELAN, R. F. (1957b). Reflex changes in vasoconstrictor tone in human skeletal muscle in response to stimulation of receptors in a low-pressure area of the intrathoracic vascular bed. J. Physiol. 139, 369-376.