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THE ACTION OF ADRENALINE ON MUSCLE BLOOD FLOW AND BLOOD LACTATE IN MAN

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Intravenous infusions of adrenaline in man cause a large transient followed by a smaller sustained vasodilatation in skeletal muscle (Allen, Barcroft & Edholm, 1946; Whelan, 1952). According to Celander (1954) the sustained dilatation in cat's muscle is probably secondary to an increase in the rate of carbohydrate metabolism and of lactic acid formation (Lundholm, 1949). In view of this we have compared the changes in the blood flow in the human forearm during intravenous adrenaline infusions with those in the lactate content of the venous effluent from the forearm muscles.

METHODS

Healthy men aged 20–30 years acted as subjects. Room temperature was about 22° C. Under local anaesthesia venepuncture was performed near the ante-cubital fossa, the needle being inserted towards the hand. A fine nylon catheter was threaded through the needle into a muscle vein (Mottram, 1955). Heparin saline was infused at the rate of 1 ml./min to prevent clotting. A plethysmograph was fitted to the same forearm and filled with water maintained at 34° C (Barcroft & Edholm, 1945). A second needle was inserted into a forearm vein in the opposite forearm through which 0·9% (w/v) saline was infused throughout the experiment at 3 ml./min. Adrenaline could be added to this saline so that it entered the vein at the rate of 10 μg/min.

Blood flows were recorded at minute intervals throughout the experiment, except immediately after the beginning of the adrenaline infusion when they were recorded every $\frac{1}{4}$ min. Blood samples were obtained as follows. The circulation through the hand having been arrested, the catheter was disconnected from its infusion apparatus and about 1 ml. of blood was withdrawn to clear it of saline. A further 1–1$\frac{1}{2}$ ml. of blood was withdrawn into a sterile lactate-free syringe, and was deproteinized as rapidly as possible with 10% trichloracetic acid to prevent accumulation of lactic acid. In most experiments there was an initial period of 20 min, followed by a single infusion of adrenaline lasting for 25 min, and a final recovery period of 40 min.

Altogether twenty-four blood samples were usually taken. Their timing is seen in Fig. 1. Four were in the preliminary rest period; six at the beginning of the adrenaline infusion, covering the phase of the initial vasodilatation; six more during the sustained dilatation and eight during the recovery period. At the end of every experiment a silver wire was passed down the catheter and the whereabouts of the catheter was established by X-ray photography. Blood lactates were determined by Hullin & Noble's (1953) modification of Barker & Summerson's method (1941).

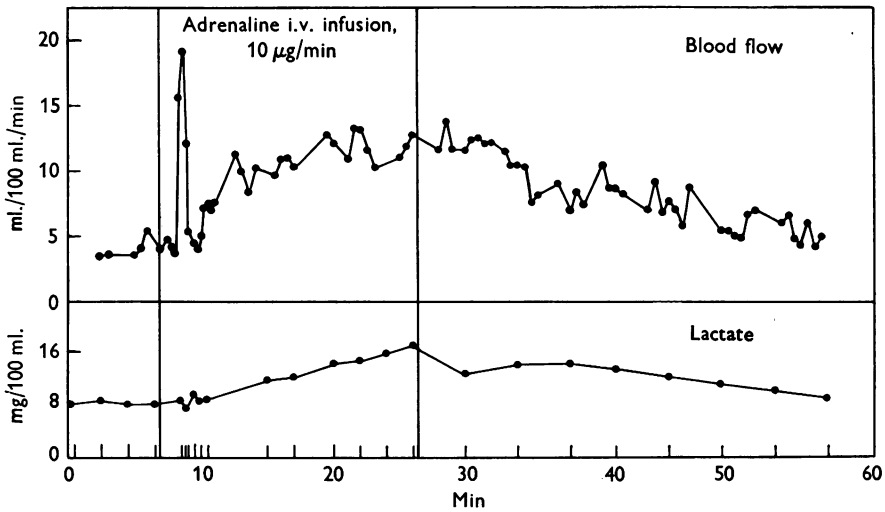

Fig. 1. Results obtained in one subject showing the action of intravenous adrenaline on forearm blood flow and on the lactate content of the blood from the forearm muscles. 0·9% NaCl infused throughout the experiment. Blood samples taken at the points indicated by the short vertical lines on the time axis.

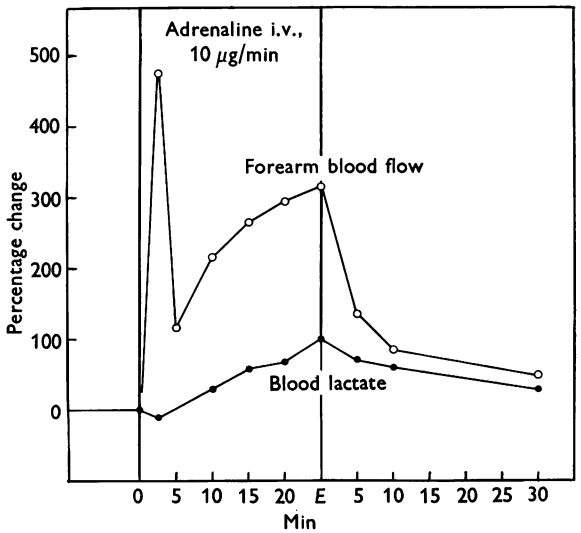

Fig. 2. Averaged results of experiments on eight subjects.

RESULTS

Fig. 1 shows the results of a typical experiment. The results of eight experiments in which the catheter was in a muscle vein are shown in Table 1. Fig. 2 shows the averaged results.

In all subjects the forearm blood flow showed the typical response to intravenous adrenaline, namely an initial transient followed by a sustained vasodilatation; after the infusion the blood flow decreased rapidly at first and then more slowly, to approach the pre-infusion level at the end of the recovery

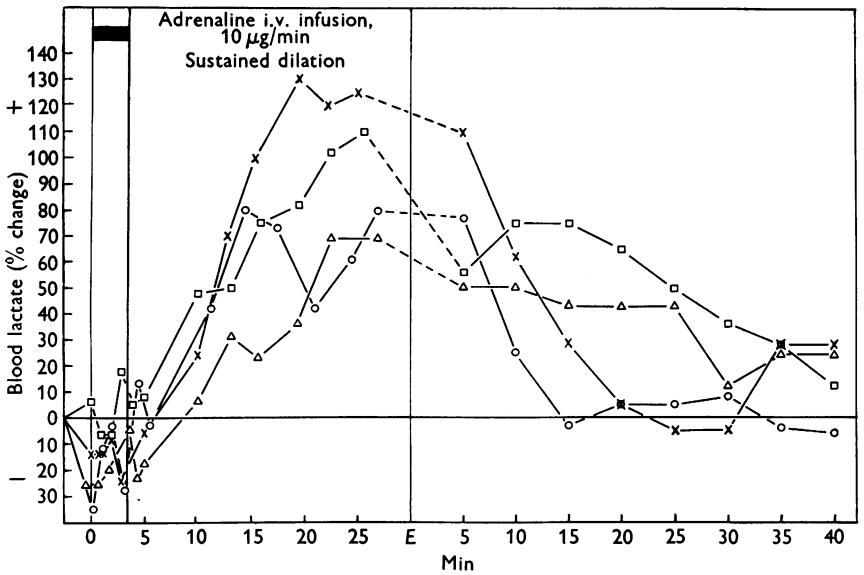

Fig. 3. Results obtained in four subjects showing the percentage change in blood lactate level during and after intravenous infusions of adrenaline. The black rectangle indicates the period corresponding to the initial transient dilatation. *E*, end of infusion.

period. The response of the blood lactate also followed a regular pattern (Fig. 3). During the initial vasodilatation there was usually a small fall in lactate concentration. This was followed by a steady rise during the sustained vasodilatation, reaching a maximum at or just after the end of the infusion. Blood lactate declined steadily during the recovery period and reached the pre-infusion level in 20–45 min.

DISCUSSION

Bell & Stead (1952) examined the effect of intra-femoral-artery adrenaline injections and infusions upon calf volume and lactate content of the femoral venous blood. The initial transient increase in calf volume was not accompanied by any significant alteration in the blood lactate. The results we have

TABLE 1. Forearm blood flow and lactate content of venous effluent from forearm muscles before during and after intravenous infusions of adrenaline

Blood flow (ml./100 ml. forearm/min)

Subject	Before adrenaline	During adrenaline: During initial vaso-dilatation	During adrenaline: Min after beginning of infusion 5	10	15	20	25	After adrenaline. Min after end of infusion 5	10	30
1	4·0	19·3	10·0	11·0	12·0	12·0	11·5	8·0	5·0	4·5
2	2·9	16·8	7·0	8·7	10·0	—	10·5	5·0	2·8	—
3	3·1	15·0	7·0	8·6	11·0	11·0	13·4	6·0	4·0	4·5
4	3·5	10·1	4·0	6·2	6·5	—	7·5	5·2	6·0	4·0
5	1·9	14·3	5·6	5·5	7·5	8·5	8·5	5·5	5·2	2·2
6	0·4	17·4	2·7	3·6	4·9	4·5	5·5	4·0	2·0	2·0
7	2·5	10·7	4·8	6·0	6·0	7·0	7·5	4·5	4·0	3·2
8	3·7	13·8	7·8	8·5	9·0	11·5	11·5	5·0	5·0	4·0
Mean	2·3	13·3	5·0	7·3	8·4	9·1	9·5	5·4	4·2	3·4

Blood lactate (mg/100 ml.)

Subject	Before adrenaline	During adrenaline: During initial vaso-dilatation	During adrenaline: Min after beginning of infusion 10	15	20	25	After adrenaline. Min after end of infusion 5	10	30
1	8·0	8·5	14·0	14·5	15·75	17·0	12·5	14·0	12·0
2	16·5	13·0	14·5	—	—	28·0	—	19·0	—
3	11·0	11·6	15·5	27·5	19·5	30·0	20·0	20·0	20·0
4	14·5	14·5	18·0	19·0	—	20·5	16·5	16·5	14·5
5	11·2	10·1	16·5	18·5	19·5	26·0	25·0	24·0	15·0
6	8·7	5·7	11·5	12·0	16·5	18·7	18·0	19·5	16·0
7	9·5	11·2	14·0	14·75	15·75	16·0	18·0	14·5	10·7
8	5·2	4·5	7·5	9·0	11·75	11·75	10·0	8·0	5·0
Mean	10·6	9·9	13·9	16·8	17·8	21·2	18·0	16·9	13·8

The figures for the blood flow and blood lactate before adrenaline are averages, so are those for the blood lactate during the initial vasodilatation. The figures for the blood flow during the initial vasodilatation are those for the greatest blood flow recorded.

obtained in the forearm are in accordance with those which Bell & Stead obtained in the calf. As we did not determine the lactate content of the arterial blood it is impossible to say what effect the adrenaline may have had upon the lactate output from the muscles during the initial transient vasodilatation. Further work is needed to clarify this point.

It is well known that adrenaline given subcutaneously or intravenously increases blood lactate (Cori & Buchwald, 1930; Courtice, Douglas & Priestley, 1939), and also that the lactate comes mainly from the skeletal muscles (Griffith, 1951). It is clear from the results which we have described that lactate enters the blood throughout the phase of sustained vasodilatation, and it appears from Fig. 2 that part of the sustained vasodilatation and most of the hyperaemia in the recovery period during the phase of gradual subsidence could be due to the action of vasodilator products of muscle carbohydrate metabolism, as for example lactic acid (McDowall, 1938).

Other considerations also suggest that there may be a relation between muscle blood flow and carbohydrate metabolism. Hildes, Sherlock & Walshe (1949) found that intravenous infusions of adrenaline caused the breakdown of muscle glycogen and lactacidaemia. Since this did not occur when adrenaline was infused into the artery of a limb Hildes, Purser & Sherlock (1949) concluded that adrenaline has no direct effect on muscle glycolysis. It is possible that the rates of their intra-arterial infusions (average 7 μg/min) were rather large and their failure to find any direct effect of adrenaline on muscle carbohydrate metabolism may have been due to vasoconstriction in the limb. Nevertheless, their conclusion is in keeping with the results obtained by Whelan (1952), who found that only the initial vasodilatation was present during intra-arterial infusions. The absence of the sustained dilatation, coupled with the absence of a glycolytic effect under these conditions, supports the view that there may be a relationship between muscle blood flow and muscle carbohydrate metabolism. If this is so then the dilator substance may well be lactic acid, as our results show.

The absence of the glycolytic effect and of the sustained vasodilatation during intra-arterial infusions of adrenaline also suggests that intravenous adrenaline may lead to the presence in the blood of some other substance which plays an important part in the development of the sustained vasodilatation. The existence of such a substance has been postulated by Whelan (1952) and by Celander (1954).

Nothing definite is known about the nature of this substance (or substances). Celander (1954) suggested that intravenous adrenaline might release the substance from the muscles themselves and, if this be so, it is possible that during intra-arterial infusions the amount released into the general circulation might be so small as to have a negligible effect. It is unlikely that the substance is histamine (Mongar & Whelan, 1953). Hildes, Purser & Sherlock (1949) and

also Whelan recalled that adrenaline released ACTH from the pituitary. Recently, Kitchin (1954) has shown that the sustained vasodilatation in muscles takes place normally when intravenous adrenaline is administered to hypophysectomized patients. We may be concerned here with the cycle liver glycogen→blood glucose→muscle lactic acid→liver glycogen, and it will be recalled that this cycle was first described in the rat following the subcutaneous injection of adrenaline (Cori & Cori, 1928). Further work is needed to see if the sustained vasodilatation in man is connected with the action of adrenaline on carbohydrate metabolism in the muscles and in the liver.

SUMMARY

1. Simultaneous determinations of the rate of the blood flow in the forearm and of the lactate content of the venous effluent from the forearm muscles have been made before, during, and after intravenous infusions of adrenaline.

2. During the infusions there was a large transient followed by a smaller sustained vasodilatation. After the infusions the blood flow decreased abruptly at first and then subsided gradually to approach the initial level in about half an hour.

3. Muscle blood lactate did not change significantly during the transient dilatation. During the sustained vasodilatation it increased progressively. Following the infusion it subsided gradually, reaching the pre-infusion level in about half an hour.

4. The results are discussed, and it is suggested that the sustained vasodilatation may be caused in part by products of muscle carbohydrate metabolism.

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