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THE OXYGEN CONSUMPTION OF HUMAN SKELETAL MUSCLE *IN VIVO*

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Attempts to measure metabolic activity of skeletal muscle *in vivo* began with the experiments of Chauveau & Kaufmann (1887). These authors stated the principles on which most later work has relied. These are '(1) to collect and measure the blood flowing through a muscle of known or ascertainable weight; (2) to collect this blood uncontaminated by blood from any other source whatever; (3) to find the amounts of chemical substances in a given volume of this blood; and (4) to compare these amounts with those found in simultaneously drawn samples of arterial blood.' They found in the levator labii superioris of the horse a muscle they could study in the unanaesthetized animal.

Holling (1939) has followed the same principle in studies on the human forearm muscles. Blood flow was recorded with the plethysmograph, and samples of venous blood were taken from the deep branch of the median cubital vein immediately distal to its junction with the superficial branch. He was concerned primarily with O_2 consumption of the tissues. Another method, used by Jarisch & Gaisböck (1929) and by Asmussen, Christensen & Nielsen (1939), was to estimate the fall in respiratory O_2 intake that occurs following vascular occlusion of the legs.

METHOD

In the present work a variant of Holling's method for studying O_2 uptake of muscle has been used. Total forearm blood flows have been measured and from them, using the data of Cooper, Edholm & Mottram (1954, 1955) an estimate of the forearm muscle blood flow has been made. Blood samples were obtained by retrograde catheterization of the deep veins of the forearm from the median cubital vein and their O_2 content estimated. Sixteen healthy young adults of both sexes were used for these experiments. During experiments they lay on a couch in a room maintained at 23° C. Subjects wore their normal indoor clothing without jackets, and were covered with a blanket if they felt cold.

Blood flows were recorded using a venous occlusion plethysmograph filled with water maintained at 34° C (Barcroft & Edholm, 1946). The collecting cuff was placed on the upper arm 2–3 in. above. the plethysmograph and inflated to 60 mm Hg for 10 sec at 20 sec intervals. Ten of these 10 sec inflow records were obtained beginning 1 min following application of arterial occlusion to the wrist (Kerslake, 1949), and the average flow rate for the period calculated. Blood samples were withdrawn 30 sec following the last inflow, and before the arterial occlusion cuff was released.

Catheterization was performed using the following technique. The venous occlusion cuff was inflated until the veins in the antecubital fossa were distended. In most subjects the median cubital vein and its deep branch were immediately apparent, and the latter could often be felt by palpation to be emerging from under the pronater teres or brachio-radialis muscles which form the lower limits of the antecubital fossa. After release of the venous compression a bleb of procaine 2% was raised in the skin over the vein. Venepuncture was performed through this bleb with the needle directed distally, using a thin-walled needle with an internal diameter of 1·1 mm. A nylon catheter, having an outer diameter of 0·9 mm and a lumen of over 0·5 mm was then threaded through the needle and down the vein. The free end of the catheter was connected to a constant infusion pump and saline containing some heparin was run in at about 0·4 ml./min. The catheter was passed 4–8 cm down the vein. It was found possible in many cases, by gentle persuasion, to guide the tip of the catheter through valves until it was in a suitable position. This was checked at the time of introduction of the catheter by observation with an X-ray screen or at the end of the experiment by taking radiographs in two planes at right angles to each other. Both for screening and taking pictures a stainless steel wire was introduced down the catheter to render it radio-opaque.

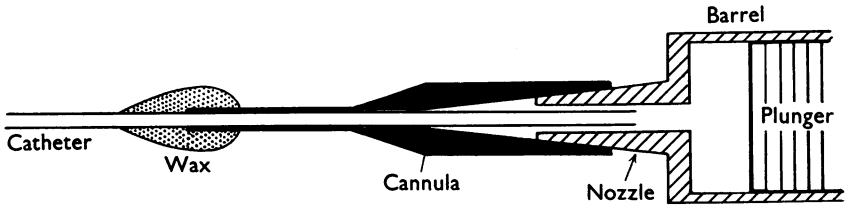

Fig. 1. The technique of sealing the catheter into the metal cannula and the attachment of the sample syringe.

Blood samples were withdrawn through the catheter into 1 ml. syringes, the dead spaces of which had previously been filled with NaF solution. This was used instead of heparin as it assists the effect of chilling on the respiration of blood. Two techniques were used for obtaining an air-free connexion between syringe and catheter. At first a fine gauge needle was attached to the syringe, filled with NaF solution and its tip inserted into the lumen of the catheter. This technique only allowed a slow rate of withdrawal of blood, owing to the narrow bore of the needle. Later a technique developed by Barcroft (personal communication) was used. The catheter was sealed with a low melting-point wax into a metal cannula as in Fig. 1. The tip of the catheter was allowed to project from the end of the cannula in such a way that it lay within the nozzle of the sampling syringe when this was attached to the cannula. Before obtaining samples by either technique at least 30 sec elapsed between disconnecting the infusion pump and taking the sample. During this interval blood was allowed to drain away from the free end of the catheter.

0·5 ml. samples were taken in 10–30 sec. As soon as the syringe was disconnected from the catheter it was sealed and stored by Roughton & Scholander's technique (1943). Usually four sets of blood flows and four corresponding samples of blood were obtained in a single experiment. Some subjects had several experiments performed on them, and some only one.

As soon as possible following the end of the experiment the O_2 content of the blood samples was estimated by the Roughton-Scholander syringe technique (1943). Duplicate analyses were always performed. 0·3 division ($c. \simeq 0{\cdot}3$ vol. %) was the largest difference between duplicate analyses accepted.

Some samples were stored for a further 18–24 hr after being analysed. It was found that practically no fall in O_2 content had occurred after this time. At least one sample from each set was saturated with O_2 and its O_2 capacity estimated. It was assumed that, as the subjects were at rest, the O_2 capacity would remain constant throughout an experiment and that arterial blood was 95% saturated.

Fig. 2 shows the relative positions of the plethysmograph, cuffs, and catheter about the subject's forearm. Supports were placed under the arm and the hand in such a way that the cuffs were clear of them. It should be noted that although the antecubital fossa appears in the diagram to be on the upper surface of the arm, the hand is fully pronated. This position was adopted by many of the subjects when asked to make themselves comfortable.

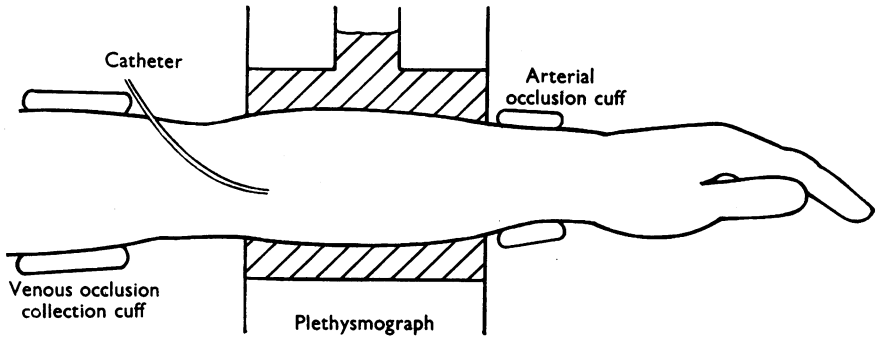

Fig. 2. The assembly of plethysmograph, etc., about the subject's forearm.

RESULTS

Arteriovenous oxygen differences

Samples of blood (174) were obtained in forty experiments in which the catheter was undoubtedly in the deep tissues of the forearm as judged by the X-ray pictures obtained. A further forty-six were taken in eleven experiments in which the catheter tip was in the superficial tissue.

Fig. 3 shows a histogram of the arteriovenous (A-V.) O_2 difference of the samples of blood drawn from deep veins during these experiments and also one for the samples obtained from superficial veins. Although there is some overlap it is clear that these two anatomically distinct sets of veins contain blood of different composition.

In eighteen experiments a sample of blood was obtained with the wrist cuff free. Nine of these samples contained more O_2 than samples taken during the experiments when the wrist cuff had been applied for nearly 5 min. In some of these cases the catheter was in such a position that it might well have been in a vena comes of the radial or ulnar arteries. In five of the other nine cases in which application of the wrist cuff made no difference to venous blood O_2 content, the catheter was in a vein running along the line of the interosseous artery.

The possibility that some forearm skin venous blood was entering deep veins was investigated by performing an adrenaline iontophoresis of a forearm with a catheter inserted into a deep vein. This was attempted on four occasions. None was entirely satisfactory, but in two it appeared that the virtual cessation of skin blood flow produced no change in deep venous blood O_2

content. This rose, however, when a hyperaemia of deep tissues occurred due to general absorption of adrenaline.

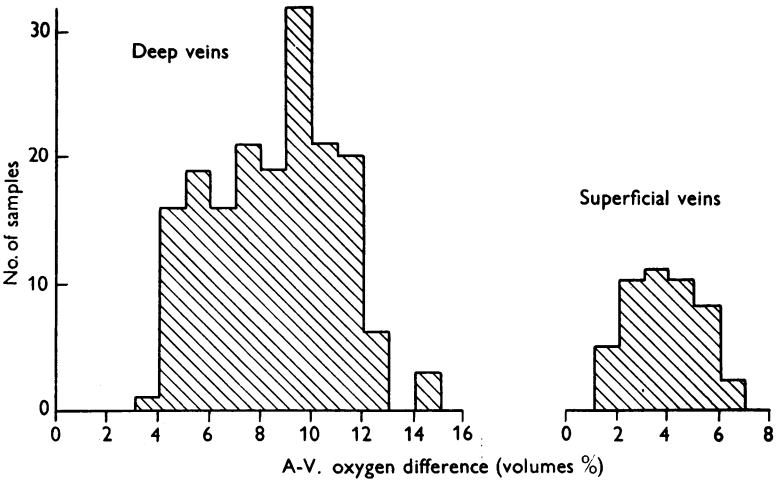

Fig. 3. A-V. O_2 difference for deep and superficial venous blood.

Blood flows

Before true O_2 uptake of muscle could be calculated the 'muscle' blood flow had to be estimated. This was done by using the data in the paper by Cooper *et al.* (1955) on partition of forearm blood flows. In that paper there is shown a regression line for blood flow/100 ml. muscle tissue against blood flow/100 ml. forearm. This was derived from the results of some thirty experiments in which blood flow in a forearm had been measured before and after iontophoresis with adrenaline, and from estimation of proportions of forearm tissues by dissecting and measuring the volume of the various component tissues.

Fig. 4 shows a histogram of the total forearm flows obtained, each observation as graphed being the mean flow calculated from a set of ten inflow slopes as already described. For comparison there is a second histogram of the muscle blood flows calculated from the total flows. The mean of the observed flows is 3·2 ml./100 ml. forearm/min, and that of the muscle flows is 2·9 ml./100 ml. muscle/min. The range of muscle blood flows is less than that of the observed total blood flows.

Oxygen consumption

The Fick principle was used for estimating O_2 consumption, thus O_2 consumption = A-V. O_2 difference × rate of flow of blood. Using the conventional units this becomes ml. O_2 consumed/100 ml. muscle/min = A-V. O_2 difference/ml. blood × ml. blood flow/100 ml. muscle/min.

In practice all A-V. O_2 differences were worked out as so many ml./100 ml. blood, so had to be divided by 100 to fit this form of equation.

Fig. 5 is a histogram of the 174 individual estimations made on the sixteen subjects during these investigations. The mean O_2 consumption was 0·24 ml./100 ml. muscle/min and the range was from 0·09 to 0·52 ml.

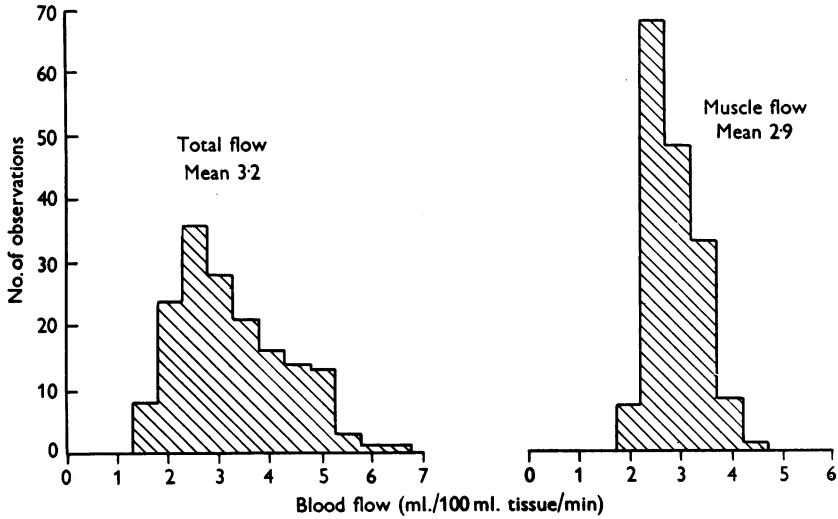

Fig. 4. Histograms of observed forearm blood flows and the calculated muscle blood flow.

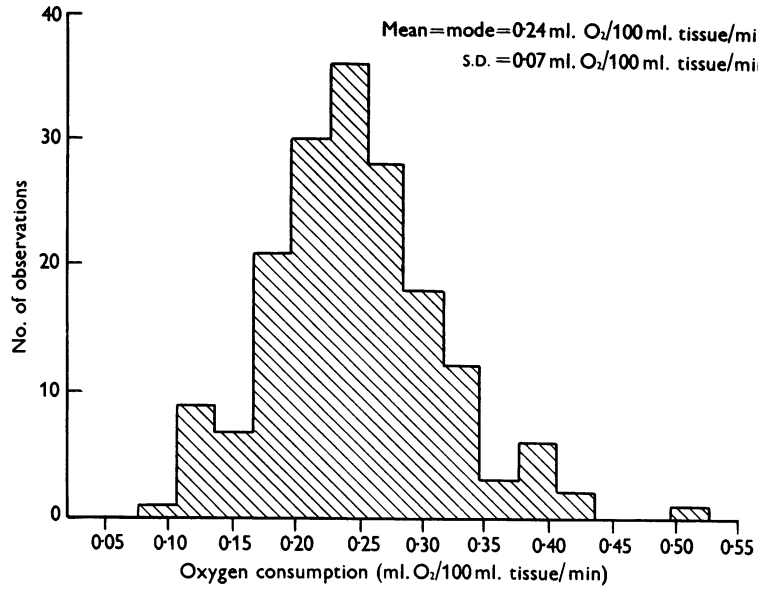

Fig. 5. A histogram of the 174 individual estimations of O_2 consumption of muscle obtained during this work.

Table 1 gives the mean result for each experiment on each of the sixteen subjects. The scatter of the results that is shown in Fig. 5 is seen to be due in part to differences between repeat experiments and between the two arms on one subject, and to differences between subjects.

TABLE 1. Mean O_2 consumption (ml./100 ml.muscle/min) found for each experiment on each of sixteen subjects, divided into right and left arms

Subject no.	Right arm, mean	Left arm, mean
1	0·18	0·16
	0·21	0·25
	0·23	0·15
	0·20	0·29
2	0·23	—
3	0·23	0·12
4	0·31	0·24
	0·42	—
	0·36	—
5	0·24	0·25
	0·22	—
6	0·25	—
7	0·25	0·26
	0·23	0·30
	—	0·25
8	0·36	0·38
9	0·19	0·27
10	0·18	0·24
	—	0·24
11	0·19	0·29
12	0·12	—
13	—	0·20
	—	0·30
14	—	0·19
	—	0·17
15	—	0·26
16	—	0·34

Any one estimation is subject to an error of up to 0·03 ml. O_2/100 ml. muscle/min, due to faults in estimation of blood flows and A-V. O_2 differences. In the sixty-five individual estimations made on subjects nos. 1, 4 and 7, fifteen estimations deviated from their respective experiment means by more than this amount.

DISCUSSION

The estimation of 'muscle' blood flow from total forearm flows is an approximation, as is stated by Cooper *et al.* (1954, 1955). As a result, any one estimation of O_2 consumption may vary by $\pm 30\%$ from the true value at that time. To obtain an approximation to the true O_2 consumption, several individual estimations have to be made and their average taken. This procedure will tend to reduce errors arising from this source.

On the basis of the radiographs taken in each experiment there was usually no doubt about the site of the catheter. In six of the experiments the position of the catheter tip could not be allocated to either the deep or the superficial

tissues. Results from these experiments have been excluded from those reported here.

The possible tissues drained by the deep veins can be classified as (1) hand tissues, (2) forearm skin, (3) forearm muscles (treated as 1 unit of tissue), and (4) forearm bones, tendons, nerves, fat, etc. The hand was excluded from the circulation for nearly 5 min before blood samples were taken, so it need not enter into consideration as being a possible site of samples taken in these experiments.

The results of the eighteen experiments in which samples of blood were taken with wrist cuff free show that, in those conditions, hand venous blood flows in the venae comites of radial and ulnar arteries, but not in those of the interosseous artery. In the two experiments in which adrenaline iontophoresis was successfully carried out there was no evidence that blood passed from the skin into the deep veins of the forearm.

For the purpose of the calculation of muscle oxygen consumption, it has been assumed that the venous blood sampled represents pure muscle venous blood. In fact about 10% (Cooper *et al.* 1955) may have come from the supporting tissues, etc., so the O_2 consumption figures recorded here should be those for all deep tissues of the human forearm. Furthermore, it had to be assumed that all muscle tissue of the forearm used O_2 at the same rate.

In some cases, the between-experiment variation observed in one subject might be due to different veins being sampled on the different occasions, but variation as great sometimes occurred when the catheter was in the same position in the repeat studies on one subject. The within-experiment and the between-experiment variations were sometimes as much as 0·06 ml. O_2/100 ml. tissue/min from their respective mean values. These changes could be due to local factors, such as change in tone of the muscle, or be part of a general change in the metabolic rate of the subjects, or, in part at least, to faults in measurement, which may give rise to an error in estimation of 0·03 ml. above or below the correct value.

The values estimated by other workers are shown in Table 2, together with those presented here.

It will be observed that the results found in the present work are higher than any found before for man. Holling's experiments were performed with a plethysmograph water temperature of 30° C, at which a substantial cooling of tissues is known to occur. The chief difference in the two sets of observations was the low blood flows found by Holling. Furthermore, his blood samples, though taken from the deep branch of the median cubital vein, were from the subcutaneous portion of this vessel, before the valves could prevent mixing of the blood samples with blood derived from the skin passing up the superficial branch of the vein.

Nielsen has stated in a personal communication concerning the work of

Jarisch & Gaisböck (1929) and Asmussen *et al.* (1939) that he doubts whether their subjects could have remained at rest following the application of arterial occlusion cuffs to the thighs. This had to be maintained for at least 10 min in order to allow the collection of expired air samples sufficient to determine the O_2 consumption of the subject. The actual falls in consumption observed were about 22 ml. O_2/min from the levels found before the legs were cut off from the circulation. On the basis of O_2 consumption at the rate of 0·24 ml. O_2/100 ml. tissue/min, the fall in respiratory O_2 intake should have been 26 ml. O_2/min, which is only 4 ml. higher than that reported by these workers.

TABLE 2. Estimation by various authors of the O_2 consumption of skeletal muscle, using different techniques

Author	Material	Method	O_2 consumption ml./100 ml. tissue/min
Holling (1939)	Forearm	Blood flows and ante-cubital vein samples	0·12
Jarisch & Gaisböck (1929)	Legs	Reduction in O_2 consumption by body following arterial occlusion in both legs	0·18
Asmussen, Christensen & Nielsen (1939)	Legs		0·17
Green (1950)	Human muscle	Calculated from blood flows and femoral A-V. oxygen differences	0·18
Mottram	Forearm	Blood flows and deep vein samples	0·24

Green's figure (1950) depends on the O_2 content of venous blood draining both skin and muscle. In fact the figure of 6 vol. % which he gives for A-V. O_2 difference can be seen to be midway between the values for deep and superficial veins obtained in the present work.

The total muscle mass is approximately 40 % of body weight. If the mean O_2 consumption value of 0·24 ml./100 ml. tissue/min applies to the whole muscle mass, then the total O_2 consumption attributable to skeletal muscle in a 70 kg man = 67 ml./min. This approaches 25 % of the O_2 consumption of the whole body at rest. On the basis of Holling's figure the skeletal muscles would account for 12 % of O_2 consumption of the body and on those of other workers, about 17 %.

SUMMARY

1. Methods are presented for recording blood flows in human forearm with simultaneous collection of blood samples from the deep and superficial veins of the forearm.

2. The O_2 contents of these samples were estimated and the arteriovenous (A-V.) difference for deep veins was 8·5 vol. % and for superficial veins about 4 vol. %.

3. From the A-V. difference of samples and the corresponding blood flow records (converted to 'muscle' blood flow) the O_2 consumption of human forearm muscle has been calculated. The mean value obtained for 174 estimations on sixteen subjects in forty experiments is 0·24 ml. O_2/100 ml. tissue/min and the S.D. = 0·07.

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