J. Physiol. (1956) 133, 255–265

THE EFFECT OF VENOUS PRESSURE ON THE OXYGEN CONTENT OF VENOUS BLOOD IN THE DEEP FOREARM VEINS

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(*Received* 15 *December* 1955)

It has been shown (Werner, Moreira & Edholm, 1953; Edholm, Moreira & Werner, 1954) that the forearm blood flow declined as venous pressure rose. This fall was less than that predicted from the change in arterio-venous pressure gradient, so these authors suggested that a rise in venous pressure caused an arteriolar dilatation. It was decided to investigate the change in venous blood oxygen content during changes of venous pressure. Friedland, Hunt & Wilkins (1943) had already shown that the oxygen content of venous blood, sampled 10 min after occlusion, was reduced, a finding compatible with the occurrence of a fall in the blood flow.

METHODS

Subjects for the experiments were healthy adults of both sexes. During experiments they lay at rest on a comfortable couch in a room at 23–25° C. Deep forearm veins were catheterized (Mottram, 1955) and blood samples were obtained from them. The catheter was made of nylon, 0·9 mm in external diameter and with a wall thickness of 0·2 mm approximately. When it was passed along the deep branch of the median cubital vein the tip usually reached the plexus of veins formed by the junction of the venae comites of the radial, ulnar and interosseous arteries, or lay in one of the venae comites. All these veins usually have internal diameters greater than 1 mm (Mottram, unpublished observations). In practice it has usually been found possible to withdraw blood through a catheter up to 4 ml./min. Attempts to draw blood at greater rates leads to a collapse of the vein wall on to the catheter tip and a complete cessation of blood flow up the catheter. The negative pressure required to draw blood from a vein under experimental conditions has not been measured, but a dummy vein was made using 0·1 mm-thick rubber sheeting. This was filled with heparinized blood and two lengths of nylon catheter, similar to those used in the catheterization of veins, were sealed into the 'vein' so that their tips were 2–3 mm apart. Capacitance manometers were attached to both catheters and blood was withdrawn from the side arm of a two-way

* Aided by a Scholarship from the Rockefeller Foundation.
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tap placed between one manometer and the catheter. Blood was withdrawn from the dummy vein at varying rates between 0·5 and 2·5 ml./min and records were taken of the pressures at both the outer end of the sampling catheter and in the vein. It was found that a negative pressure of 150–400 mm Hg was applied by the syringe and that the pressure in the rubber vein, which tended to remain circular in cross-section, fell by 3–6 mm, both pressures depending on the rate of withdrawal of blood from the vein.

A cuff pressure of 60 mm Hg was used for venous occlusion. The circulation to the hand was stopped by a wrist cuff inflated at 200 mm Hg 1 min before venous occlusion. In some experiments forearm volume changes were recorded with the plethysmograph. Occlusion was applied for periods of 1, 2, 3 or 4 min, at the end of which time the tubing from the saline-heparin infusion pump was disconnected, a syringe attached to the catheter and 1 ml. of blood collected; after completion of the sampling, the infusion tubing was re-attached to the catheter and the wrist and venous cuffs released. Blood samples were stored using Scholander's technique, and their oxygen content found by the Roughton–Scholander (1943) analyser. In some experiments adrenaline iontophoresis (Cooper, Edholm & Mottram, 1955) had been performed before the experiment began.

An oxymeter (Handforth, 1955) was used to study the oxygen saturation of the blood during the first minute of venous occlusion. In the model used the cuvette was inserted into the tube holder of a portable (Evans Electroselenium) colorimeter. The galvanometer of this instrument has a pointer which moves over a logarithmic scale, reading zero for full transmission and infinity for complete extinction of light, so changes in scale reading are proportional to changes in oxygen content of the blood in the cuvette. A change of one scale unit = a change of $3\frac{1}{3}$% saturation or 0·67 vol. oxygen %. Handforth found that 95% of estimates of oxygen percentage saturation, using both the Van Slyke manometric method and the oxymeter, differed by less than 8% saturation. The oxymeter was used to obtain a continuous record of blood oxygen content by attaching the cuvette directly to the catheter and drawing through it a stream of blood from the vein at the rate of 2 ml./min, taking readings of the galvanometer deflexion every 5 sec. The effects of 1 min periods of continuous occlusion, and of intermittent occlusions at 5, 7·5, 10 or 15 sec intervals on and off for a total of 2 min, were studied by this method.

RESULTS

In samples taken after 1, 2, 3 or 4 min of occlusion the oxygen percentage saturation was found to be high at 1 min, thereafter progressively declining to reach approximately control level at 2–3 min and showing a fall below control values at 4 min. These changes persisted after adrenaline iontophoresis, indicating that this response to venous occlusion was probably taking place in the muscle vessels (Fig. 1).

The rise in oxygen content of venous blood during the first minute of venous occlusion was then investigated using the oxymeter. The responses of the oxymeter when a continuous stream of blood was passing through it were first studied in two ways:

(1) Blood was passed through the cuvette at 0·4 ml./min from a mixed sample of heparinized blood in a syringe, using a constant infusion pump. Readings were taken at 5 sec intervals for two periods of 6 min. Between the two periods the syringe was removed from the pump and the contents remixed. The standard deviation of the 144 readings was 0·4 scale division (= 1·2% saturation).

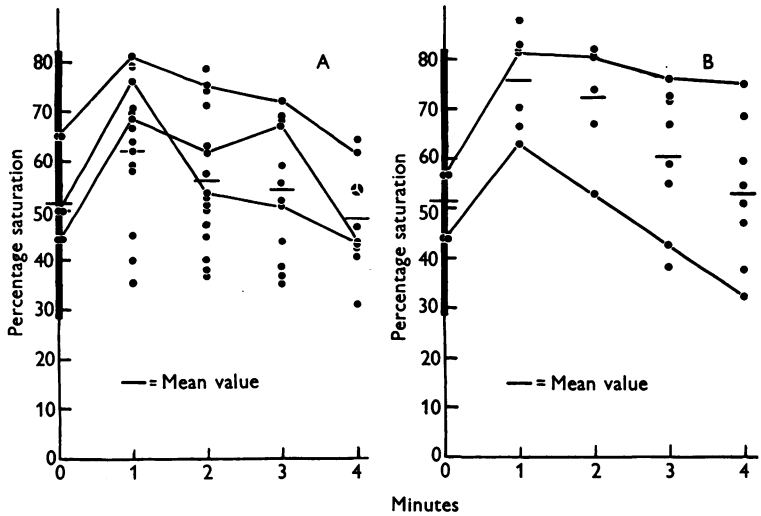

Fig. 1. The percentage saturation of venous blood samples obtained immediately after 1, 2, 3 and 4 min venous occlusion are shown, together with the mean value for samples obtained at each time. The shaded area on the Y-axis shows the mean and range of the oxygen content of a control series of samples (Mottram, 1955). Some control samples were taken in the present series. The dots on the Y-axis indicate their oxygen content. *A* = normal arms. *B* = arms subjected to adrenaline iontophoresis. The points connected with lines are the results obtained when it was possible to take the samples serially during a single occlusion period.

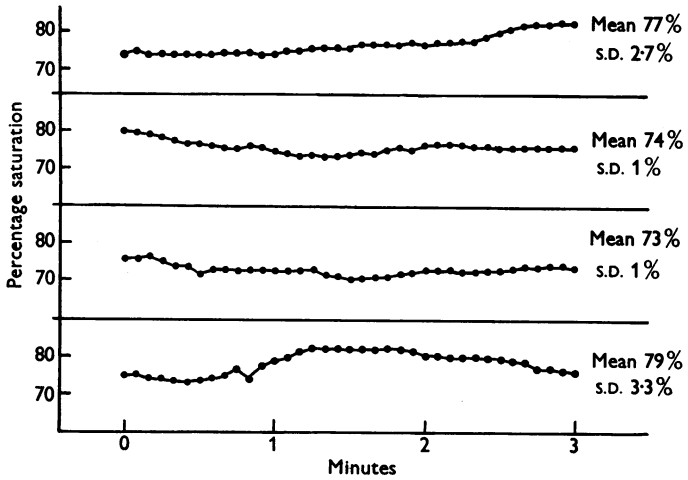

Fig. 2. O_2% saturation of blood determined by oxymeter readings made each 5 sec for four periods of 3 min, during which blood was being drawn continuously from a vein through the oxymeter cuvette. The mean and S.D. are given alongside each run.

(2) From a vein in a resting subject blood was withdrawn continuously at 2 ml./min through the oxymeter for 3 min periods, readings of the galvanometer being taken at 5 sec intervals. Fig. 2 shows the results of four periods of observation obtained at 5–15 min intervals on this subject. It is seen that the spontaneous variation in oxygen percentage saturation of venous blood in two runs was little more than that found when a mixed sample of blood from a syringe was passed through the oxymeter. In the other two runs the standard deviations of the thirty-six observations were 3·3 and 2·7% saturation respectively. In all the following experiments the galvanometric deflexion was recorded at 5 sec intervals for 1 min before any experimental procedure was

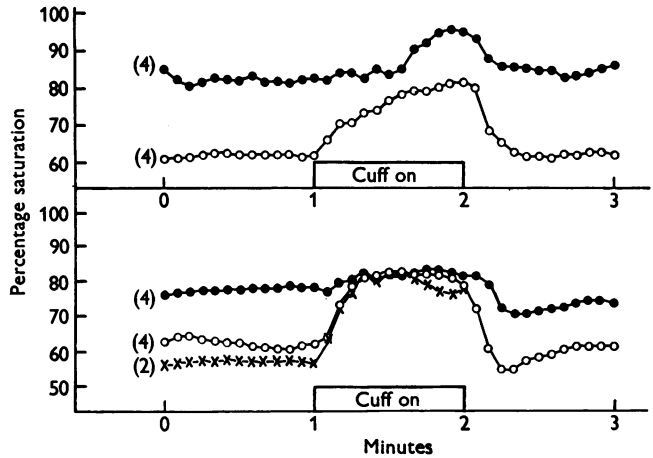

Fig. 3. The change in O_2% saturation of deep venous blood produced by 1 min of venous occlusion and determined by an oxymeter. Each line is the result of a separate experimental session and represents the mean of the galvanometer readings taken at corresponding times during 3 min periods, in the second minute of which venous occlusion was applied. The figures in brackets indicate the number of repeat runs for each experiment. Three experiments were performed on one subject and two on the other.

applied. The variation in these control periods was similar to that observed in the 3 min periods of recording described above. It can therefore be assumed that any change in oxygen saturation greater than 6·6% (twice the greatest standard deviation) will be a significant deviation from the normal level.

The oxymeter was then used to study the change in venous blood which occurred during a 1 min period of venous occlusion sustained at 60 mm Hg. Galvanometer readings were taken at 5 sec intervals for 1 min before, during and after occlusion. This procedure was repeated several times on each subject and the corresponding readings averaged. Fig. 3 shows the response given by one subject on three separate occasions and by another subject on two occasions. Galvanometer readings are plotted against time and the period of

cuff inflation indicated on the time scale. The rise in oxygen content of venous blood may be apparent within 5 sec of occlusion, or it may take as long as 30 sec to appear. The rise in oxygen content varied from about 5% saturation (a fall of 1½ scale divisions) to as much as 25% saturation (a fall of 7½ scale divisions). In all, ten subjects, in three of whom three separate experiments have been performed, have shown this response to varying degrees. Twice only, in sixteen experiments, has no rise in oxygen content of venous blood occurred with venous occlusion. These were both in subjects in whom on other occasions a definite reaction occurred. In one subject the response was observed to change from run to run, though the occlusions followed each other at 10 min intervals. In the first run no change of saturation occurred during occlusion for 1 min. In the second, third and fourth runs the response progressively increased, until the maximum rise in oxygen content was of the order of 20% saturation (Fig. 4).

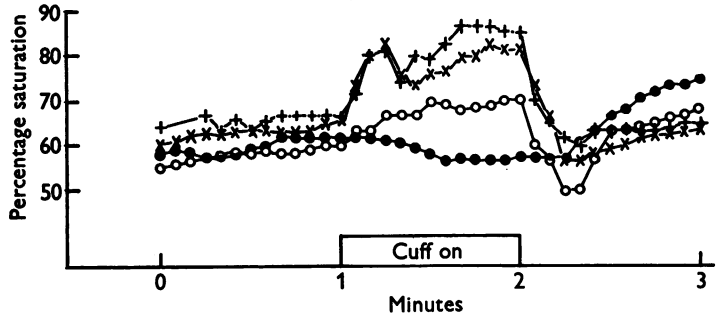

Fig. 4. O_2% saturation, determined by the oxymeter readings taken at 5 sec intervals during four periods of 3 min separated by 7 min rest periods, for blood drawn continuously from a deep vein of one subject. In each period venous occlusion was applied during the second minute. Note the progressive change in response from run 1 to run 4. ●, run 1; ○, run 2; ×, run 3; +, run 4.

In four further subjects the effect of venous occlusion on oxygen content of a superficial vein was investigated. In three of these no change occurred, but in the fourth a rise of 16% saturation was seen. This occurred after a delay of 20 sec from the onset of occlusion and was present in each of four occlusion periods.

In two subjects venous occlusion was applied for 1 min alternately to either arm, blood being drawn from a deep vein in the right arm. When occlusion was applied to the left arm, no change occurred, but when the right arm veins were occluded a rise in saturation occurred of 16% in one subject and of 10% in the other (Fig. 5).

In further experiments the forearm veins were alternately occluded and released at varying rates, occlusion being equal in duration to release and lasting

for periods of 5–15 sec. During a 2 min period, while these intermittent occlusions were being applied, observations were made on the forearm deep venous blood on five subjects. In all cases, including one experiment using 5 sec occlusions, the oxygen content of venous blood rose and fell as occlusion was alternately applied and released (Fig. 6). In one out of the six sets of observations the mean oxygen content during the intermittent (10 sec) occlusions was the same as that before occlusion began. In all the others (with cuff alternately applied and released for 15, 10, 7·5 or 5 sec) the mean oxygen content during occlusion was higher than during the control periods (Fig. 7).

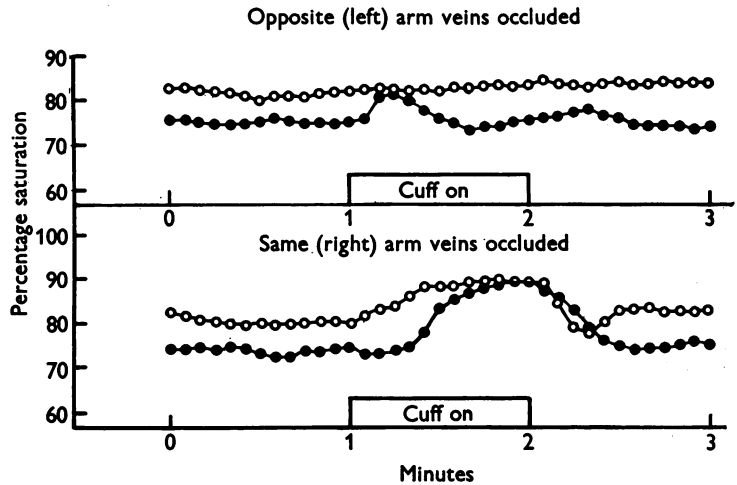

Fig. 5. The change in O_2% saturation of blood drawn from a deep vein of the right arm when 1 min occlusions were applied to each arm in turn. Two subjects were investigated. ●, subject 1; ○, subject 2.

Haemoglobin determinations were performed on samples of blood drawn before and 45–60 sec from the start of venous occlusion. Three subjects were investigated and fourteen pairs of samples were obtained. The mean difference between the pairs of samples was 0·2 g Hb/100 ml., the sample taken during occlusion containing the greater amount of haemoglobin. This difference was found, on statistical analysis, to be insignificant. Similarly, no increase or decrease in haemoglobin was found during the first 15 sec of occlusion.

DISCUSSION

The fall in optical density, that was found to occur in blood drawn from the deep veins of the forearm when the pressure within them rose, could be due either to a fall in the haemoglobin content of the blood or to a rise in the saturation with oxygen of the haemoglobin. That it could be due to a fall in

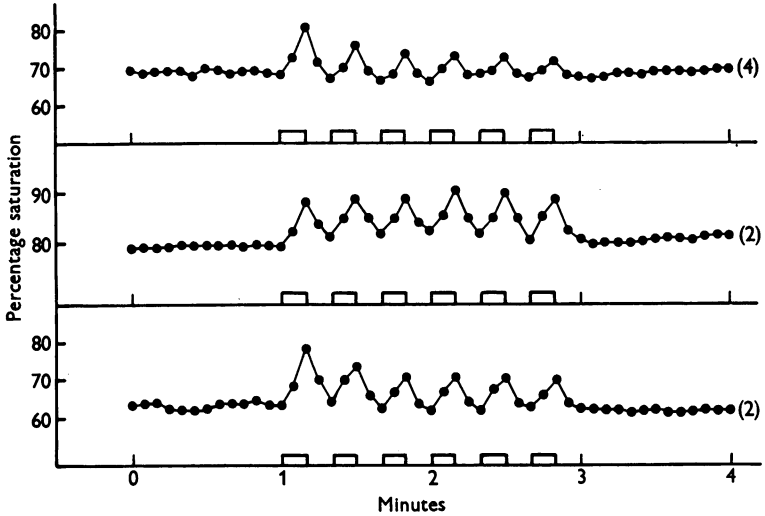

Fig. 6. The response of the O_2% saturation of deep venous blood in a 2 min period during which venous occlusion was applied for 10 sec in every 20 sec. Each line is from a separate subject and is the mean of two or more runs as indicated by the number in brackets. The rectangles on the abscissae indicate the periods of occlusion.

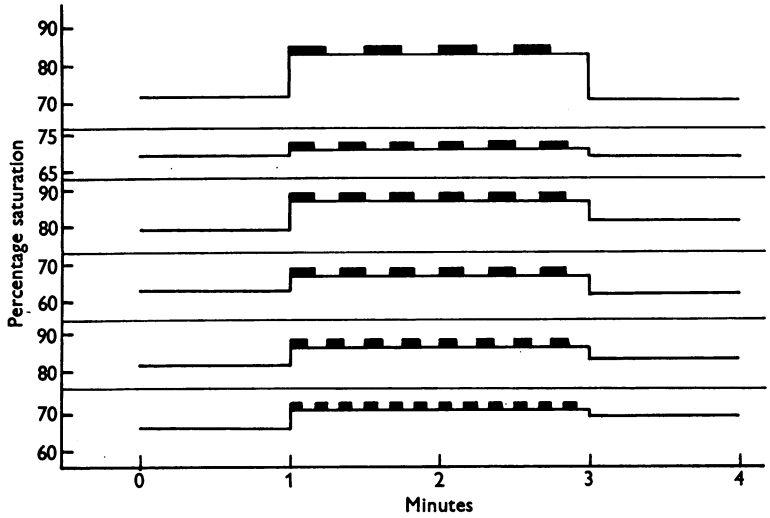

Fig. 7. The percentage saturation of blood drawn continuously through the oxymeter during 2 min of intermittent occlusion, compared with that found for the 1 min before and after the occlusions. The dark portions on each line indicate the periods of venous occlusion.

haemoglobin in these experiments is disproved by the observation that 1 min of venous occlusion produces no significant change in haemoglobin concentration. Thus no separation of plasma from cells occurred owing to stagnation or any preferential shunt mechanism. The change in optical density must therefore be due to a change in oxygen percentage saturation of the blood. This is confirmed by the results on the first series of experiments, in which the oxygen content of blood samples was found with the Roughton–Scholander syringe analyser.

Venous occlusion, or even the mere suction of blood from a vein, might result in altering the source of the blood in the vein. With the circulation completely occluded at the wrist, the deep veins of the forearm contain blood draining from the muscle tissue, from bone, and possibly from skin. Skin venous blood contains more oxygen than does that of the deeper tissues (Mottram, 1955). Venous occlusion could divert blood from the skin into the deep veins and thus account for the rise in saturation (Green, Cosby & Radzow, 1944). However, this cannot be the only factor, because the rise in saturation was not abolished by adrenaline iontophoresis which stops the skin blood flow. Furthermore, a rise in saturation was even seen to follow venous occlusion in one out of the four superficial veins that were catheterized. Therefore the change in oxygen saturation of deep venous blood is probably not solely due to a diversion of blood from the skin.

It is possible that within the deeper tissues themselves there may be areas with a high blood flow and therefore with effluent blood rich in oxygen, and conversely areas with a low blood flow and more desaturated venous blood. It is not known whether this is in fact true. Were it to be so and should the onset of venous occlusion always cause a change in oxygen saturation of blood passing the catheter tip, a fall in saturation might be expected as often as a rise. In fact, either a rise, or no change, but never a fall in oxygen saturation, was observed on venous occlusion.

Changes in venous pressure by altering the level of limbs relative to that of the heart have also been produced by Wilkins, Halperin & Litter (1950) and by Rosensweig (1955). The former found in eleven subjects lying prone that lowering the legs by flexion at the hips, to an angle of 60° below horizontal, led to a rise of oxygen content of popliteal vein blood up to 5–10% saturation after 5 min, and that returning the legs to the horizontal led to a fall of 7% saturation. Provided no obstruction to venous blood flow occurred, this change in posture would result in a hydrostatic increase of about 30 mm Hg in popliteal venous pressure. It appears that at this pressure increase elevation of venous blood oxygen saturation persisted for longer than at the pressures used by ourselves. Rosensweig alternately held the arm horizontal at the level of the sternal angle, or lowered it until the wrist was 50 cm below its original level. He found a mean rise of 16·5% oxygen saturation in antecubital and

forearm vein blood samples when the arm was dependent and observed that the change persisted for up to 14 min.

Werner *et al.* (1953) and Edholm *et al.* (1954) have shown that during periods of venous occlusion or congestion lasting up to 4 min the blood flow of the part was reduced when measured with the plethysmograph. Since this reduction of flow was less than that expected from the reduction in arterio-venous pressure gradient they suggested that a rise of venous pressure is accompanied by a progressive fall in arteriolar resistance.

The results described here show that, as the venous pressure is raised in the muscular part of a limb, blood of a progressively higher oxygen content appears in the veins. Simultaneous venous pressure and oxymeter records have not been made, but by comparison of results shown in Fig. 3 with records of venous pressure taken in the experiments of Werner *et al.* it seems likely that the observed change in oxygen content of the blood occurs after the rise in venous pressure has begun. Fig. 2 shows the change in oxymeter readings when blood was drawn through it from a deep vein while the subject remained at rest. The fluctuations in reading that occurred, though rather variable, were both smaller and slower than those observed when venous pressure was raised. Fig. 5 shows that the response to applying the cuff is one that only occurs in the limb with occluded veins. It is not obtained by occluding the veins of the other arm.

Our results thus confirm the suggestion put forward by Werner *et al.* that, as venous pressure rises, an arteriolar dilatation develops. The appearance in the veins of blood approaching arterial blood in oxygen content when the flow rate is reduced suggests that there are non-metabolic channels which are opened by this arteriolar dilatation. Passage of oxygen from red blood corpuscles to tissue fluid would be hindered if the cells passed very rapidly through the capillary, or if their distance from the capillary wall were much increased. Overall flow rate is, however, diminished, therefore corpuscular flow rate could not, under these circumstances, be increased as corpuscles tend to 'fall out' of the stream if it is slowed down. Capillary diameter would have to increase many times to interfere with diffusion of oxygen sufficiently to produce any effect.

Evidence already exists for the presence of a second, non-metabolic system of small vessels in skeletal muscles, in addition to the normal capillary vessels. Thus post-exercise hyperaemia is not altered in size by adrenaline infusion (Dornhorst & Whelan, 1953). The hyperaemia produced by adrenaline infusion or by deep nerve block can be detected by the plethysmograph but not by ^{24}Na clearance or by measuring the rate of tissue fluid formation (Miller & Wilson, 1951; McGirr, 1952; Walder, 1953; Kitchen, 1953, 1954). These latter methods give an indication of blood flow through channels where metabolic exchange is occurring, whereas the plethysmograph records the

total inflow of blood to the limb segment. On the basis of this evidence the hypothesis of a double circulation in skeletal muscle has been put forward by Barcroft & Swan (1953). The observations recorded in this paper add confirmatory evidence to this hypothesis, the non-metabolic channels being opened by: (1) release of sympathetic vasoconstrictor tone by nerve blocking; (2) infusion of adrenaline at 10 μg/min; and (3) by raising venous pressure.

Three ways in which a raised venous pressure could, theoretically, open non-metabolic or shunt vessels are as follows: (1) distension due to back pressure, (2) local liberation of vasodilator substances, (3) reflex mechanisms.

(1) It is not possible to make any suggestions concerning the effect of back pressure on the shunt vessels without knowing something about their place of origin from arteries or arterioles or about their histological structure. If they are branches from the distal end of arterioles, then they could be distended by a raised venous pressure transmitted back through the capillaries, but if their origin were from the proximal ends of arterioles this could not be so.

(2) Metabolites, accumulating as flow falls owing to the rise in venous pressure, could not open the shunts, for these open before blood flow is decreased. The specific release of a substance like bradykinin (Hilton & Lewis, 1955) may occur in response to a rise in venous pressure.

(3) Although vasodilator fibres are known to exist in skeletal muscle (Folkow, 1955) baro-receptors on the vein wall and afferent fibres from them will have to be demonstrated before it can be stated that the opening of shunts following a rise in venous pressure is due to a reflex mechanism.

SUMMARY

1. During a 4 min period of venous congestion of the human forearm at 60 mm Hg an initial rise, followed by a fall, occurs in the oxygen content of blood withdrawn from the deep veins.

2. By continuous suction of blood from a deep vein through an oxymeter it is found that blood with increased oxygen content could be withdrawn from the vein within 5 sec of the onset of occlusion, and that the peak of this rise, reached after 1 min, may be 25% saturation above the control level.

3. Venous blood withdrawn during periods when the cuff is alternately inflated and deflated at 5–15 sec intervals may contain up to 2 vol. % more oxygen than during the period before inflation begins.

4. The vascular dilatation postulated as occurring during venous occlusion must be such that blood flows from artery to vein through shunt channels and not through capillaries.

The authors wish to thank those people who acted as subjects for these experiments, and the technical staffs of both departments who gave them valuable assistance. One of us (R.F.M.) wishes to express his gratitude to the Medical Research Council for a grant for the provision of apparatus. Part of this work was presented by R. F. M. in a thesis for the degree of Doctor of Philosophy in the University of London.

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