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THE ABOLITION OF REACTIVE AND POST-EXERCISE HYPERAEMIA IN THE FOREARM BY TEMPORARY RESTRICTION OF ARTERIAL INFLOW

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

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Following a period of circulatory arrest or exercise in a limb there is a period of hyperaemia. It has been pointed out by many workers that under certain conditions there is a close relationship between the duration of circulatory arrest or the severity of the exercise and the size of the subsequent hyperaemia (Freeman, 1935; Abramson, Katzenstein & Ferris, 1941; McArdle & Verel, 1956; Coles & Cooper, 1959; Clarke & Hellon, 1959). However, many other workers have found that the relationship is by no means exact (Eichna & Wilkins, 1941; Dornhorst & Whelan, 1953; Patterson & Whelan, 1955; Wood, Litter & Wilkins, 1955; Patterson, 1956; Holling & Verel, 1957). The present experiments were devised to account for this apparent discrepancy.

METHODS

Experiments were performed on four healthy young men. The subjects wore normal indoor clothing, and lay on a couch in a laboratory maintained at 18–20° C. Both forearms were inserted into plethysmographs (Greenfield, 1954) maintained at 35° C, and throughout the experiment flows were recorded at 15 sec intervals. The subject rested for 30 min before any measurements were made.

Reactive hyperaemia. An occlusion cuff which could be inflated to a pressure of 250 mm Hg was applied on top of the venous collecting cuff on each arm. After resting flows were recorded for 3 min the occlusion cuffs were inflated for a 5 min period. On release of the occlusion, flows were recorded for a further 10 min; for the first 45 sec of this period a lower pressure (30–40 mm Hg) was used in the collecting cuff (Eichna & Wilkins, 1941; Patterson & Whelan, 1955). This constituted a control run. The first experimental run commenced 10 min later. Previously the position of both brachial arteries in the antecubital fossae had been located and marked with a skin pencil. The procedure was the same as in the control run, but at the end of the occlusion period two fingers were placed on the brachial artery on one side and compression was applied so that the blood flow was prevented from rising above the previous resting level. The couch was arranged so that the person applying compression could see the plethysmograph record on the kymograph, and it was found that with a little practice it was possible to regulate the flow down the artery. In the first series of experiments this compression was maintained for the first 5 min following circulatory arrest. Compression was then released and the flow measurements

continued for another 5 min. The second experimental run commenced 10 min later; this time the previous experimental arm became the control arm and vice versa.

In the second series of experiments the brachial artery in one arm was compressed to restrict arterial inflow for various times immediately after circulatory arrest. During five experimental runs compression was applied for 1, 2, 3, 4 and 5 min respectively.

Exercise hyperaemia. A similar set of experiments was carried out on the same four subjects using a 1 min period of rhythmic exercise of the forearm in place of the 5 min period of circulatory arrest. The exercise was standardized as far as possible by squeezing a rubber bulb connected to a water-filled burette to raise the water column a fixed height in time with a metronome. However, it was difficult to ensure that this type of exercise caused identical muscular activity in the two arms and in the same arm from time to time.

RESULTS

Reactive hyperaemia

Figure 1 illustrates part of a typical experiment. Blood flow was measured in the forearms before and after bilateral arrest of the arm circulation for 5 min. After release of the circulation, reactive hyperaemia was allowed to proceed

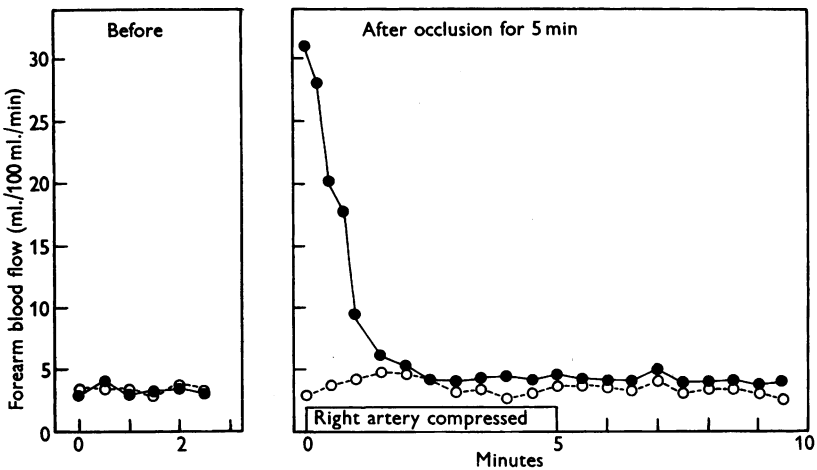

Fig. 1. The effect of restricting arterial inflow on reactive hyperaemia in the forearm. Left panel, before circulatory arrest. Right panel, after arrest of the forearm circulation for 5 min. During the period represented by the rectangle digital compression was applied to the right brachial artery to prevent the forearm blood flow rising above the previous resting level. ●, left forearm; ○, right forearm.

normally on the left side. On the right side the blood flow was prevented from rising above the previous resting level for 5 min by digital compression of the brachial artery. When the compression was released there was no increase in blood flow; that is, there was no 'repayment' of the 'debt' incurred during the period of circulatory arrest. The same result was obtained when the left side was compressed, and the right side used as a control. When neither side was compressed the hyperaemia was of similar size in both forearms.

The results from all experiments of this type are shown in Fig. 2. The sizes of the black and white rectangles indicate the blood flow repayments following a 5 min period of arterial occlusion on the left and right sides respectively. The blood flow repayment has been calculated as the amount of blood flowing during the 10 min period following the release of the occlusion cuff in excess of the previous resting level. In the control runs in which arterial compression was not applied to either arm the repayments were reasonably symmetrical.

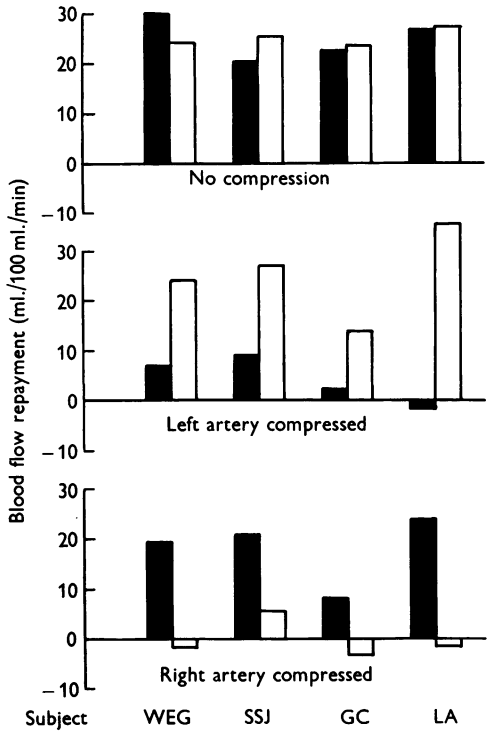

Fig. 2. The effect of restricting arterial inflow on reactive hyperaemia in the forearm. The rectangles represent the size of the hyperaemia after arrest of the circulation for 5 min in the left (■) and right (□) forearms. In the experiments illustrated in the top panel no arterial compression was applied. In those illustrated in the middle panel the left brachial artery was compressed for the first 5 min after circulatory arrest. In those illustrated in the lower panel the right brachial artery was compressed for the first 5 min after circulatory arrest.

These are illustrated in the top panel. The experimental runs are illustrated in the lower panels. In four of these eight runs where the brachial artery on one side was compressed there was no increase in flow on release of compression; in fact throughout the 10 min period after circulatory arrest the blood flow on the experimental side remained at a lower average level than the previous resting level. This is expressed as a 'negative repayment'. In the other four experiments on release of compression there was a small rise above the resting

level, but it can be seen that this repayment was always small compared with that on the control side.

Digital compression of the brachial artery might interfere with venous drainage from the forearm, causing venous congestion. This does not seem to have been the case since digital compression of the brachial artery did not cause any increase in the resting forearm volume; a small decrease was the usual finding. Inspection of the plethysmographic record showed that on release of the collecting cuff the limb volume rapidly returned to its resting level. There was no rise in venous pressure during compression in two experiments, in which venous pressure was measured with a capacitance manometer distal to the site of arterial compression. These findings indicated that com-

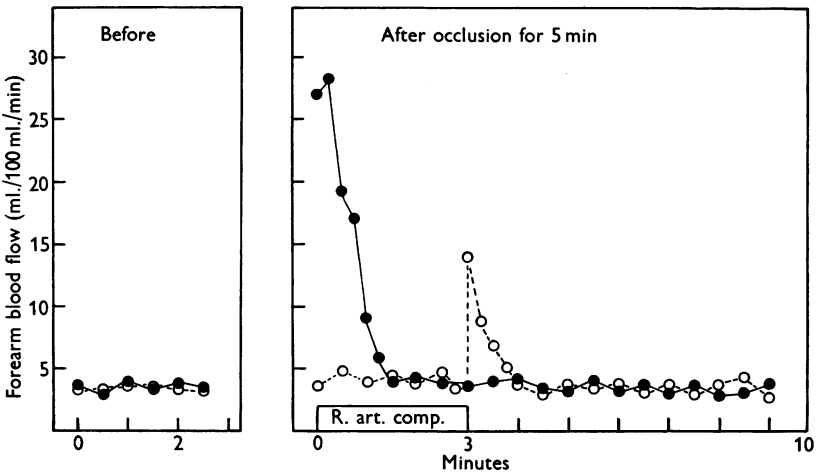

Fig. 3. The effect of compressing the right brachial artery for 3 min; conventions as in Fig. 1.

pression of the brachial artery did not cause venous congestion in the forearm and there was thus no reason for believing that the plethysmographic estimations of blood flow were not valid.

Following a 5 min period of circulatory arrest the reactive hyperaemia is normally over in 2–3 min, but in some of the experiments described above a small hyperaemia was seen after 5 min of restricted arterial inflow. This suggested that the resting rate of blood flow on the compressed side might take longer to restore the forearm to its previous resting state than the increased rate of flow in the control arm. To investigate this point a second series of experiments was carried out. As before, forearm blood flow was measured before and after bilateral arrest of the arm circulation for 5 min. In six successive runs the arterial inflow was restricted in the experimental arm for 0, 1, 2, 3, 4 and 5 min respectively, immediately after release of the circulation. Figure 3 illustrates a run from one of these experiments. On

release of restriction after 3 min a small hyperaemia was seen in the experimental limb although at this time the blood flow in the control forearm had returned to its resting level. The hyperaemia was much smaller than that on the control side but it was still greater than that usually found after 5 min

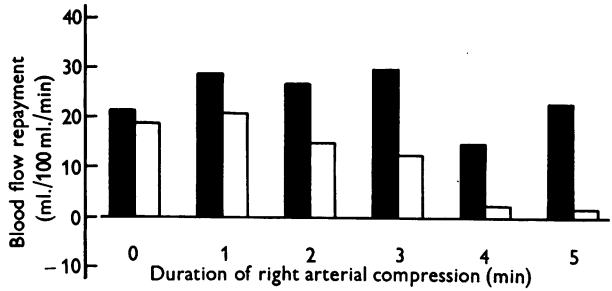

Fig. 4. The effect on the size of the subsequent hyperaemia of restricting arterial inflow to the right forearm for various times after arrest of the circulation for 5 min. ■ size of the hyperaemia in the control (left) and □ experimental (right) forearms.

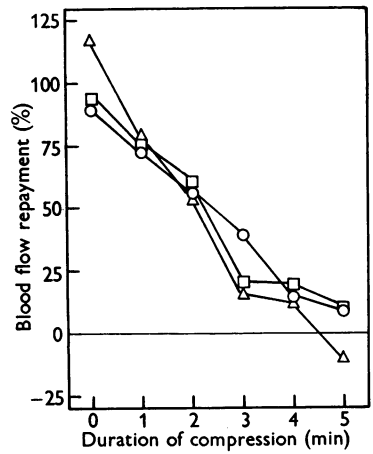

Fig. 5. The effect of restricting arterial inflow to the forearm for various times after arrest of the circulation for 5 min. The blood flow repayment in the compressed side is expressed as a percentage of that on the control side. ○, Subject I.C.R.; □, D.A.B.; △, W.E.G.

of restricted inflow. The results from the complete experiment are shown in Fig. 4. There was some variation in the size of the repayments on the control side, but there was a progressive fall in the size of the repayments on the experimental side relative to those on the control side as the restriction time was increased. In Fig. 5 the repayment on the experimental side in this and two other such experiments is expressed as a percentage of that on the control side. The size of the repayment in the experimental limb gradually decreased as the compression time was increased and after about 5 min of such compresions was practically zero. It is apparent that following a 5 min period of

arterial arrest the resting level of flow can discharge the blood-flow debt progressively over the next 5 min. It seems that the advantage of the high flows of a normal hyperaemia is that the blood-flow debt is discharged in about half the time.

Exercise hyperaemia

The same type of result was obtained in similar experiments on post-exercise hyperaemia. Figure 6 illustrates one of the experiments of the first series. In this and in most of the experiments in this group, the exercise

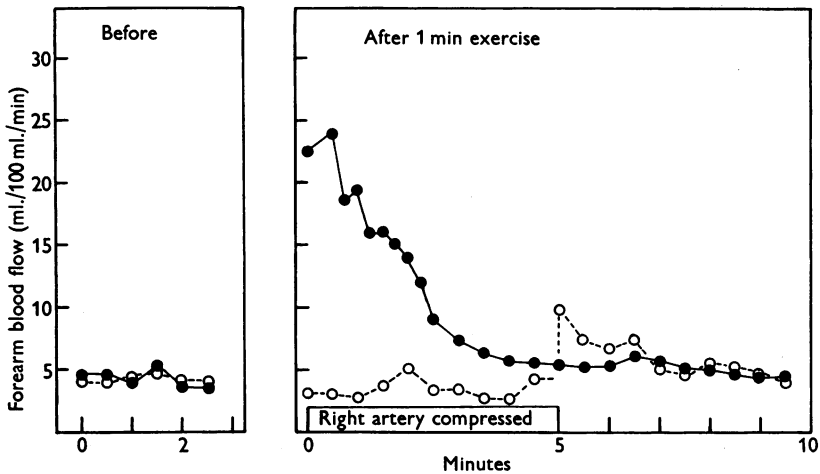

Fig. 6. The effect of compression of the right brachial artery on post-exercise hyperaemia in the forearm. Left panel, before exercise; right panel, after 1 min rhythmic exercise. Conventions otherwise as in Fig. 1.

hyperaemia lasted about 4 min on the control side. Once again there was only a small hyperaemia on the experimental side when the restriction was released after 5 min. The results from all the experiments in this series are shown in Fig. 7. In the control runs illustrated in the top panel arterial compression was not applied to either arm and the repayments were reasonably symmetrical; but it can be seen by comparison with Fig. 2 that they were much greater than the repayments after 5 min of circulatory arrest. The experimental results are illustrated in the lower panels. In all but one of the eight runs the repayments were much smaller on the side where arterial inflow had been restricted. These results indicate that it is not necessary to have an increase in blood flow after exercise to repay the debt incurred during exercise.

Figure 8 shows the effect of restricting the arterial inflow to the experimental limb for various times after exercise on the size of the repayment. Although the results of these three experiments were not as consistent as those of the reactive hyperaemia experiments, once again the size of the

repayment tended to decrease as the restriction time increased, though it was still not completely abolished after 5 min of restricted flow. It would seem that, had the compression been maintained for longer periods, the repayment might have been completely abolished. In the reactive hyperaemia experiments the blood flow on the normal side had returned to the resting level in

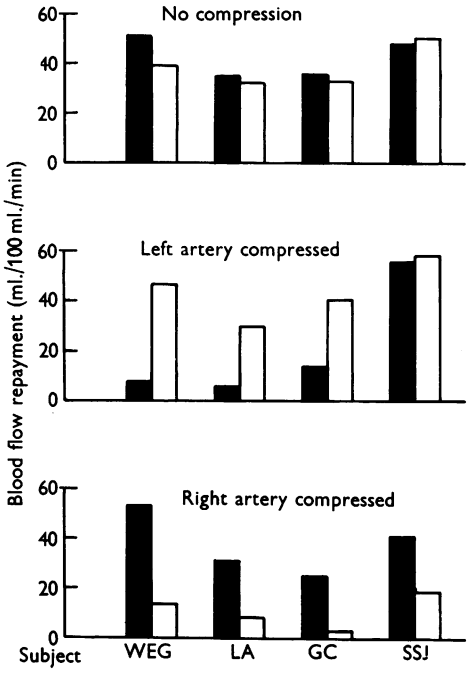

Fig. 7

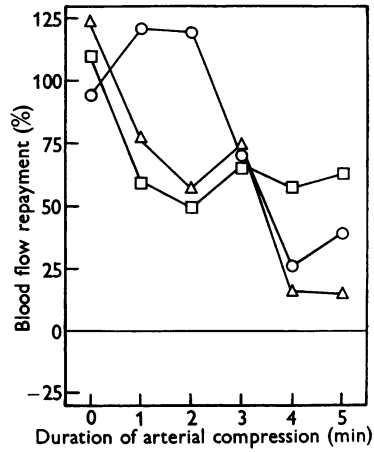

Fig. 8

Fig. 7. The effect of compression of the brachial artery on post-exercise hyperaemia in the forearm. The rectangles represent the size of the hyperaemia after 1 min rhythmic exercise in the left (■) and right (□) forearms. Top panel, neither artery compressed. Middle and bottom panels, left and right brachial arteries compressed respectively during the first 5 min after exercise.

Fig. 8. The effect of restricting arterial inflow to the forearm for various times after rhythmic exercise of the forearm for 1 min. The blood flow repayment on the compressed side is expressed as a percentage of that on the control side. Symbols for subjects as in Fig. 5.

2–3 min, and there was little or no repayment after 5 min of restricted flow. After 1 min of rhythmic exercise, the hyperaemia in the normal side took 4 min to subside; perhaps 8 min of restricted flow would have abolished the repayment.

The effect of brachial artery occlusion on the circulation in the resting forearm

When the brachial artery was occluded by digital compression (Fig. 6) there was an immediate reduction in the forearm blood flow. However, in spite of

compression maintained over the next 4 min the flow gradually increased to the previous resting level (Shepherd, 1950*b*). When the compression was released there was no increase in flow above the resting level. Similar results were obtained in six other experiments on four subjects. On release of compression in one experiment there was a transient increase in flow above the resting level but this was small compared with the 'debt' incurred during compression. The results indicate that under resting conditions the blood flow through the forearm is considerably higher than that required to satisfy the metabolic needs of the tissues. The flow can be lowered considerably without causing any metabolic disturbance.

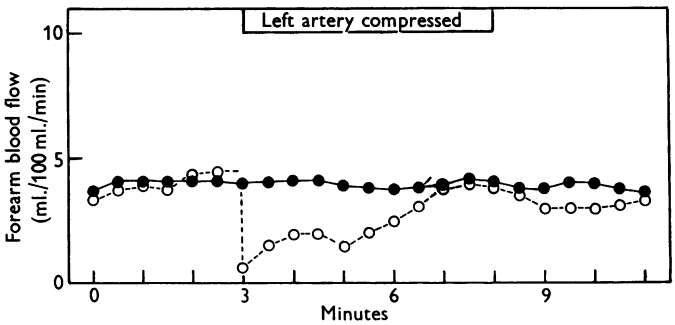

Fig. 9. The effect of brachial arterial compression on the blood flow in the forearm. Compression was applied to the left brachial artery during the period represented by the rectangle. ○, left forearm; ●, right forearm.

DISCUSSION

It is generally accepted that post-exercise hyperaemia is due to vasodilator metabolites produced during muscular contraction (Grant, 1938), and Hilton (1953) has found evidence that these metabolites act indirectly by initiating an axon reflex. There is less agreement however on the mechanism of reactive hyperaemia. One factor is believed to be the accumulation of metabolites which are normally washed away or destroyed by the circulation of the blood (Lewis & Grant, 1925). A second factor is thought to be the decrease in vascular tone that results from the fall in transmural pressure when the circulation is arrested (Bayliss, 1902; Folkow, 1949; Patterson, 1956). There is also some evidence that histamine may play a part in the hyperaemia after the circulation has been arrested for longer periods (Duff, Patterson & Whelan, 1955). The purpose of the present experiments, however, was not to investigate the mechanism of these two types of hyperaemia, but to study the relationship between the blood flow 'debt' during ischaemia or muscular exercise (the metabolic disturbance) and the size of the subsequent hyperaemia. As previously observed, some workers have found that there is a close relationship, and the assumption that the size of the hyperaemia indicates the

degree of metabolic disturbance has frequently been made in the interpretation of results of experiments designed to investigate the mechanism of reactive or post-exercise hyperaemia. Others have found that the relationship is by no means exact, and in the present experiments we have found that after exercise or ischaemia, the 'debt' can be discharged without the appearance of any hyperaemia. It is clear therefore that the degree of metabolic disturbance cannot be deduced from the changes in the volume of the hyperaemia if the local circulation has been affected by other conditions. One cannot say that because reactive or post-exercise hyperaemia is smaller in a cold limb or a limb with arterial obstruction that the metabolic disturbance is less than in the control limb. It appears that no particular volume of blood is necessary after a period of circulatory arrest and the excess volume that does flow depends on many things, including the prevailing perfusion pressure.

These experiments also show that the resting level of blood flow in the forearm is well in excess of the metabolic requirements of the tissues. Thus when the forearm blood flow was lowered by digital compression of the brachial artery no hyperaemia occurred on removal of the compression. This is in agreement with the findings of Holling & Verel (1957) who lowered the effective perfusion pressure in the forearm by elevating the limb, and found that on returning the limb to heart level there was no hyperaemia. These results are not surprising, since the blood vessels in the forearm are subjected to a high degree of nervous control, and the level of flow is varied in response to the body's needs in circulatory homoeostasis and temperature regulation. The blood flow 'debt' during a period of circulatory arrest is usually taken as (resting level of flow) $\times$ (time of arrest), but as the resting level of flow is in excess of the metabolic requirements this apparent debt must be greater than the real metabolic debt (metabolically determined flow $\times$ time). Furthermore, the amount by which the resting level exceeds the metabolic requirements is not taken into consideration when the 'repayment' is calculated (average flow in excess of resting level $\times$ time), and therefore this apparent repayment must be less than the real repayment (average flow in excess of the metabolically determined flow $\times$ time). It would seem that the traditional methods of calculating both 'debt' and 'repayment' are subject to an error, the size of which depends on the difference between the metabolically determined level and the resting level of blood flow. It is therefore not surprising that many discrepancies have been reported in the relationship.

It also follows that, after a period of circulatory arrest or exercise, any blood flowing in excess of the resting metabolic requirements can be used to restore the tissues to the resting state. This appears to be the explanation of the finding that the hyperaemia is abolished by restricting the flow to the previous resting level. It is clear, however, that the rate of recovery is much slower when the flow is restricted than when it is free. Thus in the reactive

hyperaemia experiments the tissues appeared to recover in $2\frac{1}{2}$–3 min with a free circulation, but needed about 5 min with restricted flow; and in the post-exercise experiments the respective times would appear to be 4 and 8 min. This indicates that the rate of recovery is dependent on rate of blood flow and the function of the high flows of the hyperaemia is to return the tissues to the resting state as quickly as possible. This is in keeping with the findings of Shepherd (1950*a*) and Edholm, Howarth & Sharpey-Schafer (1951) that the increase in blood flow following exercise in a limb with occlusive vascular disease had a smaller maximum and a greater duration than normal. It is also in agreement with the finding of Holling & Verel (1957) that reducing the size of post-exercise hyperaemia by elevation of the arm led to a prolongation of the hyperaemia.

However, Dornhorst & Whelan (1953) have shown that exercise or reactive hyperaemia can be reduced to some extent without prolonging its duration, and Holling & Verel (1957) obtained the same result with reactive hyperaemia. This would suggest that the rate of recovery is independent of the rate of blood flow but the reduced rate of blood flow in their experiments was much higher than the resting level of flow. It would appear that somewhere above resting level there is a rate of flow above which the rate of recovery becomes time-limited rather than flow-limited.

In conclusion, these results show that it is impossible to make deductions about the metabolic disturbance brought about by exercise or ischaemia from the volume of the subsequent hyperaemia, unless all other variables in the local circulation remain constant. Such deductions have frequently been made in the interpretation of results of experiments designed to investigate the mechanism of reactive or post-exercise hyperaemia. Such interpretations must only be made with considerable caution and in many cases are unjustified.

SUMMARY

1. Forearm blood flow was measured in four subjects before and after bilateral arrest of the arm circulation for 5 min.

2. In one forearm, immediately the occlusion cuff was deflated the blood flow was prevented from rising above the resting level by digital compression of the brachial artery for 1, 2, 3, 4 and 5 min. The size of the hyperaemia in the compressed side fell as the time of compression increased, and after 5 min there was usually no hyperaemia.

3. Similar observations were made after rhythmic exercise of the forearm for 1 min. The results were similar to those of the reactive hyperaemia experiments.

4. It is concluded that it is not necessary to have an increase in blood flow after circulatory arrest or exercise to 'repay' the 'debt' incurred during these procedures. It follows that no particular volume of excess blood flow is

necessary after a period of circulatory arrest or exercise and that the size of the hyperaemia might well vary with the prevailing state of the circulation. However, by supplying the tissues with an excess of blood the normal reactive and post-exercised hyperaemias return the tissues to the resting state more quickly than does the resting level of blood flow.

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