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THE REACTIONS OF THE BLOOD VESSELS OF THE HUMAN CALF TO INCREASES IN TRANSMURAL PRESSURE

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Following observations on dogs, cats and rabbits, Bayliss (1902) concluded that an increase in intravascular pressure, which increased the transmural pressure, acted as a mechanical stimulus to the smooth muscle cells in the walls of the vessels and resulted in a vasoconstriction, while a decrease in intravascular pressure led to a vasodilatation. These conclusions have been supported by the experiments of Folkow (1949, 1953) who has shown that in animals it is the resistance vessels which react in this way. Evidence is now accumulating that a similar mechanism operates in man (Patterson & Shepherd, 1954; Greenfield & Patterson, 1954; Wood, Litter & Wilkins, 1955; Coles & Greenfield, 1956; Patterson, 1956).

This response of the peripheral blood vessels to changes in transmural pressure probably plays a part in the adjustment of the circulation to gravity. Observations in man have been confined to the forearm and hand. The responses of the resistance vessels in the leg to increases in transmural pressure are of greater interest, however, as these vessels are normally subjected to larger increases in pressure than those of the arm. In the present experiments, therefore, the blood flow through the human calf has been measured plethysmographically following exposure of the leg to subatmospheric pressures of the same order as those employed by Greenfield & Patterson (1954) on the arm. The results of some of these experiments have already been briefly described (Coles, Kidd & Patterson, 1956).

METHODS

The subjects were three healthy men, and the observations were made in a laboratory at a temperature of 22–24° C. The subject rested on a couch for 30 min before any measurements were made. The blood flow was measured simultaneously in both calves by venous occlusion plethysmography (Barcroft & Swan, 1953). The right leg was used throughout as a control; the left leg and its plethysmograph were enclosed in a tank in which the pressure could be varied as desired (Greenfield & Patterson, 1954). The arrangement of the legs in relation to the tank and cuffs is shown in Fig. 1. The plethysmographs were filled with water, maintained at 35° C throughout the

experiment. The ankle cuffs were inflated to 250 mm Hg to arrest the circulation through the foot 1 min before flow measurements started. At least four measurements of resting flow were made before each pressure exposure. In each experiment the collecting pressure was that which gave the highest apparent rate of blood inflow; this was usually in the range 50–70 mm Hg. The air lead from the plethysmograph was then temporarily connected to the inside of the enclosing tank instead of to the float recorder and the pressure in the tank reduced to the desired level for the desired time. The plethysmograph lead was reconnected to the recorder as soon as the tank pressure returned to atmospheric, and the collecting cuffs were inflated for 12 sec in every 15 sec for the next 2½ min. The first inflation usually started 10–15 sec after the return of the pressure in the tank to atmospheric. Observation showed that the air in the transmitting system from the plethysmograph to the float recorded assumed, for practical purposes, a constant volume within

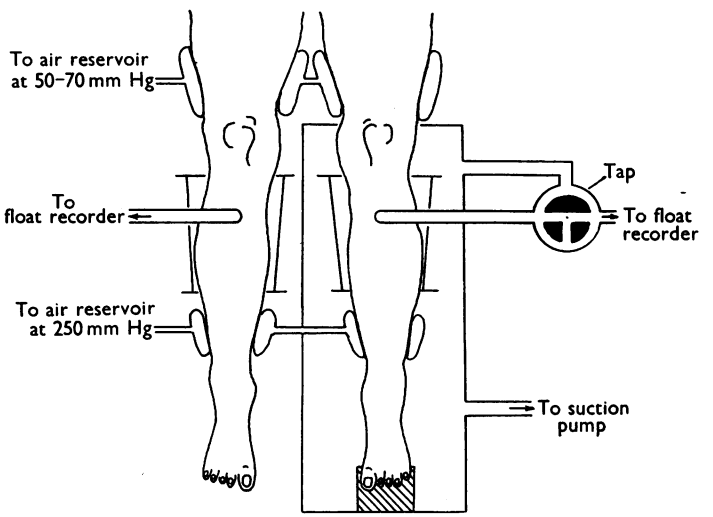

Fig. 1. Arrangement of the tank, plethysmographs and cuffs. The tap connects the plethysmograph air lead to either the float recorder or the inside of the tank.

5 sec of release of the pressure in the tank. The leg was exposed to pressures of 0 (blank experiments), 50, 100, 150 and 200 mm Hg below atmospheric for periods of 30 and 60 sec. A few observations were made after exposure of the leg to a pressure of 100 mm Hg below atmospheric for periods of 5 and 10 min. The pressure differing least from atmospheric was applied first; second and subsequent exposures were made only when examination of the recordings indicated that the flow in each calf had returned to a resting level.

A few measurements of the volume changes of the calf were made in the course of the present experiments. During these the ankle cuffs were inflated to 300 mm Hg throughout, and the position of the water meniscus in a calibrated tube attached to the plethysmograph was read, before, at 5 sec intervals during, and for 1 min after exposure of the leg to each pressure used in the blood-flow experiments.

RESULTS

The results are expressed as the percentage of the simultaneous flows through the control calf after making allowances for any lack of symmetry on the two sides before the exposure of the experimental calf to pressure changes (Greenfield & Patterson, 1954). Each of the three subjects (D.R.C., B.S.L.K. and

G.C.P.) was exposed on two occasions to the full range of pressures for both 30 and 60 sec. A typical series of plethysmographic recordings is shown in Fig. 2. The pressure in the tank enclosing the left (experimental) leg was reduced to 100 mm Hg below atmospheric (−100 mm Hg) for 30 sec. The rate of blood inflow to the right (control) leg remained almost unchanged, but that to the experimental leg was much diminished and returned only slowly to a steady level. The mean of four flows immediately preceding suction in the experimental calf was 6·0 ml./100 ml./min, and for the control side 5·0. After exposure the flows in the experimental calf were 1·5, 3·0, 5·5 and 5·9, and the corresponding flows for the control were 5·1, 5·1, 5·1 and 4·8. The calculated values of percentage blood flow after exposure are 25, 49, 90 and 102. In this example there was relatively little disturbance of the blood flow in the control

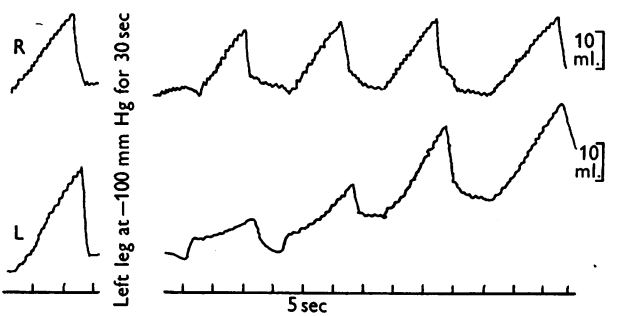

Fig. 2. A typical plethysmographic recording of blood flow through the right and left calves before and after exposure of the left leg to a pressure of 100 mm Hg below atmospheric for 30 sec.

leg and this was generally the case. In all experiments the changes in the absolute rate of blood inflow in the experimental calf were closely parallel to the changes in the percentage flow.

Fig. 3 shows the results of blank experiments in which the exposure was to 0 mm Hg below atmospheric pressure for 30 sec. As expected, the blood flow remained close to 100% after exposure.

Fig. 4 shows the results of all the experiments in which the left leg was exposed to subatmospheric pressures for 30 sec. Exposures to −50 mm Hg had little effect on the blood flow. Exposures to −100, −150 and −200 mm Hg were followed by a transient decrease in flow, the flow after −200 mm Hg being reduced by 55–75%; the flows then gradually increased, reaching the previous level in about 1 min following −100 mm Hg and in about 2 min following −200 mm Hg. Exposure to the same pressures for 60 sec (Fig. 5) gave similar results, except that the blood flow was reduced even more than after the corresponding pressures for 30 sec. This transient decrease in flow was fairly regular in all experiments.

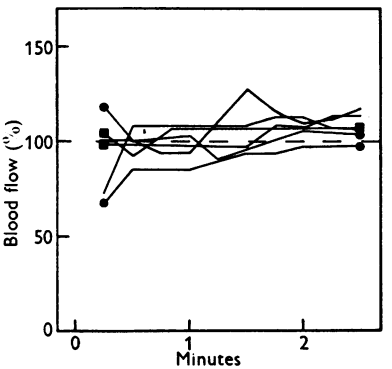

Fig. 3. Percentage blood flow following 'exposure' to atmospheric pressure only. Plain lines subject G.C.P., lines ending in solid circles D.R.C., and in solid squares B.S.L.K. Time in minutes from end of 'exposure'.

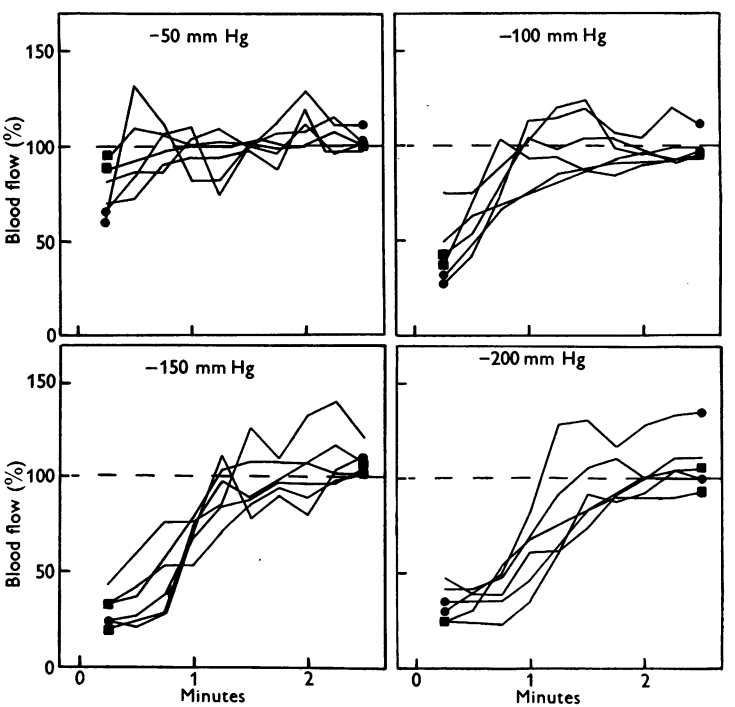

Fig. 4. Percentage blood flow following exposure to subatmospheric pressures for 30 sec. Conventions as in Fig. 3.

In one experiment on each of two subjects the leg was exposed to −100 mm Hg for periods of 5 and 10 min. The decrease in flow after such exposure was similar to that seen following exposure for 1 min.

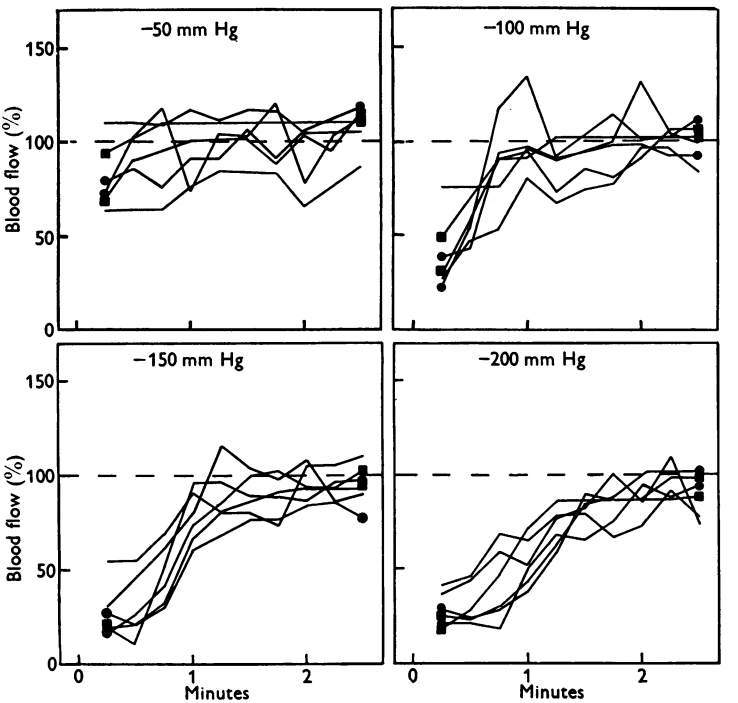

Fig. 5. Percentage blood flow following exposure to subatmospheric pressures for 60 sec. Conventions as in Fig. 3.

Evidence that the reduction in inflow depends upon the distension of the blood vessels of the calf

If the circulation to the leg is arrested for 1 min by inflating a thigh cuff to 350 mm Hg, on exposure of the leg to −100 mm Hg no blood can enter and distend the vessels. On release of the circulation the reactive hyperaemia is no different from that following simple arrest of the circulation (Fig. 6A, B); but if the leg is exposed to −100 mm Hg and the circulation in the distended vessels is then arrested for 1 min the reactive hyperaemia is abolished, whether or not the exposure to −100 mm Hg is continued (Fig. 6 C, D). From these experiments it is concluded that the reduction in blood flow following suction depends upon the distension of the blood vessels of the calf and is independent of the effects of reduced pressure on other structures of the limb.

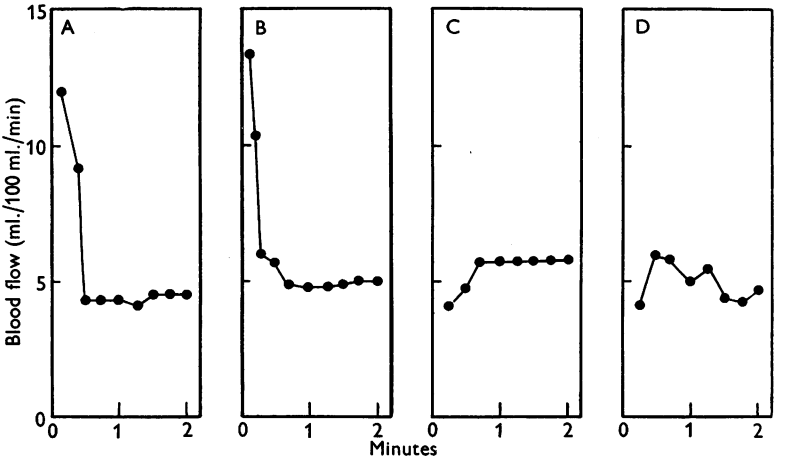

Fig. 6. A comparison of the effects during the subsequent 2 min on the blood flow through the calf after: A, arrest of the circulation through the calf for 1 min; B, exposure of the leg to −100 mm Hg for 1 min during arrest of the circulation for the same minute; C, arrest of the circulation for 1 min in a leg distended with blood by suction at −100 mm Hg for the previous minute; D, arrest of the circulation for 1 min in a leg distended with blood by suction at −100 mm Hg for the previous minute, with the suction continuing during the minute of arrest.

Sensations

At pressures of 50 and 100 mm Hg below atmospheric the leg is felt to fill up but is not uncomfortable. At −150 mm Hg the sensation is mildly unpleasant, and at −200 mm Hg the leg feels very tense.

Volume changes

During exposure to subatmospheric pressures the volume of the calf within the plethysmograph increased and water was displaced from the plethysmograph to a calibrated side tube. The increase in the volume of the calf could therefore be measured directly. The increase in volume included an artifact due to movement of the leg relative to the plethysmograph. To measure this artifact the cuffs shown in Fig. 1 were inflated to 350 mm Hg; exposure to subatmospheric pressure caused a rapid initial increase in volume due to movement, followed by a very slow increase presumably due to leakage of blood past the cuff. It was assumed that the volume changes in the first 5 sec of exposure to subatmospheric pressures and in the first 5 sec after release of the pressures were due to, and represented the whole of, the tissue movement relative to the plethysmograph. The mean volume changes due to movement were 0·20, 0·40, 0·46 and 0·53 ml./100 ml. of calf tissue during exposures to −50, −100, −150 and −200 mm Hg respectively. Provided the heel had a firm abutment the volume artifact due to movement was both small and

constant, and thus the increase in volume of the calf during exposure to suction, which was of the order of 5–10 ml./100 ml., could be determined. Fig. 7 shows the volume changes for D.R.C. during and after exposure to subatmospheric pressures for 60 sec. Each point is the mean of two observations. During exposure the volume rapidly increased for the first 15 sec at all pressures, more rapidly with −200 mm Hg than with −100 mm Hg. Thereafter the increase was slow. Following exposures to −50, −100 and −150 mm Hg the calf volume had returned to a steady level, within 0·25% of the resting level, by 15–30 sec. After −200 mm Hg there was a persistent residual volume increase of 0·9%. The cause of this is not known; it may be due to the accumulation of blood or of tissue fluid.

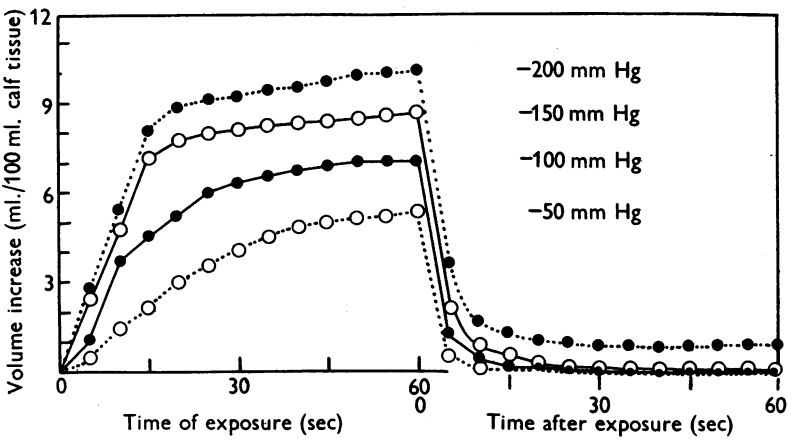

Fig. 7. Volume changes during and after exposure to subatmospheric pressures for 60 sec: each curve is the mean of two experiments.

DISCUSSION

The validity of the observations of reduced inflow

During exposure to subatmospheric pressure the veins and other capacity vessels are distended. If this distension persisted, the rate of inflow as measured by the venous occlusion plethysmographic method might be an underestimate of the true rate of inflow. At the time, 15–30 sec after exposure to −50, −100 and −150 mm Hg, when the lowest flows were recorded, the volume of the limb had reverted to a steady level, within 0·25% of the resting value (Fig. 7). From then onwards the volume was almost constant but the flows progressively increased. After exposure to −200 mm Hg, there was a persistent residual volume increase which was for D.R.C. 0·9% and for B.S.L.K. 0·75%. Coles & Kidd (unpublished), however, have shown that increases of calf volume of as much as 1·5%, brought about by venous congestion, have no significant effect on the apparent rate of blood inflow. It is concluded that in

the present experiments any residual venous distension was insufficient to invalidate the measurements of blood flow. These observations therefore show that following exposure of the leg to pressures of from 100 to 200 mm Hg below atmospheric, the blood flow through the calf is reduced. The reduction in blood flow is a local reaction, since simultaneous observations on the opposite leg failed to show any major circulatory disturbance. The reduction is seen only when the vessels are allowed to become distended during suction, and is therefore not due to the effects of reduced pressure on other structures in the limb.

During the blood-flow measurements the perfusion pressure and viscosity of the blood in the two limbs is presumed to be similar; hence the reduction in blood flow, seen in the experimental leg following suction, must indicate an increase in the local peripheral resistance resulting from a vasoconstriction.

Decreasing the local atmospheric pressure increases the differential pressure between the lumen of the blood vessels and the surrounding air by an equal amount. The pressure in the tissues follows closely the local atmospheric pressure (Coles, Greenfield & Kidd, unpublished). Thus the differential pressure across the walls of the blood vessels, or transmural pressure, is increased by very nearly the same amount as the atmospheric pressure is decreased.

The calibre of the blood vessels depends on a balance between transmural pressure, tending to dilate the vessel, and the wall tension tending to constrict it. The present experiments give no information concerning the reaction of the blood vessels of the calf during exposure to subatmospheric pressures. It may be that the reaction in the vessel wall is strong enough to cause a vasoconstriction while the suction is applied. However, Coles & Greenfield (1956) and Coles (1956) have made calorimetric observations on the hands and feet during local exposure to subatmospheric pressures of the same order as those used in the present experiments. They have shown that during exposure to -100 mm Hg there is little alteration in the rate of heat elimination from the hands and toes, and from this they concluded that there is little alteration in the calibre of the blood vessels. This suggests that there is a local mechanism causing an increase in the contractile force in the walls of the blood vessels just sufficient to oppose the greater transmural pressure. On sudden removal of the increase in pressure, a persistence of this contractile force would lead to the vasoconstriction seen in our present experiments. The evidence concerning the responses of the human blood vessels to increases in transmural pressure is, however, fragmentary, and it is possible that the resistance vessels of the hand and foot differ in their responses to increases in transmural pressures from those of the calf.

The vasoconstriction in the calf following exposures to subatmospheric pressures is similar to that observed in the forearm by Greenfield & Patterson (1954). Within the range of changes in transmural pressure likely to be

encountered in the forearm under normal conditions, the forearm vessels have a slightly more marked vasoconstrictor response than those of the calf. Within the range of changes in transmural pressure likely to be encountered in the calf, the calf vessels react more regularly and more strongly than those of the forearm. They are also more able to withstand very large increases in transmural pressure, since exposure of the leg to −200 mm Hg was invariably followed by a vasoconstriction whereas exposure of the forearm was frequently followed by a prolonged vasodilatation. Petechial haemorrhages were not seen after any of the present exposures, while they were seen after exposure of the forearm to the same pressures. The sensations were much less unpleasant than in the forearm.

The present experiments throw no light on the mechanism of the local response to increases in transmural pressure. Patterson & Shepherd (1954) showed that the blood flow through the forearm is regularly decreased below the resting level following congestion of the veins for 5 min by inflation of a cuff around the upper arm to 80–110 mm Hg. This reaction was similar in normally innervated, sympathectomized and apparently completely denervated arms. From these observations they concluded that the contractile response was independent of the nervous pathways which had been interrupted. Although their results do not rule out the possibility of a humoral mechanism, they can be readily explained as a direct response to a mechanical stimulus of the muscular elements in the walls of the resistance vessels as was first suggested by Bayliss in 1902. Such an explanation may account for our present findings.

SUMMARY

1. The rate of blood flow through the calves of both legs has been measured after exposure of one leg to pressures of 50, 100, 150 and 200 mm Hg below atmospheric for periods of 30 and 60 sec.

2. After exposure to −100, −150 and −200 mm Hg for 30 and 60 sec there was a reduction in blood flow due to a local vasoconstriction. After exposures to −50 mm Hg there was little alteration in the rate of blood flow. The rate of blood flow in the control calf was little changed in any experiment.

3. Evidence is presented to show that this reaction depends on the distension of the blood vessels of the limb.

4. It is concluded that the vasoconstriction is a response to the increase in transmural pressure produced by increasing the differential pressure between the lumen of the blood vessels and the outside air.

5. The range of pressures to which the vessels of the calf react differs from that to which the vessels of the forearm react, but corresponds to the transmural pressures likely to be encountered in the calf under normal conditions of life.

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