ARTERIAL TONE DURING PROLONGED HYPOTENSION CAUSED BY BLOOD LOSS

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Prolonged hypotension produced in dogs by blood loss leads to a marked increase in the tone of the blood vessels of the limbs, kidneys, and intestine, which persists until the time of death of the animals. The author considers that the maintenance of arterial tone in the late phase of hypotension is due mainly to humoral rather than nervous factors.

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The phenomenon of vascular spasm and increased vascular tone during blood loss is not now disputed. It was Wiggers [10] who pointed out originally that the body's first response to blood loss is an increase in the vascular resistance. It is uncertain, however, how long this spasm persists and whether it is replaced by vasodilatation during the development of the decompensation preceding death.

Petrov and Vasadze [1] consider that in the late phase of shock and blood loss an inhibition of vascular tone develops soon after disturbance of the reflex control of the circulation. Hardaway [5] associates the development of the essential changes in shock with a hypothetical paralysis of the arterioles, previously in a state of spasm. Rothe and co-workers [7] found in experiments on dogs that in the early phase of hypotension, when the arterial pressure was 50 mm, the total peripheral vascular resistance was doubled, but in the course of hypotension it fell with a decrease in the cardiac output.

Growell and Guyton [4] consider that the role of the vessels in the development of irreversible changes is less important. In their experiments with prolonged blood loss the peripheral vascular resistance remained unchanged.

In the present investigations the arterial tone was studied in the limbs, intestine, and kidneys during prolonged hypotension.

EXPERIMENTAL METHOD

Experiments were performed on dogs anesthetized with urethane (0.3 g/kg) and chloralose (0.05 g/kg). Clotting of the blood was prevented with heparin. The vascular resistance was measured by Khayutin's method [2]. The artery to be investigated was perfused with blood by means of a pump delivering blood at a constant volume velocity throughout the experiment. The pressure at the outlet of the pump reflected

TABLE 1. Perfusion Pressure (as percentage of initial value) during Prolonged Hypotension Caused by Blood Loss (arterial pressure 40 mm), M ± m

Vessel perfused	Immediately after blood loss	Time after blood loss (in h)						
		1	2	3	4	5	6	7
Art. femoralis (n=11)	130±7	133±9	126±7	141±9	154±5	157±4	155±8	
Art. renalis (n=6)	197±12	183±19	174±21	196±31	207±18			
Art. mesenterica superior (n=6)	157±10	173±22	210±14	155±4				

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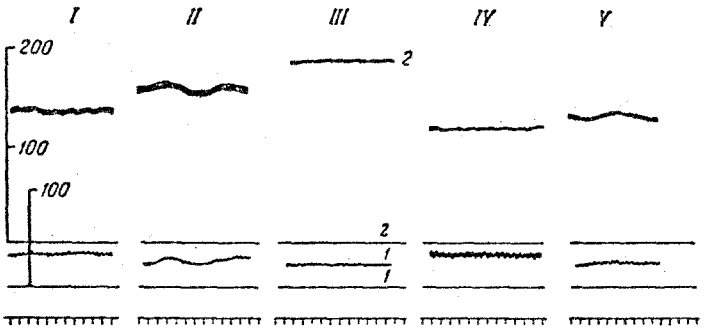

Fig. 1. Perfusion pressure in superior mesenteric artery during prolonged hypotension. I) Immediately after blood loss; II) 1 h; III) 3 h after blood loss; IV) after addition of diluted blood to reservoir; V) 4 h after blood loss. 1) Arterial pressure and its zero line; 2) perfusion pressure and its zero line. Time marker 5 sec. Scale for pressure on the left (in mm).

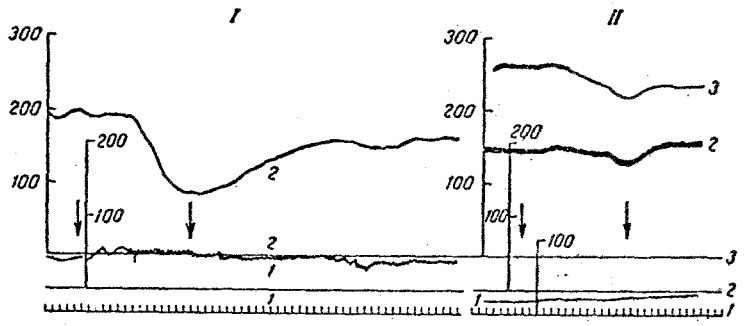

Fig. 2. Reaction of vessels to intra-arterial injection of polyglucin (I) and blood (II). I: 1) arterial pressure and its zero line; 2) perfusion pressure in femoral artery and its zero line. Time marker 5 sec. Arrows denote beginning and end of injection. II: 1) arterial pressure and its zero line, time marker 5 sec; 2) perfusion pressure in femoral artery of denervated limb and its zero line; 3) perfusion pressure in femoral artery of intact limb and its zero line. Arrows denote beginning and end of injection. Scale for pressure on the left (in mm).

changes in vascular tone. Blood entered the pump through a catheter inserted into the abdominal aorta. The arterial and perfusion pressures were recorded with mercury manometers. Prolonged hypotension was produced by Wiggers's method. The blood was collected in a special reservoir, joined by a catheter to the iliac artery. The pressure in the reservoir balanced the pressure in the aorta and was kept at 40 mm. The blood loss amounted to 30-40 ml/kg. At hourly intervals during the experiment all these indices were recorded. At the same time tests were carried out to determine the state of the vessels: the magnitudes of the pressor carotid sinus reflex, the response to injection of adrenalin (1 ml of a 10^{-5} dilution), and the reaction to intra-arterial injection of blood or blood substitutes was determined. The values of the perfusion pressure were expressed as percentages of its initial value.

EXPERIMENTAL RESULTS AND DISCUSSION

The periods of survival of the animals varied within very wide limits (from 3 to 7 h).

As the blood was withdrawn and the arterial pressure fell, the arterial tone in all investigated regions increased and remained high throughout the period of hypotension, until the onset of an agonal state. The highest increase in perfusion pressure was observed in the renal vessels (Table 1).

TABLE 2. Perfusion Pressure (as percentage of initial value) in Femoral Artery of Normal and Denervated Limb during Prolonged Hypotension Caused by Blood Loss (arterial pressure 40 mm), M ± m

Limb	Immediately after blood loss	Time after blood loss (in h)		
		1	2–3	4–5
Normal (n = 5)	139±15	143±28	158±19	142±14
Denervated (n = 5)	120±16	142±23	165±21	182±17

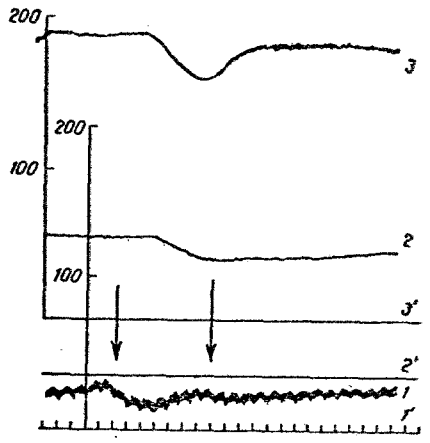

Fig. 3. Changes in pressor carotid sinus reflex during prolonged hypotension. Trace made 4 h after beginning of hypotension. 1) Arterial pressure and its zero line, time marker (5 sec); 2) perfusion pressure in femoral artery and its zero line; 3) perfusion pressure in superior mesenteric artery and its zero line. Scale for pressure on the left (in mm). Time of compression of both carotid arteries indicated by arrows.

The results of our experiments differ somewhat from those obtained by Abel and Murphy [3], who, after a blood loss of 20 ml/kg, found that the resistance of the renal vessels increased by 85%, the limb vessels by 130%, and the intestinal vessels by 75%.

In the initial stage of hypotension, a certain volume of blood passed from the animal's arterial system into the reservoir until a state of equilibrium was established, which lasted for 1.5-2.5 h, after which blood again began to leave the reservoir. The greatest increase in vascular resistance was observed both in the initial period and in the terminal state, when all the blood from the reservoir had reentered the dog's blood vessels. This process was not reflected in Table 1, which gives the mean values, because changes in vascular resistance developed at different times in different animals, and when the mean values were calculated these did not appear. They are more marked when each experiment is considered separately.

An experiment in which a dog's superior mesenteric artery was perfused is illustrated in Fig. 1. To maintain the arterial pressure (Fig. 1, IV), 150 ml of blood diluted with an equal volume of physiological saline was introduced into the reservoir. As a result, the arterial pressure rose to an assigned level but the perfusion pressure fell and became lower than immediately after the blood loss. After 4 h the diluted blood left the reservoir and the arterial pressure rose again, but did not reach its level 3 h after blood loss. The changes in perfusion pressure during lowering of the arterial pressure in the stage of decompensation and in response to the entry of diluted blood into the animal's vascular system demonstrate that the control of arterial tone remained intact even in the late stage of hypotension.

In every case when the test of intra-arterial injection of small volumes of blood or blood substitutes was carried out, a depressor reaction in fact was observed (Fig. 2), while in the case of dilution of the blood and a decrease in its oxygen capacity, the perfusion pressure remained at lower levels although the arterial pressure was the same. A rapid decrease in the resistance of the mesenteric vessels in response to blood transfusion during hypotension was observed by Selkurt and Brecher [8].

Meanwhile, during hypotension, the pressor carotid reflex showed the fluctuating changes described by I. R. Petrov and his school, indicating disturbance of central control of the blood vessels (Fig. 3).

To determine the role of the nervous system in the regulation of vascular tone, experiments were carried out during which both femoral arteries were perfused, one of the arteries having been isolated from the nervous system by division of the femoral and sciatic nerves and also of the artery itself. The level of the perfusion pressure after denervation was taken as the initial pressure for the denervated limb (Table 2).

As Table 2 shows, the reaction of the blood vessels of the denervated limb was somewhat smaller immediately after blood loss, when it was indistinguishable from normal, and in the terminal stage it actually exceeded normal. The depressor reaction to intra-arterial injection of blood and blood substitutes remained after denervation. The decrease in perfusion pressure in the vessels of the normal and denervated limbs after injection of 50 ml blood is shown in Fig. 2, II. In the course of hypotension it is evident that the nervous

regulation is disturbed, and humoral influences on the blood vessels become predominant. As shown previously [9], hypotension and acidosis in shock act as a stimulus for an increased secretion of adrenalin. Renin is also of great importance in the development and maintenance of vascular spasm [6]. Other biologically active substances appearing in the tissues naturally also play a role in these changes.

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