FEATURES DISTINGUISHING THE DEVELOPMENT OF HEMORRHAGIC COLLAPSE DURING HYPERTHERMIA

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Hyperthermia is one of the unfavorable factors which may complicate the course of hemorrhagic collapse [1, 3, 5]. The mechanism of the "increased sensitivity to blood loss at high temperature requires appropriate experimental investigation" [3].

The object of the present investigation was to study some of the hemodynamic, hematological, and biochemical aspects of the mechanism of development of hemorrhagic collapse against the background of hyperthermia.

EXPERIMENTAL METHOD

Experiments were carried out on 75 dogs weighing 13 ±1 kg. In the experiments of series I, acute blood loss was produced in 45 animals in normothermic conditions, and in those of series II in hyperthermic conditions, by withdrawing blood through a cannula from the femoral artery at the rate of 1%/kg body weight/min until the arterial pressure was stabilized at 10-20 mm. The lost blood was replaced by intravenous or, in the case of resuscitation, intraarterial transfusion of the blood of the experimental animals or of a blood substitute (hemoliquorin) possessing high osmomolar and protein-replacing properties [2]. The animals were heated for 51 ±2 min under a well ventilated electric heater producing an air temperature of 40-45° until their rectal temperature had risen by 1.6 ±0.1°. The conditioned (natural food) reflexes and the pupillary, corneal, swallowing and pain reflexes of the experimental animals were investigated. The changes in the frequency and amplitude of the cardiac contractions and respiratory movements, and in the arterial and venous pressure were recorded by a kymographic method, and the ECG was recorded in standard leads. The velocity of the blood flow was determined by the cytisine method, and the true circulating blood volume by dilution of the dye T-1824 (with the FEK-M photoelectric colorimeter). The theoretical (estimated) blood volume was calculated as the difference between the volume of blood lost and the original true circulating blood volume. The difference between the true and theoretical volumes of circulating blood (plasma) gave an indication of the volume of blood stored in depots and the volume of tissue fluid brought into or excluded from the circulation in the stage of hemorrhagic collapse. The ordinary methods were used to investigate the principal hematological changes. The blood protein concentration was determined by the refractometric method and the protein fractions by electrophoresis on paper. From the concentration of total protein and the protein fractions and knowing the true volume of plasma, the total mass of circulating proteins could be calculated. Besides this, the theoretical mass of proteins in the estimated volume of circulating plasma was calculated. The state of the permeability of the vascular wall was judged by the difference between the theoretical and true amounts of the plasma proteins, for the rapid increase of the protein deficiency in the period of hemorrhagic collapse, after the blood loss has ceased, is due to the escape of the blood proteins through the vessel walls into the intercellular space. Determinations were also made of the blood sugar (by the Hagedorn-Jensen method), the total cholesterol (by the method of Mrskos and Tovarek), and the alkaline reserve (by Van Slyke's method). The internal organs of the dying animals were investigated by the usual histological methods. The numerical results were analyzed by statistical methods.

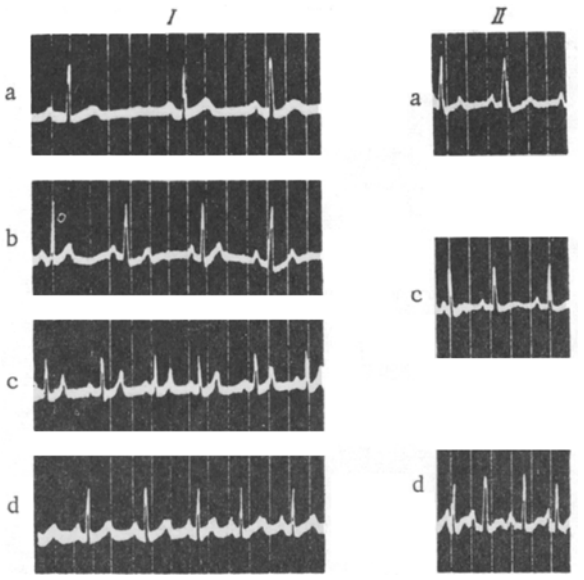

Fig. 1. ECG_2 curves of dogs following acute massive blood loss in normothermic (II) and hypothermic (I) conditions. a) Initial state; b) hyperthermia; c) collapse (high, pointed T wave against the background of hyperthermia, and low T wave against a normothermic background); d) 3 h after blood transfusion.

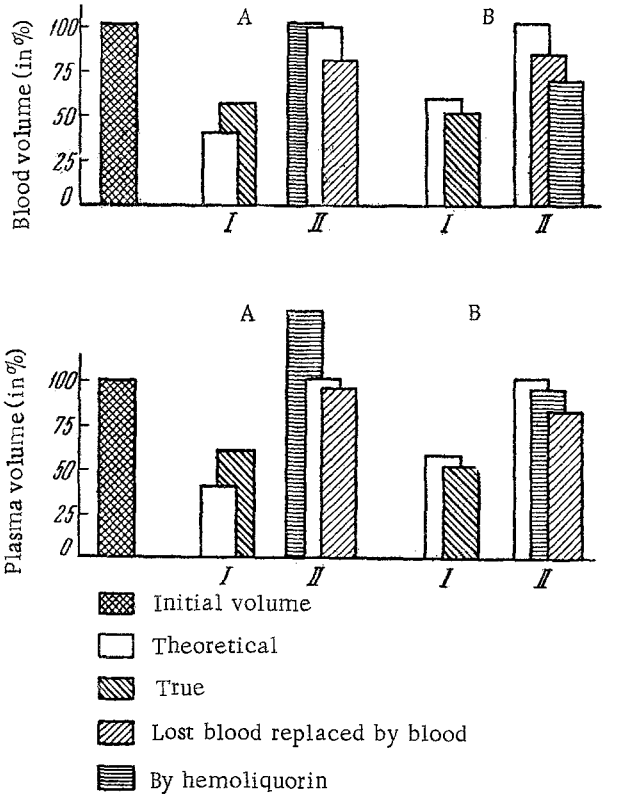

Fig. 2. Changes in volume of circulating blood and plasma after acute massive blood loss (I) and subsequent replacement (II) in normothermic (A) and hyperthermic (B) conditions.

EXPERIMENTAL RESULTS AND DISCUSSION

In hyperthermic conditions the animals developed severe hemorrhagic collapse after a smaller blood loss (3.80 ±15%/kg) than in normothermic conditions (4.30 ±0.15%/kg, $P = 0.05$). In these circumstances most of the heated animals died within 14 ±1 min after the start of hemorrhagic collapse as a result of paralysis of the respiratory center, whereas during blood loss in normothermic conditions the terminal period lasted more than twice as long (32±7 min, $P < 0.05$). The rapidly developing extinction of the conditioned, the pupillary, the pain and, frequently, the corneal reflexes demonstrated the earlier (compared with the controls) exclusion of the functions of the various parts of the brain: from the cerebral cortex to the medulla. In the period of hemorrhagic collapse weakness of the cardiac activity developed rapidly, as shown by an increase in the pulse rate, a lowering of the amplitude of the cardiac contractions and the voltage of the R wave on the ECG, and also a decrease of the Q-T and R-R intervals, and often by inversion of the T wave and a change in its apex, which became pointed. The ECG_2 of the dogs illustrating the special features of the T wave may be seen in Fig. 1. Since the pointed T wave persisted after transfusion of the autologous blood of the experimental animals, when the myocardial hypoxia was eliminated, it is justifiable to attribute the changes in the T wave to a toxemic factor in the hyperthermic organism. The development of toxemia during hyperthermia is confirmed by data in the literature [4].

Consequently, during acute blood loss against the background of hyperthermia, myocardial hypoxia was complicated by the influence of a toxic factor. As a result of the blood loss associated with hyperthermia the animals' arterial pressure fell sharply—to 9 ±1%—and the venous pressure fell less severely—to 81 ±7% of the original level. The velocity of the blood flow at the height of the blood loss in hyperthermic conditions was slowed, as it was in the control animals, by more than 50%. In the period of hemorrhagic collapse against the background of hyperthermia the true volume of the circulating blood, plasma, and erythrocytes was much smaller (by 8, 6, and 9% respectively) than the theoretical volume, whereas in normothermic conditions the true volume of the blood, plasma, and erythrocytes, on the contrary, was greater than the theoretical (by 14, 19, and 8% respectively). Hence it follows that in the period of hemorrhagic collapse against the background of hyperthermia new mechanisms develop, which aggravate

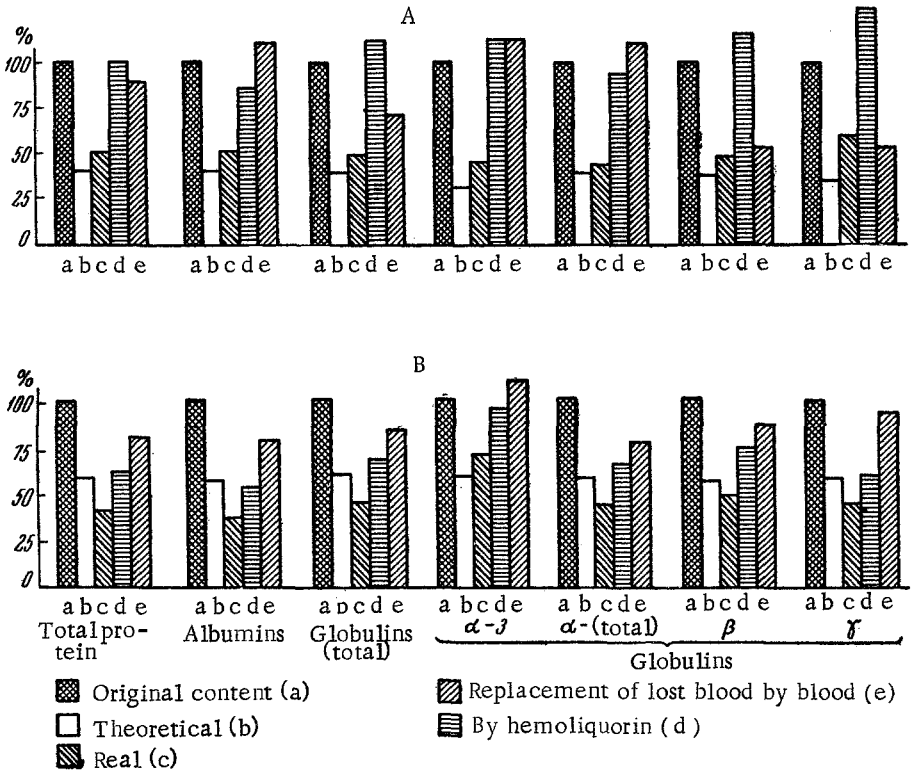

Fig. 3. Changes in total content of circulating protein and its fractions after acute massive blood loss and its replacement in normothermic (A) and hyperthermic conditions (B). a) Initial state; b, c) collapse; d, e) recovery period.

the deficit of circulating blood and plasma on account of the retention of blood in the depots, the pathological impounding of blood in the depots, and the transudation of plasma from the blood stream. Data are given in Fig. 2 which illustrate the course of the changes in the volume of circulating blood and plasma.

In the period of hemorrhagic collapse against the background of hyperthermia a lowering of the hemoglobin level and pancytopenia were observed, with an ill defined eosino-, lymphocyto-, and monocytopenia and a neurophilia with a slight nuclear shift to the left, whereas in the control animals a marked nuclear shift to the left was present (an increase in the number of stab cells to 11 ±1%) without eosinopenia. After blood loss against the background of normothermia and hyperthermia the ESR and the clotting power of the blood (by Burcher's method) were elevated. However, the degree of hydremia of the animals was much smaller in hyperthermic conditions than in the control experiments (the hematocrit reading was reduced respectively from 47 ±1 to 45 ±1 and from 46 ±1 to 41 ±1 vols. %). After blood loss in hyperthermic conditions a hypoproteinemia developed, with a relative increase in the blood concentration not only of the α_3-globulins, as in normothermia, but also of the β-globulins. The A/G ratio fell (from 0.8 to 0.7), whereas in normothermic conditions it remained at the initial level. It is clear from Fig. 3 that in acute blood loss against the background of hyperthermia, in contrast to the control experiments, the actual content of total protein, albumins, and α-, β-, and γ-globulins was below the theoretical (by 11, 20, 15, 10, and 15% respectively). Only the true mass of the α_3-globulins exceeded the theoretical value in normothermic (by 5%) and hyperthermic (by 10%) conditions. The decrease in the mass of total protein, albumins and, in particular, of coarsely dispersed globulins (α-, β-, and γ-fractions) by a larger margin than their amount lost as a result of the bleeding suggests that the increased deficit of plasma proteins may be explained by their escape from the blood stream on account of the increased permeability of the vessel wall, whereas in normothermic conditions the opposite processes developed—the return of the reserve proteins into the blood stream (see Fig. 3). The development of hyperglycemia and hypercholesteremia and the decrease in the alkaline reserve after acute blood loss were similar when accompanied by normothermia or hyperthermia.

After blood transfusion (osmomolarity of blood plasma 310 meq/liter) 12 of the 15 control dogs survived for a long time, giving a survival rate twice as high as that of the animals subjected to hyperthermia before the blood loss

and also treated by blood transfusions. After infusion of the blood substitute (osmomolarity 510-530 meq/liter) 23 of the 30 control animals survived for a long time, compared with 8 of the 15 dogs in the series of experiments with hyperthermia. It is clear, therefore, that the survival rate of the animals in both series of experiments was identical ($P > 0.05$). The early morphological changes, discovered during the first 48 h after blood transfusion, of the type of fatty degeneration (in the liver and kidneys) and focal necrosis (in the liver), more clearly marked in the experimental animals, suggest that hepato-renal insufficiency is concerned in the cause of death after acute blood loss in hyperthermic conditions.

Hence the lowering of the animal's resistance to acute blood loss in hyperthermic conditions is associated with the development not only of hypoxia of the central nervous system, respiratory failure, cardiac weakness, and vascular hypotonia, but also of a whole group of pathogenetic factors complicating the issue, such as toxemia, retention of blood in the depots, the formation of pathological blood depots, transudation of the blood plasma, and diffusion of the plasma proteins from the blood vessels into the intercellular space, an increase in the permeability of the vascular membranes, inhibition of the hydremic reaction, and hepato-renal failure.

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