However, the greatest changes took place in the region of maximal damage caused by nephritis, namely in the renal cortex, for that is where the largest quantities both of fibrin and of denatured, degraded proteins, which may also focus TPA, are found [9]. FA in the renal cortex was increased by almost 300%, whereas in the medulla it was increased by only 12%. FA increased a little in other tissues, also showing some changes as a result of the development of experimental nephritis, after injection of the preparation. A significant increase in FA in the liver tissue, where usually none is found in either affected or healthy animals, after injection of TPA is evidence of the important role of the liver in metabolism of the enzyme.

The TPA preparation obtained from the culture fluid of calf kidney, after injection into the blood stream of animals with experimental nephritis, thus restores normal values of parameters of hemostasis and fibrinolysis in the blood. The lowered FA in the renal cortex also is restored to normal.

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BLOOD RHEOLOGIC DISTURBANCES IN SHOCK OF VARIED ETIOLOGY

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UDC 616-001.36-07:616.151.4-07

KEY WORDS: blood rheology; hemorrhagic, traumatic, and burn shock.

One of the basic signs in the pathogenesis of shock of whatever etiology is a disturbance of the circulation leading to reduced tissue perfusion and the development of anoxia. Under these circumstances, substantial changes are found in the rheologic properties of the blood [1, 2, 5, 6]. The study of rheologic disturbances of the blood and their dependence on the etiology of shock is important for the elucidation of their role in the mechanism of the circulatory disturbance under extremal conditions.

The aim of this investigation was a comparative study of the rheologic properties of the blood in the stage of relative compensation and decompensation of hemorrhagic, traumatic, and burn shock.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 300-400 g. Hemorrhagic shock was induced by prolonged posthemorrhagic hypotension by a modified Wiggers' method [6], traumatic shock by Cannon's method [11], and a model of burn shock was created by thermal trauma, using water immersion (the area of the burn was 20-25% of the total body surface area and the duration of exposure was 75-80 sec). The stages of shock were evaluated on the basis of the

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(Presented by Academician of the Academy of Medical Sciences of the USSR O. K. Gavrilov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 106, No. 10, pp. 426-428, October, 1988. Original article submitted September 19, 1987.

0007-4888/88/0010-1412$12.50

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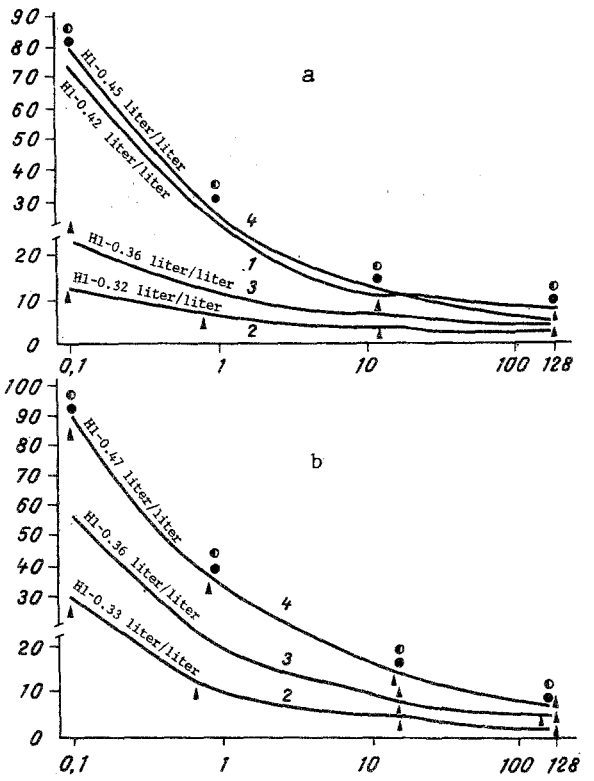

Fig. 1. Dependence of viscosity of blood on shear velocity in intact rats (1) and in animals in a stage of relative compensation (a) and decompensation (b) of hemorrhagic (2), traumatic (3), and burn (4) shock. Abscissa, shear velocity (in sec^{-1}); ordinate, blood viscosity (in mPa·sec). Filled triangles — significance of differences between control and experiment; half-filled triangles — significance of differences between hemorrhagic and traumatic shock; filled circles — significance of differences between burn and hemorrhagic shock; half-filled circles — significance of differences between burn and traumatic shock.

time of development of the pathological process, the blood pressure (BP) level, the blood pH, and the animal's body temperature. The rheologic parameters and pH were investigated in blood samples taken from the carotid artery. The viscosity of the blood was determined over the range of shear velocities from 0.1 to 128 sec^{-1}, and the viscosity of plasma by means of a rotary rheometer ("Contraves," Switzerland). The degree of deformity of the erythrocytes was studied by filtration of their suspensions [15]; the rigidity index [14] and coefficient of aggregation [13] of the erythrocytes also were determined. Test parameters of the experimental animals were compared with those of control rats of the same line, sex, and weight.

EXPERIMENTAL RESULTS

In the experiments of series I the rheologic properties of the blood were studied in animals in a stage of relative compensation of hemorrhagic, traumatic, and burn shock 2-3 h after bleeding or the application of a chemical or burn trauma. In the case of hemorrhagic and traumatic shock BP was maintained during this period at 40 mm Hg, whereas in the case of burn shock, it remained almost at the initial level (135 ± 7.4 mm Hg). The stage of relative compensation of burn shock was tested by measuring the time of development of shock and the degree of burning. Necrosis of all layers of the skin and muscle fibers was discovered in biopsy material (these data were obtained by A. N. Loginova, working in the laboratory of Pathological Anatomy, Central Research Institute of Hematology and Blood Transfusion — Head Professor M. P. Khokhlova.) In all forms of shock, pH fell to 7.3 ± 0.03 (7.46 ± 0.02 in the control); the body temperature of the rats fell to 28-31°C (33 ± 0.4°C in the control).

In the stage of relative compensation of hemorrhagic and traumatic shock, autohemodilution was observed. The hematocrit index fell from 0.43 to 0.32-0.36 liter/liter. Hemodilution

led to a decrease in the viscosity of the blood at all shear velocities, but was more marked in hemorrhagic shock (Fig. 1a). The viscosity of plasma (on average by 10%) and the coefficient of aggregation of the erythrocytes (by 50%) were significantly reduced. Improvement of the rheologic properties of the blood during this period of shock was protective—adaptive in character, and was aimed at maintaining the blood flow in the microvessels at a time of depressed BP. However, the state of the erythrocytes had improved, as shown by a reduction by more than half in the degree of deformation of these cells and an increase in their rigidity index.

In the stage of relative compensation of burn shock the hematocrit index and dynamic viscosity of the blood were the same as in the control (Fig. 1a). The viscosity of the plasma (on average by 0.27 mPa·sec) and the coefficient of aggregation (by 12%) were significantly increased. The degree of deformation of the erythrocytes was reduced and their rigidity index increased more than in hemorrhagic and traumatic shock. Disturbance of the rheologic properties of the blood in this stage of burn shock increased the resistance of the peripheral blood flow, thus predisposing it to reduction of perfusion of the microcirculatory bed. Under these conditions, one of the compensatory mechanisms ensuring an adequate degree of perfusion of organs and tissues may perhaps be a sufficiently high BP.

In the experiments of series II the rheologic properties of the blood were studied in animals in the stage of decompensation of hemorrhagic, traumatic, or burn shock. This period of shock occurred 4-5 h after bleeding or trauma (both mechanical and thermal). The stage of decompensation is characterized by failure of the protective—adaptive mechanisms and by aggravation of certain pathological processes. BP began to fall, to reach 18 ± 2.3 mm Hg, the pH fell to 7.1-7.2, and the body temperature to 22-26°C.

The rheologic properties of the blood in the stage of decompensation of hemorrhagic and traumatic shock worsened by comparison with the previous period. The previous level of autohemodilution was preserved, but the viscosity of the blood was increased at low shear velocities (Fig. 1b); the increase was greater, moreover, in traumatic shock than in hemorrhagic shock, due to intensified erythrocyte aggregation. During progression of the pathological processes, the degree of deformation of the erythrocytes continued to decrease. The rigidity index of these cells was increased to 1.12 and 1.18 in hemorrhagic and traumatic shock. The more marked rheologic disturbances of the blood in traumatic than in hemorrhagic shock evidently reflect the more severe course of traumatic shock, when, as a result of excessive shifts in the sphere of neuroendocrine regulations, more profound changes of homeostasis take place [8]. In traumatic shock anoxia developed earlier and to a greater degree, and this affects the state of the erythrocyte membranes [10, 12].

In the stage of decompensation of burn shock a progressive increase is observed in the rheologic disturbances of the blood compared with those found in the stage of relative compensation, with the appearance of new changes in the rheologic parameters. The viscosity of the blood was increased at all shear velocities, and the viscosity of the plasma and coefficient of aggregation of the erythrocytes continued to increase by 23 and 25% respectively. The degree of deformation of the erythrocytes was reduced by almost 80% and the rigidity index of the cells was increased by 20%.

The more marked disturbances of blood rheology in burn shock than in hemorrhagic and traumatic shock reflected the severity of the pathogenesis of burn shock, with its characteristic hemoconcentration, plasma-loss, and destructive changes in the erythrocytes [4, 7, 9].

Regardless of the etiologic factor, during deepening of shock and progression of the pathological processes, notably anoxia, in the affected organism, changes in the state and properties of the plasma and the state of the erythrocyte membranes, etc. [3, 6, 9], disturbances of the rheologic properties of the blood continued to progress, and in turn they led to worsening of perfusion of the microcirculatory bed. The rheologic disorders reflected the pathogenesis of shock, depending on its origin. The most marked rheologic disturbances of the blood were observed in burn shock, the least marked in hemorrhagic shock.

Information on changes in the rheologic properties of the blood at a certain period of shock, and depending on its etiology, are not only of theoretical, but also of great practical importance in the development of differential, pathogenetically based treatment programs.

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EFFECT OF "MURINE" TOXIN OF *Yersinia pestis* ON CARBOHYDRATE METABOLISM IN RATS

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UDC 615.919.579.842.23].015.4:[616.153.453+616.154.37

KEY WORDS: "murine" toxin of *Yersinia pestis*; carbohydrate metabolism; rat blood and liver.

Many bacterial toxins, when administered intravenously and parenterally, give rise to toxic-infectious shock and to death of the experimental animals, which develops against the background of a profound disturbance of carbohydrate metabolism. Endotoxin shock is known to be accompanied by phasic changes in the blood glucose level, by hyperlactatemia [7, 10], and also by an increase in the blood concentrations of insulin and glucagon [9]. Accumulation of glucose in the blood plasma in the early stages of the action of lipopolysaccharides takes place on account of intensive catecholamine release and an increase in the intensity of glycogenolysis in the liver [5]. Besides an endotoxin of lipopolysaccharide nature, *Yersinia pestis* also contains a so-called "murine" toxin, which is firmly bound with the bacterial cell wall. The "murine" toxin is a thermolabile protein [8], and its parenteral or intravenous administration causes the development of shock and death of mice and rats [11]. The pathogenetic importance and biochemical mechanisms lying at the basis of the action of the "murine" toxin of *Y. pestis* has not been adequately studied. It is suggested that its toxic action is connected with its ability to induce "functional adrenalectomy" in animals [8, 12]. The sympathicoadrenal system plays an important role in the regulation of metabolic processes and, in particular, of carbohydrate metabolism.

The aim of the present investigation was to accordingly study carbohydrate metabolism in rats in the course of development of toxic-infectious shock due to "murine" plague toxin.

Central Research Institute of Epidemiology, Ministry of Health of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR V. I. Pokrovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 106, No. 10, pp. 428-430, October, 1988. Original article submitted December 14, 1987.

0007-4888/88/0010-1415$12.50 © 1989 Plenum Publishing Corporation