stimulation chosen were similar to those of stimulation of "kindling" type [10]. However, by contrast with the kindling effect, the rabbits in the present experiment did not develop convulsions, and the epileptiform activity on the EEG was limited in character. It can be tentatively suggested that the conditions of CES used in the present experiments led not only to the formation of a long-term excitation generator, but also to the development of certain restraining, antiepileptic mechanisms, preventing excessive generalization of the excitation process.

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MECHANISM OF ACTION OF BLOOD PLASMA IN POSTRESUSCITATION STATES

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KEY WORDS: postresuscitation syndrome; defibrinated plasma; peripheral circulation; low cardiac output syndrome; thrombohemorrhagic syndrome.

Unfavorable consequences of the terminal state in the form of disturbances of blood rheology and the development of a thrombohemorrhagic syndrome [4, 8, 12] are the immediate cause or an aggravating factor of postresuscitation circulatory disorders [6]. To combat these complications, solutions of low-molecular-weight dextrans and anticoagulants have been used with success [1, 2]. It has been shown in recent years that native plasma possesses antithrombin properties [13, 14].

In this connection it was interesting to study the effect of plasma on some indices of the clotting system and viscosity of the blood, and also the state of the central and peripheral hemodynamics after prolonged circulatory arrest.

EXPERIMENTAL METHOD

Experiments were carried out on 28 dogs anesthetized with trimeperidine (8-10 mg/kg) and pentobarbital (10-15 mg/kg); circulatory arrest was induced for 17 min in the animals by electric shock. The dogs were revived by the method of Negovskii et al. In 11 experiments

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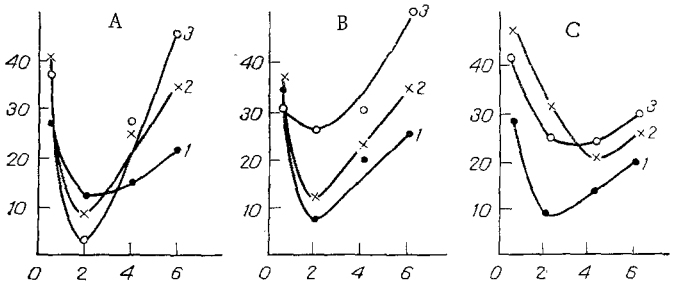

Fig. 1. Curves of thrombin generation in blood samples from two groups of animals in terminal state and after resuscitation. Abscissa, time of incubation of sample (in min); ordinate, time of formation of standard plasma clot (in sec). A: 1) Initial state, 2) clinical death (2 min), 3) clinical death (15 min); B: 1) 5 min, 2) 1 h, 3) 3 h of postresuscitation period; C) the same times of the post-resuscitation period for animals treated with plasma during the first hour.

TABLE 1. Changes in Indices of Central and Peripheral Hemodynamics, Oxygen Consumption, and Blood Viscosity after Injection of Donor's Plasma into Animals in Recovery Period after resuscitation (M ± m)

Index	Before electric shock		Recovery period			
			1 h		3 h	
	control group	main group	control group	main group	control group	main group
Mean arterial pressure, mm Hg	104±3	101±6	117±3*	117±7	111±4	121±8
Cardiac index, ml/kg/min	156±22	122±28	119±18	159±19	58±5*	116±13
					$P<0,001$	
Total peripheral resistance, dynes·sec·cm^{-5}	3503±415	5526±961	4741±526	4507±756	8670±703*	6210±853
					$P<0,001$	
Blood flow in limb, % of initial	100	100	114±22	140±40	73±10*	142±35
					$P<0,001$	
Blood viscosity in standard plasma:						
arterioles	4,31±0,05	5,04±0,27	5,14±0,31*	4,35±0,23	4,94±0,19*	4,46±0,28*
venules	7,42±0,5	9,3±1,4	8,9±0,9	7,5±0,7	9,4±0,7*	6,3±0,3*
					$P<0,01$	
pre- and postcapillaries	11,7±1,03	17,9±2,4	16,2±1,8*	12,1±2,3	19,7±1,5*	10,2±1,6*
					$P<0,01$	
Fibrinogen, %	100	100	93,8	93,9	84,7	137,0
Ht, %	47±0,5	55±2,1	52±1,4*	51±2,4*	50±2,6	50±2,7
					$P<0,01$	
Oxygen consumption, % of initial	100	100	128±15	179±51	93±12	170±25
					$P<0,01$	

Legend. *P < 0.05 relative to initial level, P relates to differences between groups.

the main group of animals was treated by previously defibrinated plasma together with micro-doses of heparin (1.9 units/ml plasma). The plasma was injected by intravenous drip for 3 h after restoration of cardiac activity (total dose 20 ml/kg). Administration of plasma was combined with bleeding from the right heart. The volume of plasma injected and of blood withdrawn by the 3rd hour of the recovery period was 20 and 14.1 ml/kg, respectively. After 24 h the plasma was reinjected (10 ml/kg). Seventeen untreated animals served as the control.

The cardiac output in the experiments was measured by Fick's method, the volume velocity of the blood flow was determined in the limb [10], and the oxygen consumption and acid–base balance of the blood were measured. The fibrinogen concentration [15], thrombin generation, and deficiency of factors VIII and IX [5, 11] were determined. The viscosity of the blood was measured by means of the VIR-75-MA rotation microrheometer.

EXPERIMENTAL RESULTS

In all animals a considerable increase in the rate of thrombin generation in the blood was observed during circulatory arrest, evidence of the sharp activation of the first stages of blood clotting, actually during the period of clinical death (Fig. 1).

In the recovery period the more rapid generation of thrombin in the blood persisted in dogs of the control group, and it was most marked at the 5th minute of resuscitation (8 ±.1.5 sec). By the end of the first hour, besides accelerated thrombin generation, consumption of clotting factors VIII and IX was observed. Their deficiency progressively increased until 3 h (Fig. 1B). Meanwhile under these conditions the fibrinogen concentration fell (by 15%, $P < 0.01$; Table 1). These observations indicated the development of a thrombohemorrhagic syndrome, in agreement with data in the literature [8, 12]. The blood viscosity was significantly increased after 1-3 h of the recovery period compared with its initial value at all levels of the peripheral blood flow, but the increase was particularly marked at the level of the microvascular system (Table 1). Under these conditions the hematocrit index also increased somewhat (by 6-11%).

Disturbances of hemostasis and of the rheologic properties of the blood, developing during clinical death, thus are not abolished after the beginning of resuscitation measures, but continue to progress.

The changes indicated above were accompanied by considerable disturbances of the peripheral and central hemodynamics (Table 1). For instance, 3 h after the beginning of resuscitation, against the background of near-original levels of systemic and pulmonary arterial pressure, the cardiac output was reduced to 46% of its initial value, the stroke volume to 26%, whereas the total peripheral resistance was increased to 247.4% and the volume velocity of the blood flow in the limb reduced to 73%, i.e., a "low cardiac output syndrome" [7] developed. All the animals of this group died during the first 2 days after resuscitation.

In the dogs of the main group administration of plasma inhibited the more rapid thrombin generation resulting from hypoxia after the 3rd-5th minutes of resuscitation. After 1 h of the recovery period, the formation time of a standard plasma clot in the treated animals (Fig. 1C) was lengthened to 31 ± 6.16 sec, whereas in the control group at this time it was 11 ± 1.92 sec, and 3 h after resuscitation its value was 45 ± 6.44 and 35 ± 2.69 sec, respectively ($P < 0.02$). The blood viscosity was significantly reduced after 3 h at all levels of the microcirculation. The increase in the fibrinogen concentration at this period by 37% was evidently compensated by the moderate hemodilution: The hematocrit index was lowered by 9-11%.

The values of the cardiac output, limb blood flow, and total peripheral resistance after injection of plasma were close to the initial levels at all stages of investigation in the postresuscitation period (Table 1). It is essential to note that the stable state of the hemodynamics in animals of the main experimental group compared with the control was accompanied throughout the period of investigation by higher oxygen transport (twofold) and consumption (by 1.7 times), and also by more rapid compensation and correction of the metabolic disturbances of the blood acid–base balance.

The corneal reflexes recovered sooner in the animals treated with plasma. Nine of the 11 animals in this group survived with apparent full recovery of their neurological status.

Improvement of the end results of resuscitation after treatment with plasma was evidently due to its many-sided positive action, including detoxication [10], replenishment of the blood proteins, hemodilution, prevention of a fall in circulating blood volume, and maintenance of normal hemostasis. Inhibition of thrombin generation by plasma in all media of the body is evidently a leading factor, because it not only prevents the development of decompensated hypercoagulation, but also prevents the harmful action of thrombin on the ultrastructure of the parenchymatous organs [3].

Partial prevention of the thrombohemorrhagic syndrome and improvement of the rheologic properties of the blood in the early postresuscitation period by injection of defibrinated plasma with microdoses of heparin thus prevent posthypoxic circulatory disturbances and improve the end results of resuscitation.

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HYPOTHALAMIC OBESITY IN OLD RATS

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KEY WORDS: hypothalamic obesity; aging; endocrine functions.

Together with atherosclerosis and diabetes, obesity is a widespread disturbance of metabolism in old age. In the development of obesity in general and of obesity during aging in particular, great importance is attached to disturbances of hypothalamic mechanisms of regulation. During aging significant changes take place in the functions of the hypothalamus and, according to some data [3], they are expressed unequally in its different structures. Production of an experimental model of hypothalamic obesity in animals of different ages, through injury to the ventromedial hypothalamic nuclei (VMN), could help, first, to shed light on the special features of development of this form of obesity at different ages and, second, to establish some age differences in hypothalamic regulation of endocrine functions.

In the investigation described below changes in the degree of obesity, the quantity of food and water consumed, the concentrations of insulin, growth hormone (GH), thyroid-stimulating hormone (TSH), corticosterone, sugar, total lipids, cholesterol, and free fatty acids in the blood, and also the concentration of GH in the pituitary gland were compared in relation to the time elapsing after destruction of VMN and the degree of obesity which developed.

EXPERIMENTAL METHOD

Bilateral electrolytic injury to VMN was produced in 12 male albino rats ages 24-26 months (old) and in 41 rats aged 8-10 months (young). Intact animals (15 old and 32 young) and animals undergoing a mock operation (12 old and 29 young) served as the control. The conditions of keeping, determination of body weight, food consumption, sacrifice, and methods of determination of GH in the pituitary, and of total lipids, cholesterol, free fatty acids (FFA), and sugar in the blood were described previously [4]. Immunoreactive insulin (IRI), GH, TSH, and corticosterone levels in the blood plasma were determined by the competitive binding method. To describe the degree of obesity, the percentage of gain in body weight was used (20-29% – degree I, 30-49% – degree II, 50-99% – degree III, over 100% – degree IV). The numerical results were subjected to statistical analysis.

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