On morphological investigation of the aorta of rabbits receiving local injections of physiological saline, no evidence of pathology of the aorta tissue could be found any of the ten control animals (Fig. 1a).

The method described above thus enables a model of atherosclerosis to be obtained in rabbits with a high degree of reproducibility and in a relatively short time. On the other hand, the results described above indicate an essential role of the cholinergic structures of the mesencephalic reticular formation in the mechanisms of formation of this pathological condition, and the model can be used to study the neurochemical mechanisms lying at the basis of development of atherosclerosis, and also experimentally to develop new methods of treatment of this disease.

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EFFECT OF EXTREMAL FACTORS ON THE MECHANISMS OF HEMOLYSIS

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Under extremal influences (hypoxia, low atmospheric pressure, blood loss, injection of foreign agents) a stereotyped response of the blood system was observed: hemolysis (erythrodieresis), followed by activation of erythropoiesis, stimulation of nonspecific resistance, and regeneration of the tissues [2, 4, 6-8, 11-14]. The mechanisms of the so-called extremal erythrodieresis have not been explained. A definite role in the origin of increased erythrocyte destruction under the influence of stress has been attached to an increase in the titer of antierythrocytic antibodies, tissue hemolysins, and an intracellular defect of the erythrocytes. A probable role of the kidneys in this process has been mentioned in some publications [10].

The aim of this investigation was to study an autoimmune humoral and cellular component of erythrodieresis (ED), dependent on the kidney and induced by injection of phenylhydrazine and of a uranyl–glycerol mixture, and by acute blood loss.

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TABLE 1. Properties of Erythrocytes during Perfusion of Rats Exposed to the Action of Extremal Factors through the Kidneys (M ± m)

Series of experiments	Total acid resistance of erythocytes, %	Percent of erythrocytes, %/min		EPME, μ/sec/V cm	Potassium of supernatant,
		low resistant	High resistance		
Before perfusion	391,5±13,91	22,0±2,06	35,4±2,87	1,51±0,01	5,1±0,49
After perfusion of kidneys					
With blood loss	301±9,70*	32,1±2,40*	13,2±3,16**	1,32±0,043**	10,41±0,64**
Without blood loss	352,6±20,41	24,7±2,68	28,1±4,66	1,60±0,040*	5,2±0,42
Withblood loss + euphylline	311,4±5,20**	30,4±2,20*	15,4±3,26**	1,40±0,031**	9,1±0,70**
With blood loss + ink	339,5±10,11**	23,8±3,50	30,4±5,10	—	6,5±0,30*
With uranyl-glycerol	492,1±20,67**	12,1±3,20*	54,7±6,43*	1,38±0,028**	8,2±0,53**

Legend. *$p < 0.05$, **$p < 0.01$ Compared with values before perfusion.

EXPERIMENTAL METHOD

Experiments were carried out on 140 Wistar rats weighing 200-230 g and 95 CBA, BALB/c, and Swiss mice weighing 20-25 g, aged 1.5-2 months, anesthetized with ether. ED was activated by injection of phenylhydrazine (8 mg/100 g), or of uranyl–glycerol mixture (1 ml/100 g), and by acute blood loss (35-40% of CBV, determined with the aid of T-1824 dye and ^{51}Cr). The intensity of hemolysis was judged by a change in acid resistance [1, 5], electrophoretic mobility of the erythrocytes (EPME) [9], free serum hemoglobin, deposition of hemosiderin in the tissues, and the protein content in the erythrocyte stroma, determined by PAG electrophoresis. Autoimmune cellular ED was scavenging assessed by the number of zones of local hemolysis [3]. The scavenging activity of cells of the mononuclear phagocytic system (MPS) was studied by the results of seeding completeness a culture of Listeria (strain 1457) from the blood and completeness of phagocytosis. The erythrodleretic activity (EDA) of the blood serum was determined quantitatively after incubation (37°C, 3 h) with reference (syngeneic) erythrocytes, by measuring the change in total acid resistance of the erythrocytes and comparing it with the control. The properties of the erythrocytes were studied separately in "young" and "old" fractions after centrifugation (10 min, 70 g) in hematocrit capillary tubes. The results were subjected to statistical analysis by Student's test.

EXPERIMENTAL RESULTS

The intensity of phenylhydrazine hemolysis in bilaterally nephrectomized rats was found to be 23.4% less than in animals with intact kidneys; the number of circulating erythrocytes per 100 g body weight in rats undergoing mock nephrectomy 48 h after injection of phenylhydrazine was reduced by 67.2%, and in nephrectomized rats by 44.1% ($p < 0.05$). The intensity of deposition of hemosiderin in the animals of this group was 2.5 times less than in the control, and hemolysis of hemoglobin also was correspondingly less marked after nephrectomy, despite an evident increase in its elimination from the blood ($1.84 \cdot 10^{-3} \pm 0.091 \cdot 10^{-3}$ g/100 g compared with $2.29 \cdot 10^{-3} \pm 0.073 \cdot 10^{-3}$ g/100 g in the control).

The total acid resistance of the erythrocytes 15 min after acute blood loss rose by 14.2% in animals with intact kidneys, with a maximum toward the 3rd hour after hemorrhage (543.3 ± 17.20%/min); after nephrectomy and blood loss it was 460.2 ± 12.60%/min (compared with 427.4 ± 24.20% in the control). The mechanism of posthemorrhagic EA is linked with release (activation) of humoral factors of renal origin, EDA of posthemorrhagic blood serum from rats with bilateral nephrectomy was reduced by 3.5 times during investigation of target cells (erythrocytes of the old fraction), and by 7.3 times relative to erythrocytes of the young fraction, The study of the hemolytic properties of the serum in the late posthemorrhagic period with the aid of ^{51}Cr is evidence of a secondary rise of EDA toward the 3rd day after blood loss, to a level of 3.3% of hemolyzed erythrocytes.

Erythrodieresis following blood loss also is associated with injury to erythrocytes as they pass through the renal microvessels of the anemic (1 h) animals (Table 1), as is reflected in the reduced acid resistance, EPME, and percentage of erythrocytic stromal proteins of medium and low molecular weight. Injection of the uranyl–glycerol mixture also potentiates the kidney-dependent local mechanism of ED, which is confirmed by changes in the physicochemical properties of the erythrocytes in experiments with perfusion of the kidneys with homologous blood (Table 1) and the increase in EDA of dialyzed blood serum of the animals by 28% on account of destruction of erythrocyte populations with low resistance. Blockade of the phagocytic cells of the kidneys with ink reduced the kidney-dependent local erythrodieresis by 37.6%, whereas preliminary injection of euphylline into the perfused blood did not cause abolition of the renovascular ED in the early posthemorrhagic period.

The study of the autoimmune cellular mechanism of ED revealed a decrease in the number of reactive populations of autologous plaque-forming cells (APFC) in the blood by 14.8 times in bilaterally nephrectomized animals, associated with a 2.1-fold increase in APFC in the spleen. After bleeding, the number of APFC in the blood of the mice undergoing mock nephrectomy was increased by 3.2 times, whereas the number of APFC in the spleen fell to 10,500 ± 460/10^6 nucleated cells. The mechanism of erythrocyte destruction in the posthemorrhagic period also was associated with a 1.8-fold increase in the number of APFC in the kidneys compared with the number of spontaneous APFC.

The study of the effect of MPS on the intensity of extremal ED showed an increase in the number of positive blood cultures of LI-1487, especially 20 min after infection (20.6 ± 5.20%), and the degree of phagocytosis after 20 and 30 min was 3.0 ± 0.3 and 63.4 ± 3.80% compared with mice undergoing the mock nephrectomy (corresponding values 0.2 ± 0.03; 95.5 ± 6.5, and 99.0 ± 8.23%).

Thus the mechanism of ED under the influence of extremal factors (hypoxia of hemic, posthemorrhagic origin) is associated with erythrodieretically active humoral factors, formed with the participation of the kidneys The hemolytic effect is supplemented by renoprival euphylline-independent mechanism of destruction of low-resistant fractions during passage of the blood through the kidneys of the animals while subjected to the action of extremal factors, with a process of local elimination and injury by means of reactive populations of APFC and phagocytic elements of the kidneys.

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