during immobilization. It can be tentatively suggested that the specific nature of changes in the cardiovascular functions during emotional stress is largely connected with the character of functioning of LC neurons. The results of the present investigation confirm earlier views on the homeostatic function of LC [1].

By contrast with LC, no correlation was found in NSC between changes in the CA level and the response of BP and of the gastric mucosa (Fig. 2). Consequently, two noradrenalin-synthesizing brain formations, in close proximity to one another, play an essentially different role in the organization of the emotional stress reaction.

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"SHOCK LUNG" AND BLOOD RHEOLOGY IN EXPERIMENTAL PANCREATITIS

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KEY WORDS: "shock lung"; blood rheology; hemorheologic disorders; pancreatic necrosis.

The syndrome of acute pulmonary disturbances ("shock lung") is one of the most serious complications of pancreatic necrosis and it develops against a background of marked disturbances of both the systemic and the pulmonary circulation [7]. An important role in the pathogenesis of the syndrome is played by changes in the rheologic properties of the blood arising during progression of pancreatogenic shock [3, 7]. The aim of the present investigation was to study the hemorheologic disorders and their effect on development of the syndrome of acute pulmonary disturbances in pancreatic necrosis.

EXPERIMENTAL METHOD

Altogether 22 experiments were carried out on mongrel dogs weighing 18-22 kg. Pancreatic necrosis was induced by the method of Anderson et al. [1]. Under intravenous thiopental anesthesia (20 mg/kg), after premedication with trimeperidine (5 mg/kg), the cranial vena cava, pulmonary artery, and thoracic aorta were catheterized. For the pulmonary artery a Swan–Ganz triple-barreled balloon catheter was used; the position of the catheter was verified by monitoring the intracardiac pressure curve on an oscilloscope.

The pressure in the orifice of the venae cavae (CVP), in the pulmonary artery (P_{mean}), and in the thoracic aorta (AP_{mean}) was recorded on a Mingograph-82 apparatus (from Siemens). The circulating blood volume (CBV) and cardiac output (CO) were determined by a radiocardiographic method with [^{131}I]albumin. The gas composition of the arterial (P_aO_2) and mixed venous blood was determined by the micro-Astrup method on a Radelkis apparatus (Hungary) and the oxygen saturation of hemoglobin was measured on an Oximeter apparatus (Denmark). The pulmonary shunt Q_s/Q_t was determined after hyperoxygenation for 20 min in accordance with Berrgren's equation and with the aid of the nomogram of Stadler et al. [6]. To estimate the rheologic properties of the blood, the structural viscosity of mixed venous blood (η_0), the

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TABLE 1. Indices of Hemodynamics, Gas Exchange, and Blood Rheology in Control Animals (M ± m; n = 6)

Index	Stage of investigation		
	background	3rd hour	7th hour
CBV, liters	1,93 ± 0,07	1,88 ± 0,06	1,83 ± 0,07
CO, liters/min	2,57 ± 0,14	2,35 ± 0,09	2,25 ± 0,12
APmean, mm Hg	110,8 ± 4,6	111,7 ± 4,4	108,3 ± 5,2
Pmean, mm Hg	13,1 ± 0,6	13,7 ± 0,6	14,6 ± 1,1
CVP, mm water	60,0 ± 10,6	56,7 ± 6,7	43,3 ± 6,7
TPR, dyn · sec · cm^{-5}	3571 ± 150	3816 ± 177	3867 ± 164
PAR, dyn · sec · cm^{-5}	190,8 ± 15,1	234,2 ± 18,2	325,0 ± 21,3
Pa_{O_2}, mm Hg	86,7 ± 5,0	94,0 ± 2,9	89,0 ± 4,1
$\frac{Q_s}{Q_t}$, %	7,3 ± 0,7	6,7 ± 0,9	6,0 ± 1,0
BE, meq/liter	−5,4 ± 1,2	−6,3 ± 1,1	−5,8 ± 0,9
η_0, cP	16,12 ± 1,26	19,0 ± 1,40	21,54 ± 3,54
Aer, %	0,15 ± 0,01	0,16 ± 0,01	0,18 ± 0,01
HI, %	43,5 ± 1,0	45,2 ± 1,0	45,0 ± 2,0

TABLE 2. Indices of Hemodynamics, Gas Exchange, and Blood Rheology in Experimental Animals (Series II) with Experimental Pancreatitis (M ± m)

Index	Stage of investigation		
	background	3rd hour	7th hour
CBV, liters	1,92 ± 0,04	1,20 ± 0,11[a,b]	1,03±0,12[a,b]
CO, liters/min	2,48 ± 0,05	1,68 ± 0,16[b]	1,11±0,11[a,b]
APmean, mm Hg	110,6 ± 3,8	120,3 ± 1,6[a]	62,3±3,2[a,b]
Pmean, mm Hg	12,7 ± 0,2	19,6 ± 1,0[b]	19,2±1,2[b]
CVP, mm water	65,5 ± 2,2	8,3 ± 2,8[a,b]	0[a,b]
TPR, dyn · sec · cm^{-5}	3599 ± 112	7086 ± 292[a,b]	4735±336
PAR, dyn · sec · cm^{-5}	193,3 ± 3,6	738,0 ± 30,2[a,b]	834,4±34,2[a,b]
Pa_{O_2}, mm Hg	86,3 ± 4,6	79,2 ± 1,28[b]	65,3±4,1[a,b]
$\frac{Q_s}{Q_t}$, %	8,4 ± 0,7	9,1 ± 0,4	21,9±0,6[a,b]
BE, meq/liter	−5,4 ± 0,3	−16,3 ± 0,9[a,b]	−17,8±1,2[a,b]
η_0, cP	17,09 ± 1,27	22,0 ± 2,20	50,57±6,20[a,b]
Aer, %	0,15 ± 0,01	0,29 ± 0,02	0,29±0,02[a,b]
HI, %	43,6 ± 0,5	46,0 ± 4,0	53,1±1,0[a,b]

a) Changes significant compared with initial data ($P < 0.05$).
b) Changes significant compared with data for corresponding stage of control series ($P < 0.05$).

intensity of aggregation activity of the erythrocytes (A_{er}), and the hematocrit index (HI) were determined.

Anesthesia was maintained throughout the experiment by intravenous drip injection of thiopental in a dose of 3 mg/kg per hour. The investigation was carried out immediately after premedication and induction of anesthesia (background), and at the 3rd and 7th hours of the experiment. There were two series of experiments: series I (control) — laparotomy only was performed on six dogs; series II — a model of acute pancreatitis was produced in 16 dogs and led to severe hemodynamic and respiratory disturbances and ultimately to the animal's death.

The results were subjected to statistical analysis by Student's t test, and by the use of Wilcoxon–Mann–Whitney nonparametric criteria and the chi-square test.

EXPERIMENTAL RESULTS

All the animals of series II died between 6 and 14 h after the time of induction of acute pancreatitis. Autopsy revealed pancreatic necrosis with a hemorrhagic effusion into

the peritoneal cavity. The diagnosis of pancreatic necrosis was confirmed histologically in all cases. The lungs of the animals of series II were edematous, with multiple subpleural hemorrhages. Under the light microscope, in 8 of the 16 case signs of injury to lung tissue were found: collapse of the alveoli, edema of the interstitial tissues, and microthrombi in the lung capillaries. No such changes were found in the animals of series I, nor were there any significant changes in the blood rheologic and gas exchange indices ($P_{\chi^2} < 0.05$, $P_t < 0.05$).

The results of investigation of the hemodynamics, gas exchange, and blood rheology in experimental pancreatitis and in the control animals showed (Tables 1 and 2) that induction of acute pancreatitis leads to a sharp fall in CBV and CO connected with extensive loss of plasma, and to an increase in the hematocrit index. This was accompanied by an increase in the total peripheral and pulmonary arterial resistance (TFR and PAR respectively), which enabled the perfusion pressure to be maintained in both the systemic and the pulmonary system. Despite this, perfusion of the peripheral tissues and of the lungs was impaired, as shown by a decrease in the CO/CBV ratio, and the development of borderline arterial hypoxemia and metabolic acidosis. Stimulation of the cardiorespiratory mechanisms of compensation thus leads to a redistribution of the blood flow between vitally important organs and the microcirculatory system. In the literature this state is characterized as the "inadequate circulation syndrome" [4], for the circulatory disturbances in the lungs, kidneys, abdominal organs, and other regions progress despite the high perfusion pressure. At this stage, p_aO_2 and Q_s/Q_t remain at a subnormal level, indicating satisfactory conditions for the circulation and gas exchange in the pulmonary system. In the early stages of pancreatic necrosis the main cause of peripheral tissue hypoxia is evidently a fall in the cardiac output, whereas the gas-exchange function of the lungs remains intact.

Despite the marked peripheral vasoconstriction, only a slight change was observed in the rheologic properties of the blood: an increase in viscosity and aggregation activity of the erythrocytes and also in the hematocrit index. In this case, probably because of activation of the sympathico-adrenal system, a considerable part of the microcirculation was shut off from the general circulation, so that massive transport of microaggregates and tissue metabolites into the pulmonary capillary system was prevented. This explains the satisfactory indices of the pulmonary circulation observed at the 3rd hour of the investigation.

Later a decrease in TPR was observed, and against the background of the low values of CO, this led to a critical fall in the mean arterial pressure (7th hour of the experiment). The venous return to the heart was reduced, as shown by the fall in CVP to zero and further decline in CBV. The fall in TPR was evidently due to hypoxic injury to the resistive vessels, evidence of profound disturbances of the peripheral circulation [5]. Under these circumstances the viscosity and aggregation activity of the erythrocytes in the mixed venous blood rose sharply. Disturbance of the rheologic properties of the blood in experimental pancreatitis can be explained by the extensive loss of plasma, the increased hematocrit index, the rise of metabolic acidosis, the formation of cell conglomerates, and also the action of fatty acids, enzymes, and toxic agents entering the blood stream in pancreatogenic shock [3, 7]. Against the background of these changes disturbances of the gas exchange function of the lungs develop. For instance, the pulmonary shunt at the 7th hour of the investigation reached $21.8 \pm 0.6\%$ ($P_t < 0.01$) and this was accompanied by a decrease in p_aO_2 to 65.3 ± 4.1 mm Hg ($P_t < 0.05$). Meanwhile, the results of the histological investigation show that edema of the interstitial tissue of the lungs, collapse of the alveoli, and microembolism of the pulmonary capillaries developed. Consequently it can be postulated that in the late stages of pancreatic necrosis, peripheral vasodilation, and the flushing out of microaggregates, tissue metabolites, and other toxic agents from the systemic microcirculation lead to their large-scale transportation into the pulmonary circulation. Against this background, thrombosis and embolism of the pulmonary capillaries lead to a decrease in the surface area of the pulmonary capillary bed and to a disturbance of pulmonary perfusion. This is one of the chief causes of the increase in PAR, the pressure in the pulmonary artery, and the pulmonary shunt observed in the late stages of pancreatic necrosis [7]. These data, together with the characteristic histological picture, lead to the conclusion that microcirculatory disturbances in the pulmonary circulation develop in acute pancreatitis and are characteristic of the early stages of the "shock lung" syndrome [2, 3].

In pancreatic necrosis a disturbance of the rheologic properties of the blood is thus observed, and it increases in severity during progression of the pancreatogenic circulatory

shock. These disturbances are accompanied by impairment of the circulation in the pulmonary capillary system and they play an important role in the pathogenesis of "shock lung" in pancreatic necrosis.

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CATECHOLAMINE CONTENT IN THE STRIATUM, HYPOTHALAMUS, AND ADRENALS OF RATS GENETICALLY PREDISPOSED TO EPILEPSY

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The results of previous experiments on rats genetically predisposed to epileptiform convulsions (KM rats, bred by L. V. Krushinskii and L. A. Molodkina) led to the hypothesis that correlation exists between genetic predisposition to epilepsy and a generalized defect of catecholamine (CA) metabolism [4, 5]. The following facts served as the basis for this hypothesis: First, it was shown that the dopamine (DA) antagonist bulbocapnine does not cause catalepsy in KM rats although it invariably arises in audiogenically insensitive Wistar rats (AIWR). Second, it was shown that signs of inadequate sympathetic activation of the cardiovascular system are found in KM rats, compared with AIWR, under conditions of immobilization stress judging from such ECG parameters as the area of the P wave, the P/T ratio, Macruz index, and the area of the T wave [4, 5, 6].

Investigation of the tyrosine hydroxylase kinetics in the striatum and hypothalamus showed that values of K_m and V_{max} in KM rats are significantly lower than in AIWR. These observations suggested hyperproduction of DA in both structures in KM rats. However, the "sympathetic activation deficiency" under conditions of immobilization stress and the low thresholds of the avoidance reaction in response to electrical stimulation of the ventromedial hypothalamus in KM rats suggested that the CA content in their hypothalamic structures is lower than in AIWR.

The object of the present investigation was, accordingly, the direct determination of the content of DA, noradrenalin (NA), and of DA metabolites in the striatum and hypothalamus, and also the CA content in the adrenals of KM rats and AIWR differing in their predisposition to seizures.

EXPERIMENTAL METHOD

Experiments were carried out on 16 male rats weighing 180-270 g (9 KM rats, 7 AIWR, selected by triple testing with a bell with an intensity of 105 dB*).

*It should be pointed out that at the present time at least 60-80% of Wistar rats are audiogenically sensitive, i.e., they react by typical audiogenic epileptiform seizures to the ringing of a bell of the above intensity.

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