Depression of the febrile response in diabetes is thus associated not with a change in the number of leukocytes in the focus of inflammation, but with changes in their qualitative features. The liberation of leukocytic pyrogen is determined by the state of metabolism in the leukocytes and requires energy [12]. It can tentatively be suggested that in connection with the marked disturbances of the energy metabolism of the leukocytes in diabetes [5, 6, 11] and a change in their reactivity under the unfavorable conditions for their vital activity in the inflammatory focus, their ability to secrete pyrogenic products is weakened.

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CHANGES IN SOME INDICES OF LIPID METABOLISM AFTER LETHAL EXSANGUINATION AND RESUSCITATION

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The lipolytic activity of adipose tissue (LAAT), the concentration of nonesterified fatty acids (NEFA) in the blood and adipose tissue, and the concentrations of ketone bodies and β-lipoproteins in the blood of dogs were determined after lethal exsanguination and in the postresuscitation period. During agony activation of lipolysis was found in the adipose tissue, the levels of NEFA and β-lipoproteins were lowered, and the concentration of ketone bodies in the blood was increased. At the end of the third minute of clinical death inhibition of lipolysis developed and the NEFA concentration in the adipose tissue increased. The blood levels of NEFA and β-lipoproteins fell 1 h after resuscitation, whereas the level of ketone bodies rose; these changes were accompanied by some decrease in LAAT. In the late postresuscitation period (1st, 3rd, and 7th days) LAAT and the blood levels of NEFA, ketone bodies, and β-lipoproteins all increased. The NEFA concentration in the adipose tissue was low in the postresuscitation period.

KEY WORDS: lipid metabolism; terminal relationships; postresuscitation period.

Many studies of metabolic changes during terminal states and in the recovery period after resuscitation have been published. Particular attention has been paid to the study of carbohydrate–phosphorus [1, 6-8], protein [1, 2, 9, 10] and electrolyte and mineral [2] metabolism. Yet lipid metabolism in these states has hardly been studied at all. Considering the important role of lipids in energy metabolism [3, 11], it was decided to

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TABLE 1. Dynamics of Changes in NEFA Concentration in Adipose Tissue (μeq/g) and LAAT (μeq/ml/g) after Lethal Exsanguination and Resuscitation

Indices n = 5	Initial background	Pentobarbital–heparin background	Agony	End of third minute of clinical death	Postresuscitation period			
					1 h	24 h	72 h	1 h
NEFA								
$M \pm m$	22,6±1,08	18,8±1,22	19,1±1,0	22,4±0,79	11,47±1,24	7,5±0,92	9,5±0,82	8,46±0,99
P	—	<0,05†	>0,5*	<0,05*	<0,01*	<0,001†	<0,001†	<0,001†
LAAT								
$M \pm m$	1,36±0,165	3,21±0,429	4,5±0,192	1,9±0,223	2,66±0,202	5,19±0,329	3,72±0,2	4,44±0,442
P	—	<0,01†	<0,05*	<0,05*	>0,5*	<0,001†	<0,001†	<0,01†

Legend. Here and in Table 2: *) P compared with pentobarbital–heparin background, †) compared with initial background.

study some aspects of lipid metabolism in terminal states and in the recovery period after resuscitation.

EXPERIMENTAL METHOD

Two groups of experiments were carried out on mongrel male dogs weighing 14-17 kg. In group 1 the dynamics of changes in lipolytic activity of the adipose tissue (LAAT), the concentration of nonesterified fatty acids (NEFA) in the blood and adipose tissue, and the blood levels of β-lipoprotein and ketone bodies was studied in terminal states; in group 2 the same indices were studied in the postresuscitation period. Clinical death for a period of 3 min was produced by acute exsanguination from the femoral artery after injection of heparin. Resuscitation was carried out by Negovskii's combined method. Considering the effect of these substances on lipid metabolism, neither adrenalin nor glucose was added to the injected blood. The dogs were anesthetized with pentobarbital (25-30 mg/kg body weight, intraperitoneally). The NEFA concentration was determined by the method of Barreto and Mano in Duncombe's modification, LAAT by the method of Cordon and Cherkes, the β-lipoprotein level by the method of Burstein and Samaille in Ledvina's modification, and the ketone body concentration by Peden's method in the modification of Baev and Bulakh.

EXPERIMENTAL RESULTS AND DISCUSSION

During agony LAAT was increased by 40.1%, but at the end of the third minute of clinical death it was lowered by 40.9% (Table 1). An increase in LAAT over the previous period was observed 1 h after the appearance of spontaneous breathing, but compared with the pentobarbital–heparin background, the LAAT level was low. In the late postresuscitation period activation of lipolysis was observed. For instance, on the first day of the postresuscitation period LAAT was 3.8 times higher than initially, and it still remained high on the third and seventh days.

Investigation of the NEFA concentration in adipose tissue during agony revealed no special changes; toward the end of the third minute of clinical death their concentration was increased by 11.9%. In the postresuscitation period, on the other hand, the NEFA concentration in the adipose tissue fell. For instance, 1 h after resuscitation the NEFA concentration was reduced by 39%. It remained low also during the later stages of the postresuscitation period.

During agony the NEFA and β-lipoprotein concentration in the blood fell (by 39.6 and 31.1%, respectively) compared with their initial background (Table 2). The level of these indices was still low 1 h after reappearance of spontaneous breathing. During the first day after resuscitation the NEFA level was increased by 3.8 times and the β-lipoprotein level by 2.2 times. These indices remained high on the third and seventh days. As regards ketone bodies, during agony they were increased by 23.4%, and 1 h after the reappearance of spontaneous breathing their level was 150% higher than initially. This index still remained high in the late postresuscitation period.

Extraordinary stimuli not only mobilized carbohydrates [13], but also mobilized the lipid reserves of the body by intensifying the supply of NEFA from the fat depots into the bloodstream [4, 12]. These stimuli act through excitation of the sympatho-adrenal

TABLE 2. Dynamics of Changes in NEFA (μeq/ml), Ketone Bodies (mg %), and β-Lipoproteins (mg %) in Blood after Lethal Exsanguination and Resuscitation

Indices	Initial background	Pentobarbital–heparin background	Agony	Postresuscitation period			
				1 h	24 h	72 h	1 h
NEFA							
$M \pm m$	0,25±0,031	0,442±0,056	0,267±0,033	0,265±0,045	0,825±0,118	0,548±0,083	0,568±0,108
n	10	7	5	7	8	9	9
P	—	<0,01†	<0,05*	<0,05*	<0,001†	<0,01†	<0,02†
Ketone bodies							
$M \pm m$	1,13±0,051	1,75±0,071	2,16±0,074	4,37±0,238	1,74±0,125	2,04±0,217	1,75±0,244
n	12	10	10	6	7	10	5
P	—	<0,001†	<0,001*	<0,001*	<0,001†	<0,001†	<0,05†
β-Lipoproteins							
$M \pm m$	216,9±21,2	302,9±21,8	208,8±24,5	236,7±16,9	490,3±40,0	519,1±71,6	526,1±32,8
n	5	5	5	5	6	5	5
P	—	<0,05†	<0,05*	<0,05*	<0,001†	<0,01†	<0,001†

and pituitary-adrenal systems [5, 15]. It can accordingly be postulated that massive blood loss leads to activation of lipolysis in the period of agony as a result of an increase in tone of the sympatho-adrenal system and the liberation of catecholamines into the blood stream. Glucocorticoids play a permissive role under these circumstances in relation to the lipid-mobilizing action of catecholamines [5]. The concentration of NEFA in the blood is known to depend on the intensity of their supply from the fat depots and on the degree of uptake of these acids by the cells of the various organs. It thus seems likely that the discrepancy between the increased LAAT and the reduced blood level of NEFA in the period of agony is evidence of intensive uptake of NEFA by the tissues of the body, probably in order to maintain the essential concentration of glucose to supply the nervous system with energy under the conditions of stress. During clinical death, when the circulation stops, the fat cells are no longer bathed with blood; NEFA accumulate in them and, probably by the feedback principle, give rise to the observed inhibition of lipolysis in the adipose tissue.

On the basis of data on the secondary activation of the sympatho-adrenal system in the late recovery period after resuscitation [10], the activation of lipolysis on the first and subsequent days after resuscitation can be partly explained. Stimulation of lipolysis in the adipose tissue can also be connected with the endocrine function of the pancreas, for insulin is the most powerful and long-acting metabolic regulatory factor in the body. There is evidence that insulin insufficiency develops in the postresuscitation period [8], and this also probably leads to stimulation of lipolysis in the adipose tissue. The high blood level of NEFA in this period is evidence of their intensive mobilization from the fat depots, and this can be regarded as a compensatory reaction enabling fatty acids to be used as a source of energy. However, under the conditions of insulin deficiency, as a result of inhibition of the Krebs' cycle, incomplete combustion of fatty acids takes place, thereby giving rise to the hyperketonemia observed in the postresuscitation period. Furthermore, elevation of the level of ketone bodies can also be explained by delay of resynthesis of fatty acids as a result of depression of the pentose cycle. There is evidence that during insulin deficiency lipoprotein lipase is inhibited [14] and the redistribution in the associations of lipids with protein fractions is also observed [3]. The possibility cannot therefore be ruled out that the hyper-β-lipoproteinemia observed in the late postresuscitation period can be attributed both to the inhibition of intravascular lipolysis and to increased stability of associations of triglycerides with proteins.

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ROLE OF CORTICOSTEROIDS IN THE REGULATION OF NUCLEIC ACID METABOLISM IN THE SPLEEN AFTER SEVERE MECHANICAL TRAUMA

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The RNA and DNA concentration in the spleen of adrenalectomized rats and of rats receiving ACTH was studied before trauma and 10 min and 5 and 10 h after the beginning of crushing of the soft tissues of the hind limbs. The results suggest that corticosteroid hormones influence the changes in nucleic acid metabolism in the spleen following mechanical trauma.
KEY WORDS: shock; metabolism; corticosteroids; nucleic acids.

Many pathological processes are known to cause changes in nucleic acid metabolism and structure [1]. However, little information is available on the changes in the splenic nucleic acids during severe mechanical trauma. A significant increase in the nucleic acid content spleen, mainly on account of DNA, has been demonstrated under the influence of mechanical trauma. The view has been expressed that the increase in the nucleic acid concentration in the spleen is evidence of activation of the genetic apparatus of the cells caused by pituitary and adrenocortical hormones. Meanwhile many aspects of this problem remain inadequately explained. In particular, there is no information on the role of pituitary and adrenocortical hormones in the mechanism of the disturbance of nucleic acid metabolism in the spleen during shock.

The object of this investigation was to study this problem.

EXPERIMENTAL METHOD

Experiments were carried out on 240 male albino rats weighing 180-220 g. Mechanical trauma was inflicted on the animals by crushing the soft tissues of the hind limbs. RNA and DNA were determined by a quantitative spectrophotometric method [4] and expressed in mg % phosphorus. The animals were divided into three main groups: 1) control, 2) adrenalectomized rats, and 3) rats receiving ACTH before trauma and also 10 min and 5 and 10 h after the beginning of trauma (different series of experiments). Ten rats were used in each series of experiments.

EXPERIMENTAL RESULTS

Mechanical trauma led to marked changes in the DNA content in the spleen. At all periods of the investigation it was significantly below the initial level. The RNA concentration rose sharply but only 10 h after the beginning of trauma ($P < 0.01$; Table 1).

When these facts are assessed it can tentatively be suggested that during adaptive responses of the injured animal intracellular mechanisms of nucleic acid and protein synthesis in the spleen are activated. How-

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