METABOLIC RESPONSE OF LEUKOCYTES AS AN INDICATOR OF THE INDIVIDUAL REACTION OF AN ANIMAL TO STRESS AND TO SHOCK-INDUCING INJURY

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KEY WORDS: leukocytes; metabolism; individual reactivity; shock.

The formation of traumatic shock and the severity of its course are determined by the initial functional state of the individual [2, 3, 8] and are associated with adaptive reactions which are based on metabolic processes [7-9, 11]. It has been shown that a change in the composition of the white blood cells and corresponding changes in the metabolism of these cells reflects differences in individual reactivity and can be regarded as a criterion of adaptive reactions in stress situations [5, 6, 12, 13].

The object of this investigation was to study the connection between the biochemical individuality of the organism, based on the results of a study of substrate–enzyme systems for the basic energy cycles of leukocytes, and the severity of the response to shock-inducing trauma (the erectile phase), depending on the outcome of traumatic shock.

EXPERIMENTAL METHOD

Experiments were carried out on 30 male dogs weighing 13-15 kg after preliminary preparation of the animals for the experiments, during which the animals were kept in the animal house for 1 week and adapted to laboratory conditions. Shock was produced by Cannon's method on anesthetized animals. Leukocytes were isolated [13] from 10-12 ml blood. Activity of the following enzymes was determined: glucose-6-phosphate dehydrogenase (G6PDH; E.C. 1.1.1.49) and hexokinase (HK, E.C. 2.7.1.1) [13], succinate dehydrogenase (SDH; E.C. 1.3.99.1) by the tetrazolium method [15], and cytochrome oxidase (CCO; E.C. 1.9.3.1) [10]; the concentration of the substrates lactate and pyruvate also was determined [14]. The results were calculated per milligram protein.

EXPERIMENTAL RESULTS

Despite the standard preparation of the animals before the experiments, the response to fixation in the frame took the form of "immobilization stress," the intensity of which was determined by the individual features of the animals and was characterized by changes in activity of the various enzymes and concentrations of their substrates, in different directions (Table 1). After infliction of standard shock-inducing trauma and analysis of the character of the course of the shock, the animals were divided into two groups.

Retrospective analysis of metabolic processes in the leukocytes of the two groups of animals showed that in dogs with mild shock the "immobilization stress" was characterized by increased activity of enzymes of glucose metabolism (G6PDH and HK) by 50 and 60%, respectively, compared with the control. The indices of oxidation–reduction processes (the lactate and pyruvate levels and CCO activity) were 65, 50, and 70%, respectively, higher than the control. It was noted that in the animals of this same group the SDH activity in the leukocytes was 34% lower than in the control. These results are in harmony with views on biochemical resistance, for it has been shown [4] that resistance to hypoxia can be increased by means of a reduction in SDH activity.

In the primary metabolic response to "immobilization stress," characterized by a fall in activity of the enzymes of glucose metabolism by 17 and 56%, respectively, compared with the control, a fall in the lactate and pyruvate concentrations by 37 and 36%, by depression of

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TABLE 1. Enzyme Activity and Substrate Levels in Leukocytes in Immobilization Stress and Traumatic Shock of Varied Severity (M ± m)

Index, μmoles/mg	Control	Immobilization stress		Erectile phase	
		group 1	group 2	group 1	group 2
G6PDH	11,7±0,7	19,7±0,1	9,7±0,7	14,3±0,6	8,3±1,3
P_1		<0,01	<0,05		
P_2				<0,05	>0,5
HK	7,7±0,9	12,5±1,4	3,4±0,5	4,1±0,08	2,5±0,4
P_1		<0,01	<0,001		
P_2				<0,001	<0,5
CCO	3,3±0,1	5,6±0,5	2,1±0,4	1,4±0,3	2,7±0,5
P_1		<0,05	<0,05		
P_2				<0,05	>0,5
SDH	0,4±0,02	0,27±0,05	1,3±0,2	0,11±0,01	1,4±0,3
P_1		<0,001	<0,05		
P_2				<0,001	>0,5
Lactate	0,37±0,07	0,61±0,08	0,21±0,04	0,14±0,003	0,24±0,006
P_1		<0,01	<0,05		
P_2				<0,001	>0,5
Pyruvate	0,04±0,005	0,08±0,002	0,06±0,005	0,12±0,01	0,04±0,006
P_1		<0,001	<0,05		
P_2				<0,001	<0,5

Note: Group 1) animals with a mild course of subsequent shock, group 2) animals developing severe shock. P_1) Level of significance compared with control, P_2) level of significance compared with corresponding "immobilization stress" group.

CCO activity by 36.4%, and by elevation of SDH activity by 236.6%, shock-inducing trauma was accompanied by a severe type of shock.

It is of the utmost importance to be able to detect latent decompensation in the early stages of shock formation [1, 2, 8]. In the erectile phase in dogs which subsequently developed severe shock the leukocyte count fell sharply by 58.7%. In dogs with mild shock and in the animals which survived, the leukocyte count was practically unchanged in the erectile phase. This "binding" of the shock process, following production of shock by a standard method, was thus accompanied by different responses of the animal's leukocytes which correlated with the severity of the subsequent course of the shock. In animals resistant to shock, metabolic changes were most clearly observed in the erectile phase and were characterized by a fall in the intensity of the metabolic reactions compared with values obtained in "immobilization stress." Activity of HK fell significantly by 67%, activity of G6PDH fell by 24%, of SDH by 59% and of CCO by 74.3%; the lactate level fell by 77%. Pyruvate, the concentration of which rose by 50%, was the exception. The irreversibility of the shock was connected with low individual mobility of the changes in energy metabolism in the erectile phase and, as will be clear from Table 1, it was characterized by less marked quantitative changes, which were not statistically significant. In a critical situation the formation of resistance evidently depends on individual organization of the control of homeostasis and, in particular, on the energy-generating level of cell metabolism and the degree of mobilization of structural and energy-producing processes.

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RNA SYNTHESIS IN ORGANS OF MICE WITH CHRONIC FLUORINE POISONING

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A prolonged excessive intake of fluorine causes a severe illness known as fluorosis, which is characterized not only by specific changes in the bony skeleton and teeth, but also by destructive changes in other internal organs. Fluorosis is thus a systemic disease affecting the body as a whole [1]. This suggests that the morphological changes in fluorosis are preceded by injury to metabolic stages common to all cells.

For these reasons, in the investigation described below, changes in RNA synthesis were studied in different organs of mice with experimental fluorosis.

EXPERIMENTAL METHOD

Sodium fluoride was injected subcutaneously in a dose of 12 μg/g body weight daily into male CBA mice weighing 18-20 g in two series of experiments. Animals of the control group received the corresponding volume of physiological saline. The mice were decapitated 1, 2, 3, and 4 weeks after the beginning of the experiment. An intraperitoneal injection of ^{3}H-uridine in a dose of 10 μCi/g body weight, with a specific activity of 10 Ci/mole, was given to the animals 1 h before sacrifice, so that the intensity of synthesis of high-turnover RNA in the cells could be determined. Pieces of various organs were excised from the animals soon after decapitation, washed in Hanks' solution, and placed in concentrated formic acid in the proportion of 1 ml acid to 20 mg tissue. After hydrolysis of the tissue (12 h at 37°C) the samples were examined on a liquid scintillation counter. The results were subjected to statistical analysis on a Nairi computer.

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