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CELL COMPOSITION OF SUBCUTANEOUS CONNECTIVE TISSUE AFTER SINGLE AND REPEATED GENERAL OVERHEATING

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KEY WORDS: overheating; histiocytes; fibroblasts; mast cells; subcutaneous connective tissue

Generalized overheating leads to morphological and functional changes in the cardiovascular and respiratory systems and in the kidneys and liver [2-5]. During and after hyperthermia the content of lipid peroxidation products, which exert a toxic action [6], increases in all the organs and in the blood. The increase in blood levels of biologically active substances and also of products of incomplete metabolism [4] gives rise to autointoxication.

The aim of this investigation was to study the cell composition of subcutaneous connective tissue (SCCT) in the early and late stages after single and repeated general overheating.

EXPERIMENTAL METHOD

Experiments were carried out on 198 noninbred male rats weighing from 170 to 200 g. The animals were kept on a standard diet with free access to water. The rats were subjected to a single period of overheating for 1 h or to three separate periods (45 min every 3 days) at 43.5°C in a ventilated heat chamber. Animals kept at 20°C served as the control. The rats were decapitated immediately and 1, 3, 7, 11, 15, 30, and 62 days after a single period of overheating and 6, 7, 9, 13, 17, 21, 36, and 68 days after the initial period of repeated overheating. The cell composition of SCCT was studied in intervascular regions of film preparations by the random samples method. The leukocyte formula of the peripheral blood was determined. After a single overheating, the biological toxicity of the blood serum was estimated by an express method (the paramecium test).

EXPERIMENTAL RESULTS

The conditions of overheating chosen were extremal and in some cases death ensued. Mortality depended on the duration of exposure: 20.7% after an exposure of 1 h and 1.3% after an exposure of 45 min. On repetition of overheating, the number of fatal cases increased: 1.3% after the first exposure, 7.7% after the second, and 13.9% after the third. Single and repeated whole-body overheating led to dehydration: the animals lost about 6% of their total body weight after a single overheating lasting 1 h, and up to 4% after overheating for 45 min. The body weight was restored 3 days later. The survival rate of the animals after exposure to a high temperature is evidently determined by individual features of the adaptive capacity of the physiological systems and also by the duration and repetitiveness of the overheating.

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TABLE 1. Cell Composition (in %) of SCCT of Noninbred Rats in Control and in Late Stages after Whole-Body Overheating (M ± m; 10,000 cells, n = 5 in each group)

Time after overheating	Single whole-body overheating				Time after overheating, days	Repeated whole-body overheating			
	fibroblasts	histiocytes	mast cells	leukocytes		fibroblasts	histiocytes	mast cells	leukocytes
Control	72,1±0,5	26,3±0,5	0,3±0,1	1,3±0,1	Control	70,4±1,0	28,4±1,0	0,2±0,1	1,0±0,1
60 min	71,9±0,5	26,9±0,4	0,5±0,1	1,6±0,2	6	68,3±1,4	30,0±1,4	0,3±0,1	1,4±0,4
1 day	71,9±0,5	25,9±0,4	0,2±0,1	2,0±0,2	7	66,9±1,0	31,0±0,8	0,4±0,2	1,7±0,6
3 days	68,3±0,6	30,2±0,6	0,6±0,1	0,9±0,1	9	67,4±1,2	30,7±0,8	0,5±0,2	1,4±0,3
7 days	60,4±0,7	37,2±0,5	1,2±0,2	1,2±0,2	13	65,3±2,9	32,2±2,5	0,7±0,4	1,8±0,7
11 days	66,1±0,6	31,1±0,5	1,0±0,2	1,8±0,2	17	66,3±1,7	32,0±1,5	0,5±0,2	1,2±0,1
15 days	67,1±0,6	31,0±0,6	0,2±0,1	1,5±0,2	21	69,9±1,0	28,7±1,0	0,2±0,1	1,2±0,6
30 days	68,8±0,5	29,4±0,5	0,2±0,1	1,6±0,2	36	70,0±0,3	28,5±0,2	0,1±0,1	1,4±0,2
62 days	72,1±0,5	26,4±0,5	0,2±0,1	1,3±0,1	62	70,7±0,8	28,4±0,9	0,2±0,1	2,1±0,8

A single exposure to whole-body overheating led to an increase in the biological toxicity of the blood serum: immediately after overheating, paramecia died three times faster than in the control. The maximal increase in biological toxicity of the blood serum (five times higher than the control values) was recorded 7-11 days after a single overheating. It was still three times higher than the control after 30 days. The increase in biological toxicity of the blood serum may be due to prolonged circulation of toxic metabolites of endogenous origin in the body under conditions when the excretory function of the kidneys and the detoxication function of the liver are disturbed [7, 8].

After single general overheating the composition of the cell population in SCCT changed: after 3 days the relative percentage of histiocytes was increased and that of fibroblasts reduced (Table 1). Since no signs of destruction of fibroblasts were observed in the film preparations, the relative change in the number of histiocytes and mast cells in SCCT can be regarded as absolute. A single overheating led to a prolonged increase in the number of histiocytes: after 3 days to 443 ± 21 (365 ± 9 in the control); the maximal increase in the number of histiocytes was observed after 7 days, when it reached 602 ± 62 per 1000 fibroblasts.

Immediately after a single overheating the number of mast cells in SCCT was increased; the maximal increase occurred on the 7th day, when they were five times as numerous as in the control.

After repeated overheating an increase in the number of histiocytes also took place. The maximal increase was recorded 13 and 17 days after the initial exposure to overheating: 502 ± 65 and 486 ± 36 per 1000 fibroblasts respectively compared with 406 ± 20 in the control. The number of histiocytes 21 days after overheating was the same as in the control. The change in the number of mast cells after repeated overheating was synchronized with the change in the histiocyte population.

By contrast with dehydration [1] whole-body overheating led to an increase in the average size of the histiocytes. The area of a "statistical mean" histiocyte 7 days after single overheating was 55% greater than in the control, and 17 days after repeated overheating it was 15% greater. The increase in the number of mast cells was accompanied by a decrease in their size.

The response of SCCT, expressed as an increase in the number of histiocytes, was smoother after repeated overheating than after a single exposure. Compared with the control values, the number of histiocytes after single overheating was increased by 70%, and after repeated overheating by 24%. The response after single overheating was more prolonged than that after repeated overheating. The degree of the response of SCCT may perhaps be determined by the activation of adaptive mechanisms.

Determination of the peripheral blood leukocyte formula of the experimental animals after a single overheating showed an increase in the number of monocytes after 24 h from 4.9 ± 0.4 to 10.2 ± 2.7%. The increase in the number of monocytes was observed for 1 month and reached a maximum 7 days after single overheating (17.7 ± 3.2%).

Changes in the cell composition of SCCT arising after single and repeated whole-body overheating reflect a reaction that is evidently aimed at maintaining metabolic homeostasis. It can be tentatively suggested that the collagen-glycosaminoglycan structures of the ground substance of SCCT are a "sorbent," which retains and removes from the circulation incompletely oxidized metabolic products. Saturation of the "sorbent" necessitates its replacement, and this takes place as a result of the combined function of histiocytes and fibroblasts: the proteases of the histiocytes destroy and cause lysis of the collagen-glycosaminoglycan complexes, and the fibroblasts synthesize them. It is accepted that histiocytes can also perform a detoxication function through "assimilation" and enzymic lysis of toxic metabolites.

The possibility cannot be ruled out that mast cells, together with histiocytes, perform a detoxication function and can be regarded as elements of "emergency aid" in autointoxication arising as a result of overheating.

The increase in number of histiocytes in SCCT takes place on account of the existence of a pool of bone marrow monocytes. The macrophage population of SCCT is probably a "running total" and the rate of its renewal is determined by the degree of the load on SCCT.

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EFFECT OF A TERRILYTIN–NICOTINIC ACID MIXTURE ON THE STRUCTURAL AND FUNCTIONAL STATE OF THE MYOCARDIUM IN EXPERIMENTAL ISCHEMIA

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Research is currently in progress into the therapeutic properties of the Soviet preparation terrilytin, obtained from the culture fluid of *Aspergillus terricola* [2]. The writers showed previously that terrilytin, in conjunction with nicotinic acid, prevents hypercoagulation in the lymph and blood and has a favorable influence on the course of experimental myocardial infarction [1, 3-5].

The aim of this investigation was to study the effect of a terrilytin–nicotinic acid mixture (TNA) on the state of the ischemic myocardium.

EXPERIMENTAL METHOD

Two series of experiments were carried out on 35 rabbits. The animals of series I served as the control, and in series II, 30 min after ligation of the anterior interventricular branch of the left coronary artery a mixture of TNA was injected intravenously in the following doses: terrilytin 50 proteolytic units/kg, nicotinic acid 5 mg/kg. Tests were carried out before and 1, 3, and 7 days after the experiment (five rabbits at each time). Several oxidation-reduction enzymes and carbohydrates were studied by histochemical methods in the necrotic, perinecrotic, and intact zones of the myocardium.

EXPERIMENTAL RESULTS

One day after the production of an acute myocardial infarct (AMI) the diformazan concentration in the zone of necrosis was increased, but under these circumstances signs of "enzymic diffusion" were observed, in the form of precipitation of a homogeneous histochemical reaction product. A change in its standard parameters was observed on demonstration of glucose and, in particular, of glycogen. The increase in the cytophotometric density of cardiomyocytes in the necrotic zone must be regarded as most probably due to dissociation of the enzymes and substrates studied from the corresponding ultrastructures on which they function. This was confirmed by the subsequent sharp fall (by more than half) of the concentration of the histochemical reaction products after the third and, in particular, the seventh day (Table 1).

In the perinecrotic zone after 1 day the cardiomyocytes showed increased activity of NADPH and lactate dehydrogenases. The small increase in the glycogen and glucose concen-

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