EFFECT OF A HIGH AMBIENT TEMPERATURE ON THE STATE OF CELLULAR IMMUNITY

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A high ambient temperature is an unfavorable factor to which man is frequently exposed and which causes disturbances of the state of organs and systems [2, 6]. This necessitates a study of the principles governing changes in functional systems during hyperthermia and adaptation to heat, and a search for ways of increasing the resistance of an individual under these conditions. The most important functional system of the body as regards maintenance of its vital activity is the immune system. However, data in the literature on the effect of a high ambient temperature on the immune processes of the body are limited and contradictory.

One reason for the urgency of a study of the state of immunity in hyperthermia is the fact that the latter is widely used in clinical practice and, in particular, as a component of combination treatment of cancer patients. The use of the thermal factor in the treatment of cancer is often accompanied by general hyperthermia. The study of the state of immunity in hyperthermia, which largely determines the success or failure of treatment of cancer patients, is therefore essential for practical purposes [3, 5].

The aim of this investigation was to study some parameters of cellular immunity in acute hyperthermia and also during long-term intermittent exposure of the body to a high ambient temperature.

EXPERIMENTAL METHOD

First generation hybrid (CBA × C57BL/6)F_1 mice weighing 24-26 g were used. Hyperthermia of the animals was produced in a hot chamber at 43-44°C with constant ventilation. Acute hyperthermia was produced by keeping the animals in the hot chamber once up to a rectal temperature of 42°C and to the stage of heat shock. Long-term intermittent hyperthermia was produced by keeping the mice daily in the chamber for 20 min. The animals were exposed to the action of heat for 3, 5, 10, 20, 30, and 40 days. The rectal temperature rose during the first exposure to hyperthermia on average to 42°C. Material for investigation, in the case of a single exposure to hyperthermia, was taken immediately after removal of the animals from the hot chamber. The state of the parameters chosen for study in the case of chronic hyperthermia was studied 24 h after the last exposure. To assess cellular immunity, the proliferative activity of the spleen cells (SC) in response to stimulation by alloantigens was determined in a unidirectional mixed lymphocyte culture (MLC) [1] and the blast transformation reaction of the lymphocytes (BTRL) [4] in response to stimulation by polyclonal T-cell mitogens: phytohemagglutinin (PHA) and concanavalin A (con A). The reacting cells in MLC were SC from experimental and control F_1 hybrid mice. As stimulators we used irradiated spleen cells from BALB/c mice. The cells were cultured in medium RPMI-1640, with the addition of human serum (5-10%), L-glutamine (2 mM), 2-mercaptoethanolamine ($5 \cdot 10^{-5}$ M), and HEPES buffer (10 mM). The cellular response was recorded as incorporation of ^{3}H-thymidine into DNA of the proliferating cells, with calculation of the index of stimulation (IS):

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TABLE 1. Proliferative Response of SC (indices of stimulation) during Acute Hyperthermia (M ± m)

Type of stimulation	Series of investigations			
	hypothermia to 42°C		hypothermia to heat shock	
	control	experiment	control	experiment
PHA	6,53±0,41	9,61±0,92*	9,85±0,47	1,37±0,26*
con A	13,03±0,71	17,41±1,70*	18,01±0,59	2,06±0,56*
Alloantigens	37,00±4,78	71,89±13,35*	58,72±19,24	6,09±4,15*

Legend. Here and in Table 2: *p < 0.05 indicates significant differences.

TABLE 2. Proliferative Response of SC during Long-Term Hyperthermia (M ± m)

Type of stimulation	Series of investigations, days											
	3		5		10		20		30		40	
	control	expt.	control	expt.	control	expt.	control	expt.	control	expt.	control	expt.
PHA	11,17 ±1,08	14,67 ±1,61*	4,88 ±0,66	7,85 ±1,81	11,85 ±1,66	6,83 ±1,45*	5,68 ±0,33	4,52 ±0,31*	6,94 ±1,33	5,40 ±0,50	13,88 ±2,19	13,69 ±2,24
con A	10,79 ±0,93	12,56 ±1,09	11,38 ±1,52	13,49 ±1,84	22,34 ±2,22	12,49 ±1,93*	17,45 ±1,12	12,25 ±1,50*	13,68 ±1,37	8,48 ±0,84*	25,49 ±3,58	21,06 ±3,82
Alloantigens	14,72 ±2,42	20,48 ±4,37	12,85 ±3,97	19,27 ±3,29	54,16 ±9,47	28,59 ±7,47*	30,70 ±5,40	15,07 ±4,81*	39,58 ±8,43	9,17 ±4,10*	55,35 ±20,04	49,97 ±15,48

The series of experiments were conducted on 6-12 animals. Each variant was set up in 6-9 tests. The results were subjected to statistical analysis by Student' test.

EXPERIMENTAL RESULTS

In animals with hyperthermia and a rectal temperature of up to 42°C, functional activity of the lymphocytes was increased, as shown by an increase in the proliferative capacity of SC to respond to stimulation by alloantigens and by polyclonal T-cell mitogens PHA and con A. Hyperthermia of the mice up to heat shock led to abrupt suppression of the proliferative response of SC to stimulation both by alloantigens and by mitogens (Table 1).

Long-term intermittent hyperthermia of the animals was accompanied by a change in proliferative activity of the lymphocytes, the degree and direction of which depended on the duration of hyperthermia (Table 2). For instance, hyperthermia of the animals for 3 days led to an increase in the proliferative activity of SC in response to stimulation by PHA, but the response to con A and to alloantigens was unchanged. Hyperthermia of the mice for 5 days caused no changes in lymphocyte function. Exposure of the animals to a high temperature for 10 days led to inhibition of the proliferative activity of SC in response to stimulation by PHA, con A, and alloantigens. The proliferative response of SC to mitogens and alloantigens still remained depressed 20 days after the beginning of hyperthermia. Exposure to a high ambient temperature for 30 days was marked by restoration of the proliferative ability of SC to respond to stimulation by PHA; the response to con A and alloantigens remained depressed.

Hyperthermia of animals up to heat shock, and also intermittent hyperthermia for 10, 20, and 30 days were thus accompanied by inhibition of the cellular immune response, as shown by depression of the proliferative activity of the spleen cells of the experimental mice to stimulation both by alloantigens and by polyclonal T-cell mitogens.

During long-term hyperthermia of animals the functional activity of the lymphocytes was restored as the animals became adapted to exposure to a high temperature, as shown by restoration of normal values of proliferative activity of the spleen cells 40 days after the beginning of hyperthermia in response to stimulation by mitogens and alloantigens.

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