SPORTS MEDICINE

Relationship between the Degree of Cardiovascular Adaptation and Th1/Th2 Polarization of Immune Response

A. E. Donnikov, M. U. Shkurnikov*, E. B. Akimov*, and A. G. Tonevitsky*

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 146, No. 10, pp. 442-445, October, 2008
Original article submitted July 31, 2008

The main parameters of humoral immunity during medium intensity exercise were studied in oarsmen with high and low cardiovascular adaptation. A relationship between high cardiovascular adaptation to exercise and immune response polarization by the Th2 mechanism was demonstrated. Increased production of IL-10 in response to physical stress plays a key role in this relationship.

Key Words: *immunoglobulin E; physical activity; allergy; interleukin-10; Th1/Th2 balance*

Adaptation to intensive muscular activity is a systemic response aimed at attaining high training status with minimum biological expenditures. The immune system provides homeostasis of the internal medium of the body and plays an important role in its adaptation, including adaptation to exercise [3]. Professional athletes, particularly during intensive training, are highly susceptible to infections, for examples, infections of the upper airways [4]. Immunosuppression caused by exercise is assumed to be mainly responsible for this [1]. The key role in this process is played by interactions between $CD4^+$ T lymphocyte subpopulations. Normally type 1 T-helpers (Th1) are involved in the reaction to antigen. Predominant involvement of type 2 T-helpers (Th2) in response to antigen leads to development of atopy [6], while Th1 cells inhibiting Th2 reactions suppress IgE synthesis (Fig. 1). Stress, *e.g.* physical strain, leads to formation of allergic liability [11], while exposure to an allergen is just as a triggering mechanism.

It was experimentally proven that physical activity switches over the immune response from Th1 to Th2 variant [4]. Long intensive training reduces the count of Th1 cells in the bloodstream in humans [9]. A possible mechanism of this switch-over is changed Th1/Th2 cytokine proportion.

The data on increased level of IgE in normal subjects are scanty and contradictory. It is known that the level of total IgE increases under extreme conditions, for example, during work in space [10]. This is paralleled by an increase in the content of $CD8^+$ lymphocytes and serum IgG and reduction of the $CD16^+$ lymphocyte count.

The majority of studies were focused on highly intensive exercise, while medium and low-intensity exercises were virtually never studied. However, more than 80% training time is spent for low- and medium-intensity exercises [8].

We studied the main parameters of humoral immunity in medium-intensity exercises in subjects with different degree of adaptation to physical work.

DNA-Technology Company; *National Institute of Physical Culture and Sports, Moscow, Russia. ***Address for correspondence:*** donnikov@dna-technology.ru. A. E. Donnikov

0007-4888/08/1464-0462

MATERIALS AND METHODS

The study was carried out in the academic rowing young team members (Table 1). All athletes signed informed consent to participation in the experiment, which was approved by Ethic Committee of National Institute of Physical Culture and Sports. The study was carried out during common training sessions over a complete mesocycle consisting of four one-week microcycles. Each microcycle consisted of six training days, including the morning and evening training session, and a day of rest.

Before the study, the threshold anaerobic metabolism (TANM) heart rate was evaluated by invasive lactate method in each athlete in a step-wise test on a Concept II rowing simulator and individual pulse zones were calculated: zone 1 (aerobic): heart rate <80% TANM; zone 2: heart rats 80-100% TANM; and zone 3 (anaerobic/glycolytic): more than 100% TANM.

The entire training activity of athletes was controlled by continuous pulsometry using Polar S610 heart rhythm monitors (Polar Electro).

Immunological and allergological history of the examined subjects was collected by interviewing. On day 1 of the study, the main laboratory values of humoral immunity were evaluated. Total IgA, IgG, IgM, and C3 and C4 complement components were evaluated using commercial test systems (Roche Diagnostics) on a Hitachi 912 automated analyzer (Roche Diagnostics).

Total IgE was measured on an Elecsys 2010 electrochemiluminescent analyzer (Roche Diagnostics) at the beginning, in the middle, and at the end of the mesocycle.

The levels of IL-10 were measured on days 1 and 6 of microcycles. Blood was collected after overnight fasting before training and 1 h after it and analyzed by enzyme immunoassay (IL-10-EIA-BEST; Vector-Best).

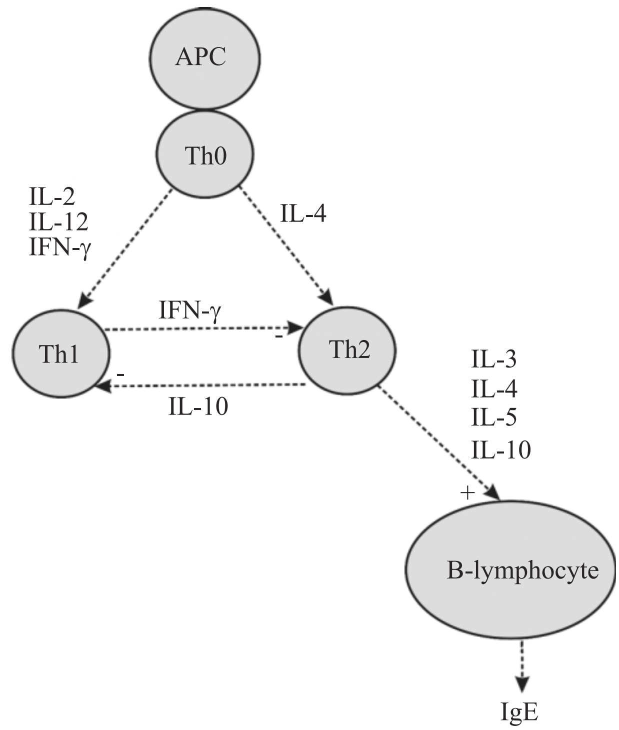

Fig. 1. Scheme of IgE synthesis activation in immune response polarization by Th2 mechanism. APC: antigen-presenting cells; Th0: “naive” T-helpers.

The differences between the values were statistically verified using Mann—Whitney *U* test.

RESULTS

All athletes were trained according to a universal plan, but the degree of cardiovascular adaptation to this exercise was different. The degree of adaptation was evaluated by the percent of athlete’s work in zones 2 and 3. Hence, the participants were divided into 2 groups: with high (group 1) and low (group 2) exercise tolerance. The mean percentage of work in zones 2 and 3 was 11.3% in group 1

TABLE 1. Physiological Parameters

Parameters	Group 1	Group 2
Number of examined subjects	5	6
Age, years	17.0 (16.5-17.2)	17.8 (17.3-18.1)
Body height, cm	191.0 (187.5-196.5)	190.5 (188.5-193.5)
Body weight at the start of the study, kg	93.0 (85.3-98.3)	96.2 (75.9-103.75)
Heart rate at rest, bpm	75.0 (68.5-80.0)	78.0 (72.0-80.0)
TANM heart rate, bpm	179.1 (173.6-181.6)	172.7 (169.0-187.4)
Heart $rate_{max}$, bpm	197.0 (194.5-203.0)	200.0 (188.0-203.0)
MOC, ml O_2/kg/min	49.4 (47.1-57.5)*	45.1 (44.6-46.9)*

Note. Here and in Table 2: the median is shown; the lower and upper quartiles are shown in parentheses. *p<0.05 compared to group 1.

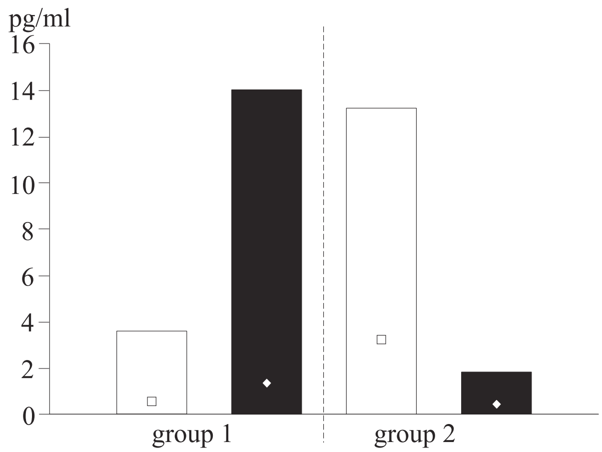

Fig. 2. Serum level of IL-10 before and after training (median, upper and lower quartiles). Light bars: before training; dark bars: after training.

from 159.3 to 536.7 U/ml and all subjects in this group had high levels of total IgE in comparison with the population level. In group 2 none of athletes had so high levels, the IgE level being 12.0-95.4 U/ml. Serum level of IgE did not change in athletes throughout the study. Hence, group 1 athletes exhibited obvious liability to allergy, which was not characteristic of group 2 athletes. The level of IgG was elevated in group 1 ($p<0.05$), while the levels of IgA and IgM were elevated negligibly.

The level of IL-10 before training was somewhat lower in group 1 than in group 2, while after training the picture was opposite (Fig. 2). Individual reactions of IL-10 to training were analyzed (increment of IL-10 level in response to exercise; Table 3). The decrease in IL-10 level in response to physical activity was more characteristic of group 2 than of group 1 athletes ($p<0.05$).

TABLE 2. Results of Immunological Study

Parameter (reference interval)	Group 1	Group 2
Total IgG (7.00-16.00, g/liter	14.80 (13.60-15.77)*	12.75 (8.69-13.50)*
Total IgA (0.70-4.00), g/liter	3.30 (2.53-3.64)	2.06 (1.72-2.13)
Total IgM (0.40-2.30), g/liter	1.26 (1.09-1.51)	0.96 (0.94-2.80)
Total IgE (0.10-100.00), U/ml	301.95 (201.00-443-.90)**	40.28 (12.35-72.97)**
C3 (0.90-1.80), g/liter	1.28 (0.62-1.69)	1.04 (0.49-1.84)
C4 (0.10-0.40), g/liter	0.26 (0.22-0.30)	0.27 (0.19-0.33)

Note. *$p<0.05$, **$p<0.001$compared to group 1.

and 23.1% in group 2, the maximum oxygen consumption (MOC) being 49.4 and 45.1 ml O_2/kg/min, respectively. No statistically appreciable differences were detected for other physiological parameters.

No clinical signs of allergy were detected in any of athletes. No cases of high eosinophil content in the blood were detected. None of the examinees had a history of specialized testing for allergy. The use of scoring system for description of allergic history (1 point corresponding to every symptom) showed a significantly higher incidence of symptoms of allergy in group 1 ($p<0.05$).

Anamnesis was confirmed by laboratory results (Table 2). In group 1, the levels of total IgE varied

TABLE 3. Variants of Individual Reaction of IL-10 to Exercise (%)

Individual reaction to training	Group 1	Group 2
Reduction of IL-10 level	36	59
No reaction	32	36
Increase of IL-10 level	32	5

The increase in IgE level in the group with high exercise tolerance can result from immune response polarization by the Th2 dependent type in these athletes. Type 2 helpers produce also IL-5, stimulating the production and secretion of Ig (particularly IgA) by B-cells. We observed a trend to elevation of serum Ig level in group 1 athletes, which can serve as an indirect evidence of this hypothesis. It is assumed that normal reaction to a stress exposure is activation of the cytokine component by the Th1 mechanism, while the observed switch-over to Th2 is a compensatory mechanism, preventing hyperactivation of the cellular component of the immune system [2]. The most probable mechanism of this switch-over is increased production of IL-10 in response to exercise in the presence of constant IFN-γ level [7]. An increase of IL-10 level in response to physical stress is characteristic of athletes with high cardiovascular adaptation, while a reduction of IL-10 level is associated with poor adaptation to exercise.

Hence, the relationship between the immune status and degree of adaptation to exercise, detected in our study, may prove to be the key to understanding of individual reactions to physical stress. Relationship between high cardiovascular adaptation to exercise and polarization of immune response by the Th2 mechanism has been shown. Activation of Th2 component results in high liability to allergic reactions. Alteration of the Th1/Th2 cytokine balance at the expense of increased production of IL-10 in response to physical stress plays the key role in this process.

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