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TITLE

ENDURANCE EXERCISE WITH AND WITHOUT A THERMAL CLAMP: EFFECTS ON LEUKOCYTES AND LEUKOCYTE SUBSETS

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Endurance exercise with and without a thermal clamp: effects on leukocytes and leukocyte subsets

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Defence and Civil Institute of Environmental Medicine, North York, Ontario M3M 3B9, Departments of Community Health and Anaesthesia, Faculty of Medicine, and School of Physical and Health Education, University of Toronto, Toronto, Ontario M5S 1A1, Canada

Cross, M. C., M. W. Radomski, W. P. VanHelder, S. G. Rhind, and R. J. Shephard. Endurance exercise with and without a thermal clamp: effects on leukocytes and leukocyte subsets. *J. Appl. Physiol.* 81(2): 822–829, 1996.—To test how leukocyte responses to endurance exercise were modified by clamping body temperature, nine men (27.3 ± 6.0 yr) completed four 80-min immersions to midchest at water temperatures of 23 or 39°C; two tests included 40-min of cycle ergometer exercise at 65% of aerobic power. When the subjects were exercising, rectal temperature peaked at 39.1 ± 0.4°C in the warm water and 37.8 ± 0.3°C in the cool water. When the subjects were sitting in warm water, rectal temperature closely matched the core temperature during exercise in cool water, whereas when they were sitting in cool water, rectal temperatures decreased to 36.4 ± 0.6°C. Total and differential white cell counts were determined by using a Coulter counter, and cortisol and growth hormone concentrations were determined by radioimmunoassay; all data were adjusted for changes of blood and plasma volumes. Heat clamping during exercise substantially reduced the rise in white cell, lymphocyte, and granulocyte counts but not the increase in monocyte count. Clamping also abolished previously observed associations between cell counts and cortisol and weakened associations with growth hormone concentrations (D. A. McCarthy and M. M. Dale. *Sports Med.* 6: 333–363, 1988). We conclude that both exercise and a rise of core temperature contribute to the changes in white cell and subset counts during and immediately after moderate exercise. Both cortisol and growth hormone concentrations appear to be mediators of these responses.

granulocytes; heat exposure; hormones; lymphocytes; monocytes

THE LEUKOCYTOSIS OF EXERCISE was well described by Garrey and Bryan (11) and has since been reviewed in detail by McCarthy and Dale (20). However, it is less clear whether the observed changes are related to the exercise-induced increase of cardiac output (30), to associated microtraumata (18) or hormone release (5, 31, 32), to the increase in core temperature (4), or to some more general stress response (15).

One method of examining the possible triggering role of core temperature is to compare leukocyte responses with exercise under conditions where body core temperature is allowed to rise with the reactions observed when core temperature is clamped by some external mechanism. Use of an air- or water-perfused suit by the subjects is difficult while they are exercising. An alternative option, adopted here, is to place a suitably grounded cycle ergometer in a large and well-stirred water bath, allowing subjects to exercise with the head and neck above the water line. Young et al. (34) have recently applied this type of technique to study metabolic adaptations to training sessions conducted under warm and cool conditions. A preliminary trial of various water temperatures established that when the present group of subjects were exercising at 65% of their maximal oxygen intake, a water temperature of 23°C largely eliminated the rise of core temperature and that the same water temperature led to a moderate fall of core temperature when the subjects were sitting at rest (unpublished observations). In contrast, when the subjects were seated in water at 39°C, there was a substantial increase of core temperature compared with while they were exercising, and under resting conditions there was a small increment of core temperature that closely matched that observed when they were exercising in the cool water. For the purpose of this report, we have designated the four conditions as hot-control, hot-exercise, cold-control, and cold-exercise, respectively.

Observations made with and without the thermal clamp have included the total white cell count and its subsets (granulocytes, monocytes, and lymphocytes). Our specific objectives were to determine *1*) whether an increase of core temperature augmented the leukocyte responses to exercise and *2*) how far the changes in leukocyte count observed under cool and warm conditions, respectively, were mediated by associated increments in plasma cortisol and growth hormone concentrations.

MATERIALS AND METHODS

Subjects

The subjects were nine moderately fit young men, aged 27.3 ± 6.0 (SD) yr, recruited from the community of our Institute and the University of Toronto in accord with a protocol approved by the Human Experimentation Review Committees of our Institute and the University of Toronto. Their physical characteristics were height of 1.79 ± 0.07 (SD) m and body mass of 80.9 ± 11.9 kg. Their peak oxygen intake, determined by cycle ergometer exercise to subjective exhaustion while they were immersed in thermally neutral water (33°C), was 41.5 ± 5.1 $ml \cdot kg^{-1} \cdot min^{-1}$. All nine subjects had remained free of infection for 6 wk before study, and none of the group was currently taking any medications.

Experimental Plan

The subjects sat on a well-grounded, electrically braked cycle ergometer (Pedalmate, Collins, Braintree, MA; modified to include a positive-pressure water seal) for each of the four immersion experiments, which were assigned according to a random-block design (Table 1). To avoid intertrial differences

Table 1. *Illustration of random block experimental design*

Time, min	Session A (hot-control)	Session B (hot-exercise)	Session C (cold-control)	Session D (cold-exercise)
0–40	Sitting at 39°C	Exercise at 39°C	Sitting at 23°C	Exercise at 23°C
40–80	Sitting at 39°C	Sitting at 39°C	Sitting at 23°C	Sitting at 23°C

Subjects are immersed to midchest in water at 23 or 39°C, and in 2 of their 4 sessions they exercise at 65% of aerobic power during first 40 min of exposure.

of circadian phase, all sessions began at the same time of day (1300), 5 h after a standard 280-ml intake of a liquid meal (Ensure Plus, Ross Laboratories, Montreal, PQ, Canada). An interval of at least 7 days was allowed between exposures.

Subjects were submerged to midchest level in a well-stirred water bath throughout each session, with the water temperature being either 23 or 39°C. Exercise at 65% of the individual's directly measured maximal oxygen intake (corresponding to an oxygen consumption of ~2 l/min) was performed for the first 40 min of two of the four sessions.

Oxygen consumption and rectal temperatures were recorded continuously and averaged for 5-min intervals. Blood samples for determination of leukocyte counts and hormone levels were collected throughout the 40-min bout of exercise and a 40-min recovery period.

Blood Sampling

Samples of blood (8 ml) were drawn from an indwelling catheter inserted into the median antecubital vein at each of 14 selected time points, for a total blood withdrawal of 112 ml per session.

For cytology, 5 ml of the blood collected at each time point were drawn into chilled, sterile liquid-EDTA glass vacutainers (Becton-Dickinson, Oakville, ON, Canada) and were immediately placed on ice.

For serum separation and subsequent hormone analysis, the remaining, additive-free 3 ml of the blood collected at each time point were allowed to clot and were then centrifuged (Beckman Instruments, Missisauga, ON, Canada) at 2,800 *g* for 10 min. Serum separation was completed within 30 min. The separated serum was immediately transferred to a freezer (−80°C).

Leukocyte Counts

Total blood cell counts, white cell differential counts (granulocytes, monocytes, and lymphocytes), and hemoglobin and hematocrit determinations were performed by using an automated counter (Coulter hematology analyzer, Coulter Electronics, Hialeah, FL). White cell counts and hormone concentrations were corrected to the immediately preceding resting blood volume and plasma volume, respectively, by using the formula of Dill and Costill (6).

Hormone Assays

Total plasma concentrations of cortisol and growth hormone were determined by radioimmunoassay, using the procedures of standard commercially available kits (Allegro Nicholls Institute, San Juan Capistrano, CA, for human growth hormone; Diagnostic Products, Los Angeles, CA, for cortisol).

Core Temperature Determinations

Core temperatures were determined by a thermistor (Baxter Pharmaseal, Valencia, CA), inserted 0.12 m above the anal sphincter.

Other Laboratory Measurements

Peak oxygen intake was determined by the subjects performing a progressive cycle ergometer test while immersed in thermally neutral water at 33°C. The pedal pace was 60 revolutions/min. After a warm-up of pedaling against water resistance (~75 W), loading of the ergometer was increased by 25 W at 1-min intervals until subjective exhaustion, reached in 8–10 min. Expired gas was collected breath by breath and was analyzed for respiratory minute volume and oxygen consumption by using a custom-built metabolic measurement unit (EMTEK). The apparatus was calibrated before and after use, by means of a 3-liter syringe and precision-analyzed cylinder gases.

Statistical Analyses

Differences between the four conditions were tested by repeated-measures analysis of variance, with post hoc location of significant differences by application of the least squares-difference method. Backward stepwise multiple-regression analyses were used to assess the influence of core temperature and cortisol and growth hormone concentrations on total leukocyte count and subsets under each of the four conditions.

RESULTS

Oxygen Consumption and Core Temperature Changes

Oxygen consumption did not differ significantly between the hot-control and cold-control conditions, averaging 1.98 ± 0.28 and 1.99 ± 0.24 l/min, respectively. When the subjects were sitting in the cool water, oxygen consumption rose slowly, terminating at an average value of 0.43 l/min, compared with 0.34 l/min when they were sitting in the warm water. Four of the nine subjects developed slight shivering during the final 15 min of the experiment.

Exercise in the warm water led to a progressive rise of rectal temperature (Fig. 1). As expected, the rectal readings were somewhat slow to respond, peaking at 39.1 ± 0.4°C 15 min after the subjects ceased exercise. In the cool water, the core temperature was held to a peak of 37.8 ± 0.3°C at the end of exercise, dropping to 37.5°C during the recovery period. When the subjects were sitting in warm water, the temperature response closely matched the response to exercise in cool water, whereas their sitting in cool water led to a steady decrease of core temperature, with a final reading of 36.4 ± 0.6°C.

Blood and Plasma Volume Changes

Blood and plasma volume changes followed the expected pattern. The decrease in blood volume peaked at an average of 5.9% for exercise in cool water, 7.1% for exercise in warm water, 2.7% for sitting in warm water, and 3.4% for sitting in cool water. Changes in mean corpuscular volume were generally <0.5%, and the

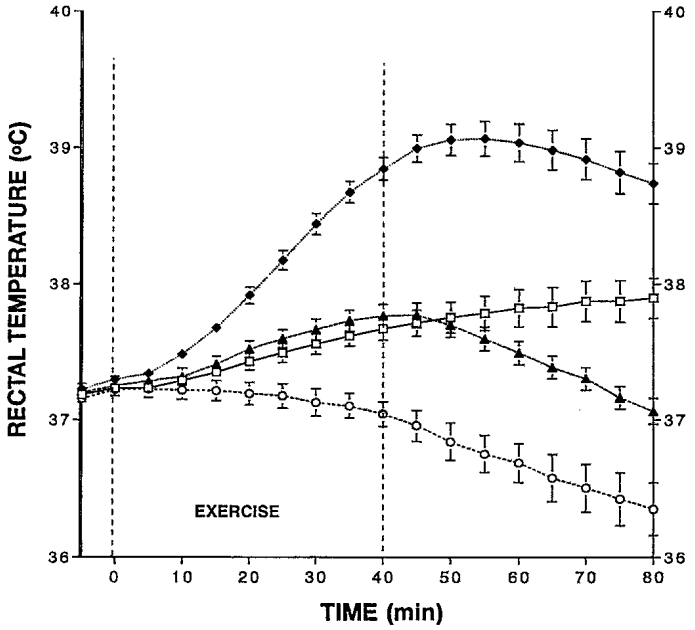

Fig. 1. Rectal temperature readings under the 4 experimental conditions. Values are means ± SE of data for 9 subjects. □, Hot-control; ◆, hot-exercise; ○, cold-control; ▲, cold-exercise.

corresponding peak decreases in plasma volume averaged 9.8, 12.9, 4.7, and 5.9%.

White Cell Count

The average white cell count (Fig. 2) was initially within the expected normal limits of 4.8–10.8 × 10^9 cells/l (33). There were significant increases when the subjects exercised, whether under cool or warm conditions, although the two curves differed significantly from each other between 10 min of exercise and 40 min of recovery. Counts remained below the ceiling of normality throughout exercise and quickly reached a plateau (particularly in the cold-exercise condition). When in the warm water, the subjects showed a significant secondary rise of white cell count during the recovery period. During seated rest in the warm water, subjects developed a small, progressive increase in white cell count, which was first statistically significant when core temperature had risen to 37.5°C. The subjects sitting in the cool environment produced no significant changes in white cell count.

Lymphocyte Count

Lymphocyte counts rose rapidly at the beginning of exercise (Fig. 2), before there had been any appreciable increase in core temperature. In the hot-exercise condition, counts continued to rise, peaking somewhat above the normal range of 1.2–3.4 × 10^9/l at 30 min of effort, but in the cold-exercise there was a subsequent decline of cell count as exercise continued; the two curves differed significantly from each other between 5 min of exercise and 20 min of recovery. After exercise, counts dropped significantly below the initial resting level, although remaining within the normal range; this effect was much larger for the cool than for the warm condition.

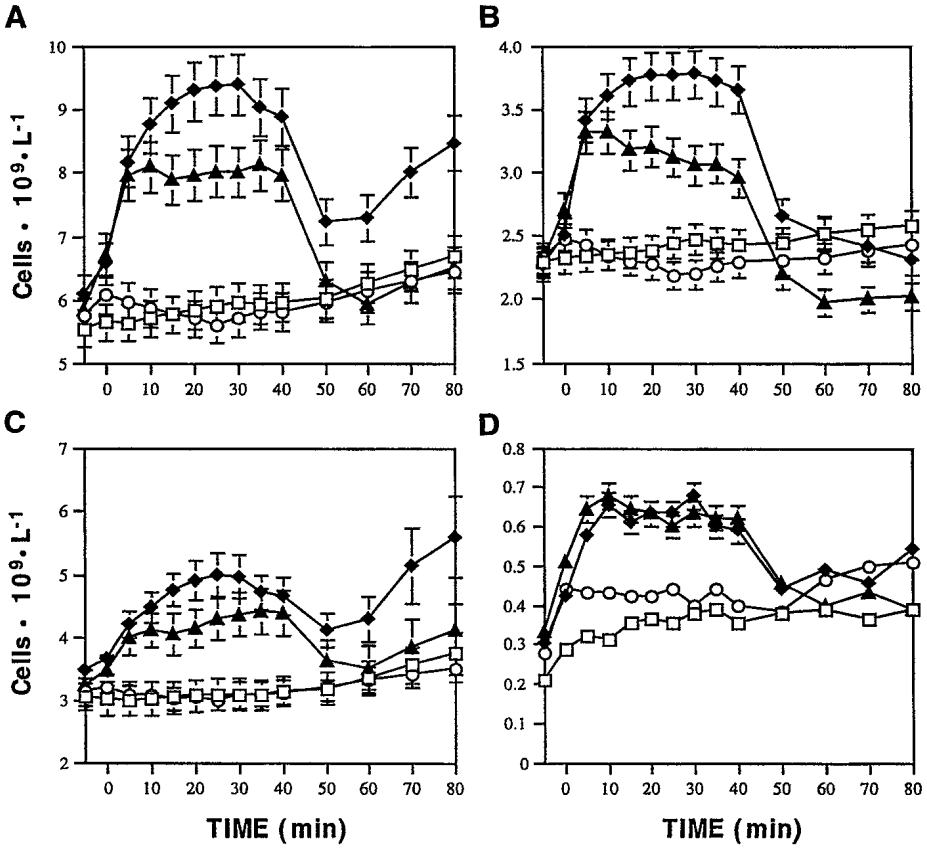

Fig. 2. White cell (*A*), lymphocyte (*B*), granulocyte (*C*), and monocyte (*D*) counts under the 4 experimental conditions. □, Hot-control; ◆, hot-exercise; ○, cold-control; ▲, cold-exercise.

Seated rest induced a progressive increase of lymphocyte count, significant from 50 to 80 min, in the hot-control condition, whereas in the cold-control there was a small decrease in count, significant from 25 to 35 min of exposure.

Granulocyte Count

Exercise in the warm environment produced a progressive increase in granulocyte count (Fig. 2), already significant at 5 min, before core temperatures had risen appreciably; counts peaked within the normal range of 1.4–6.5 × 10^9/l at 30 min of exercise and decreased subsequently despite the continuing rise of core temperature. Exercise in the cool environment produced a slower increase in granulocyte count; the response was statistically significant from 5 to 40 min of exercise, but there were also significant differences between the two curves both for 15–25 min of exercise and throughout the recovery period (when the hot-exercise condition was associated with a steep secondary rise in granulocyte count).

There was little change in granulocyte count during seated rest, except that in the hot-control condition counts were significantly increased for the 70th and 80th min of exposure.

Monocyte Count

The monocyte count rose quickly to exceed normal limits of 0.11–0.59 × 10^9/l when the subjects were exercising in both environments (Fig. 2). Significant gains were seen at 5 min, before there had been any appreciable increase of core temperature. In the cold-exercise condition there was then a trend to a downward-sloping plateau as exercise continued, with significant differences between the two environments at 20–30 min of exercise and throughout recovery. During the hot-exercise experiments, counts continued to climb to 30 min of exercise, but again a downward-sloping plateau was seen during the final 10 min of exercise. The hot-control condition induced a small but progressive increase of monocyte count, first significant at quite a small increment of core temperature (0.2°C at 20 min of exposure). The cold-control condition gave no significant changes, although there was a slight trend toward an increase in monocyte count during the final 15 min of the experiment, when some of the subjects had begun to shiver.

Cortisol

When the subjects were exercising in the heat, cortisol concentrations (Table 2) rather closely mirrored the changes in rectal temperature (Fig. 1). Increments were first statistically significant after 15 min of exercise, and values peaked at a mean of 22.2 ± 6.6 (SD) μg/dl 10 min postexercise, with a subsequent decline of cortisol concentrations in parallel with the decrease of core temperature. When the subjects were exercising in cool conditions, there was a much smaller peak of 12.2 ± 4.6 μg/dl, statistically significant from 10 to 40 min of exercise; however, the values differed significantly from those for hot-exercise at all times except 15 and 20 min of exercise.

Table 2. *Concentrations of cortisol and growth hormone at selected points during four experiments*

Time, min	Hot-Control	Hot-Exercise	Cold-Control	Cold-Exercise
		Cortisol		
0	7.5 ± 1.4	7.5 ± 0.7	7.7 ± 0.9	9.3 ± 1.6
20	6.0 ± 0.6	11.4 ± 1.2	8.0 ± 0.8	12.5 ± 1.2
40	6.7 ± 0.8	18.6 ± 2.4	7.3 ± 0.7	11.5 ± 1.5
60	8.6 ± 0.9	20.0 ± 2.1	7.9 ± 0.8	9.9 ± 1.1
80	10.2 ± 1.2	16.3 ± 1.9	8.1 ± 1.1	8.4 ± 0.8
		Growth hormone		
0	0.7 ± 0.4	0.5 ± 0.3	0.2 ± 0.1	0.2 ± 0.1
20	1.2 ± 0.4	1.6 ± 0.5	0.2 ± 0.1	0.7 ± 0.3
40	1.2 ± 0.4	2.0 ± 0.4	0.1 ± 0.05	1.2 ± 0.3
60	1.0 ± 0.3	1.0 ± 0.3	0.04 ± 0.02	0.7 ± 0.2
80	0.6 ± 0.2	0.7 ± 0.2	0.05 ± 0.03	0.4 ± 0.2

Values are means ± SE for 9 subjects given in μg/dl.

Seated rest led to no significant changes of serum cortisol in either warm or cool conditions (Table 2).

Growth Hormone

When the subjects were exercising in the warm environment, serum growth hormone concentrations increased by some 1.5 μg/dl to a peak of 2.0 ± 1.3 μg/dl, with changes from baseline being significant from 10 to 80 min (Table 2). Exercise in the cool environment produced a much smaller increase of growth hormone concentrations, to a peak of 1.2 ± 0.9 μg/dl; although statistically significant from 15 to 60 min, the peak value was marginally less than the value of 1.2 ± 1.1 μg/dl reached when the subjects were sitting in the hot-control condition at a similar core temperature. When the subjects were sitting at rest in the cold-control condition, no significant changes of growth hormone concentration were seen.

Multiple-Regression Analyses

Leukocytosis. A combination of cortisol and growth hormone concentrations and rectal temperature readings accounted for 77–86% of the observed variance in white cell count under the four experimental conditions (Table 3). When the subjects were exercising in the heat, all three of the measured variables showed substantial increments, and all made independent contributions to the description of variance in white cell count: growth hormone and rectal temperature had positive associations, and cortisol provided a negative association. When the subjects were exercising under cool conditions, there was still a substantial increase of growth hormone concentration, but the multiple-regression analysis showed no significant association of growth hormone with leukocyte count. Moreover, in contrast to the hot-exercise condition, cortisol now showed a positive association with the white cell count. In the hot-control condition, there was little change in either hormone, and the only significant association revealed by the multiple-regression analysis was a decrease in cell count as rectal temperatures fell.

Table 3. *Multiple-regression equations fitted by backward stepwise procedure, relating white cell count to concentrations of cortisol and growth hormone and to rectal temperature for four experimental conditions*

Variable	Hot-Control	Hot-Exercise	Cold-Control	Cold-Exercise
White cell count ($\times 10^9$/l)				
r^2	0.86	0.83	0.77	0.80
Cortisol (μg/dl)		−0.55 ± 0.15		0.56 ± 0.08
Growth hormone (μg/dl)		1.52 ± 0.29		
Temperature (°C)	1.19 ± 0.14	3.79 ± 1.16	−0.68 ± 0.13	
Residual	−38.7 ± 5.2	−130.7 ± 42.1	31.2 ± 4.8	1.19 ± 0.88
SEE	0.13	0.51	0.10	0.43
Lymphocyte count ($\times 10^9$/l)				
r^2	0.85	0.93	0.10	0.87
Cortisol (μg/dl)		0.08 ± 0.01		0.39 ± 0.05
Growth hormone (μg/dl)	0.70 ± 0.09	1.23 ± 0.10		−0.65 ± 0.20
Temperature (°C)	0.015 ± 0.002			
Residual	1.74 ± 0.09	2.73 ± 0.16	2.43 ± 0.09	−1.07 ± 0.44
SEE	0.04	0.19	0.08	0.21
Granulocyte count ($\times 10^9$/l)				
r^2	0.93	0.67	0.87	0.82
Cortisol (μg/dl)		−0.40 ± 0.11		0.22 ± 0.05
Growth hormone (μg/dl)	−0.48 ± 0.07			1.87 ± 0.43
Temperature (°C)	0.82 ± 0.07	3.31 ± 0.79	−0.48 ± 0.05	−2.70 ± 0.71
Residual	−27.13 ± 2.71	−116.5 ± 28.9	21.1 ± 2.0	101.7 ± 26.3
SEE	0.06	0.36	0.06	0.18
Monocyte count ($\times 10^9$/l)				
r^2	0.83	0.76	0.64	0.82
Cortisol (μg/dl)		−0.05 ± 0.02		0.07 ± 0.01
Growth hormone (μg/dl)	0.10 ± 0.03	0.15 ± 0.03	0.87 ± 0.27	
Temperature (°C)	0.13 ± 0.03	0.34 ± 0.14	−0.25 ± 0.06	
Residual	−4.76 ± 0.94	−11.76 ± 4.98	9.71 ± 2.11	−0.24 ± 0.11
SEE	0.02	0.06	0.04	0.05

Values are β-coefficients. SEE, standard error of estimate.

Lymphocytes. Hormonal and thermal measurements accounted for 10–93% of the variance in lymphocyte counts (Table 3). When the subjects were exercising in the heat, lymphocyte counts increased in relation to increments in both cortisol and growth hormone. Exercise under cool conditions strengthened the association between lymphocyte count and cortisol readings but changed the effect of growth hormone from a positive to a small negative association. When subjects were sitting in the heat, the cortisol term that had been seen when they were exercising at a comparable rectal temperature was eliminated from the equation, but a small, independent thermal term was added. When subjects were sitting in the cool environment, there were no statistically significant regression coefficients.

Granulocytes. Hormonal and thermal data described 67–93% of the variance in granulocyte counts (Table 3). When the subjects were exercising in the heat, cortisol had a strong negative association with granulocyte counts and temperature had an independent positive association, but there was no significant growth hormone term in the prediction equation. When the subjects were exercising under cool conditions, the smaller increase in cortisol concentration had a positive association, and growth hormone also had a positive association, but rectal temperature had a negative association with granulocyte counts. In the hot-control condition, there was a large temperature term in the equation and a smaller negative association with growth hormone concentration, whereas in the cold-control condition, only the negative temperature coefficient was statistically significant.

Monocytes. Hormonal and thermal data accounted for 64–83% of the variance in monocyte counts. When the subjects were exercising under warm conditions, cortisol had a negative association with monocyte count, whereas growth hormone concentration and rectal temperature made positive contributions to description of the data (Table 3). However, when the subjects were exercising under cool conditions, the only contribution was a significant positive association with cortisol concentration. The hot-control condition stood in contrast with cold-exercise, despite a similar core temperature; the hot-control data showed associations with both growth hormone and temperature but no association with cortisol. In the cold-control condition, there was a significant association with growth hormone and a negative term in the equation relating to rectal temperature.

DISCUSSION

Choice of Experimental Conditions

The experimental conditions chosen for the present experiment seem well suited to determining the respective contributions of heat and of exercise to the changes in white cell count and subsets observed during exercise of the immersed subject, although both thermal and metabolic responses could conceivably differ when the subjects are exercising in air.

When the subjects were exercising in warm water, there was a substantial associated rise of rectal temperature, but when they were exercising in the cool water, there was only a minor thermal change, almost exactly matched by the response observed when they were sitting in warm water. The responses observed thus represent the effects of slight body cooling, slight body heating, exercise with an equivalent small increase of core temperature, and exercise plus heat. Our data do not allow a precise assessment of the relative contributions of core and skin temperatures to the changes described, but from the similarity of control data when the subjects were sitting in hot and cool water, it appears that any contribution of the cutaneous receptors was small.

Effects of Heat

The present data for immersed subjects show a clear reduction of white cell, lymphocyte, and granulocyte responses from the hot-exercise to the cold-exercise condition (Fig. 2). The findings agree with and extend earlier observations (4, 28) showing that the exercise responses observed at normal air temperature were exacerbated when the environmental air temperature was warm (40°C, 30% relative humidity), particularly if the exercise bout was repeated with a short rest interval that did not allow a completion of body cooling.

Given that our cold-exercise condition still allowed a modest rise of rectal temperature, it might be asked whether even the leukocytosis seen in these experiments was triggered by the rise in core and/or skin temperature. However, Fig. 2 shows that this is not the case. The hot-control condition increased skin temperatures to near 39°C and generated a higher final peak rectal temperature than did exercise in the cool water, yet there was almost no associated white cell response [again mirroring the findings of Severs et al. (28)]. Does a rise of body temperature produce a response only when heat exposure is accompanied by exercise, or does exercise merely bring the thermal stimulus to a threshold level where a leukocyte response is observed? The latter explanation seems correct, because [as reviewed by Brenner et al. (3)] passive exposures to either hot air or hot water generate a substantial leucocytosis, given a sufficient increase of core temperature. The threshold for such a response seems to be a core temperature of ~38°C; Severs et al. (28) saw no change when their subjects sat in warm air until core temperatures had increased by 0.7°C, but Beisel et al. (1) and Kappel et al. (17) both observed substantial increments of total white cell count when heat exposure in a climatic chamber or a water bath, respectively, had elevated the subjects' core temperature to 38°C.

The increment of total white cell count reflects increases in several leukocyte subsets: lymphocyte, monocyte, and granulocyte. The changes in lymphocyte and granulocyte counts are similar to those noted for the total white cell count, but in the case of the monocytes, all of the change seems attributable to exercise, with no additional effect from the warm environment. Although we discovered quite a clear-cut, exercise-only response in the present study, Severs et al. (28) found that if subjects performed a second bout of exercise before they had fully recovered from the first, then the monocytosis during and after the second bout of exercise was greater if the environment was warm.

Mediators of the Leukocytosis

All data were adjusted for changes of blood volume (cell counts) or plasma volume (hormones), an important precaution in view of the substantial changes in these variables induced by exercise and heat.

Heat exposure alone gave rise to some increase in the corrected plasma concentration of growth hormone, but cold-exercise induced higher plasma levels of cortisol and growth hormone than those that were seen when the subjects were sitting in warm water at a similar core temperature (Table 2). Concentrations of both hormones were further increased by the combination of exercise and heat exposure (hot-exercise condition in Table 2).

The backward stepwise multiple regression provides some indication of the extent to which these hormonal changes may have mediated the observed changes in cell counts.

Exercise

When the subjects were exercising in a cool environment, cortisol was associated with increases of both total white cell count and the various subsets. Growth hormone concentration was positively associated with the granulocyte count, although it was negatively related to lymphocyte count. Core temperature had an independent negative association only with granulocyte count. Hoffman-Goetz and Pedersen (15) previously pointed to the high surface density of growth hormone receptors on human mononuclear leukocytes. However, in support of the present findings, infusion of growth hormone primarily affects the neutrophil count (16).

Heat

The responses of the subjects when they were sitting in the warm water may have been limited because peak temperatures remained below the response threshold. Nevertheless, core temperature readings in the hot-control condition were positively associated with white cell, lymphocyte, granulocyte, and monocyte counts. Kappel et al. (17) have demonstrated that passive heating induces only minor changes in plasma catecholamine concentrations. We saw no changes in cortisol and only minor increments in growth hormone concentrations, but, nevertheless, granulocytes showed a small negative association and monocytes a positive association with growth hormone levels.

Heat Plus Exercise

The combination of heat plus exercise consistently reduced the positive association between cortisol and the various cell counts that had been observed when the same exercise was performed under cool conditions; moreover, associations of cortisol with granulocyte and

monocyte counts became negative. Differences in the duration of exercise and recovery observations and interactions between hormones may explain conflicting earlier reports on association (22, 23, 25) or lack of association (7, 12, 14, 19, 26) between cortisol and white cell or neutrophil counts.

In the present experiments, the early increase in cell counts diminished as exercise continued. During the latter half of the exercise period, circulating cortisol concentrations approached the capacity of the corticosteroid-binding globulin (~20 μg/dl; Refs. 13, 20), and rising free cortisol concentrations would have facilitated egress of leukocytes into the active muscles (2, 9, 10, 29).

The association of cell counts with growth hormone concentrations was also modified relative to cold-exercise, with positive associations being seen with respect to white cell, lymphocyte, and monocyte counts. Probably because core temperatures rose above the response threshold, temperature also showed strong independent associations with white cell, granulocyte, and monocyte counts but not with lymphocyte count.

Other Possible Mediators

Core temperature in itself could provoke a change in cell counts simply by increasing cardiac output and thus flushing additional cells into the central circulation (8, 19, 24, 30). The temperature of the water bath (39°C) was enough to cause near-maximal cutaneous vasodilation, although the maximal skin blood flow (5–6 l/min; Ref. 27) remains small relative to the likely muscle blood flow (~13 l/min at an exercise oxygen consumption of 2 l/min).

Catecholamines also cause a demargination of splenic leukocytes and thus increased white cell counts (4, 5, 29, 31, 32), although it remains unclear whether norepinephrine (4) or epinephrine (31, 32) is the more important mediator. Passive elevation of core temperature by water immersion leads to only minor changes in catecholamine levels (17), but the intensity of exercise adopted would have been sufficient to increase plasma catecholamine levels. Unfortunately, available blood samples were insufficient to permit analyses of catecholamines in the present study.

Conclusions

Both exercise and a rise of core temperature contribute to the changes in white cell and subset counts during and immediately after moderate exercise. Cortisol and growth hormone concentrations appear to play significant roles in mediating these responses; the observed counts reflect the interaction among core temperature, hormonal influences, and other effects of exercise.

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