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LEUCOCYTOSIS, THROMBOCYTOSIS, AND PLASMA OSMOLALITY DURING REST AND EXERCISE: AN HYPOTHESIS

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The mechanism for inducing leucocytosis (increase in white blood cells) and thrombocytosis (increase in platelets) during exercise is unclear. Because plasma osmolality (Osm) may influence T-cell proliferation, Osm and the number of leucocytes (WBC) and platelets in blood were measured periodically during a 90 min rest period, and were compared with those during upright sitting ergometer exercise in six untrained, healthy men who cycled for 70 min at 71% of their maximal oxygen uptake ($\dot{V}O_{2max}$). There were 6 experiments in which the subjects drank different fluid formulations (10 $ml \cdot kg^{-1}$) of various ionic and osmotic concentrations intermittently during 60 min of the rest period and during the exercise period. Osmolality, and WBC and platelet counts increased significantly ($p < 0.05$) within the first 10 min of exercise, but the additional 60 min of exercise did not significantly change the leucocytosis or thrombocytosis. There were low but significant correlations between individual values of total WBC and total Osm during exercise ($r_{0.001(2),284} = 0.39$) and during rest plus exercise ($r_{0.001(2),499} = 0.43$). With combined data from the six experiments, mean Osm correlated highly and significantly with both mean WBC ($r_{0.001(2),6} = 0.95$, $p < 0.001$) and mean platelets ($r_{0.001(2),6} = 0.94$, $p < 0.01$) during the exercise phase. These data indicate that increases in leucocytes, thrombocytes, and osmolality occur primarily within the first 10 min of high-intensity exercise, but neither hypovolemia nor hyperthermia during exercise contributed to the leucocytosis, thrombocytosis, or hyperosmolality. The high correlations between plasma Osm and WBC or platelet counts suggest changes in osmolality may contribute to the mechanism of leucocytosis and thrombocytosis induced by exercise.

Key words: *immune parameters, white blood cells, platelets*

INTRODUCTION

The mechanisms for exercise-associated increases in white blood cell counts (leucocytosis) and platelet counts (thrombocytosis) have not been elucidated. Whether acute leucocytosis confers only transient immuno-enhancement or

long-term resistance to infection is not clear (1). Thrombocytosis during the first min of exercise (2) may result in myocardial infarction (3). Understanding the mechanisms for thrombocytosis and leucocytosis may have applications for hospitalized deconditioned patients, trained athletes, and immunosuppressed individuals (2).

Suggested mechanisms for leucocytosis during exercise include: increased cardiac output (4) and blood flow or pressure (5—7); elevated level of catecholamines that facilitate release of stored leucocytes from the spleen, liver, and lungs (6, 8—11); elevated corticosteroid levels that stimulate delayed leucocytosis (primarily neutrophils) from the bone marrow (9, 12, 13); and hyperthermia (14, 15) or muscle damage (16) associated with exercise which mobilizes leucocytes. The predominant hypothesis is the catecholamine release response; however, there is significant opposing evidence (17, 18). Possible mechanisms for exercise-associated thrombocytosis are similar in that increased circulation may contribute (7, 19, 20), and other data (13) implicate rising catecholamine and lactate levels; however, there is contradictory evidence from Dawson and Ogston (17).

Such variable and contradictory factors and responses suggest incomplete understanding of the mechanisms involved, and the probable action of undefined factors. One such additional factor could be increased plasma osmolality which appears to be associated with lower T-lymphocyte $CD4^+/CD8^+$ ratios after exercise (21). This is supported by evidence of increased T-cell proliferation in vitro with concentrations of NaCl or KCl up to 40 mM; however, proliferation decreases with ionic concentrations higher than 40 mM (22). Also, mitogenic stimulation of PNA-negative murine thymocytes is enhanced with increased osmolality (by NaCl or KCl) of the culture medium (23).

Thus, the purpose for this study was to further examine the role of plasma osmolality on white blood cell (WBC) and platelet responses at rest and during submaximal exercise.

MATERIAL AND METHODS

Subjects

Six healthy untrained men (age 22—39 yr) gave written, informed consent to participate in this study which was conducted at Ames Research Center (ARC) in the Laboratory for Human Environmental Physiology and approved by the ARC and San Francisco State University human subjects' committees. The subjects passed a comprehensive medical exam including a treadmill exercise test. Their anthropometric and physiological measurements ($\bar{X} \pm$ SD) were 76.84 ± 16.19 kg, 182 ± 7 cm ht, $3{,}124 \pm 505$ ml plasma vol, and $5{,}522 \pm 923$ ml blood vol. Peak exercise data were: work load = 253 ± 21W, heart rate = 187 ± 17 bpm, $\dot{V}O_{2max} = 2.99 \pm 0.19$ L · $_{min}^{-1}$ or 40 ± 10

$mL \cdot min^{-1} \cdot kg^{-1}$, pulmonary ventilation ($\dot{V}_{E\,BTPS}$) = 126 ± 15.04 $L \cdot min^{-1}$, and respiratory exchange ratio (R_E) = 1.25 ± 0.09.

Procedure

After familiarization sessions with the equipment, the subjects underwent a peak oxygen uptake ($\dot{V}O_{2peak}$) ergometer exercise test (model 846 ergometer, Quinton Instruments Co., Seattle, WA). Each subject arrived at the laboratory at 0700 hr weekly for six consecutive weeks. After consuming 220 mL of reconstituted frozen orange juice and two English muffins with jelly, the subjects urinated and inserted a rectal thermister about 16 cm. Dressed in shorts (weighed dry), they were weighed (±5 g) on a digital scale (model 5780, National Controls, Inc., San Carlos, CA). The subjects then sat for 90 min to have EKG sensors attached and a venous catheter (Quik-Cath, Travenol Laboratories, Inc., Deerfield, IL) was inserted into an antecubital vein. They drank fluids of various content intermittently for 60 min during rest, but drank the same formulation intermittently during subsequent exercise. Rest was 90 min followed by a 15-min repositioning period, then 70-min of sitting submaximal exercise (71 ± SD 7 % $\dot{V}O_{2max}$, 134 ± 22 W load) followed by 30 min of recovery (*Fig. 1*).

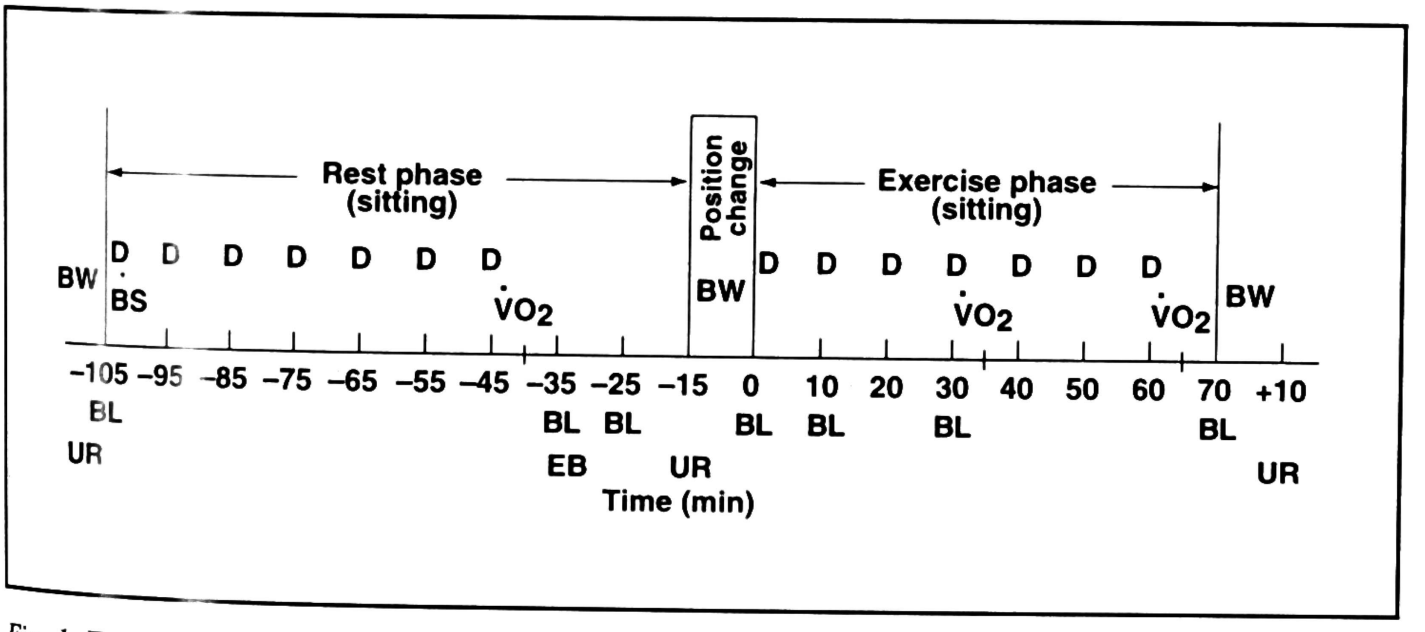

Fig. 1. Experimental Protocol. BW = body wt, UR = urinate, BL = Blood draw, $\dot{V}O_2$ = oxygen uptake, D = Drink (1/7 of total vol.), EB = Evans blue dye

Drinks

There were four fluid formulations used in the six-weekly treatments: Performance 1 (P1); Performance 2 (P2); Performance 2G (P2G); and AstroAde (AA) (*Table 1*). In one treatment the subjects drank nothing (0). During the rest phase the drinks, ingested semi-randomly, differed according to the treatment: during subsequent exercise P1 was consumed in five treatments and there was no drinking in the sixth; P2 and P2G were double the concentration of P1, and P2G contained 4% glycerol. These drink formulations were used to change plasma osmolality to test the hypothesis. The formulation designations for the six treatments for the respective rest/exercise periods were: P1/P1; P2/P1; P2G/P1; AA/P1; 0/P1; or 0/0. Drink volume was 10 $mL \cdot kg^{-1}$ body weight for both rest and exercise phases. P1 is a commercial product of Yamanouchi Shaklee Pharma (San Francisco, CA) and AA was formulated at Ames Research Center. Each drink was reconstituted from powder with demineralized water immediately prior to testing.

Table 1. Measured drink solute concentrations.

	P1[a]	P2[b]	P2G[d]	AA[d]
Na^+ ($mEq \cdot L^{-1}$)	55.2	97.1	112.7	163.7
K^+ ($mEq \cdot L^{-1}$)	5.3	10.3	10.7	<0.1
Osmolality ($mOsm \cdot kg\ H_2O^{-1}$)	365	791	1,382	253
Glycerol ($mg \cdot dL^{-1}$)	2.0	4.0	2,916	1.0
Glucose ($mg \cdot dL^{-1}$)	2,049	3,579	3,543	<0.5
Citrate ($mg \cdot dL^{-1}$)	416	753	731	854

[a] Shaklee Performance.
[b] Double-strength Shaklee Performance.
[c] Double-strength Shaklee Performance plus 80 ml glycerol.
[D] AstroAde — NaCl/Na citrate.

Physiological measurements

Heart rate was measured with a cardiotachometer (model 78203C, Hewlett Packard, Waltham, MA). Mean room dry bulb temperature was 21.8 ± SD 3°C and relative humidity was 50 ± SD 2%. A fan increased airflow to 16.2 ± SD 1.2 $m \cdot min^{-1}$.

A 15 mL blood sample was drawn with an 18-gauge catheter from the right antecubital vein at each time interval (*Fig. 1*), except at −25 min and −35 min when 20 mL were drawn. Total blood withdrawn was 115 mL per experiment.

Blood hemoglobin (Hb) was determined *via* the cyanomethemoglobin method with a Coulter Diluter II and Hemoglobinometer (Coulter Electronics, Hialeah, FL). After centrifugation for 10 min at 11,500 rpm (model MB, International Equipment Co., Needham Heights, MA), four microcapillary tubes were read with a microcapillary tube reader (model CR International Equipment Co.) for hematocrit (Hct). Plasma was frozen (−20°C) for later analysis.

Percent change in plasma volume (PV) was calculated (25): $\% \Delta PV = 100[Hb_B / Hb_A \times \times (1 - Hct_A \times 10^{-2} / 1 - Hct_B \times 10^{-2})] - 100$ where: A is after and B is before an interval of time.

Plasma osmolality (Osm) was measured by freezing-point depression (model 3DII, Advanced Instruments Digimatic Osmometer, Needham Heights, MA). Plasma volume was measured from frozen plasma with the Evans blue dye (T-1824, New World Trading Corp., DeBary, FL) dilution technique from one 10-min post-dye injection blood sample (24, 25). Total WBC and platelets in whole blood were determined with a Cobas Helios hematology analyzer (Roche Diagnostic Systems, Inc., Branchburg, NJ). Rectal temperature was measured with series 400 thermistors (Yellow Springs Instrument Co., Yellow Springs, OH) and monitored *via* computer with a Squirrel meter-logger (Grant model 1200, Science/Electronics, Inc., Miamisburg, OH).

Statistical analysis

The data were analyzed by one-way analysis of variance, nested analysis of variance, and correlation coefficients using Minitab version 8.3 statistical program (Minitab Inc., State College, PA). The null hypothesis was rejected when $p < 0.05$. Nonsignificant differences were noted by NS. All data are expressed as mean ± SE unless indicated otherwise.

RESULTS

Leucocytes (WBC)

All subjects had resting WBC counts within the normal range of $3.4 - 11.0 \times 1000/mm^3$, with the exception of one subject during rest in P2/P1

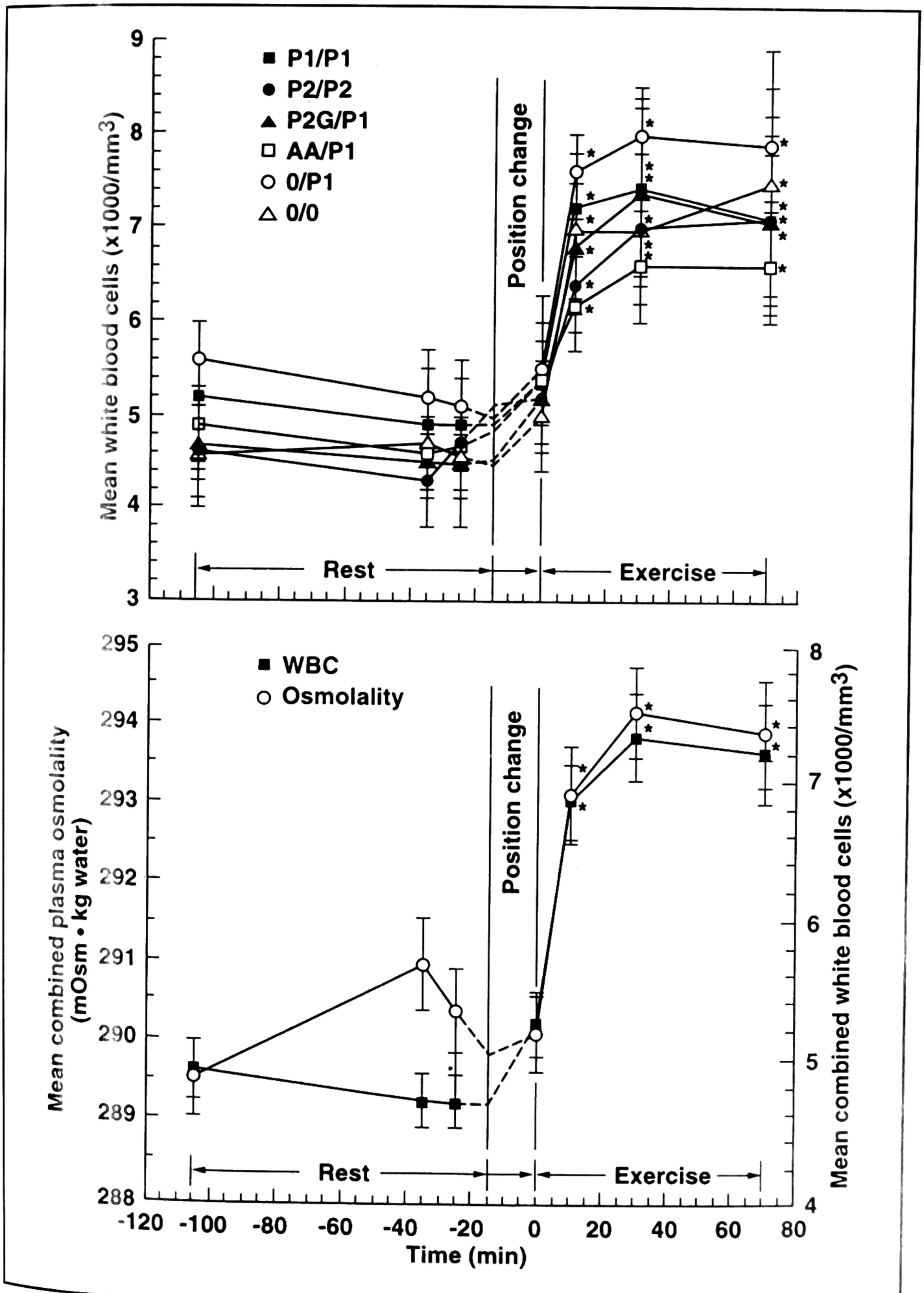

Fig. 2. Upper panel: Mean (±SE) white blood cells for each treatment. Lower panel: Mean (±SE) combined plasma osmolality and white blood cells for all treatments and subjects during rest and exercise. * ($p < 0.05$) from time 0.

and another during rest in P2G/P1, AA/P1 and 00 (*Fig. 2*, upper panel). A rapid change in WBC occurred during the first 10 min of exercise ($p < 0.001$) with the treatments and the elevation was sustained throughout the exercise period (*Fig. 2*, upper panel). In the first 10 min of exercise the mean combined WBC (sum of all values) increased from 5.2 ± 0.2 to $6.9 \pm 0.3 \times 1000/mm^3$ ($\Delta = 31\%$, $p < 0.001$, *Fig. 2*, lower panel). From 10 to 30 min of exercise the WBC increased slightly by 8.9% (NS) and then leveled off throughout the remaining 40 min.

Plasma osmolality (Osm)

Resting Osm of all subjects ranged from 283—299 $mOsm \cdot kg^{-1}$ and were within the normal range of 280—295 $mOsm \cdot kg\ H_2O^{-1}$ 95% of the time (*Fig. 2*, lower panel). Exercise Osm levels ranged from 284 to 310 $mOsm \cdot kg^{-1}$ and were within the normal range 82% of the time. Osm was unchanged at rest and increased significantly from 290.1 ± 0.5 at time 0 to 293.1 ± 0.6 $mOsm \cdot kg^{-1}$ ($p < 0.001$) at 10 min of exercise and remained at this level thereafter (*Fig. 2*, lower panel).

Platelets

All subjects had resting platelet numbers within the normal range of $150—450 \times 1000/mm^3$ (*Fig. 3*, upper panel). Mean combined platelet counts increased significantly from 210.1 ± 7.2 at time 0 to $232.9 \pm 7.4 \times 1000/mm^3$ during the first 10 min of exercise ($\Delta = 10.9\%$, $p = 0.031$, *Fig. 3*, lower panel). Number of platelets changed further by +4.1% (NS) from 10 to 30 min of exercise, and by 6.8% (NS) from 30 to 70 min, with a total change during exercise of 21.8% ($p < 0.001$). The number of platelets was significantly higher at 10, 30, and 70 min when compared to that at the start of exercise (0 min).

During exercise there was a low but significant correlation between Osm and WBC ($r_{0.001(2),284} = 0.39$, $p < 0.001$) with individual data, and a low nonsignificant correlation between Osm and platelets ($r_{0.001(2),284} = 0.02$). However, there were significant correlations during exercise between mean combined Osm and WBC ($r_{0.001(2),6} = 0.95$, $p < 0.001$, *Fig. 2*, lower panel), between mean combined Osm and platelets ($r_{0.001(2),6} = 0.94$, $p < 0.01$, *Fig. 3*, lower panel), and between mean combined platelets and WBC ($r_{0.001\,(2),\,6} = 0.94$, $p < 0.01$) suggesting these two cell populations responded similarly.

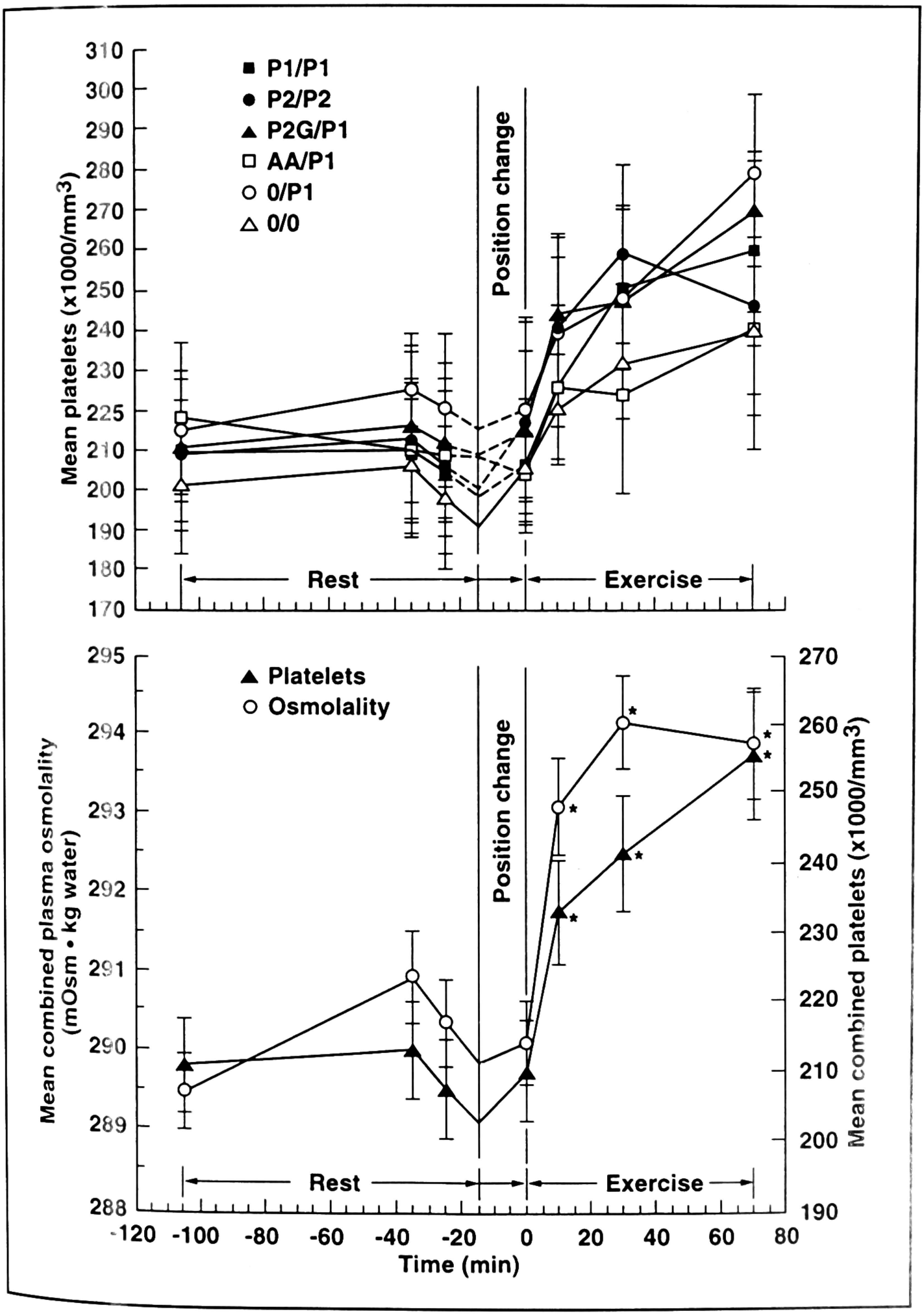

Fig. 3. Upper panel: Mean (±SE) platelets for each treatment. Lower panel: Mean (±SE) combined plasma osmolality and platelets for all treatments and subjects during rest and exercise. * ($p < 0.05$) from time 0.

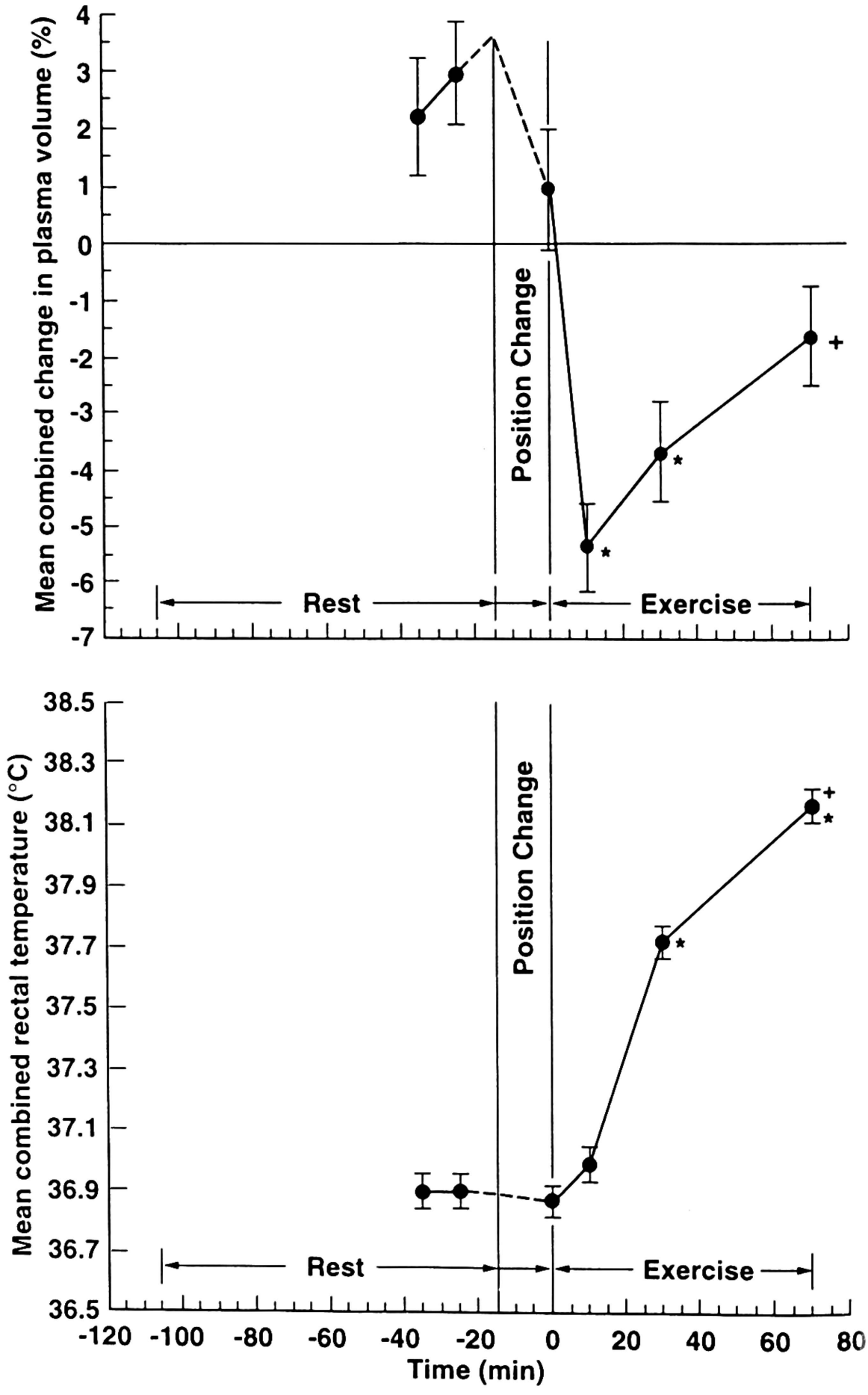

Fig. 4. Upper panel: Mean (±SE) combined percent change in plasma volume for all treatments and subjects during rest from −105 min, and during exercise from 0 min. Lower panel: Mean (±SE) combined rectal temperature for all treatments and subjects during rest and exercise. * $p < 0.05$ from time 0.

Plasma volume

Mean combined percent change in plasma volume (%ΔPV) decreased significantly by 5.4 ± 0.8% ($p < 0.001$) in the first 10 min of exercise (*Fig. 4*, upper panel). Thereafter, it tended to increase to −3.7 ± 0.9% at 30 min ($p < 0.05$) and to −1.6 ± 0.9% at 70 min; the latter was not significantly different from that at time 0. All correlation coefficients at rest and during exercise between %ΔPV and WBC, platelets, and Osm were not significant: WBC rest $r = 0.05$, exerc. $r = -0.07$; platelets rest $r = 0.07$, exerc. $r = 0.05$; Osm rest $r = 0.10$, exerc. $r = -0.19$ indicating that the changes in WBC, platelets, and Osm were not due to loss of PV.

Rectal temperature (Tre)

Mean combined Tre increased from 36.9 ± 0.1°C at time 0 to 37.0 ± 0.1°C (NS) at 10 min, to 37.7 ± 0.1°C ($p < 0.001$) at 30 min, and to 38.2 ± 0.1°C ($p < 0.001$) at 70 min of exercise (*Fig. 4*, lower panel). The Tre increases between 10 and 30 min and 30 and 70 min were significant ($p < 0.001$). The correlation coefficients between mean combined Tre and WBC and between Tre and platelets were not significant during rest or exercise indicating that changes in core temperature did not affect these cellular responses.

DISCUSSION

Regardless of the different composition of the drinks consumed; WBC, platelets, or Osm did not change significantly and there were no differences among treatments during rest or after the change in body position. This apparent lack of significant interaction between Osm and WBC or platelets at rest does not negate the possible Osm effect during exercise, because there is no stimulus to induce change in the cells at rest.

Exercise-induced leucocytosis

A significant leucocytosis of 31.0% occurred within the first 10 min of exercise, with an additional 8.9% increase (NS) by 70 min of exercise. Mean WBC were significantly higher at 10, 30, and 70 min of exercise when compared to that at time zero. This finding is consistent with results of Gabriel *et al.* (26) who reported a 47% lymphocytosis (primarily NK cells) and a 62% monocytosis within the first 10 min of ergometer exercise in 14 healthy subjects, with an additional 17% increase in lymphocytosis at the end of exercise (100% of

individual „anaerobic threshold" for 83.8 ± 22.2 min). Our exercise was shorter but of similar intensity while our values were lower but still significant. There is a direct positive relationship between exercise intensity and the magnitude of leucocytosis (2, 9, 16). While the duration of our exercise between 10 and 70 min did not further change leucocytosis significantly, the magnitude of the initial leucocytosis was similiar to that reported by Davis *et al.* (19), suggesting a release or mobilization of WBC from storage areas. There is no general consensus that immunological benefits are derived from changes in numbers of circulating immune cells, which may reflect just transient movement into and from the blood.

Exercise-induced thrombocytosis

The significant thrombocytosis of 10.9% that occurred within the first 10 min of exercise, with an additional 10.9% increase (NS) by 70 min of exercise, is within the reported range of 9—36%; however, the magnitude of thrombocytosis appears to be proportional to exercise intensity (2, 19, 20, 27). Wang *et al.* (2) reported an 18% rise in platelets after moderate exercise (55% VO_{2max}), and a 25% rise after strenuous (100% $\dot{V}O_{2max}$) ergometer exercise. We found a 22% rise in platelets after 70 min of 71% $\dot{V}O_2$ peak ergometer exercise. Here also there appears to be a direct relationship between exercise intensity and magnitude of thrombocytosis (6, 18, 28). There is some evidence that exercise duration affects the level of thrombocytosis (27, 29). We found a small additional non-significant increase from 10—70 min. Herren *et al.* (27) observed in trained men that the magnitude of thrombocytosis was greater after a 7- to 12-hr 100 km run than after a one-hr run. Thus, there appears to be a bi-phasic response, with an initial surge followed by a prolonged slower increase in platelets. This early significant thrombocytosis may cause exercise-induced myocardial infarction which often occurs in the first minutes of exercise (3).

Mechanisms for leucocytosis and thrombocytosis

It has been suggested that increased levels of plasma catecholamines trigger leucocytosis (9—11); however, significant increases in plasma epinephrine and norepinephrine levels occur with low-intensity exercise without accompanying lymphocytosis or neutrophilia (18). Tvede *et al.* (11), in his investigation with 8 men, found that exercise induced a greater lymphocytosis than that resulting from epinephrine infusion at rest. This suggests that epinephrine is not entirely responsible for the WBC surge. Administration of propranolol during exercise

to block β-adrenergic receptors also lowers cardiac output (4, 8). Cardiac output during muscular work has been positively correlated with leucocytosis, and it has been suggested that the increased cardiac output, not catecholamines, facilitates leucocytosis (4). Hypovolemia was not primarily responsible for the accompanying leucocytosis or thrombocytosis: the 5.4% decrease in PV in the present study was not sufficient to explain the much larger increase of 31.0% in WBC in the first 10 min of exercise, and there was no significant correlation between mean %ΔPV and mean WBC. Furthermore, while PV returned to baseline by 70 min of exercise, the WBC remained significantly elevated. Others have reported significant leucocytosis when cell counts were corrected for PV changes (9, 26), and even when there was no change in hematocrit (30). Another possible mechanism is that exercise-induced hyperthermia mobilizes leucocytes, mimicking a fever response (14, 15). However, when WBC and platelets in the present study changed significantly early during exercise, T_{re} did not; and vice versa. Also, there was no significant correlation between T_{re} and WBC or platelets. Our data indicate that elevated body temperature has minimal influence on exercise-associated leucocytosis, or that an increase in rectal temperature greater than 1.25°C is necessary to activate the WBC.

However, the evidence indicates that increased sympathetic stimulation and plasma catecholamine concentration, together with increased blood flow and decreased plasma volume, probably act in concert to induce the early leucocytosis.

Mechanism for thrombocytosis

Dawson and Ogston (17) found no significant difference in the magnitude of thrombocytosis in seven subjects after 15 min of ergometer exercise with or without propranolol even though heart rate (and presumably cardiac output) were lowered significantly. These results also suggest that β-adrenergic activation is not a primary mechanism for inducing thrombocytosis during exercise and questions the extent to which increased circulation is involved. Hemoconcentration is not primarily responsible for exercise-induced thrombocytosis; despite correction for hemoconcentration a significant increase in platelets still occurs (31), and the magnitude of the platelet surge is much greater than the level of hemoconcentration (17, 20). In the present study the magnitude of thrombocytosis (10.9%) was greater than the reduction in plasma volume of 5.4% at 10 min of exercise, in agreement with Davis *et al.* (19). Furthermore, we found no significant correlation between mean %ΔPV and mean platelets; PV returned to pre-exercise levels by 70 min of exercise, yet platelets remained significantly higher.

Osmotic hypothesis

Results from the present study suggest an additional hypothesis that links plasma osmolality to this exercise-associated WBC and platelet surge (21, 22). In spite of the low nonsignificant correlation between plasma volume and WBC, there were low but significant correlations between total Osm and WBC during exercise ($r_{0.001(2),284} = 0.39$), and with combined data from rest and exercise ($r_{0.001(2),499} = 0.43$). These relationships suggest that Osm per se, not hemoconcentration, is associated with the leucocytosis. This hypothesis is further supported by the significant correlation between mean Osm and mean WBC ($r_{0.001(2),6} = 0.95$) with combined data. These results are consistent with those of Novogrodsky *et al.* (23) who suggested that osmotic effects may enhance T-cell proliferation. When they increased osmolality (by 25mM or 50mM with NaCl, KCl, sucrose, or fructose) in a peanut agglutinin (PNA) negative murine thymocyte medium, incubated with 12-O-tetradecanoyl-phorbol (TPA; 100 $ng \cdot ml^{-1}$) and suboptimal levels of phytohemaglutinin (PHA; 2 $\mu g \cdot ml^{-1}$), the increased osmolality enhanced [^{3}H]thymidine incorporation; i.e., increased osmolality enhanced the mitogenic response of thymocytes. PHA-treated thymocyte activity was higher in an interleukin-2 (IL-2) medium when osmolality was higher. Furthermore, they found osmotic enhancement of mitogenic stimulation in mouse splenocytes and in human peripheral lymphocytes.

When Junger *et al.* (22) increased extracellular sodium concentration by 25—30 mM above isotonicity in human and rabbit peripheral blood mononuclear cells *in vitro*, T-cell proliferation and monocyte function [denoted by 300% increase in tumor necrosis factor (TNF) production] were increased by 100%. However, when increasing hypertonicity beyond 30 mM (> 40 mM in human cells and > 80 mM in rabbit cells), T-cell proliferation was suppressed progressively suggesting a limit to which increased osmolality can facilitate lymphocytosis. Hypertonic saline injection also increased cell-mediated immune function (delayed-type hypersensitivity reaction) in rabbits *in vivo*. These results indicate why risk of sepsis in hypovolemic shock victims is reduced and their survival rates are higher if resuscitated with hypertonic saline. Based on their *in-vitro* data, Junger *et al.* (22) predicted that immune responses would be enhanced by 60% in trauma patients who received hypertonic saline (7.5% sodium chloride in 6% dextran 70) resuscitation treatment.

Greenleaf *et al.* (21) found an inverse relationship between T-lymphocyte $CD4^+/CD8^+$ ratios and plasma osmolality. Regression of mean $CD4^+/CD8^+$ ratios on mean plasma osmolality resulted in a pre-exercise correlation of -0.76 ($p < 0.10$) and a post-exercise correlation of -0.92 ($p < 0.01$). Thus, 58% (0.76^2) and 85% (0.92^2) of the ratios variability, respectively, could be attributed to osmotic changes.

How could plasma osmolality influence WBC or platelets? Novogrodsky *et al.* (23) suggested that increased osmolality of a culture medium stimulated Na^+/H^+ exchange, which enhanced mitogenesis. Introduction of sodium promoted T-cell proliferation suggesting that hyperosmolality enhances an early event in thymocyte activation, possibly IL-2 production. Junger *et al.* (22) agreed that early introduction of hypertonic solutions to peripheral blood mononuclear cells (PBMC) is important; i.e., T-cell proliferation in a PBMC medium was greatest when extracellular Na^+ was added before or within 5 hrs; reduced or no proliferation occurred if Na^+ was added after 5 hr, or at 60 hr, respectively. Increased osmolality enhanced monocyte accessory function which indirectly increased T-cell proliferation. Addition of Na^+ did not significantly increase Ca^{2+} levels of non-stimulated PBMC, suggesting that intracellular Ca^{2+} signaling was not responsible for enhanced T-cell proliferation and supporting the suggestion that enhanced monocyte function may increase T-cell proliferation indirectly. Greenleaf *et al.* (21) suggest that a generalized stress response is induced in test-subjects by dehydration which may depress immune function by a glucocorticoid-mediated mechanism (32).

These results support the hypothesis that the increases in WBC and platelets during exercise may be induced by concomitant increase in plasma osmolality which may contribute to the common mechanism.

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