Antihypertensive and Volume-Depleting Effects of Mild Exercise on Essential Hypertension

HIDENORI URATA, YOICHI TANABE, AKIRA KIYONAGA, MASAHARU IKEDA, HIROAKI TANAKA, MUNEH1RO SHINDO, AND KIKUO ARAKAWA

SUMMARY After a general clinical observation period of over 4 weeks, 20 essential hypertensive subjects (Japanese) were randomly divided into two groups. One group (n = 10; 4 men and 6 women; 51.4 ± 2.8 years of age) agreed to physical training using bicycle ergometer exercise with the intensity at blood lactate threshold for 60 minutes three times a week for 10 weeks, while the other group (n = 10; 4 men and 6 women; 51.0 ± 2.9 years of age) did no particular physical training and was followed once a week as the control. Changes in blood pressure, hemodynamics, and humoral factors of the exercised group were compared with values in the controls. The following significant changes were found only in the exercised group. Blood pressure was significantly (p<0.01) reduced. Whole blood and plasma volume indices were significantly reduced (p<0.05, p<0.01, respectively). The change in ratio of serum sodium to potassium positively correlated with the change in systolic blood pressure (r = 0.76, p<0.02). Plasma norepinephrine concentrations both at rest and at the workload of blood lactate threshold during graded exercise tests were significantly reduced (p<0.05, p<0.02 respectively) after 10 weeks of exercise training. The change in the resting level of plasma norepinephrine positively correlated with that in the mean blood pressure. No such changes were observed in the control group. In both groups, body weight and urinary sodium excretion showed no statistically significant changes. In conclusion, the antihypertensive effect of mild exercise training was confirmed in a well-matched, controlled study, and reduction in blood volume and plasma norepinephrine concentrations had an apparent association. (Hypertension 9: 245–252, 1987)

KEY WORDS • blood pressure • training • electrolytes • catecholamines • lactate

DESPITE widespread interest in nonpharmacological therapy for hypertension, physical exercise has not gained acceptance for its antihypertensive effectiveness and mechanisms.1,2 This may be attributed to the fact that there has been no well-controlled study of factors such as age, sex, race, number, and life-style in matched hypertensive control subjects. Even when positive effects3–8 were obtained, the related mechanisms remained unclear.

We reported the antihypertensive effect of exercise training with the workload at blood lactate threshold and noted a significant reduction of plasma catecholamine concentration and an elevation of plasma prostaglandin E concentration.9,10 In addition, we found a significant positive correlation between changes in mean blood pressure and the initial levels of plasma renin activity.9,10 These observations suggest that volume depletion is linked to the antihypertensive effect. The present study was undertaken in an attempt to confirm the depressor effects of exercise, in comparison with data on well-matched nonexercised hypertensive controls, and to analyze changes in hemodynamics, with special reference to blood volume and humoral factors.

Subjects and Methods

Subjects

Twenty Japanese with essential hypertension and a blood pressure above 140/90 mm Hg (mean, 155/100 mm Hg), aged 32 to 60 years (mean, 51.2 years) were
randomly divided into an exercised group ($n = 10$) and a nonexercised group ($n = 10$) after general clinical observations of over 4 weeks in our outpatient clinic. Careful physical and laboratory examinations were performed, and secondary hypertension and serious cardiovascular and cerebrovascular complications were ruled out. None had a serum creatinine level exceeding 1.5 mg/dl, World Health Organization Stage III complications, severe obesity, or heart failure. Table 1 lists the pertinent factors in both groups. These 20 subjects were asked to maintain their usual casual life-style, including sodium and caloric intake, sleeping habits, alcohol ingestion, smoking habits, and other activities, during the entire study. These events were periodically monitored along with the exercise course, through measurements of body weight, 24-hour urinary sodium collection, and a questionnaire. Medication, if any, was withdrawn at least 6 weeks before initiation of the study.

All participating subjects signed a consent form after being well informed of the nature and purpose of the study.

**Blood Pressure Measurements**

Blood pressure was measured indirectly using a mercury sphygmomanometer. The fifth phase of Korotkoff's sound was used as an approximation of the diastolic pressure, except for the measurement during exercise, when the fourth phase was used for the diastolic blood pressure. Blood pressure was measured in the left arm with the subject sitting in a chair, after more than 5 minutes of rest, and was expressed by an average of duplicate measurements. Before the study, we confirmed the validity and reproducibility of the blood pressure values measured by all practitioners taking part in the study. All measurements were performed by the same instructor and physician in an air-conditioned, quiet room. Blood pressures were measured once weekly during the observation period of more than 4 weeks. During the first few weeks, systolic blood pressure decreased slightly but not significantly. The blood pressure at rest in both groups remained stable during the observation period. The average blood pressure value of the last two visits of the observation period was used as a prestudy value for each subject. Blood pressures were measured at each visit more than 48 hours after the last exercise session (i.e., on three occasions each week). It was measured once a week in the nonexercised group, since we knew from our previous study that the blood pressure was well stabilized after a 4-week observation and did not change in the following 12 weeks. The average blood pressure of the last two visits in each period served for a comparison between the two groups.

**Predetermination of the Exercise Intensity to Be Loaded**

Before and after 10 weeks of exercise to determine the intensity of the exercise and aerobic capacity, the subjects in the exercised group were subjected to multistage testing of submaximal graded exercises on an electric bicycle ergometer (Electric Bicycle Ergometer, Lode's Instrumenten B.V., Groningen, Holland) as described. Graded exercise tests were administered between 0900 and 1300 in an air-conditioned room. With subjects in the sitting position, the initial workload was 0 W for 4 minutes, and the workload was increased by 10 or 15 W every 4 minutes, depending on their physical fitness, until exhaustion set in. The electrocardiogram was monitored continuously on the oscilloscope so that the subject's condition and heart rate could be carefully watched. The following parameters were measured every 4 minutes: heart rate, blood pressure, oxygen uptake, and blood lactate concentration. Expired gas from the subjects was collected in a Douglas bag and directed to a continuous-recording respirometer (Model CR-20; Fukuda Sangyo, Tokyo, Japan) to measure minute ventilation. Mixed expired gas samples were simultaneously analyzed by a gas analyzer (Model MGA-1100; Perkin-Elmer, Pomona, CA, USA) previously calibrated for O2 and CO2. Twenty microliters of blood from an earlobe was used to measure lactate levels, using a lactate analyzer (Model 640; Roche Bio-Electronics, Basel, Switzerland), and was plotted against the exercise workload (in watts). Lactate levels passed through three phases during the graded exercise, and the workload at the first breaking point of lactate (blood lactate threshold) was used to calculate the exercise training intensity in each subject. This workload reflects the relative equal metabolic stress for each subject and corresponds to approximately 40 to 60% of the maximum oxygen uptake ($V_{O2\text{max}}$). Estimated $V_{O2\text{max}}$ was calculated from data of heart rate and workload during the graded exercise test and was adjusted by age and sex. Physical working capacity at a heart rate of 150 beats/min was calculated from the heart rate plotted against the workload (in watts).

**Method of Exercise**

The subjects in the exercised group performed bicycle ergometer exercise in our laboratory three times a week for 10 weeks. Each session began with a 5- to 10-minute warm-up period of light calisthenics and stretching exercises, followed by 60 minutes of exer-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exercised ($n = 10$)</th>
<th>Nonexercised ($n = 10$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>4:6</td>
<td>4:6</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>51.4 ± 2.8</td>
<td>51.0 ± 2.9</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>157.6 ± 2.4</td>
<td>156.5 ± 2.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>62.4 ± 3.5</td>
<td>60.1 ± 2.1</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>0.86 ± 0.18</td>
<td>0.91 ± 0.18</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>156.3 ± 4.0</td>
<td>154.0 ± 3.9</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>102.8 ± 3.5</td>
<td>98.0 ± 2.9</td>
</tr>
<tr>
<td>Mean BP (mm Hg)</td>
<td>120.7 ± 3.3</td>
<td>117.9 ± 3.2</td>
</tr>
</tbody>
</table>

All values are means ± SE. BP = blood pressure.
cise on a bicycle ergometer with a weight and rhythm box (Cyclotek, Monark-Crescent A.B., Varberg, Sweden) at the predetermined work intensity for each subject, and ended with a 5-minute cooling-off period. The exercise was supervised by a physical education instructor. Pulse rates, blood pressure, and physical condition during and after the exercise were also monitored by a physician or physical education instructor. Heart rate and workload averages of the exercised group during a session were 101.0 ± 3.3 beats/min and 33.5 ± 3.3 W, respectively. Reading books, listening to the radio, or watching television were freely allowed during the exercise.

Hemodynamic Parameters

Before and after the 10-week study period, cardiac output and blood volume were determined after an 8-hour fast from solid food. Drinking water was allowed. Cardiac output was measured by a dye-dilution method (Model MLC-4100M; Nihon Kohden, Tokyo, Japan) using 2 ml of indocyanine green (2.5 mg/ml) injected from the femoral vein as indicator and an earpiece detector (Model JQ-410V; Nihon Kohden). The average value of triplicate measurements was used for comparison. Since the average variable coefficient calculated in 107 hypertensive subjects in our laboratory was 5.4%, reproducibility of this method was adequate for estimation of the data. Total peripheral resistance (mm Hg/L/min) was calculated from the cardiac output and the mean blood pressure measured simultaneously. Whole blood and plasma volume were determined by using 131I-labeled human serum albumin, according to the method of Crispell et al. and was described as an index divided by body surface area. In the exercised group, these hemodynamics at rest were examined 48 to 72 hours after the last exercise session.

Humoral Factors

Twenty-four-hour urine and 12-hour fasting blood samples of the exercised group were collected before and after exercise, while such samples in the nonexercised group were collected at Weeks 0 and 10 in the control period. Blood samples for plasma were drawn from the antecubital vein into vacuum tubes after a 15-minute rest period (sitting position), immediately placed on ice, and centrifuged at 1800 × g at 4°C. The plasma and serum were stored at −30°C until analysis. Blood samples for the measurement of plasma norepinephrine during submaximal graded exercise test were obtained using a 20- or 22-gauge elastic tube that had been inserted into the antecubital vein 20 minutes before the sampling. Twenty-four-hour urine samplings were performed using a simple portable device according to the method of Tochikubo et al.

Plasma renin activity was measured according to the method of Haber et al. Serum aldosterone concentration was measured using aldosterone assay kits. Plasma norepinephrine and epinephrine levels were measured by the trihydroxyindole method after extraction by high performance liquid chromatography. Serum angiotensin converting enzyme activity was determined according to a modification of the method of Cushman and Cheung; the tripeptide hippuryl-histidyl-leucine was used as a substrate. Liberated hippuric acid was measured spectrophotometrically. Serum sodium and potassium concentrations were determined by the flame photometric method (Flame Photometer 775; Hitachi, Tokyo, Japan). Serum chloride concentration was measured by the amperometric method (Chloride Counter CL-5; Hiranuma Sangyo, Mito, Japan).

All procedures during the study (i.e., the measurement of blood pressure, hemodynamic examination, blood sampling, graded exercise test, and exercise training) were performed under the same temperature (20–22°C) and humidity (40–60%) conditions throughout 1 year.

Statistical Analysis

All values are expressed as the mean ± SE. Student's t test was used for statistical assessments. An analysis of variance was performed for all data and was also used for the results obtained with Student's t test. There was no difference between the results using these two methods. Correlation coefficients were calculated by Pearson correlations.

Results

Changes in Blood Pressure and Hemodynamic Parameters

Figure 1 shows the time course of changes in blood pressure in both groups. During observation for over 4 weeks, a slight but not significant decrease in systolic blood pressure was observed. The resting blood pressure of the exercised group decreased from 156.3 ± 4.0/102.8 ± 3.5 mm Hg to 143.6 ± 5.3/98.0 ± 5.4 mm Hg after the 10-week exercise period, and the mean blood pressure of the exercised group also decreased significantly, from 120.7 ± 3.3 mm Hg to 113.1 ± 5.3 mm Hg, in contrast to no change in the nonexercised control group after 10 weeks. A significant difference was found in blood pressure changes between the exercised and the nonexercised groups (systolic blood pressure: p < 0.001; mean blood pressure: p < 0.01; diastolic blood pressure: not significant). There were some nonsignificant differences in the average values of the initial diastolic blood pressure between groups; these differences occurred incidentally because of the random division of the two groups. The depressor effect in systolic and mean blood pressures reached the significant level in the 7th week of the exercise period. The levels of diastolic blood pressure were significantly reduced in the 5th, 8th, and 9th weeks of exercise, but not in the 10th week.

Figure 2 shows changes in blood pressure during exercise in the 1st, 10th, 20th, and 30th exercise sessions. The gradual reduction in blood pressure elevation during exercise was evident as training progressed. Systolic blood pressure in the 10 minutes after exercise was significantly lower than that before exer-
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FIGURE 1. Comparison of the time course of blood pressure changes in the exercised and the nonexercised hypertensive subjects. During the observation period, there was a slight but insignificant decrease in systolic blood pressure (SBP) in both groups. Within the exercised group, a significant antihypertensive effect of systolic and mean blood pressure (MBP) was found after 10 weeks of exercise, as well as a trend toward diminution in diastolic blood pressure (DBP), in contrast with no significant changes in the nonexercised hypertensive subjects. There was also a significant difference between changes in SBP and MBP in both groups. Shaded bars represent the mean values of the exercised group, and open bars represent the mean values in the nonexercised controls. NS = not significant. Single (p<0.05) and double asterisks (p<0.01) indicate significant change compared with the initial value at Week 0. Values are means ± SE.

FIGURE 2. Changes in blood pressure during exercise at the 1st, 10th, 20th, and 30th exercise sessions. The gradual reduction of blood pressure during 60 minutes of exercise and at the resting level are evident. Systolic blood pressure 10 minutes after the 60-minute exercise session was significantly lower than the preexercise resting level. Asterisk (p<0.05) indicates significant difference compared with the corresponding values before exercise (resting levels). Dagger (p<0.01) indicates significant difference compared with the corresponding values during the initial exercise session. Each dot shows the average value in 10 essential hypertensive subjects during each exercise session.

FIGURE 3. Whole blood and plasma volume indices of the exercised (shaded bars) and nonexercised (open bars) groups before and after 10 weeks of training. A significant decrease in whole blood and plasma volume was found only in the exercised group. NS = not significant. Values are means ± SE.

Exercise training was performed throughout 1 year, and no seasonal difference in the depressor effect was observed.

Whole blood and plasma volume indices were significantly reduced in the exercised group, from 3406 ± 210 ml/m² to 3021 ± 120 ml/m² and from 1941 ± 86 ml/m² to 1723 ± 52 ml/m², respectively, but not in the non-exercised group (Figure 3). There were no significant changes in other parameters (i.e., heart rate, resting cardiac index, stroke volume, total peripheral resistance, and body weight) in either group (Table 2), and resting heart rate, cardiac index, and body weight in the exercised group tended to decrease slightly.

Exercise intensity and oxygen uptake at the blood lactate threshold, estimated maximum oxygen uptake, and physical working capacity at a heart rate of 150 beats/min had improved significantly in the exercised group by the 10th week of exercise (Table 3).

TABLE 2. Comparison of Hemodynamic Changes Between Exercised and Nonexercised Hypertensive Subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Exercised</th>
<th>Nonexercised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0</td>
<td>62.4 ± 3.5</td>
<td>60.1 ± 2.1</td>
</tr>
<tr>
<td>Week 10</td>
<td>61.9 ± 3.6</td>
<td>59.1 ± 2.1</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0</td>
<td>74.0 ± 2.0</td>
<td>73.3 ± 2.5</td>
</tr>
<tr>
<td>Week 10</td>
<td>72.1 ± 2.2</td>
<td>71.2 ± 2.0</td>
</tr>
<tr>
<td>SV (ml/stroke)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0</td>
<td>87.8 ± 4.9</td>
<td>80.5 ± 6.6</td>
</tr>
<tr>
<td>Week 10</td>
<td>81.0 ± 7.1</td>
<td>78.7 ± 4.8</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0</td>
<td>3.70 ± 0.28</td>
<td>3.58 ± 0.34</td>
</tr>
<tr>
<td>Week 10</td>
<td>3.28 ± 0.23</td>
<td>3.54 ± 0.33</td>
</tr>
<tr>
<td>TPR (mm Hg/L/min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 0</td>
<td>21.8 ± 1.9</td>
<td>22.8 ± 1.7</td>
</tr>
<tr>
<td>Week 10</td>
<td>22.9 ± 2.3</td>
<td>22.4 ± 2.0</td>
</tr>
</tbody>
</table>

Values are means ± SE. HR = heart rate; SV = stroke volume; CI = cardiac index; TPR = total peripheral resistance.
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TABLE 3. Changes in Parameters of Graded Exercise Test Before and After 10 Weeks of Exercise

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before</th>
<th>After</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBPLA1 (W)</td>
<td>33.5±3.3</td>
<td>42.5±3.3*</td>
</tr>
<tr>
<td>HR at WBPLA1 (beats/min)</td>
<td>102.6±3.6</td>
<td>98.5±3.3</td>
</tr>
<tr>
<td>V̇O₂ at WBPLA1 (ml/kg/min)</td>
<td>12.9±0.6</td>
<td>13.3±0.5†</td>
</tr>
<tr>
<td>Estimated V̇O₂max (ml/kg/min)</td>
<td>27.7±0.9</td>
<td>31.0±0.8*</td>
</tr>
<tr>
<td>PWC 150 (W)</td>
<td>79.2±8.7</td>
<td>93.4±9.2†</td>
</tr>
<tr>
<td>PNE at WBPLA1 (pg/ml)</td>
<td>480±68</td>
<td>375±54†</td>
</tr>
</tbody>
</table>

All values are means ± SE. WBPLA1 = workload at the first breaking point of lactate (blood lactate threshold); HR = heart rate; V̇O₂max = maximum oxygen uptake; PWC 150 = physical working capacity at a heart rate of 150 beats/min; PNE = plasma norepinephrine concentration.

* p < 0.01, †p < 0.02, compared with preexercise values.

Changes in Humoral Factors

Exercise led to a significant reduction (p < 0.05) in the resting plasma norepinephrine level, from 287 ± 30 pg/ml to 197 ± 17 pg/ml (Figure 4), and this change correlated positively (r = 0.69, p < 0.05) with that of mean blood pressure (Figure 5). The time course of changes in plasma norepinephrine concentration is shown in Figure 6.

Plasma norepinephrine concentration measured with the workload at blood lactate threshold during the submaximal graded exercise test was significantly decreased, from 480 ± 68 pg/ml to 375 ± 54 pg/ml (p < 0.02), after 10 weeks of exercise (see Table 3). The levels of plasma epinephrine, serum aldosterone, plasma renin activity, and serum angiotensin converting enzyme activity remained unchanged (Table 4). The correlation coefficient between the logarithm of the initial value of plasma renin activity and the change of systolic blood pressure was 0.51, but this value was not statistically significant. There was also a large difference in the depressor change of systolic blood pressure between relatively high (>2.0 ng angiotensin I/ml/hr; n = 3) and low (<1.0 ng angiotensin I/ml/hr; n = 3) plasma renin activity groups. In the high plasma renin activity group, the change in systolic blood pressure was —9 mm Hg. In the low plasma renin activity group, the change in systolic blood pressure was —21 mm Hg. However, this difference was not statistically significant.

Changes in electrolytes are summarized in Table 5. The serum sodium levels in the exercised group were statistically lower after 10 weeks of exercise (i.e., from 142.5 ± 0.5 mEq/L to 140.2 ± 0.6 mEq/L), and the sodium/potassium ratio in the exercised group was decreased slightly but not significantly. The change in sodium/potassium ratio correlated positively (r = 0.76, p < 0.02) with that of systolic blood pressure (Figure 7). There were no significant changes in any other electrolyte parameters in either group.

We also calculated various differences between the data on men and women and found no statistically significant differences only for height and weight. Differences in the sexes did not seem to play any role in the results.

Discussion

In a well-controlled study, we have confirmed our preliminary findings1,10 on the depressor effect of mild exercise. The design described in this report is adequate to estimate the result and overcomes many previously experienced problems. The special characteristics are 1) the random division of subjects, 2) the long observation period before the study, 3) the strictly supervised ergometric exercise, 4) the monitoring of...
The exercise led to a significant depressor effect in association with a depletion in the blood volume and sympathetic nervous tone and improved physical fitness in the exercised but not in the nonexercised group.

Several studies have compared the depressor effect of exercise with results in a nonexercised hypertensive control group, but to our knowledge none included an observation period in which the effect of supervision in an outpatient clinic might be observed. Actually, a significant depressor effect, even in the control group, was found in some subjects during a control period.

During the subsequent 10 weeks, blood pressure in the nonexercised group was unchanged. In the exercised group, blood pressure after the institution of exercise decreased still further to a significant level, and the depressor change was significant compared with that in the control group. It is possible that more frequent blood pressure measurement in the exercised group might contribute to the difference in blood pressure reduction. However, such an effect is unlikely because the blood pressure of both groups was well stabilized after the 4-week observation period. Blood pressure elevation during exercise decreased as the exercise training progressed, as shown in Figure 2. In all subjects, the acute elevation of systolic blood pressure during exercise never exceeded 200 mm Hg. Systolic blood pressure after a 60-minute exercise was significantly lower, for at least 10 minutes, than that at the preexercise resting level at all exercise sessions.

![Figure 7](http://hyper.ahajournals.org/)

**Figure 7.** Relationship between the change in systolic blood pressure (SBP) and the ratio of serum sodium to potassium induced by mild exercise. There was a significant correlation.

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**Table 4. Comparison of Changes in Humoral Factors Between Exercised and Nonexercised Groups**

<table>
<thead>
<tr>
<th>Humoral factor</th>
<th>Exercised</th>
<th>Nonexercised</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNE (pg/ml)</td>
<td>287 ± 30</td>
<td>286 ± 29</td>
</tr>
<tr>
<td>PEPI (pg/ml)</td>
<td>197 ± 17*</td>
<td>291 ± 29†</td>
</tr>
<tr>
<td>PRA (ng ANG I/ml/min)</td>
<td>21 ± 4</td>
<td>28 ± 3</td>
</tr>
<tr>
<td>SAC (ng/dl)</td>
<td>13.5 ± 1.2</td>
<td>11.3 ± 0.9</td>
</tr>
<tr>
<td>ACE (nmol/ml/min)</td>
<td>40.3 ± 3.1</td>
<td>31.9 ± 2.8</td>
</tr>
</tbody>
</table>

Exercised Nonexercised

21 ± 4 28 ± 3

13.5 ± 1.2 11.3 ± 0.9

All values are means ± SE. PNE = plasma norepinephrine concentration; PEPI = plasma epinephrine concentration; PRA = plasma renin activity; ANG I = angiotensin I; SAC = serum aldosterone concentration; ACE = serum angiotensin converting enzyme activity.

*P < 0.05, compared with Week 0 value.
†p < 0.05, compared with value for exercised group.

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**Table 5. Comparison of Changes in Electrolytes Between Exercised and Nonexercised Groups**

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Exercised</th>
<th>Nonexercised</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Na (mEq/L)</td>
<td>142.5 ± 0.5</td>
<td>141.2 ± 0.4</td>
</tr>
<tr>
<td>Serum K (mEq/L)</td>
<td>140.2 ± 0.6*</td>
<td>139.9 ± 0.4</td>
</tr>
<tr>
<td>Serum Cl (mEq/L)</td>
<td>103.7 ± 0.6</td>
<td>103.8 ± 0.7</td>
</tr>
</tbody>
</table>

Exercised Nonexercised

36.8 ± 0.8 35.5 ± 1.0

34.7 ± 0.8 37.4 ± 0.8

All values are means ± SE. Serum Na/K ratio

*P < 0.05, compared with Week 0 value.
†p < 0.05, compared with value for exercised group.
training progressed (see Figure 2). Generally, it is difficult to accurately measure blood pressure, especially in diastole, during exercise by the indirect method, but the bicycle ergometric exercise we adopted made it much easier to do so during exercise because of the subject’s fixed positioning and a lesser degree of noise.

**Body Weight and Physical Fitness**

Despite the significant reduction in blood volume, no significant changes were observed in body weight, as noted in previous work. An increase of lean body mass induced by exercise training might contribute to this result.

A significant increase in workload and oxygen uptake at the first breaking point of lactate, physical working capacity at a heart rate of 150 beats/min, and estimated VO\(_{2}\max\) were found after 10 weeks of exercise. It could be harmful to determine direct VO\(_{2}\max\) in hypertensive subjects because of the possible extreme elevation of blood pressure during maximum exercise. To avoid this problem and to provide accurate exercise intensity, we measured blood lactate levels at each workload of submaximal graded exercise. Blood lactate threshold is the set point of blood lactate accumulation and may reflect the anaerobic threshold. After 10 weeks of exercise training, the VO\(_{2}\max\) estimated from the heart rate and workload during the graded exercise test increased significantly, concomitant with an increase in oxygen uptake and workload at the blood lactate threshold.

**Hemodynamic Effects and Humoral Responses**

Determination of the mechanism of depressor effects that occur in the exercise training has been given little attention, except for a recent report by Jennings et al. In our previous work, we pointed out a significant reduction in plasma catecholamine concentrations and increased plasma levels of prostaglandin E. We also reported that subjects with low renin hypertension responded better to exercise training (correlation coefficient, 0.78) than did subjects with other types of hypertension. In the present study, the correlation coefficient between logarithm of the initial plasma renin activity and the change in systolic blood pressure was 0.51. There was also a large difference in depressor change of systolic blood pressure between groups with relatively high (> 2.0 ng angiotensin I/ml/hr; n = 3) and low (< 1.0 ng angiotensin I/ml/hr; n = 3) plasma renin activity. These nondefinitive results probably are due to the small number of subjects studied and the error inherent in measurements of plasma renin activity. We studied the change in blood volume occurring with exercise and noted a reduction in circulating intravascular volume. This finding suggests the important role of depleted blood volume induced by mild exercise training in the depressor mechanism. In addition, the significant correlation between the changes in sodium/potassium ratio and systolic blood pressure suggests that sodium depletion may also occur. There was no significant change in 24-hour sodium excretion before and after 10 weeks of exercise training, indicating that the intake of sodium remained constant, as we had requested.

Plasma volume and cardiac output have been reported to increase after heavy physical training in normal subjects. The conflicting results obtained in the present study may be due to differences in blood pressure of the subjects and the intensity of exercise. The volume and electrolyte responses to exercise training in essential hypertensive subjects may differ from that in normotensive subjects because of genetic abnormalities in body fluid and electrolyte homeostasis. In the present study, the mild exercise at the workload of blood lactate threshold induced the same relative metabolic stress in each subject. Exercise at this workload may not stimulate to any great extent the renin-angiotensin-aldosterone system or the sympathetic nervous system. During the 10-week exercise training, there was no significant change in the resting levels of plasma renin activity, serum aldosterone concentration, or angiotensin converting enzyme activity, again reaffirming our previous findings. The more strenuous training intensity performed in other studies might activate the renin-angiotensin-aldosterone system and sympathetic nervous system, to a high degree. The present study revealed a depletion in blood volume without an alteration in the renin-angiotensin-aldosterone system. This depletion may be due to an increased level of prostaglandin E, which we also have observed. However, elucidation of mechanisms of volume depletion must await determination of other intrinsic natriuretic factors (i.e., atrial natriuretic factor, taurine), which are underway in our laboratory.

Despite the significant decreases in whole blood and plasma volume, heart rate and total peripheral resistance did not increase; conversely, heart rate tended to decrease even after training, probably because of a simultaneous decrease in the sympathetic activity. It was therefore suggested that hemodynamic changes (i.e., the slight reduction in cardiac output and lack of supplementary increase in total peripheral resistance because of simultaneously suppressed sympathetic tone) might be associated with the antihypertensive effect of exercise. Resting plasma norepinephrine concentrations were significantly reduced after 10 weeks of training and also showed a gradual decline as training progressed (see Figure 6). Changes in plasma norepinephrine concentrations also correlated positively with changes in mean blood pressure (see Figure 5). The plasma norepinephrine concentrations measured with the workload at blood lactate threshold during the submaximal graded exercise test also were significantly decreased after 10 weeks of exercise. The determinations of the blood lactate threshold workload were readjusted after 10 weeks of exercise training, so that they reflected the same metabolic stress and the same relative workload for each subject in the exercised group. Plasma norepinephrine levels at this point during graded exercise tests decreased significantly following 10 weeks of exercise (see Table 3). These findings strongly support the proposal that a reduction in sympathetic nervous tone occurred and contributed to
the depressor effect of the exercise training. Despite the reduction in plasma norepinephrine concentrations, the resting heart rate did not decrease significantly. It may be that the number of subjects was too few, the exercise intensity too mild, and the duration of exercise too short to evidence a bradycardia. As we reported, 10 20 weeks was required to see any significant reduction in the resting heart rate by the same protocol of mild exercise training.

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References

Antihypertensive and volume-depleting effects of mild exercise on essential hypertension.
H Urata, Y Tanabe, A Kiyonaga, M Ikeda, H Tanaka, M Shindo and K Arakawa

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