Exercise and Renal Function

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Abstract

SUZUKI, M. Exercise and Renal Function. Adv. Exerc. Sports Physiol., Vol. 2, No.2 pp.45-56, 1996. Research on renal function during exercise is very rare in sports medicine area because it has no direct bearing on the performance of exercise. However, the kidneys play an important role in maintaining a constant internal state, which, when disturbed by exercise in a hot environment, is normalized by means of enhanced conservation of water and electrolytes by the kidneys.

It is the purpose of this article to review the previous literature, to relate some of our findings on renal function, and to discuss the mechanisms underlying the changes in renal function and the roles of the kidneys during and/or following exercise, in relation to exercise intensity, duration and exercise environment. Mechanisms underlying exercise-induced proteinuria in healthy and obese persons are further discussed.

The renal blood flow (RBF) and glomerular filtration rate (GFR) decreased from 40% and 49% of VO2max respectively, dependent of increase in the intensity of exercise. However, RBF and GFR were not affected by the modification of exercise duration. Urinary excretion of many electrolytes was inhibited, which might have been due to the decrease in GFR in response to exercise, with increase in the intensity of exercise. The remarkable reduction of Na+ concentration in the urine observed following exhaustive exercise, in particular, might have a role in the compensation for increase in the anion gap in urine produced by the exercise. The RBF and GFR reduce in response to a hot environment. The loss of water and electrolytes caused by an increase in sweating and the urinary excretion of water and electrolytes are inhibited by enhancement of the renin-angiotensin-aldosterone (RAA) system during exercise in a hot environment. Response of the RAA system to these conditions was attenuated by replacement of fluids containing minerals and other elements. Water immersion induced increases in RBF and GFR and the excretion of water and electrolytes into the urine. A slight intensity of exercise (under about 40% of VO2max) in water (29.9 ± 0.6°C) did not inhibit the excretion of water and electrolytes into urine, and produced only slight increases in the plasma concentration of catecholamines and aldosterone, in contrast to the responses to the same intensity of exercise on land. The results suggest that light exercise in water may be preferred for individuals with sympathicotonia, patients with hypertension and obesity who have a tendency to retain water and sodium in the body, and have minor nephropathy.

The mechanism proposed to explain proteinuria of the mixed glomerular and tubular type induced by exhaustive exercise in a healthy person was that lactic acid, pyruvic acid and other organic acids produced in excess by exercise were filtered in the glomerulus and renal tubules, and excreted together with enhanced reabsorption of Cl–, and with inhibition of reabsorption of albumin and low molecular weight protein (LMWP) such as α1M and β2M in tubular cell, thereby resulting in the occurrence of proteinuria following exhaustive exercise in a healthy person. A moderate level of exercise (MLE) that does not induce any change in urinary albumin excretion (UAEx) following exercise in healthy persons is used as a provocative test of diabetic nephropathy (DN). MLE produced an increase in UAEx in some obese persons who showed higher levels of Hct, serum TC, TG, Apo B and E concentrations accompanied by a slightly impaired glucose tolerance. This result indicated that the MLE may provoke a latent renal glomerular abnormality in some obese subjects with a slightly impaired glucose-fatty metabolism.

Key words: Exercise intensity, Renal blood flow, Heat and water environments, Water-electrolyte balance, Exercise-induced proteinuria

Introduction

The kidneys play an important role in maintaining constancy of physiological factors within the body, such as pH, osmotic pressure and electrolytes in plasma, by excreting metabolic wastes and noxious products as well as excreting and reabsorbing water and electrolytes, including Na+, K+ and Cl–. These functions are performed by the renal blood flow (RBF), glomerular filtration rate (GFR), and excretion and reabsorption in the tubules. Even if the excretable noxious products were to increase, as a result of increase in metabolic rate, RBF will be reduced during exercise. Physical exercise has, therefore, a negative effect on the kidneys in terms of maintenance of renal function. However, in sports medicine, research on renal function in athletes has been given less importance, compared to other areas of study such as the respiratory, circulatory systems and neuro-muscular systems as well as the metabolism of glucose and fats, as it has no direct influence on the performance of exercise. However, exercise is also used in physical therapy for obesity, diabetes mellitus and minor hypertension. In patients with mild nephritis in whom exercise is not restricted, a knowledge of the relation between exercise and renal function is essential. Though microalbuminuria (MAU) is used as useful index for the early detection and diagnosis of diabetic nephropathy (25, 61), physical activity increases excretion of MAU into urine (1, 26) and this knowledge is indispensable for evaluating MAU of diabetic patients.

On the other hand, renal function is important in the maintenance of the fluid-electrolyte balance, even in healthy persons and athletes during exercise in warm conditions or in water. The purpose of this article is to review the previous literature, to present some of our observations on renal function and to discuss the mechanisms underlying the changes of renal function and the roles of the kidney during and/or...
following exercise.

Effects of exercise on RBF and GFR

A. Effect of body posture on RBF and GFR

Generally, RBF and GFR are measured in the supine position. However, exercise is performed in various positions of the body such as the supine, standing and sitting positions, therefore the effect of body posture on RBF and GFR and their changes must be considered during exercise. Bakris et al. (1) reported that in healthy persons, para-aminohippuric acid clearance (C_{PAH}, effective renal plasma flow ; ERPF) and inulin clearance (C_{in}, glomerular filtration rate ; GFR) were reduced to 18.5% and 13.5%, respectively, when the body posture changed from the supine position for one hour to standing for 20 minutes. Molzahr et al. (26) reported that creatinine clearance (C_{cr}) and C_{PAH} in healthy males (n = 8, 25 ± 1.6 yrs) decreased 27 ± 27% and 38 ± 27%, respectively, when the body posture changed from the supine position for 45 minutes to a 45° head up tilting position for 30 minutes. According to Ueda (59, C_{PAH} in healthy males (n = 4, 21.0 yrs), was reduced 19.8% at 60 min and 23.1% at 120 min in a continuous standing position respectively from the value of the supine position for 60 min, whereas sodium thiosulfate clearance (C_{thi}) and C_{cr} did not change significantly. The above-described studies showed that response of RBF to conscious change of body posture is different to the response to transitive change of body posture using a tilting table. Orthostasis in man may activate complex reflex and hormonal responses that preserve arterial pressure during a decrease in venous return (1, 28). It has been pointed out that the cardio-renal adjustment is maintained, in response to posture change, by increasing the secretion of norepinephrine and through the activation of renin activity and renal sympathetic nerve (1).

B. Effect of exercise intensity on RBF and GFR

With an increment in the intensity of exercise, oxygen intake (\( \text{VO}_2 \)) increases, but if the oxygen supply is less than the oxygen requirement, an oxygen debt is incurred, thereby causing increases in blood lactate (bLA) and pyruvate, which induce transient blood acidosis. As renal function has an important role in acid-base regulation, one might expect it to be activated to buffer metabolic acidosis caused by exercise. However, during exercise, as the muscular oxygen requirement increases, the blood distribution changes and blood flow to the internal organs, including the kidneys is reduced (32).

RBF and GFR are reduced in response to an increase in the intensity of exercise but the degree of reduction has varied in different studies. These differences may be due to the differences in the indices used to express the intensity of exercise (\%HR_{max}, \%\text{VO}_2{\text{max}}, speed of treadmill), and of body postures, cycle ergometer and treadmill run used in the exercise test, and of methods to measure RBF and GFR. According to the results of the author (44), Suzuki et al. (42) and Grimby (14), RBF was reduced by 44.0 ~ 57.0% following maximum exercise (100\%\text{VO}_2{\text{max}}), by 34.3 ~ 38.9% at 80% of \text{VO}_2{\text{max}}, by 24.4 ~ 38.4% at 60% of \text{VO}_2{\text{max}}, and by 2.4 ~ 23.9% following 40% of \text{VO}_2{\text{max}}. However, the relation between exercise intensity and GFR has differed to some extent, from that of RBF. Sodium thiosulfate clearance (C_{thi}), C_{in} and C_{cr} are used as indices of change in GFR. According to the author (46), at the intensity of 43 ~ 61% of \text{VO}_2{\text{max}}, there were no changes in C_{cr} immediately after exercise, but at 83% and 100% of \text{VO}_2{\text{max}}, C_{cr} was reduced to 47% and 45%, respectively. Poortman (29) has reported the absence of change in GFR (C_{in}) at a minimum to medium intensity of exercise.

Recently, Suzuki (41) has investigated relations between exercise intensity (\%\text{VO}_2{\text{max}}) and renal plasma flow (RPF) and C_{in} as well, and reported the following regression equations.

\[
\%C_{PAH} = 1.94 \times 10^4 \cdot X^3 - 3.51 \times 10^2 \cdot X^2 + 1.05 \cdot X + 95 \quad (r=0.959, \ p<0.001)
\]

\[
\%C_{\text{in}} = -8.53 \times 10^{-9} \cdot X^2 + 3.01 \times 10^{-1} \cdot X + 101 \quad (r = 0.879, \ p<0.001)
\]

Here, \%C_{PAH} and \%C_{\text{in}} are the percentage values of the resting value and X is the relative work intensity (\%\text{VO}_2{\text{max}}).

The results of the author (44), Suzuki et al. (42) and Grimby (14) largely concurred in the relation between the exercise intensity (\%\text{VO}_2{\text{max}}) and percent change of RPF (\%C_{PAH}) calculated by the above-stated Suzuki's equation (41). According to Suzuki's equation (41), RPF was reduced from 35% \text{VO}_2{\text{max}}, whereas GFR (C_{in}) started to reduce from 42% \text{VO}_2{\text{max}}, and the filtration fraction started to increase when \text{VO}_2{\text{max}} increased to over 50%. Suzuki's results (41) demonstrated that there was no reduction in RPF until the exercise intensity reached 35% \text{VO}_2{\text{max}} and there was no reduction in GFR under 49% \text{VO}_2{\text{max}}. Reductions of RPF and GFR occurred in response to exercise accompanied by increases in plasma catecholamines, renin and angiotensin II (7, 19) and decrease in blood pH (18, 52), with an increase in anaerobic metabolism induced by a gradual increase in exercise intensity. The mechanism of reduction in GFR and RPF in response to work intensity will be stated subsequently.
The results of the author (44), Suzuki et al. (42), Grimby (14) and Suzuki (41) indicated that RBF and GFR were not reduced within the intensity range of 35–40% of VO₂ max, and that the physical activity at these levels (35–40% VO₂ max) is permissible for minor nephritics patients in their daily life. Exercise duration does not have a significant concomitant effect on changes in RBF and GFR. Castenfors (4) has reported that no changes in RPF and GFR were noticed even if 45 minutes of moderate exercise was extended to 90 minutes.

The process of RBF recovery following exercise has seldom been examined at different intensities of exercise. Chapman et al. (6) reported that RPF reduced to 85% immediately after, and recovered to 89.1% 20 min after, and to 96.5% of the resting value 40 min after light exercise (treadmill speed 3.0 miles/hr, grade 0%), whereas RPF reduced to 65.5% immediately after, and recovered to 79.8% 20 min after, and to 94% of the pre-exercise value 40 min after strenuous exercise (treadmill speed 3.5 miles/hr, grade 10%). The author (54), on the other hand, examined the process of RBF recovery measured by radio-nuclide angiography (RA) following exhaustive bicycle ergometer exercise. The RBF reduced to 46.6% immediately after, 82.5% 30 min after and 78.9% of the pre-exercise level 60 min after the exercise. The results of Chapman et al. (6) and the author (54) revealed that light exercise induced a smaller reduction and rapid recovery of RBF following exercise. There were, however, no prominent differences in the process of RBF recovery following exercise, with recovery to 78.9–94% of the resting value 40 to 60 min after the exercise at a higher than moderate intensity. The author’s previous study (46) showed that the degree of Ccr reduction immediately after exercise was related to the intensity of exercise within 43–100% VO₂ max, and recovered to the pre-exercise level 30 min after exercise. Modification of RPF was greater than that of GFR during exercise, and recovery of RPF was slower than that of GFR following exercise. Therefore, the higher level of the filtration fraction (FF) was maintained throughout the exercise and post-exercise periods.

Sanders et al. (37) reported that the reduction of RBF, modifications of blood distribution in the kidneys and increase in blood flow into skeletal muscles in response to exercise were observed in miniswine using the tracer microspheres technique.

The mechanism of RBF reduction during exercise is considered to be as follows. Reduction of RBF in response to exercise might be caused by activation of renal sympathetic nerve activity and/or enhanced levels of vasoconstrictor hormones such as norepinephrine and angiotensin II (AII) (57, 58). This notion is based on the experimental finding that stimulation of the renal nerve plexus, and intravenous injections of a large amount of catecholamine constricted renal arterioles selectively (29), and on the finding by Hohimer et al. (17) in cutting off one side of the renal nerve in the baboon. Stebbins et al. (40) suggested that the renin-angiotensin (RA) system was enhanced in response to exercise involved in the reduction of RBF during exercise, but Castenfors (5) and Tidgren et al. (57, 58), negated involvement of the RA system in the reduction of RBF during exercise. Wade et al. (63) suggested that there was no involvement of AII in the reduction of RBF during exercise according to the finding obtained by administration of angiotensin converting enzyme (ACE) inhibitor prior to exercise, though it was reported that AII preferentially constricted the efferent arterioles intrarenally.

The above observations suggest that enhanced renal sympathetic nerve activity and increase in catecholamine secretion induces modifications of RBF and GFR during exercise and post-exercise periods. However, the role of the RA system has not been confirmed in relation to the reduction of RBF in response to exercise.

Responses of water, electrolytes and hormones related to the regulation of metabolism of water-electrolytes to exercise

The amount of electrolytes and water in the body is controlled strictly by consuming water, which is stimulated by the neuro-secretory system in the brain, and by a system which regulates absorption and excretion of water and electrolytes in the kidney. During exercise, RBF and GFR are reduced, and prolonged exercise induces a large loss of water and electrolytes in sweat. It is, therefore, presumed that modifications of urinary excretion of water and electrolytes, and of hormones related to the regulation of water and electrolyte balance may be enhanced.

A. Effect of exercise intensity on responses of water, electrolytes and hormones related to regulation of water-electrolyte balance

Excretion of water and electrolytes into the urine following exercise is affected by the state of hydration and the emotional state of the subject (29), and by the severity and duration of exercise. Here, the effects of severity of exercise are discussed.

Responses of hormones, electrolytes and osmolality of the blood and urine to four different intensities of exercise (42.5–100% VO₂ max) were measured in seven healthy males, during pre-exercise, ex-
exercise and 2-hr post-exercise periods. Mean duration of maximum exercise was 17.9 min, and three different levels of submaximum exercise were performed for 20 min using a treadmill. Figure 1 illustrates the responses of plasma angiotensin II (pA II), aldosterone (pAld) and prostaglandin E (pPGE) concentration to different intensities of exercise. Concentrations of pA II and pAld significantly increased immediately after exercise at an intensity above 60.5% VO2max, and pA II recovered to the pre-exercise level after 30 minutes. Recovery of pAld occurred subsequently, and a significantly higher concentration of pAld persisted for 2-hr after exhaustive exercise (100% VO2max). However, the pPGE concentration did not vary significantly throughout the four different intensities of exercise. Serum osmolality (Sosm), and Na and Ca concentrations significantly increased immediately after 83.0% and 100% VO2max exercise, and recovered to the pre-exercise levels thereafter. In contrast, the serum inorganic phosphate (Pi) concentration increased significantly immediately after exercise at intensities ranging from light (42.5% VO2max) to exhaustive (100% VO2max), and decreased to below the pre-exercise levels (p < 0.05) within 60 120 min after 83.0% and 100% VO2max exercise. Serum concentration of Mg showed a significant increase immediately after 100% VO2max, and returned to the normal level 30 min after exercise. No significant change in serum Mg was observed under the intensity of 83.0% VO2max. Figure 2 shows responses of urine volume (UV), Ccr and urine osmolality (Uosm) to exercise. UV reduced significantly immediately after severe exercise, and a transient diuretic phenomenon was observed 30 min after exercise, and reduced again thereafter. A transient reduction of UV was observed immediately after 83.0% VO2max exercise. At the intensity of 83.0% VO2max, UV responses to exercise tended to increase. Ccr showed significant decreases immediately after 100 and after 83.0% VO2max of exercise, but recovered almost to the pre-exercise levels 30 min after exercise. At levels lower than 60.5% VO2max, Ccr did not vary significantly, but tended to increase following exercise. A remarkable reduction of Uosm was seen 30 min after exercise, and the magnitude of reduction of Uosm was related to the intensities of the exercise.

An obvious effect of exercise on the urinary excretion of electrolytes was seen at 30 min after exercise. Significant decreases in Na and Cl concentrations in the urine were observed 30 min after 83.0% and 100% VO2max of exercise, and it was noteworthy that the decrease in Cl concentration was 3.6-fold compared to that of the Na concentration in urine observed 30 min after exhaustive exercise (100% VO2max). There were no significant change in the excretion of K (uK) into the urine at 83.0 100% VO2max, but below that level there were significant increases in excretion following exercise. Urinary concentrations of Ca and Mg did not vary significantly following exhaustive exercise. Below the intensity of 83.0% VO2max, significantly lower levels of Mg and Ca concentrations in the urine continued for 2-hr following exercise. In contrast, the urinary concen-

Fig. 1 Changes in plasma concentrations of angiotensin II (pA II), aldosterone (pAld) and prostaglandin E (pPGE) following various levels of exercise. Significance of differences from the pre-exercise level: *p<0.05, **p<0.01

Fig. 2 Changes in urine volume (UV), creatinine clearance (Ccr) and urinary osmolality (Uosm) following various levels of exercise. Data were presented as means and SDs of differences from the pre-exercise level. Significance of differences from the pre-exercise level: *p<0.05, **p<0.01, ***p<0.001

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The mechanisms and roles of the kidney during exercise.

The concentration of Pi showed a significant increase 30 min after both 83.0% and 100% VO_{2\text{max}} of exercise, but did not vary significantly at these intensities of exercise.

The difference between the product of GFR and the plasma concentration of solutes and the amount of reabsorption and/or excretion of solutes in the renal tubules determines the amount of solutes excreted into the urine. Excretion of electrolytes into the urine may be affected by reabsorption and/or excretion by the renal tubular cells, and by the modifications of GFR in response to exercise.

First of all, the relationships between variations in the urinary concentration of electrolytes that responded to exercise were analyzed. Change in Na concentration in urine was largely accompanied by change in the Cl concentration (r = 0.756, p < 0.001), besides the remarkable discrepancy between changes in the Na and Cl concentrations in the urine observed 30 min after exhaustive exercise. On the other hand, a relation between changes in urinary Cl and Pi concentrations in response to exhaustive exercise was presumed, as an increase in Pi concentration was correlated to decrease in Cl concentration in urine following severe exercise (r = -0.549; p < 0.001). Change in Uosm was negatively correlated with UV (r = -0.431, p < 0.001), but was independent from Ccr (r = 0.005, NS). Uosm is the sum of concentrations of solutes in the urine. Among these, Cl had considerable influence (r = 0.738, p < 0.001) on Uosm and Na (r = 0.495, p < 0.001), Mg (r = 0.478, p < 0.001) and K concentration in the urine (r = 0.364, p < 0.001) had an influence on Uosm in this order, and concentrations of Ca and Pi in the urine seemed to have less influence on Uosm (Ca; r = 0.303, p < 0.01; Pi; r = 0.218, p < 0.01). The degrees of increase in blood lactate (Δ bLA) concentration immediately after exercise and of decrease in the urinary concentration of Cl (Δ Cl) 30 min after exercise depended on the increase in the intensity of exercise. A higher negative coefficient of correlation (r = -0.886, p < 0.001) was found between the concentration of Δ bLA observed immediately after exercise and the concentration of Δ Cl in the urine 30 min after exercise. A significant negative correlation (r = -0.549, p < 0.001) was also observed between the changes in urinary Pi (Δ Pi) and Cl (Δ Cl) concentrations before and after exercise. The remarkable reduction of Cl concentration in the urine observed 30 min after exhaustive exercise was thought to be due to the preferential excretion of Pi into the urine compared to the excretion of Cl.

We (50, 53) observed changes in electrolytes and lactate (uLA) concentration in the urine following exhaustive exercise (Fig.3, Fig.4). Fig.3 shows our the significant increase in LA and Pi (PO_{4}) concentration accompanied by a marked reduction of Cl concentration in the urine 30 min after exhaustive exercise. The higher sum of LA and Pi concentrations in the urine increased, and the lower Cl concentration in the urine decreased (Fig.4). The sum of cations (Na+ + K+) in the urine was nearly equal to the sum of anions (PO_{4} + LA + Cl) in urine, and there was a markedly higher coefficient of correlation (r = 0.995, p < 0.001) between changes in the sum of cations and of anions in the urine following exhaustive exercise. The peak concentration of LA in the blood and urine was observed immediately after and 30 min after exercise, respectively. Increase in uLA concentration was related to the increase in blood LA concentration (r = 0.926, p < 0.001), and started to increase above the level of 60 mg/dl (6.7mM/L) of blood LA concentration (50). Overproduction of LA in the cell induced by severe exercise led to a reduction of pH in the blood, which induced a lower ratio of HPO_{4}^{2-} to H_{2}PO_{4}^{-} concentration (HPO_{4}^{2-}/H_{2}PO_{4}^{-}) in the blood. We postulated that H_{2}PO_{4}^{-} and LA were excreted simultaneously into the renal tubules, and resulted in a large amount of anions in the tubular fluid, and that ion balance in the tubular fluid...
might be maintained to enhance reabsorption of Cl in the tubule cell (50). Meanwhile, increases in Na, Cl and K excretions into the urine were seen following light to moderate exercise (42.5 \sim 60.5\% V\text{O}_2\text{max}). However, the lower correlation coefficient between the changes in plasma aldosterone (pAld) concentration and the urinary excretion of Na into the urine (r=0.301, p<0.001) did not suggest an important role in the absorption of Na and secretion of K in renal tubular cells following exercise. No significant correlations between the changes in pAII and the excretion of Na, K and Cl into urine were observed following exercise. After more intense exercise, higher concentrations of pAld and pAII were found, but these hormones had no obvious actions on changes in the urinary excretion of electrolytes following exercise. Particularly, pAld concentration persisted at a significantly higher level for up to 2 hrs after exhaustive exercise. This might have been caused by inactivation of Ald in the liver due to the reduction of hepatic blood flow induced by physical exercise (36, 38).

**B. Effect of prolonged exercise on responses of water, electrolytes and hormones related to regulation of water-electrolyte balance**

There have been no consistent observations with changes in electrolyte excretion into urine following prolonged exercise. Differences in observations may be attributed to the differences in severity and duration of exercise, and to the different environments, and to the replacement or non-replacement of fluid containing minerals and other elements during exercise (45, 48). Furthermore, there may have been differences in the urine sampling, which was collected only two to three hours after and 24-hr during and after exercise (9, 24, 35).

Refsum et al. (35) reported that a marked decrease in Na, Cl, Ca, Mg and urea concentrations and increase in K concentration were observed in urine collected after a 70-km cross country ski race for 4.39 to 6.52 hrs. Lijnen et al. (24) reported that 2 consecutive days of 3.5 hrs of strenuous physical exercise, which consisted of 50 km of cycling (90 min), circuit training (60 min) and running and calisthenics (60 min), led to decreases in Na and K excretion and increases in Ca, Mg and aldosterone excretion into 24-hr urine in each two-day exercise session; these values then recovered to the pre-exercise levels one and two days after the exercise, respectively. We observed modifications in plasma renin activity (PRA), pADH, pA II, pAld and serum electrolyte concentration and urinary excretion of electrolytes into 24-hr urine for one week after a 42.195-km full marathon race in six healthy middle aged elderly males and females (unpublished data). Plasma hormones and serum concentrations of almost all electrolytes increased immediately after the race, then returned to the pre-exercise levels within 60 min after the race. However, serum Mg concentration showed a significant reduction immediately after and 60 min after the race, and returned to the pre-exercise levels, as did the other serum electrolytes, on the day after the marathon race. On the other hand, excretion of Na and Cl into the urine showed a significant reduction on the next day, returned to the pre-exercise levels two days after the race, and showed no significant changes thereafter. No significant changes in excretion of Ca, K, Pi and Mg into urine for 24-hr were observed two days after the race.

As mentioned above, a short duration of significant electrolyte modification in the serum and urine following exercise was induced dependently on the intensity and duration of exercise, but urine samples collected for 24-hr during and/or after exercise showed no significant changes. Based on the absence of significant modifications of plasma ADH and Ald
concentrations, the induction of changes in electrolyte excretions into 24-hr urine might be avoided by replacements with appropriate amounts of water and minerals through the consumption of meals and sports beverages during and/or after the prolonged exercise.

Responses of renal function following exercise related to environmental conditions
A. Renal function and water-electrolyte balance during and after exercise in a hot environment

Increases in body temperature and loss of water and electrolytes from the body are produced as heat production is increased with an increase in the requirement for energy during exercise. In particular, distribution of the renal blood flow may be diminished by diversion of the blood through the skin in response to heat exposure (64), and large amounts of water and electrolytes in the body may be lost by an increase in sweat (3, 8, 27). The functions of the organs and neuro-secretory system involved in controlling the water-electrolyte metabolism and the body temperature, mainly in the kidneys, may be enhanced by exercise under a hot environment (47).

Smith, et al. (39) reported 8 ~ 10% and 5.3 ~ 15.2% lower levels of para-aminomipurate clearance (RPF) and manitol clearance (GFR), respectively, in a hot environment (50°C d.b., 26°C w.b.) compared to those in a cool environment (25°C d.b., 16°C w.b.). Smith, et al. (39) also added that remarkable reductions of RPF and GFR were observed during exercise in a dehydrated state under a hot environment. Radigan, et al. (34) reported marked decreases in RPF and GFR during exercise in a hot environment.

We (43) observed responses of serum electrolytes, pAld and pA II concentrations, and of urinary excretions of electrolytes of about 60% of VO2max exercise for 30 min in cool (6.0°C), moderate (18.6°C) and hot (32.9°C) environments in five healthy males in a dehydrated state. The greatest reductions of body weight (Δ 750g), urine volume and urinary excretions of electrolytes into urine were observed after exercise in a hot environment compared to that under other environmental conditions. As is shown in Fig.5, enhanced responses of pAld and pA II concentrations without significant modifications of serum electrolyte concentrations in response to moderate exercise were observed under hot environmental conditions. On the other hand, enhanced levels of pAld and pA II concentration occurred in response to exercise in a hot environment and returned to the pre-exercise levels after replacement by means of a sports beverage containing glucose, electrolytes and other elements.

Heat exposure leads to increase in skin blood flow (64) and to decreases in RPF and GFR (34, 39). Substantial decrease in body fluid due to the large amount of sweat loss during exercise in these environmental condition may result in further decreases in RPF and GFR (34, 39). The enhanced endocrine system involved in the regulation of water and electrolyte metabolism, induced by remarkable elevation of pADH, pAld and pA II concentrations may contribute to conservation of water and electrolytes in the body by increasing sodium and water reabsorption from the filtered tubular fluid in the kidney under these conditions.

B. Responses of renal function to water immersion and exercise in water

Reduction of blood flow in the body surface area and increase in blood flow in deeper parts of the body are induced by an increase in hydrostatic pressure on the immersed part of the body dependent on the depth of immersion. This enhanced hydrostatic pressure diverts interstitial fluid from the interstitial compartment in the body surface area into the vascular compartment, and may be responsible for hemo-
dilution, concomitantly, it may produce an increase in stroke volume and a decrease in heart rate due to the increase in venus return occurring in water immersion (12, 15, 22). Inhibition of sympathetic nervous activity and a lower concentration of plasma norepinephrine have been observed in water immersion (11).

In head-out water immersion, however, the estimated renal plasma flow (ERPF) and plasma concentration of atrial natriuretic peptide (plasma ANP) were increased, accompanied by a lower pAld concentration and PRA (10, 33) without significant modification of GFR. Urine volume and excretion of Na, Cl and K into urine increased simultaneously in the head-out immersion. If water immersion was prolonged, water excretion progressed markedly compared to the excretion of other solutes, and hemocentration occurred (13, 20).

Reductions in RPF and GFR, and inhibitory excretion of water and electrolytes occurring during exercise on land may be attenuated in head-out water immersion. We are interested in the modifications of RPF, GFR and serum hormones in the regulation of water-electrolyte balance during exercise in water. However, it is comparatively difficult to measure change in RPF in humans during exercise in water. Therefore, in a recent study performed on eight healthy males who exercised for 30 min each in water (29.9±0.6°C) and on land (25.1±2.3°C) (unpublished data), we observed changes in Ccr, urinary excretion of electrolytes and the concentrations of plasma catecholamines and pAld, without measurement of RPF, following exercise at levels corresponding to 40% and 60% of VO2max determined using a treadmill on land. Walking and/or running speed was controlled strictly to the same oxygen uptake (VO2) during exercise in water as that on land. Volunteers were assigned to maintain a standing position for 30 min immersed to the xiphoid level in water and on land, respectively, as controls to the exercise experiments both in water and on land. Increases in UV and urinary excretion of Na, and decreases in pAd, pNorad, pAII and pAld concentrations were produced, without changes in Ccr and Uosm, during quiet standing for 30 min in water. On the contrary, change in body position from sitting for 30 min to standing for 30 min on land led to significant elevations in the concentration of these plasma hormones, and significant inhibition of water and sodium excretion into the urine. The different responses to standing in water and on land occurred largely in response to light exercise (40% VO2max; 22.0 ml/kg/min) in water and on land. However, responses of pAd, pNorad and pAII to moderate exercise (60% VO2max; 33.4~34.2 ml/kg/min) resulted in smaller differences between that observed in water and on land. Fig.6 shows that the difference in increase in pAld concentration after moderate exercise observed in water and on land was not significant. Reabsorption of Na occurred in the renal tubules (TRNa%) following exercise in water, and yet, was significantly lower compared to that on land. The advantage responses to exercise in water are inhibition of the sympathetic nervous system and endocrine system, and facilitation of water and electrolyte excretion into the urine induced by water immersion, and may be maintained, if the intensity of exercise is low (around 40% of VO2max) during exercise in water. It has been reported that exhaustive exercise in water produced lower increases of plasma catecholamines, pAld and pAII concentrations, and fewer effects on the kidney compared to that produced by exhaustive exercise on.

![Fig. 6 Comparison of responses in plasma aldosterone (pAld) and tubular reabsorption of Na (TRNa%) to standing posture (30 min) and 60% of VO2max exercise (30 min) on land and in water. Signficance of differences from the pre-exercise level, and between data obtained at the same time on land and in water: *p<0.05, **p<0.01, ***p<0.001](NII-Electronic Library Service)
land (49, 51).

From the above observations, it can be concluded that light exercise in water is preferable for individuals with sympathicotonia and patients with hypertension and obesity, who have a tendency to retain water and sodium in the body, and who have minor nephropathy.

Exercise-induced proteinuria.

A. Mechanism underlying exercise-induced proteinuria in a healthy person.

Exercise induced-proteinuria (EIPU) is related to the intensity of exercise, and frequently occurs at levels over 70 – 80% VO2max (29, 30, 46). EIPU contained medium to larger molecular weight proteins such as IgG, IgA, albumin (Alb), and lower molecular weight proteins (LMWP) such as $\alpha_1$ microglobulin ($\alpha_1$M) and $\beta_2$ microglobulin ($\beta_2$M). The mechanism for exercise-induced proteinuria had been assumed extensively. EIPU was accompanied by reductions in RBF and GFR, and by increases in pAd, pNorad, pA II concentrations and PRA (21, 62). On the other hand, it has been reported that intravenous infusion of noradrenaline or A II-produced proteinuria (2, 23), and oral administration of angiotensin-converting enzyme inhibitor (ACE-inhibitor) reduced proteinuria in patients with nephropathy (16, 56). From these findings, exercise-induced modifications of renal homodynamics and the glomerular filtration fraction (FF), and activations of renal sympathetic nerve and the renin-angiotensin (RA) system has been thought to directly or indirectly increase permeability of the glomerular capillary membrane to proteins (2, 23, 29, 31, 46). We observed that an increase in pA II concentration following exhaustive exercise was inhibited by oral administration of 50 mg of the ACE inhibitor, captopril, in eight healthy males at 30 min prior to exercise (unpublished data). However, marked excretions of Alb and $\beta_2$M into urine after maximal exercise were not inhibited at all by captopril treatment, and the role of A II in the induction of post-exercise proteinuria in a healthy person remains problematic. Not only Alb, but LMWP such as $\alpha_1$M and $\beta_2$M, were found in the urine collected following exhaustive exercise, and the mechanism for the occurrence of these LMWP was not explained by the prior-mentioned mechanisms (2, 23, 29, 46). We (50) observed individuals (H-alb; n=20) who had marked excretion of Alb, and individuals (L-alb; n=20) who had little excretion of Alb into urine after exhaustive exercise performed using a treadmill among 69 healthy males. Responses to exhaustive exercise of plasma CA, pA II concentration and urinary excretion of electrolytes and lactate to exhaustive exercise in the H-alb group were compared with those in the L-alb group. On the contrary, no significant difference in the responses of pAd, pNorad and pA II concentration to exhaustive exercise was seen between the H-alb and L-alb groups. However, the H-alb group showed a greater decrease in Cl concentration, and higher increases in urine Pi and LA concentrations compared with those in the L-alb group following exhaustive exercise. Higher coefficients of correlation between changes in urinary Alb and LA, and $\beta_2$M and LA concentrations in urine are shown in Fig.7. Fig.7 shows that at higher concentrations of LA, more Alb and $\beta_2$M are excreted into the urine.

Based on the above-described observations (50), the mechanism for proteinuria of the mixed glomerular and tubular type induced by exhaustive exercise in a healthy person is thought to be that lactic acid, pyruvic acid and other organic acid excessively produced by exercise were filtered in the glomerulus and renal tubules, and markedly excreted with enhanced reabsorption of Cl, and inhibition of reabsorption of lactate. Fig. 7 Relationship between urinary excretion of lactate [uLA] and $\beta_2$M [u$\beta_2$M] and albumin[uAlb] before and after exhaustive exercise. Actual values have been converted into logarithms and plotted.
Alb and LMWP in the tubule cells, thereby resulting in the occurrence of proteinuria consisting of both Alb and LMWP. Although further study should be performed to provide a detailed explanation of exercise-induced proteinuria, we do not believe that angiotensin II plays an important role in the occurrence of proteinuria following exhaustive exercise in a healthy person.

B. Exercise-induced proteinuria in obese persons

Microalbuminuria (MAU) is defined as abnormally elevated urinary albumin excretion (UAEx; 20~200 mg/min) in the absence of clinical proteinuria as measured by standard laboratory methods. Recently, it has been generally accepted that UAEx is a useful parameter to detect early stages of diabetic nephropathy. Development from obesity with disturbed glucose-fatty metabolism to diabetes mellitus (DM) is not rare, and it is thought that obese persons may have cardiovascular disease, such as an early stage of renovascular disease or retinopathy caused by disturbed glucose-fatty metabolism. Therefore, we conducted a provocation test with exercise of latent renovascular abnormality in obese persons (55). A moderate levels of exercise (MLE) that induces no change in UAEx following exercise in healthy persons is used as one of the provocative tests of diabetic nephropathy (DN) (60). A study was undertaken to ascertain the effects of moderate exercise on UAEx after exercise, and to demonstrate the relation between glucose tolerance (GT) and the levels of lipid concentrations in blood, and UAEx after moderate exercise in twenty-one obese males (42.1 yrs, BMI 28.0). Eight normal volunteers (37.4 yrs, BMI 23.1) participated in the study as control subjects. Blood pressure (BP), serum levels of TG, TC, HDL-C, lecithin cholesterol-acyltransferase (LCAT), apoprotein (Apo) concentrations and GT ability were measured. MLE test (58.0% \( \text{VO}_{2\text{max}} \)) were performed for 30 min using a bicycle ergometer. Urine samples for the measurement of Alb, \( \beta_2 \)-M, NAG and creatinine were obtained before, directly and 30 min after exercise. Significant increases in UAEx after MLE were shown in the obese group (obesity I ; \( n = 10 \)). The other obese (obesity II ; \( n = 11 \)) and eight normal volunteers showed no change in UAEx after MLE. Obesity group I showed significantly higher levels of Het, Apo B, E concentrations and LCAT activity, and tendencies for the values of TC, TG, TC/HDL-C ratio, fasting immuno-reactive insulin (FIRI) and blood sugar (FBS) to be higher than in the obesity II and control groups. There were no significant differences in age, BMI, resting BP and heart rate and BP during exercise among these groups. The obese sub-

jects in whom an increase in UAEx was induced after MLE showed significantly higher levels of Het, TC, TG, Apo B and E accompanied by a slightly impaired GT, despite a normal range of Ccr. The results indicate that the MLE might have provoked latent renal glomerular abnormalities in obese subjects.

Further study may explain the mechanism underlying increase in urinary excretion of albumin following moderate exercise in obese persons who show high levels of Het, TC, TG, Apo B and E, and a slightly impaired glucose tolerance.

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