Is urodilatin the missing link in exercise-dependent renal sodium retention?

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Schmidt, W. A. Bub, M. Meyer, T. Weiss, D. Schneider, N. Maassen, and W. G. Forssmann. Is urodilatin the missing link in exercise-dependent renal sodium retention? J. Appl. Physiol. 84(1): 123–128, 1998.—The purpose of the present study was to investigate the behavior of plasma atrial natriuretic peptide [ANP-(99—126)] concentration ([ANP]) and renal urodilatin [Uro; ANP-(95—126)] excretion during and after exercise and their possible effects on renal Na+ retention. Ten male subjects performed a cycle ergometer test for 60 min at 60% of maximum workload. Blood and urine samples were collected before, during, and up to 24 h after exercise. During exercise, plasma [ANP] and renal Uro excretion were oppositely affected; whereas [ANP] increased from 46.5 ± 5.1 to 124.1 ± 10.6 pg/ml, urinary Uro excretion decreased from 120.8 ± 16.0 to 49.5 ± 9.8 fmol/min and remained at a lower level until 1 h after exercise. Glomerular filtration rate showed lowest values during exercise (from 164.9 ± 15.3 to 75.8 ± 10.1 ml/min), and urine flow and the fractional excretion rate of Na+ (FE Na+) and Cl− (FE Cl−) had their nadir during the first hour after exercise. Positive relationships were observed between Uro excretion and FE Na+ (P < 0.05) and FE Cl−, whereas a tendency toward a negative correlation was obtained between [ANP] and FE Na+. It seems possible that Uro may be, among other factors, involved in the exercise-related regulation of renal Na+ retention. The specific roles Uro and ANP play during exercise, however, remain to be investigated.

atrial natriuretic peptides; sodium excretion

It has been known for a long time that intensive exercise influences renal function, including changes in hemodynamics, concentration mechanisms, and electrolyte excretion (see, e.g., Ref. 22). During and immediately after exercise, urine flow decreases, which is due to 1) lower renal blood flow and subsequently lower glomerular filtration rate (GFR) and 2) increased reabsorption mechanisms at the distal tubule and medullary collecting duct. These phenomena, i.e., lower GFR and lower water excretion, can be partly explained by increased sympathetic activity. The lower sodium excretion rate during exercise, however, which is indicated by a lower percentage of the filtered sodium excreted by the kidneys and the frequently found lower urine electrolyte concentration and osmolality (2), cannot be satisfactorily explained by any hitherto known hormonal mechanism.

The plasma aldosterone concentration increases during and after exercise as a result of a sympathetically and hemodynamically stimulated increase in renin activity. However, the aldosterone effector kinetics are too slow to have any considerable early effects on tubular electrolyte retention (3, 28).

After 1981, when the atrial natriuretic peptide [ANP-(99—126)] was discovered by de Bold and co-workers (9), plasma ANP was also assumed to be an important factor in the exercise-associated regulation of renal sodium retention. In the meantime, many studies have been performed showing that ANP release increases in response to physical exercise in a dose- and time-dependent manner. That is, during longer lasting exercise such as marathon running an initial increase is followed by a return toward basal levels (13). The lower renal sodium excretion during exercise, however, is in contrast to the increased plasma ANP concentrations, excluding ANP as a main factor involved in the regulation of renal function during exercise. Furthermore, during the last few years, physiological ANP concentrations have been shown to have hemodynamic effects but no influence on the regulation of tubular sodium excretion (15, 19).

In 1988, urodilatin [Uro; ANP-(95—126)], a member of the family of the natriuretic peptides, was isolated from human urine (27). To date, the mode of its synthesis, processing, and secretion is poorly understood. Because Uro occurs in urine, but could not be detected in human plasma, it is assumed to be secreted by the kidney. Immunohistological studies give further evidence that Uro is localized in the distal tubules in the form of its precursor (12). Uro and ANP share similar functional properties, such as, e.g., diuresis, natriuresis, and vasorelaxation (25). Under physiological conditions, Uro is less inactivated by the kidney endopeptidase EC 24.11 than is ANP (14), explaining the different effects of both natriuretic peptides on the inner medullary collecting duct. Secretion of Uro is mainly regulated by circulatory central filling pressure and by extracellular sodium concentration (see Ref. 15). Thus under many physiological conditions Uro and ANP are stimulated in a similar manner.

To date, no data exist about the behavior of Uro excretion and possible natriuretic effects during physical exercise. Increasing plasma sodium concentration (e.g., Ref. 26) and central venous pressure (17) suggest a stimulation of renal Uro secretion, leading to increased sodium excretion. However, other effects may compensate for these stimuli. It was, therefore, the purpose of this study to investigate the natriuretic peptides Uro and ANP-(99—126) and their possible influences on renal sodium excretion during and after exercise. During exercise, plasma [ANP] and renal Uro excretion were oppositely affected; whereas [ANP] increased from 46.5 ± 5.1 to 124.1 ± 10.6 pg/ml, urinary Uro excretion decreased from 120.8 ± 16.0 to 49.5 ± 9.8 fmol/min and remained at a lower level until 1 h after exercise. Glomerular filtration rate showed lowest values during exercise (from 164.9 ± 15.3 to 75.8 ± 10.1 ml/min), and urine flow and the fractional excretion rate of Na+ (FE Na+) and Cl− (FE Cl−) had their nadir during the first hour after exercise. Positive relationships were observed between Uro excretion and FE Na+ (P < 0.05) and FE Cl−, whereas a tendency toward a negative correlation was obtained between [ANP] and FE Na+. It seems possible that Uro may be, among other factors, involved in the exercise-related regulation of renal Na+ retention. The specific roles Uro and ANP play during exercise, however, remain to be investigated.

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exercise. Because there were no published data available about the influence of exercise on the secretion of Uro, we used a 60-min-long bout of exercise at 60% of maximum performance, which is well known to change renal functions.

METHODS

Test subjects and exercise protocol. Ten nonsmoking male subjects participated in the study after giving their informed consent. Maximum work capacity and maximum oxygen uptake (Oxycon Sigma, Pulmocard, Iselrohn, Germany) were obtained by an ergocycle test (Excalibur, Lode, Germany) that began at 100 W and increased the workload by 16.6 W every minute until exhaustion. The anthropometric data of the test subjects and the results of the vita maxima tests are presented in Table 1. One week after the initial test all subjects performed a 60-min ergocycle test at 60% of the initially determined maximum performance. All tests were started between 11:00 and 12:00 AM, which was 3 h after the last meal. All subjects were instructed to abstain from physical exercise and to keep to their normal nutritional behavior 1 day before the beginning of the test and during the 24-h observation period. Fluid and nutrient ingestion was restricted 3 h before, and up to 1 h after, the test. Thereafter, the subjects were allowed to drink as much fluid as they had lost during the test period, i.e., 1.4 ± 0.1 liter. Room temperature was kept constant at 21 ± 0.5°C, and relative humidity and ambient pressure were 66 ± 3% and 751 ± 3 mmHg, respectively.

After 15 min, by using an indwelling catheter blood samples were taken from an antecubital vein of subjects in a sitting position on the ergometer before, during (15 and 30 min), and after exercise (immediately after and at 1, 4, and 24 h afterward). Urine samples were collected corresponding to the time points of blood sampling, i.e., from 2 h before until the start of exercise; at end of exercise; and first hour, from 1 to 4 h, and from 4 to 24 h after exercise.

Hormonal measurements. Urinary Uro concentrations were determined by radioimmunoassay as described previously (see Ref. 7). The Uro antibody showed no cross-reactivity with human or rat ANP-(99—126), brain natriuretic peptide, C-type natriuretic peptide, or several shorter ANP analogs. The antibody was used in a final dilution of 1:7,500. Synthetic Uro served as a standard (2.8–1,420 pmol/l) and was synthesized by solid-phase peptide-synthesis methods. Purity and peptide content of synthetic Uro were confirmed by capillary zone electrophoresis, amino acid sequencing, amino acid analysis, and mass spectroscopy. 125I-labeled Uro was used as tracer (Immunodiagnostic, Bensheim, Germany) with a specific activity of 500 μCi/μg.

The urine samples were pretreated by using an ethanol extraction and lyophilization of the supernatant (7). After resuspension in assay buffer (50 mmol/l sodium phosphate, 0.5% bovine serum albumin, 0.02% sodium acid, and 0.025% Tween 20, pH 7.4), samples were incubated with the Uro antibody and tracer overnight at 4°C. Precipitation was carried out by incubation with a second antibody (donkey anti-rabbit precipitation solution; Immunodiagnostic) for 30 min after centrifugation for 20 min at 4°C and 2,000 g. The supernatant was discarded, and the radioactivity of the pellet was assessed by a gamma counter. The intra- and interassay variations were 8 and 12%, respectively. When synthetic Uro was added to urine, recovery was >90%.

ANP-(99—126) was determined in trasyol-treated plasma by a specific radioimmunoassay (IBL, Hamburg, Germany). The assay is based on a sheep antiserum against pure recombinant human ANP-(99—126) and 125I-labeled recombinant human ANP-(99—126) used as tracer. Intra- and interassay variance was 3.1 and 5.5%, respectively. The recovery rate from C18 extraction in serum containing 125 pg/ml of added ANP was between 118 and 128 pg/ml, and the minimum detectable concentration was 11 pg/ml. During the exercise period (minutes 15 and 30), ANP was only determined in the blood of five subjects.

Analytic methods. During the exercise period, the arterial blood pressure was measured every 15 min, and the heart rate (Polar-Sport-Tester, Polar, Kempele, Finland) was continuously recorded. In heparinized blood, the hemoglobin concentration was determined by a spectroscopic method (OSM3, Radiometer, Copenhagen, Denmark), hematocrit by microhematocrit centrifugation (20,900 g), and lactic acid concentration by the lactate dehydrogenase method (test kit no. 124842, Boehringer Mannheim). In plasma and urine, the electrolyte concentration ([Na+, K+, Cl−]) was measured by ion-sensitive electrodes (EML, Radiometer), osmolality by the freezing-point depression method (Osmometer Röbling, Berlin, Germany), and the creatinine concentration by the Jaffe method (test kit no. 124192, Boehringer Mannheim).

Calculations. Changes in plasma volume from the preexercise values were determined by the equation of Dill and Costill (6).

\[
PV(\%) = \frac{[Hb]_a - [Hb]_b}{[Hb]_a} \times 100 - \frac{\text{Hct}_a - \text{Hct}_b}{\text{Hct}_a} \times 100 (1)
\]

where PV is plasma volume, [Hb]a and [Hb]b are hemoglobin concentration, and Hcta and Hctb are hematocrit values before and after the beginning of exercise, respectively.

Urine volume (ml/min) was calculated for the collecting periods before (2 h), during, and after exercise (1st hour, 1–4 h, 4–24 h).

Creatinine clearance was used for the calculation of the GFR, and urinary electrolyte excretion is expressed as a percentage of the filtrated mass.

Statistics. All results are presented as means ± SE. For statistical analysis of significant changes across time, we used a 1-way ANOVA with repeated measurements. Significantly different values are marked by an asterisk (*P < 0.05; **P < 0.01; ***P < 0.001). Table 2. Heart rate, arterial blood pressure, and lactic acid concentration at rest and during 60-min exercise period

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>15</th>
<th>30</th>
<th>60</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beats/min</td>
<td>69 ± 3</td>
<td>156 ± 4*</td>
<td>169 ± 4*</td>
<td>177 ± 4*</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>[Lac], mmol/l</td>
<td>4.2 ± 0.4*</td>
<td>4.4 ± 0.5*</td>
<td>3.6 ± 0.5*</td>
<td>P &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>85 ± 2</td>
<td>86 ± 4</td>
<td>87 ± 4</td>
<td>84 ± 3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 10 subjects. ANOVA indicates degree of significance obtained by 1-way ANOVA with repeated measurements. Significantly different from initial values, *P < 0.001 (Bonferroni t-test).
Changes in plasma volume and plasma electrolyte concentration

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>15 min</th>
<th>30 min</th>
<th>End</th>
<th>1</th>
<th>4</th>
<th>24</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV, %</td>
<td>100 ± 0</td>
<td>90.5 ± 1.0*</td>
<td>89.4 ± 1.2*</td>
<td>91.1 ± 0.8*</td>
<td>99.7 ± 1.1</td>
<td>103.7 ± 1.7</td>
<td>103.8 ± 1.9</td>
<td>P &lt; 0.01</td>
</tr>
<tr>
<td>Osmolality, mosmol/kgH2O</td>
<td>287.8 ± 1.0</td>
<td>296.6 ± 1.8*</td>
<td>296.8 ± 1.4*</td>
<td>296.2 ± 0.9*</td>
<td>290.7 ± 1.5</td>
<td>290.0 ± 1.2</td>
<td>288.9 ± 0.8</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>[Na⁺], mmol/l</td>
<td>142.8 ± 1.2</td>
<td>146.6 ± 1.0*</td>
<td>146.8 ± 0.9*</td>
<td>146.8 ± 1.1*</td>
<td>144.1 ± 1.0</td>
<td>144.3 ± 1.3</td>
<td>143.4 ± 1.3</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>[K⁺], mmol/l</td>
<td>4.0 ± 0.1</td>
<td>4.9 ± 0.1*</td>
<td>5.1 ± 0.1*</td>
<td>5.1 ± 0.1*</td>
<td>4.6 ± 0.1</td>
<td>4.4 ± 0.1</td>
<td>4.3 ± 0.1</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>[Cl⁻], mmol/l</td>
<td>104.8 ± 0.7</td>
<td>107.4 ± 0.7*</td>
<td>107.3 ± 0.8*</td>
<td>107.8 ± 0.8*</td>
<td>105.5 ± 0.8</td>
<td>104.5 ± 0.8</td>
<td>105.0 ± 0.7</td>
<td>P &lt; 0.001</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 10 subjects. PV, plasma volume (% initial value). [Na⁺], [K⁺], and [Cl⁻]: Na⁺, K⁺, and Cl⁻ concentration, respectively. Significantly different from initial values; *P < 0.05 (Bonferroni t-test).

used a one-way analysis of variance with repeated measurements. To establish significant differences between two different time points, e.g., variations from the initial value during the observation time, the Bonferroni t-test was used as a follow-up test.

Partial correlation analysis adjusting dependencies between the test subjects was applied to detect relationships between two variables (all tests according to Ref. 29).

RESULTS

Exercise performance data (Table 2). During the 60-min-long test period, the workload was adjusted to 60% of the individual maximum performance, corresponding to 207 ± 10 W. This exercise intensity could be maintained during the whole exercise period from all subjects. Heart rate continuously increased during exercise, whereas the systolic blood pressure and plasma lactate concentration remained on a constantly higher level than initial values during the second 30 min of the test.

Plasma volume and electrolytes (Table 3). Water and electrolyte status was markedly influenced during and after exercise. Plasma volume decreased by 8.9% at the end of exercise and was slightly overcompensated 4 and 24 h after the test. Plasma osmolality significantly increased by 8.4 mosmol/kgH₂O, and [Na⁺], [K⁺], and [Cl⁻] increased by 4.0, 1.1, and 3.0 mmol/l, respectively. After 1 h of recovery, all of these quantities had reached the preexercise values.

Renal function (Table 4). Urine volume (ml/min) was significantly decreased up to 4 h after exercise and tended to show lower values up to 24 h after cessation. The creatinine clearance, which was used as an indicator of the GFR, was lowered by >50%, reaching the preexercise values during the first hour of recovery. The fractional excretion rate of sodium and chloride decreased markedly up to 1 h after exercise, whereas the free water clearance showed the opposite behavior, increasing during and up to 1 h after the exercise period.

Partial correlation analysis was used to detect relationships between two variables (all tests according to Ref. 29). The correlation was found between plasma ANP concentration and urinary Uro excretion, Plasma ANP concentration and urinary Uro excretion were oppositely affected by physical exercise. Whereas ANP concentration increased from 46.5 ± 5.1 (83.1 ± 13, minute 15; 99.8 ± 3.1, minute 30; n = 5) to 124.1 ± 10.6 pg/ml (Fig. 1), Uro excretion decreased by ~60% during the exercise period from 120.8 ± 16.0 to 49.5 ± 9.8 fmol/min, remained on a lower level (52.5 ± 12.1 fmol/min) for 1 h, and returned to the initial level after 4 h of recovery (Fig. 1; analysis of variance; P < 0.001 for changes in both hormones).

DISCUSSION

This study shows that urinary Uro excretion is markedly reduced by exercise effects, i.e., it is oppositely affected compared with plasma ANP concentration. Increasing ANP levels during exercise, as observed here, are well established by a great number of recent studies (e.g., Refs. 13 and 26) and are mostly due to changes in cardiac filling pressure and wall tensions. Uro excretion has not yet been studied under exercise conditions. We therefore use the results of studies with other purposes to discuss our results.

Table 4. Changes in urine volume, GFR, fractional electrolyte excretion rate, and free-water clearance

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rest</th>
<th>End of Exercise</th>
<th>Recovery, h</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>URODILATIN EXCRETION DURING EXERCISE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UV, ml/min</td>
<td>1.9 ± 0.3</td>
<td>0.8 ± 0.1*</td>
<td>0.5 ± 0.1*</td>
<td>1.0 ± 0.1*</td>
</tr>
<tr>
<td>GFR, ml/min</td>
<td>164.9 ± 15.3</td>
<td>75.8 ± 10.1*</td>
<td>131.4 ± 14.6</td>
<td>179.5 ± 20.8</td>
</tr>
<tr>
<td>FE Na⁺, %</td>
<td>0.90 ± 0.14</td>
<td>0.49 ± 0.09</td>
<td>0.25 ± 0.05*</td>
<td>0.53 ± 0.09</td>
</tr>
<tr>
<td>FE K⁺, %</td>
<td>11.7 ± 1.9</td>
<td>13.0 ± 4.4</td>
<td>7.4 ± 1.7</td>
<td>8.9 ± 1.5</td>
</tr>
<tr>
<td>FE Cl⁻, %</td>
<td>1.62 ± 0.22</td>
<td>1.35 ± 0.16</td>
<td>0.60 ± 0.09*</td>
<td>0.99 ± 0.13</td>
</tr>
<tr>
<td>ClH₂O, ml/min</td>
<td>-2.2 ± 0.3</td>
<td>-0.7 ± 0.2*</td>
<td>-0.9 ± 0.1*</td>
<td>-1.9 ± 0.2</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 10 subjects. UV, urine minute volume; GFR, glomerular filtration rate (creatinine clearance); FE Na⁺, FE K⁺, FE Cl⁻, fractional excretion rate for Na⁺, K⁺, and Cl⁻, respectively; ClH₂O, free-water clearance. For further information, see Table 3.
Regulation of Uro excretion. At least three mechanisms are known to lead to changes in urinary Uro excretion.

First, as was recently demonstrated by Kirchhoff et al. (20), the release of Uro from the isolated perfused rat kidney strongly depends on the perfusion pressure, i.e., the increase in perfusion pressure from 80 to 120 mmHg led to a threefold increase in Uro excretion. In the present study, mean arterial blood pressure increased by 30 mmHg during exercise, whereas renal blood flow can be assumed to be considerably decreased (2). Because Uro excretion has not yet been determined under such conditions, we cannot decide whether Uro secretion may be influenced by changes of the renal hemodynamics during exercise.

Second, when the left atria were distended in dogs, the renal excretion of sodium and Uro as well as the plasma concentration of ANP-(99—126) were increased. In cardiac denervated dogs, however, left atria distension increased plasma ANP concentration but not Uro and sodium excretion (16). These experiments demonstrate that Uro secretion is regulated by the central venous filling pressure and is mediated by neural pathways. The lack of response in denervated dogs further implies that sodium and Uro excretion may be modified by central nervous mechanisms. With reference to our exercise study, it seems probable that increased plasma ANP concentration during exercise is caused by increased venous blood flow and higher heart rate. By this mechanism, however, Uro secretion is not stimulated under the prevailing conditions. As shown by Drummer et al. (8), infusion of 2 liters of isotonic saline solution leads to corresponding sodium and Uro excretion, which is accompanied by suppressed epinephrine and norepinephrine plasma levels. Thus it seems worthwhile to evaluate whether increased sympathetic activation during exercise may exert inhibitory effects on Uro excretion.

Third, besides central venous filling pressure, the sodium concentration in carotid blood determines urinary Uro excretion. Emmeluth et al. (9) observed a threefold increase in Uro excretion when the cephalic sodium concentration was selectively increased by the split-infusion technique by only 2 mmol/l. The sensitivity of this regulatory system was proved to be more sensitive than the antidiuretic hormone-releasing mechanism. In a recent study, however, a similar increase in carotid sodium concentration in similarly treated dogs had no effect on Uro excretion when the kidneys were completely denervated (10). These experiments indicate that the regulation of Uro secretion may also be controlled by neuronal mechanisms. Whether a similar regulation exists during and after exercise, when the plasma sodium concentration increases (in this study, by ~4 mmol/l; Table 3), remains to be investigated.

To date, only a few physiological conditions have been found, in which plasma ANP levels and urinary Uro excretion were changed to go in opposite directions (8). In some situations such as increase in plasma sodium...
concentration, long-term elevation of sodium intake, and isotonc volume loading, plasma ANP concentration was not affected, whereas renal Uro and sodium excretion were closely associated (see Ref. 15). In this study, there is a tendency toward a negative correlation between the release of both natriuretic peptides (Fig. 4), indicating that the regulation of Uro is not generally linked to that of ANP.

Uro and ANP effects. After its discovery by de Bold et al. (4), ANP was assumed to be a potent natriuretic peptide, exerting its effects especially at the inner medullary collecting ducts by formation of the second messenger guanosine 3',5'-cyclic monophosphate (cGMP). Meanwhile, ANP could be shown to have considerable hemodynamic effects but not to induce natriuresis in physiological situations. As is demonstrated in Fig. 3, there is a tendency toward a negative correlation between ANP and fractional sodium excretion rate. On the other hand, Uro is positively related to sodium excretion (Fig. 2). This is in accordance with the data of recently published studies describing positive relationships between Uro and fractional sodium excretion rate and a lack of correlation between ANP and fractional sodium excretion rate after dietary salt loading and isotonic volume loading (8, 18). Under in vitro conditions, ANP and Uro exert similar natriuretic effects mediated by the natriuretic peptide A receptors at the medullary collecting duct. In vivo, however, most of the filtered ANP molecules are degraded by the endopeptidase EC 24.11, whereas Uro is more resistant against this enzyme (14). Furthermore, Uro is probably produced in the distal parts of the nephron and is scarcely exposed to this endopeptidase (11), thus acting as a paracrine modulator of tubular electrolyte transport.

As reported in this study, there is only a short delay between exercise-associated changes in urinary Uro and the reduced fractional sodium and chloride excretion rate during and after physical exercise. Generally, Uro exerts its effects by binding to the natriuretic peptide A receptors at the inner medullary collecting ducts and stimulating the guanylate cyclase activity of the receptor protein, thereby increasing intracellular cGMP levels. cGMP reduces apical sodium channel activity by stimulation of a cGMP-dependent protein kinase (30). Inhibition of paracrine Uro secretion during exercise, therefore, may influence tubular sodium reabsorption. In this context, however, a variety of other factors such as angiotensin II and the sympathetic renal nerve activity, which are known to influence tubular sodium retention (1, 5, 21, 24), have to be considered. Whether Uro exerts a specific and measurable sodium-sparing effect during exercise needs further investigations.

As is well known from previous studies, the aldosterone concentration continuously increases during bouts of exercise as performed in these experiments (e.g., Refs. 3 and 26). Aldosterone's effects, however, may be recorded after a delay of some hours, excluding any aldosterone effects during and immediately after this type of exercise. Some hours thereafter, when Uro excretion returns to preexercise values, the aldosterone effects perpetuate the electrolyte-sparing mechanism, leading to the well-known overcompensation in plasma volume (e.g., Ref. 26).

In physiological concentrations, ANP has no direct natriuretic effects but influences the hemodynamics of the kidneys via dilatation of the vas afferentia and constriction of the vas efferentia, which normally result in an increased GFR. During exercise, however, there is a tendency toward a negative relationship between plasma ANP concentration and GFR. This discrepancy may be explained by opposite effects of ANP and the exercise-related renal sympathetic nerve activity. Most probably, ANP partly compensates for the reduced renal blood flow, which is indicated by an increased filtration fraction (2), and protects the kidney during exercise from anuria.

We conclude that Uro may be a new candidate for tubular sodium regulation under acute exercise conditions. In addition, the involvement of other factors such as angiotensin II and norepinephrine have to be considered. After exercise, when Uro excretion returns to normal values, perhaps aldosterone's effects prolongate the sodium-sparing mechanism. In contrast to former opinions, ANP seems to have only a weak influence on the regulation of tubular sodium retention.

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