Characteristics of the Relationship between

the Flow Rate of Tubular Fluid and Potassium Transport

in the Distal Tubule of the Rat

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A B S T R A C T The flow rate of tubular fluid has been suggested as one of several factors which may influence potassium transport in the distal convoluted tubule of the kidney. In the present micropuncture studies, the relationship between the flow rate of distal tubular fluid and potassium transport was examined in four groups of rats. Three groups of rats (I, II, and IV) were fed normal rat chow before study whereas one group (III) was fed chow containing 10% KCl. Group II received 10–20 μg/kg per h of d-aldosterone throughout the study. Distal tubular potassium transport in groups I, II, and III was examined before and after an increase in the flow rate of distal tubular fluid as induced by the infusion of an isotonic saline-bicarbonate solution equivalent to 10% of body weight. In group IV, distal tubular potassium transport was examined before and after enhancement of the flow rate by the infusion of hypertonic (15%) mannitol.

In all four groups, distal tubular potassium secretion increased as the flow rate of tubular fluid increased. The nature of the relationship between distal tubular potassium transport and tubular fluid flow rate, however, was influenced by the extent to which the tubular fluid to plasma potassium ratio in the late distal tubule varied as the flow rate increased. As the flow rate was increased this ratio decreased significantly and to a comparable extent in groups I and II. In groups III and IV, on the other hand, this ratio was essentially identical during hydropenia and after the increase in the flow rate of tubular fluid. As a result, the increment in the amount of potassium present at the late distal tubule, which occurred as the flow rate increased, was significantly greater in groups III and IV than in groups I and II. The contrast in the relationship between the

flow rate of distal tubular fluid and potassium transport which were observed, probably reflects differences in the net driving force for cell to lumen potassium movement. Seemingly, the net driving force for potassium movement was maintained, as the flow rate of tubular fluid increased, by chronic potassium loading in group III and by hypertonic mannitol infusion in group IV. In groups I and II, the net driving force for potassium movement decreased as the flow rate of tubular fluid increased. However, the net driving force did not decrease in proportion to the increase in flow rate since potassium secretion was increased by increments in flow rate in these groups as well.

We conclude that our results are consistent with the view that the flow rate of tubular fluid is a factor which can affect distal tubular potassium transport. However, the nature of the relationship between the flow rate of tubular fluid and potassium transport appears to depend upon the degree to which the driving force for cell to lumen potassium movement changes as the flow rate is varied.

INTRODUCTION

Variations in potassium transport in the distal convoluted tubule both of the mammalian (1–3) and amphibian (4) kidney may have a marked influence on the overall pattern of renal potassium excretion. The systemic acid-base status of the animal (5) and differences in potassium intake (6, 3) and in mineralocorticoid effect (7) are some of the factors known to modify the character of potassium transport in the distal convoluted tubule. Recently, it has been suggested that another factor, the flow rate of tubular fluid through the distal tubule, may be an important modulator of distal tubular potassium transport (8–10).

The extent to which potassium transport in the distal tubule may be flow related can be ascertained by an examination of the relationship of the distal tubular fluid

to plasma potassium ratio $(TF/P \ K^+)$[1] and the flow rate of distal tubular fluid. If the distal tubular $TF/P \ K^+$ ratio remained constant as increasingly greater fractions of the glomerular filtrate were delivered to the distal tubule, as evidenced by progressively lower tubular fluid to plasma inulin ratios $(TF/P \ In)$, the quantity of potassium present in the distal tubule, $TF/P \ K^+/In$, would progressively increase. The $TF/P \ K^+/In$ ratio in the distal tubule under these conditions would vary directly with the tubular fluid flow rate. If, on the other hand, the distal tubular $TF/P \ K^+$ ratio would decrease in proportion to the increase in fractional filtrate delivery, the quantity of potassium present $(TF/P \ K^+/In)$ in the distal tubule would remain constant, i.e., unaffected by variations in flow rate.

The $TF/P \ K^+$ ratio in the earliest portion of the distal tubule accessible to micropuncture undergoes little change with variations in tubular fluid flow rate unless, in addition, potassium reabsorption in the ascending limb of the loop of Henle is affected as well (2, 8, 11). For this reason, the relationship between the $TF/P \ K^+$ ratio and the flow rate of distal tubular fluid can best be appreciated by study of the late distal tubule. In the present experiments, we have examined the relationship between the late distal tubular puncture site (LD) $TF/P \ K^+$ ratio and the flow rate of tubular fluid at this site as the flow rate was increased by either acute isotonic saline-bicarbonate or hypertonic (15%) mannitol infusion. In additional studies, the effects on this relationship of exogenous aldosterone and of chronic high potassium feeding were examined. Finally, since tubular fluid samples were obtained from the early as well as from the late distal tubule, the absolute quantities of potassium secreted and sodium reabsorbed along the length of the distal tubule were determined under all experimental conditions.

METHODS

Four groups of male Sprague-Dawley rats weighing between 312 and 385 g were studied. Before micropuncture study, groups I, II, and IV were fed normal rat chow. For at least 7 days before micropuncture study, group III was fed normal rat chow to which KCl (10% wt/wt) was added. All rats were permitted free access to water. The four groups were studied as described below.

Group I (eight rats). For 75–90 min before the collection of tubular fluid samples, these rats were infused at 20 µl/min with a saline-bicarbonate solution (125 meq NaCl, 25 meq NaHCO₃/liter) containing 10% inulin. After this interval the initial proximal, early, and late distal tubular fluid, arterial blood, and urine samples were obtained

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[1] *Abbreviations used in this paper:* ED, early distal tubular puncture site; EDFR, tubular fluid flow rate at early distal tubular puncture site; In, inulin; LD, late distal tubular puncture site; LDFR, tubular fluid flow rate at late distal tubular puncture site; SNGFR, single nephron glomerular filtration rate; TF/P, tubular fluid to plasma ratio; TF/P K⁺/In, quantity of potassium as a fraction of the filtered load.

(period A). After period A, the infusion rate of the above solution was increased to 37.5 µl/min and a second solution of saline-bicarbonate was infused at 500 µl/min until an amount equivalent to 10% of their body weight was administered (approximately 60 min). Thereafter, the infusion rate of the latter solution was adjusted to exceed the urine flow rate by 30–100 µl/min and period B began. During period B, tubular fluid samples were recollected from the previously studied tubular sites and arterial blood and urine samples again obtained.

Group II (five rats). This group was studied as group I except that d-aldosterone (Ciba Pharmaceutical Company, Summit, N. J.) 10–20 µg/kg per h was given i.v. beginning at least 2 h before the collection of tubular fluid samples and continuing throughout the study. In addition, the saline-bicarbonate solution used contained 5.5 meq/liter KCl.

Group III (six rats). This group, prefed the diet containing 10% KCl, was studied by the same method as the rats in group I except that the saline-bicarbonate solution contained 5.5 meq/liter KCl.

Group IV (five rats). This group was studied by the same method as group I through period A. Thereafter, while the rate of the inulin-containing saline-bicarbonate solution was maintained at 20 µl/min, a second infusion of 15% mannitol was started. The mannitol solution was infused at 150 µl/min for 60 min before period B started and was continued throughout the experiment.

The surgical preparation for the micropuncture study was performed on a heated pad. After i.p. anesthesia with Inactin (Promonta, Hamburg, West Germany) 100 mg/kg, a tracheostomy was performed. Catheters (PE-50) were placed into the left femoral artery for the collection of arterial blood samples. Urine for analyses was collected from both kidneys via a catheter (PE-90) placed into the dome of the urinary bladder. The left kidney was exposed by a lateral abdominal incision, freed from its peritoneal attachments and the adrenal, and placed into a Lucite cup. The kidney was surrounded with cotton saturated with mineral oil and the surface was bathed with water-equilibrated mineral oil at 37°C. Throughout the micropuncture study the temperature of the rat was maintained at 37°C by a thermostatically heated micropuncture table.

The recollection micropuncture technique was used in all studies. In these experiments, a portion of the distal convoluted tubule between the earliest and latest surface convolutions of the same distal tubule was localized and studied. It was felt that if potassium and sodium transport were examined in the same isolated distal tubular segment before and after an experimental maneuver, a more precise comparison of changes in transport could be made. After the i.v. administration of 50 µl of 5.0% lissamine green dye, a late distal tubular convolution was localized (12). This convolution was then punctured with a small 4-5-µm (OD) glass micropipette which contained 1%, F, D, and C dye (Food, Drug, and Cosmetic Dye no. 3, Keystone Aniline and Chemical Co., Chicago, Ill.) (Na⁺ approximately 20 meq/liter, K⁺ approximately 0.5 meq/liter). With gentle pressure, the dye filled the late distal convolution and any other surface convolutions of this distal convoluted tubule. Usually no other or only one other convolution was present on the surface. The connection between the earliest and latest surface convolutions was ascertained during the collection of tubular fluid samples. If after the collection of the tubular fluid samples from the early convolution the oil droplet did not pass from the early to the late convolution, the tubule was excluded. In

TABLE I
Summary of Clearance and Micropuncture Results

	Clearance data						Micropuncture data											
	FE-K+*		U_K^+V		P_K^+		LDFR		LD TF/P K^+		LD TF/P K^+/In $\times$ 100		ED TF/P K^+		Distal K^+ secretion		Distal Na^+ reabsorption	
	%		µeq/min		meq/liter		nl/min				%				peq/min		peq/min	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
Group I (8 rats)	8.2	28.1	0.95	3.85	4.6	4.1	3.7	30.3	2.41	1.46	19.8	60.9	0.52	0.56	21	94	203	645
SEM	1.4	2.5	0.13	0.31	0.1	0.2	0.4	1.6	0.16	0.08	2.2	2.9	0.04	0.02	3.9	6.2	24.1	55.3
n	8		8		8		16		16		16		16		16		15	
P	<0.001		<0.001		0.1 > 0.05		<0.001		<0.001		<0.001		>0.3		<0.001		<0.001	
Group II (5 rats)	13.7	39.8	1.88	5.10	4.4	3.7	4.7	31.0	2.70	1.67	24.7	66.0	0.52	0.59	30	100	297	964
SEM	2.1	3.9	0.30	0.58	0.3	0.1	0.4	2.4	0.22	0.14	2.0	5.5	0.08	0.06	5.1	15.1	15.7	101.1
n	5		5		5		9		9		9		9		9		8	
P	<0.005		<0.005		<0.05		<0.001		<0.005		<0.001		>0.2		<0.005		<0.001	
Group III	26.9	78.2	3.60	9.36	4.9	3.3	5.2	29.0	3.00	2.83	33.0	115.1	0.47	0.68	49	178	226	807
SEM	3.4	6.1	0.67	0.82	0.4	0.1	0.8	1.5	0.21	0.32	4.1	13.9	0.06	0.05	10.3	31.8	19.3	86.4
n	6		6		6		12		12		12		10		10		10	
P	<0.001		<0.001		<0.005		<0.001		>0.5		<0.001		<0.01		<0.005		<0.001	
Group IV	7.9	56.5	0.61	4.81	4.0	3.8	3.8	17.1	2.16	2.29	20.4	90.7	0.48	0.57	17	96	194	556
SEM	2.1	6.3	0.10	0.39	0.2	0.1	0.4	0.8	0.21	0.21	2.3	11.9	0.02	0.03	3.4	12.7	18.3	39.4
n	3	5	5		5		10		11		10		11		10		10	
P	‡<0.001		<0.001		>0.1		<0.001		>0.6		<0.001		<0.005		<0.001		<0.001	

* A and B, refer to study periods A and B; FE-K+, fractional excretion of potassium; U_K^+V, minute excretion of potassium; P_K^+, plasma potassium; and distal K^+ secretion and Na^+ reabsorption refer to measurements made in identical distal tubular segments; n, number of observations.

‡ Unpaired t test.

addition, if the F, D, and C dye extravasated from the site of puncture either during or after the localization procedure, the tubule was excluded from further study.

Although without subsequent nephron microdissection the precise localization of the puncture sites in these early and late distal convolutions cannot be made, based on a comparison of the TF/P K$^+$ ratios in the early and late distal puncture sites during hydropenic conditions with those observed by others and verified by subsequent nephron microdissection (13). it is clear that the early sites are well within the first one-half of the distal tubule and the late sites well within the last one-half. This was confirmed by a separate study of 15 distal tubules in which the earliest and latest sites were located as described above and the puncture sites subsequently verified by microdissection. The early distal site ranged from 17 to 37% and the late distal site from 73 to 98% of the length of the distal tubule. In each rat, one to three such distal tubular segments were studied, tubular fluid samples being collected for subsequent analyses of inulin, sodium, and potassium.

The administration of the lissamine green also permitted the localization of end proximal convolutions (14). The collection of tubular fluid samples from the proximal convolutions was made over an accurately timed interval so that the single nephron filtration rate (SNGFR) could subsequently be determined. Usually three, but occasionally two, proximal tubules were studied in each rat.

In each rat, the lissamine green was administered up to five times over a 15–20-min interval. No tubular fluid samples were collected until 25–30 min after the last injection of lissamine green.

Sharply beveled Kimax® micropipettes (Kimax Laboratory Glassware, Toledo, Ohio) with tip diameters of 7–10 and 5–7 μm (OD) were used for the collection of proximal and distal tubular fluid samples, respectively. After the introduction of an oil droplet (Sudan black-stained mineral oil) of three to five tubular diameters the collection of tubular fluid samples was initiated by gentle aspiration and, as much as possible, proceeded spontaneously. No tubule, proximal or distal, was restudied if the oil droplet did not leave the puncture site shortly after the collection of the tubular fluid sample. The early distal convolution was studied only after the oil droplet had left the late convolution and had moved well downstream.

The volume of the proximal tubular fluid samples was determined in a calibrated quartz capillary with a constant internal diameter. The inulin concentration in tubular fluid samples was determined by the microfluorescence method of Vurek and Pegram (15). Sodium and potassium concentrations in tubular fluid samples were measured with a helium glow photometers (16). Preliminary studies indicated that the presence of mannitol in test samples influence the results obtained in these samples. This problem was alleviated by the use of a C_5NO_3: $NH_4H_2PO_4$ solution (diluent) containing 1% mannitol. The inulin concentration in plasma and urine was determined with the method of Führ, Kaczmarczyk, and Krüttgen (17). Sodium and potassium concentrations in plasma and urine were determined with an IL Model 143 Flame Photometer (Instrumentation Lab, Lexington, Mass.). Plasma solids were determined by hand refractometry.

The plasma inulin concentrations were collected for plasma water. No water or Donnan corrections were used for sodium or potassium.

Calculations: (a) SNGFR (nanoliters/minute) = proximal tubular fluid flow rate × proximal TF/P In ratio. (b) Distal tubular fluid flow rate (nanoliters/minute) =

SNGFR × 1/(TF/P In). (c) Nephron-filtered potassium or sodium load (picoequivalents/minute) = mean SNGFR of all proximal convolutions studied in period A or B × plasma sodium or potassium concentration (picoequivalents/nanoliter). (d) Potassium secretion and sodium reabsorption in individual distal tubular segments = early distal TF/P K$^+$ or Na$^+$/(TF/P In) minus late distal TF/P K$^+$ or Na$^+$/(TF/P In) × nephron-filtered load of K$^+$ or Na$^+$.

The results are expressed as the mean±1 SEM. The Student's t test was used in the statistical analysis of the results. Except where indicated in the text, the P values refer to a paired comparison of the results in period A to those in period B.

RESULTS

Clearance data. The fractional and absolute excretion of potassium and the plasma potassium concentration observed in both periods of all groups are listed in Table I. Under hydropenic conditions, (period A), fractional potassium excretion was approximately 8% in both untreated groups (I and IV). In group II, treated with 10–20 μg/kg per h of d-aldosterone, and group III, prefed a high potassium diet, fractional potassium excretion during period A was 13.7 and 26.8%, respectively. After the administration of either an isotonic saline-bicarbonate solution (groups I, II, and III), or the hypertonic mannitol solution (group IV), fractional and absolute potassium excretion increased significantly (period B).

The plasma potassium concentration did not change significantly in groups I and IV after either the saline-bicarbonate or hypertonic mannitol infusion. In contrast, in both groups II and III, the plasma potassium concentration decreased significantly after the saline-bicarbonate infusion despite the addition of 5.5 meq/liter KCl to the solution used in these groups.

Micropuncture data. As shown in Table I, in group I, as the late distal tubular fluid flow rate (LDFR) was increased from 3.7 to 30.3 nl/min by the saline-bicarbonate infusion, the LD-TF/P K$^+$ ratio fell from 2.41 to 1.46, $P < 0.001$. A similar pattern of response was noted in group II in which d-aldosterone was administered and the saline-bicarbonate solution contained 5.5 meq/liter KCl. In contrast, after prior oral potassium loading (group III), as the LDFR increased from 5.2 to 29 nl/min, the LD-TF/P K$^+$ ratio did not change significantly (3.00–2.83, $P > 0.5$). In group IV, the administration of the hypertonic mannitol solution did not result in an increase in the LDFR to the same extent as observed after the saline-bicarbonate infusion. However, as the LDFR increased from 3.7 to 17.1 nl/min, the LD-TF/P K$^+$ ratio remained constant, 2.16 vs. 2.29, $P > 0.6$.

In all groups, regardless of the degree of change in the LD-TF/P K$^+$ ratio which occurred as the LDFR increased, the amount of potassium present at the late distal tubule increased significantly. This can be seen in Table I where the LD-TF/P K$^+$/In (× 100%) ratio

was significantly greater in period B than in period A in all four groups. As the late distal TF/P In ratios during both periods were not significantly different from each other in all groups, variations in the responses noted reflect differences in the LD-TF/P K^+ ratio. An enhanced response was observed in groups III and IV, the groups in which the LD-TF/P K^+ ratio did not change as the LDFR increased. In groups III and IV, the absolute increases in the LD-TF/P K^+/In $\times$ 100% between periods A and B of 82.1 and 70.3%, respectively, were not different from each other, $P > 0.5$. In groups I and II, the absolute increases between periods A and B were 41.1 and 41.3%, respectively, again not different from each other, $P > 0.97$. The absolute increases in the LD-TF/P K^+/In $\times$ 100% in groups III and IV were both statistically greater than in I or II, (I vs. III, $P < 0.005$; I vs. IV, $P < 0.01$; II vs. III, $P < 0.05$; II vs. IV, $P < 0.05$). Therefore, although the amount of K^+ present at the late distal tubule increased with the increase in LDFR in all groups, the pattern of this relationship was significantly affected by the extent to which the LD-TF/P K^+ remained constant as the LDFR increased.

Although unlikely, it is possible that in association with the increase in tubular fluid flow rate to the distal tubule, the amount of potassium present at the early distal puncture site also increased so that net potassium secretion by the distal tubule decreased or remained con-
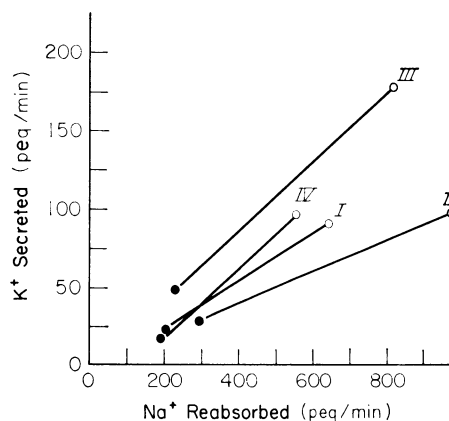
FIGURE 2 A comparison of the quantities of sodium reabsorbed and of potassium secreted in the distal tubular segments. In all groups the quantity of sodium reabsorbed exceeded the amount of potassium secreted. Similar quantities of potassium were secreted in distal tubular segments which reabsorbed widely divergent quantities of sodium, e.g., groups II and IV, period B.

stant. This could result if the TF/P K^+ ratio at the early distal tubule was increased markedly in period B in comparison to period A. As shown in Table I, although this ratio increased slightly in all groups, the modest increases were statistically significant only in groups III and IV. In Fig. 1, the relationship between potassium secretion and the mean flow rate of distal tubular fluid (EDFR + LDFR ÷ 2) is illustrated. The absolute quantities of potassium secreted in all groups is also listed in Table I. It is clear that in all groups as the mean flow rate of tubular fluid increased absolute potassium secretion increased. Therefore, not only did the fractional quantity of potassium at the LD site increase with increments in the LDFR as was shown previously, but absolute potassium secretion in the distal tubular segments of all groups increased in association with the increase in the flow rate of distal tubular fluid.

Fig. 2 graphically demonstrates the relationship between the amount of potassium secreted and sodium reabsorbed in the individual distal tubular segments. After either isotonic saline-bicarbonate or hypertonic mannitol infusion, absolute distal tubular sodium reabsorption, as well as potassium secretion, increased. The quantity of sodium reabsorbed in every group in both periods greatly exceeded the amount of potassium secreted (1). Furthermore, as shown by the absolute values of potassium secreted and sodium reabsorbed in Table I, the amount of potassium secreted at any given rate of sodium reabsorption varied considerably. For example, during period A the amount of sodium reabsorbed was not statistically different in groups I, III, and IV (Table I). Nevertheless, the amount of potassium secreted in group III, 49 peq/min, was significantly greater than in either
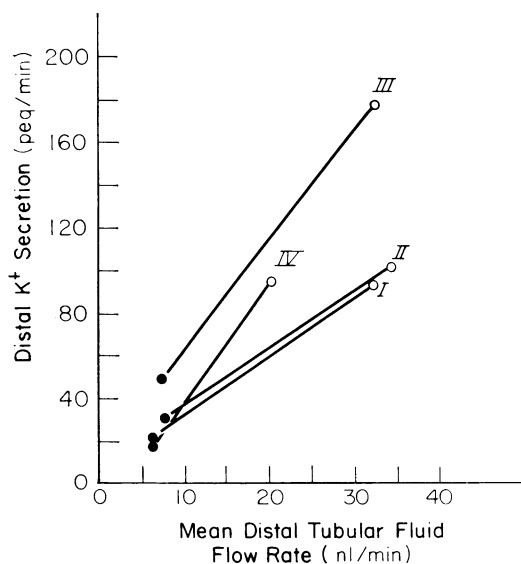

FIGURE 1 The relationship between the mean distal tubular fluid flow rate and the quantity of potassium secreted in the distal tubular segments. In this and the following figure the solid circle (●) represents data obtained during hydropenia, period A, the hollow circle (○) during period B. In all groups potassium secretion increased as the mean flow rate was increased.

group I, $P < 0.01$ or group IV, $P < 0.01$. Similarly in period B, even though the amount of potassium secreted in groups II and IV was virtually identical, 96 and 100 peq/min, respectively, the quantity of sodium reabsorbed in group II was significantly greater than in group IV, 964 vs. 555 peq/min, $P < 0.001$.

DISCUSSION

It has recently been suggested that the flow rate of distal tubular fluid is one of several factors which affects potassium transport in the distal convoluted tubule (8–10). The results of the present study provide additional evidence in favor of this view. As the flow rate of distal tubular fluid was increased by the acute infusion of either an isotonic saline-bicarbonate or a hypertonic mannitol solution, there was an associated increase in distal tubular potassium secretion. Furthermore, the relationship between the flow rate of tubular fluid and distal tubular potassium transport was significantly influenced by the extent to which the LD-TF/P K^+ ratio varied as the flow rate increased. In the rats prefed a high potassium diet and infused with isotonic saline-bicarbonate (group III) and in the rats infused with a hypertonic mannitol solution (group IV), the mean LD-TF/P K^+ ratio observed as the distal tubular fluid flow rate increased was virtually identical to that observed during hydropenia. In contrast, in rats infused with isotonic saline-bicarbonate with or without exogenous aldosterone (group II and I, respectively), the LD-TF/P K^+ ratio was significantly lower after the flow rate of distal tubular fluid was increased than it was during hydropenia. The decrease which occurred in the LD-TF/P K^+ ratio in groups I and II, however, was not proportional to the increment in the LDFR. In both groups I and II, the LD-TF/P K^+/In ratio increased significantly as the LDFR increased. However, in groups III and IV, in which the LD-TF/P K^+ ratio remained constant, a significantly greater increment in the LD-TF/P K^+/In ratio resulted as the LDFR increased.

The contrast in the relationship between the LD-TF/P K^+ ratio (and thereby the LD-TF/P K^+/In) and the flow rate of tubular fluid in groups I and II, on one hand, and groups III and IV, on the other, undoubtedly reflects differences in the movement of potassium from the distal tubular cell into the tubular lumen. Malnic, Klose, and Giebisch have shown the distal tubular TF/P K^+ ratio to be the same under stop flow and free flow conditions when examined under similar circumstances (18). These observations suggest that the distal tubular TF/P K^+ ratios observed under free flow conditions represent equilibrium values and are dependent upon the net driving force for cell to lumen potassium movement. The constancy of the LD-TF/P K^+ ratio in groups III and IV, therefore, would suggest that the net driving force responsible for cell to lumen potassium movement

remained relatively stable in spite of the increased unidirectional cell to lumen potassium flux which occurred as the tubular fluid flow rate increased. In contrast, in groups I and II the net driving force did not remain constant but decreased, as did the LD-TF/P K^+ ratio, as the flow rate of tubular fluid increased.

The present studies while demonstrating an association between distal tubular potassium transport and the flow rate of tubular fluid, did not examine the precise nature of the driving force(s) responsible for distal tubular cell to lumen potassium movement or if such forces were altered in the course of the various studies. It has been shown that a favorable electrochemical gradient is the driving force responsible for the movement of potassium from the distal tubular cell into the lumen (1). The recent studies of Mello Aires, Giebisch, and Malnic in the distal tubule of the rat (19), and Wiederholt, Sullivan, and Giebisch in the distal tubule of the Amphiuma (4), would suggest that a critical, and perhaps the most critical, factor in determining this gradient is the intracellular transport pool of potassium. One important determinant of the intracellular transport pool of potassium would appear to be the magnitude of the peritubular uptake of potassium. Chronic potassium loading has been demonstrated to increase the peritubular membrane permeability to potassium and thereby the uptake of potassium across the peritubular membrane (19). Furthermore, Silva, Hayslett, and Epstein have recently shown that chronic potassium loading in the rat can increase cortical as well as outer medullary Na^+-K^+ ATPase[a] (20). They suggested that such an increase in the cortical activity of this enzyme could result in an enhanced capacity to move potassium across the peritubular membrane into the distal tubular cell. In group III, therefore, the ability of potassium loading to facilitate the peritubular uptake of potassium and to maintain the intracellular transport pool of potassium is one means by which the gradient for cell to lumen potassium movement could be stabilized. In contrast, in groups I and II, a failure of peritubular potassium uptake to match potassium loss from the cell could result in a decrease in the gradient for cell to lumen potassium movement.

The mechanism responsible for the stabilization of the electrochemical gradient in group IV may differ from that in group III. Mudge, Foulks, and Gilman have suggested that the rate of potassium excretion may be influenced by the state of hydration of the tubular cells

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[a] As no balance studies were performed in the present studies, we are unable to state whether the potassium intake in group III was sufficient to increase cortical Na^+-K^+ ATPase. An interpretation of the daily excretion of potassium based upon excretory rates in period A, after the surgical preparation for micropuncture, would seem to be hazardous.

(21). In their studies the increase in potassium excretion observed during the infusion of hypertonic sodium chloride and urea solutions was felt to be due to a decrease in cellular hydration. When potassium excretion was diminished by water diuresis, cellular hydration was presumed to increase. It is possible that such alterations in cellular hydration may be responsible for the pattern of potassium secretion noted in group IV. The infusion of the hypertonic mannitol solution would tend to move water from the intracellular to the extracellular compartment and, together with the net loss of body water which occurred as a result of the diuretic effect of this infusion, would tend to decrease cellular hydration. Therefore, although potassium was secreted from the distal tubular cells during the mannitol infusion, a relatively greater concomitant loss of intracellular water could maintain the concentration of the remaining intracellular potassium and thereby maintain the electrochemical gradient for potassium movement.

Although the infusion of either the saline-bicarbonate or the mannitol solution resulted in increased sodium reabsorption and potassium secretion, no definite relationship between distal tubular sodium reabsorption and potassium secretion was observed in these studies. In fact, as shown in Table I and Fig. 2, the relationship between the quantity of potassium secreted and sodium reabsorbed varied considerably. These studies should not be taken to indicate that sodium is not in any manner involved in distal tubular potassium secretion (22). Rather, in agreement with others (1) they suggest that the quantity of sodium reabsorbed from the lumen and potassium secreted into it are not precisely related.

Distal tubular potassium transport in group II, in which exogenous aldosterone was administered, slightly exceeded but was not statistically different from that observed in group I in which no exogenous aldosterone was given. Of interest, however, is that the fractional excretion of potassium was significantly greater in group II than group I, $P < 0.02$, period A; $P < 0.05$, period B. As the late distal puncture sites were not subsequently localized by microdissection it is conceivable that the LD-TF/P K^+/In in group II was determined from study of earlier portions of the distal tubular in group I. However, as the selection of the late distal sites was random and as the LD-TF/P In ratio both during periods A and B in the two groups were not significantly different from one another, it would seem that, on the average, similar LD segments were studied. If this is the case, the greater urinary excretion of potassium in group II as compared to group I, in the absence of greater distal tubular secretion, would suggest that the administration of exogenous aldosterone affected potassium transport at some site(s) beyond the distal convolution.

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