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Research Article

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On the Adaptation in Potassium Excretion Associated with Nephron Reduction in the Dog

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ABSTRACT An effort to examine certain aspects of the adaptation in potassium excretion associated with nephron reduction was made in dogs with unilateral remnant kidneys. A constant intake of potassium was maintained by tube feeding and studies were performed before and after removal of the intact control kidney. The removal of the intact kidney created the need for the remaining nephrons of the remnant kidney to increase their rate of potassium excretion markedly. Sodium intake was held constant either at a normal or a low level. Mineralocorticoid hormone activity was maintained either at a high level by the administration of 0.2 mg 9-α-fluorohydrocortisone daily or at a low level by performing bilateral adrenalectomy and administering a minimal maintenance dose of deoxycorticosterone acetate (DOCA) and cortisol. Potassium excretion per nephron increased strikingly within 18 hr of contralateral nephrectomy and by 7 days, excretion rates were 600% of control values for the remnant kidney. More potassium was excreted in the first 5 hr after administration of a test dose of potassium by the remnant kidney alone in the postnephrectomy state than by both the remnant and intact kidneys in the prenephrectomy state. 24 hr excretion of potassium by the remnant kidney postnephrectomy averaged 92% of the administered load of potassium. The adaptation in potassium excretion was independent of the concurrent rate of sodium excretion and of mineralocorticoid hormone activity and persisted during constriction of the renal artery, a stimulus which presumably decreased distal delivery of sodium. The adaptation and the continued modulation of potassium excretion could not be explained adequately by an increase in impermeant anion excretion per nephron. Finally, known changes in hydrogen ion excretion per nephron associated with nephron reduction are in a direction opposite to those which would explain the acquired kaliuresis per nephron.

Part of this work has been presented in abstract form (1970 *Clin. Res.* **18**: 518.).

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INTRODUCTION

Potassium balance appears to be maintained with relatively close precision throughout the course of most forms of chronic progressive renal disease despite wide and random variations in dietary intake of this cation. This phenomenon, which is essential for life, strongly implies the continued operation of a control system which serves to monitor the amount of potassium entering body fluids and to regulate the rate of potassium excretion in accordance with both the intake and the number of surviving nephrons. The principal responsibility of the control system is to effect an increase in the rate of potassium excretion per nephron as the number of nephrons decreases. The present studies are directed to an examination of the patterns of potassium excretion in dogs subjected to experimental reduction of their nephron population.

METHODS

Experiments were performed on adult, female mongrel dogs. The renal mass of one kidney was diminished by approximately 75% by ligating most of the second and third-order branches of the ipsilateral renal artery (1). The contralateral kidney was left intact. The urinary bladder was divided into two hemibladders (2) so that urine could be collected separately from the small "remnant" kidney and the contralateral intact organ. After studying potassium excretion by the remnant kidney in the presence of the intact organ, the latter was removed and the same studies were repeated with only the remnant kidney continuing to function.

All food and electrolytes were administered by gastric tube in two equal feedings throughout the period of study. The diet was a synthetic mixture which was sodium free

TABLE I

Potassium Excretion by a Representative Animal with a Unilateral Remnant Kidney Studied before and after Removing the Contralateral Intact Kidney

Time of study	GFR		P_K	FL_K		U_KV		$\frac{U_KV}{FL_K}$		$U_{Na}V$	
	I	R		I	R	I	R	I	R	I	R
	ml/min		*mEq/liter*	*μEq/min*		*μEq/min*		%		*μEq/min*	
Control	81.0	5.9	4.1	317	23.3	30.6	2.7	9.7	11.8	19.7	3.4
Nephrectomy											
14 hr		7.2	5.0		34.5		32.1		93		13.6
7 days		7.1	4.6		34.1		50.4		146.0		56.2

Salt intake was maintained at 3.0 g/day throughout. FL_K is the filtered load of potassium calculated as GFR × plasma potassium concentration × 0.95 Donnan factor. U_KV and $U_{Na}V$ refer to the minute rates of excretion of potassium and sodium respectively; P_K is the plasma potassium concentration. The animal was maintained on oral feedings and 0.1 mg of 9-fluorohydrocortisone twice daily as described in the text.
I refers to intact kidney, R to remnant kidney.

and contained 18% casein, 72% sucrose, and 5% butter fat (Nutritional Biochemicals, Cleveland, Ohio). 125 g were administered in each of two daily feedings; this quantity provides approximately 1200 cal/day. The intake of potassium was maintained constant at 50 mEq/day, unless otherwise indicated. 25 mEq were contained in each feeding.

The intake of sodium chloride also was maintained constant either at a low level (0 to 17 mEq) or at a moderate level (51 or 85 mEq) daily. Mineralocorticoid hormone activity was controlled according to one of two regimens. In most of the dogs, 0.1 mg of 9-α-fluorohydrocortisone was administered twice daily orally in order to maintain a high level of mineralocorticoid hormone activity. In a group of five dogs, however, bilateral adrenalectomy was performed and mineralocorticoid hormone replacement was maintained at a very low level by administering 0.5 mg of DOCA per day. These animals also received 5 mg of cortisol twice daily.

All experiments were performed with the animals awake and standing quietly in a supporting sling. The morning meal containing 25 mEq of potassium was administered approximately 1 hr before the start of the clearance studies. Three or more clearance periods were obtained during each study. In one group of nine dogs, potassium excretion was measured hourly for 5 hr after the administration of 25 mEq of potassium. In three dogs, cumulative potassium excretion was measured by obtaining successive 2-hr urine collections for 24 hr. These animals received their usual two feedings containing a total of 50 mEq of potassium during the course of the 24 hr. The effects of reduction of glomerular filtration rate (GFR) on potassium excretion were studied in a group of six dogs in which only the remnant kidney contributed to renal function. The renal artery was exposed surgically 1–2 days before the study and a cord was placed loosely around the artery and brought to the exterior. On the day of study, three control clearance periods were obtained after which the band about the renal artery was tightened so as to reduce GFR. Another three or more clearance periods then were obtained. In two of the six animals additional constriction was applied and three more clearance periods were obtained.

Glomerular filtration rate was measured as exogenous creatinine clearance, and creatinine was determined according to the method of Bonsnes and Taussky (3). Sodium and potassium were measured on an Instrumentation Laboratories flame photometer, Model 143. Additional details of the experimental procedures have been described previously (1).

RESULTS

Table I depicts the results of serial measurements of potassium excretion before and after removing the intact kidney in a representative dog maintained on 50 mEq of potassium, 51 mEq of sodium chloride, and 0.2 mg of 9-α-fluorohydrocortisone daily throughout the period of study. This regimen was initiated 5 days before the control study was performed. During the control study, with the intact kidney contributing to renal function, potassium excretion averaged 2.7 μEq/min by the remnant kidney and 33 μEq/min by the two kidneys combined. The excretion rates of potassium by each of the kidneys approximated 10% of their respective filtered loads of potassium. 14 hr after removing the intact kidney, potassium excretion by the remnant kidney had increased strikingly with the excretion rate increasing to 93% of the filtered load. By the 7th day postnephrectomy, the excretion rate by the remnant kidney alone was greater than the combined excretion rates by the intact plus the remnant kidneys before nephrectomy. At this time potassium excretion was 146% of the concurrent filtered load of potassium. The plasma potassium concentration increased from a control value of 4.1 to 5.0 mEq/liter 14 hr after nephrectomy. On the 7th day postnephrectomy, the value had decreased to 4.6 mEq/liter. Sodium excretion increased in a manner which roughly paralleled the increase in potassium excretion.

A summary of similar studies performed on 18 dogs is shown in Fig. 1. Potassium excretion for the remnant kidneys before nephrectomy averaged 6.3 μEq/min

while the contralateral intact kidneys excreted 36.1 μEq/min. Within 18 hr of removal of the intact kidneys, potassium excretion by the remnant kidneys increased by an average of approximately fourfold. 7 days after nephrectomy, the excretion rate by the remnant kidneys alone was 85% of the sum of the excretion rates of the two kidneys in the control studies. In 10 of the 18 animals studied 1 wk after nephrectomy, potassium excretion rates exceeded the simultaneous filtered load of potassium. Plasma potassium concentrations averaged 4 mEq/liter in the control studies, 4.8 mEq/liter in the studies performed within 18 hr of nephrectomy, and 4.1 mEq/liter in the studies performed 7 days after nephrectomy.

Table II depicts the patterns of adaptation of potassium excretion in five dogs which had been totally adrenalectomized before the initiation of the control studies. These animals were maintained on 0.5 mg of DOCA and 10 mg of cortisol daily. Sodium intake was maintained at 17 mEq/day in two of the animals and 85 mEq/day in the other three. Potassium intake was maintained constant at 50 mEq/day. In three dogs studied within 18 hr of removal of the intact kidney, potassium excretion had increased substantially by the remnant kidneys; and in the group of five animals, the adaptation present 7 days after nephrectomy was qualitatively similar to that observed in the dogs with intact adrenal glands maintained on a large daily dose of mineralocorticoid hormone. On the 7th day after nephrectomy, the remnant kidneys excreted an average of 75% of the potassium excreted by the intact plus the remnant kidneys before the nephrectomy. Plasma potassium concentration averaged 4.4 mEq/liter in the control studies and 4.7 mEq/liter in the studies performed 7 days after nephrectomy.

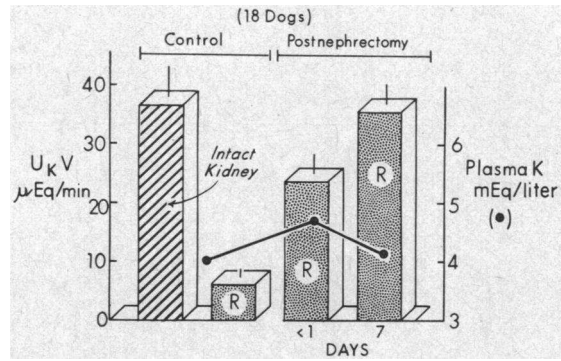

FIGURE 1 Adaptation in K^+ excretion. Potassium excretion was measured first with both the intact kidney (hatched bar) and remnant kidney (R) contributing to renal function. The intact kidney then was removed and studies were repeated. Further details are presented in the text.

TABLE II

Potassium Excretion by Five Adrenalectomized Dogs with a Unilateral Remnant Kidney Studied before and after removing the Contralateral Intact Organ

Condition	Dog	GFR		P_K	$U_K V$		$\frac{U_K V}{FL_K}$		$U_{Na} V$		Salt diet	Wt.
		I	R		I	R	I	R	I	R		
		ml/min		*mEq/liter*	*μEq/min*		*%*		*μEq/min*		*g/day*	*lb.*
Control studies	1	29.1	7.3	4.0	38.2	10.8	34.9	39.6	2.4	1.2	1	25
	2	14.6	4.5	5.0	19.7	6.6	28.6	31.8	1.8	1.1	1	28
	3	36.2	7.8	4.4	43.0	9.6	28.3	29.2	24.4	6.2	5	23.5
	4	37.1	15.1	4.1	49.5	18.4	34.1	31.0	22.7	13.1	5	24
	5	38.7	8.2	4.4	43.7	11.5	36.5	33.7	4.6	5.7	5	25.5
Mean		31.1	8.6	4.4	38.8	11.4	32.5	33.1	11.2	5.5		
14–18 hr post-nephrectomy	1		10.6	5.0		18.2		36.3		4.9	1	23.0
	2		9.1	4.9		32.0		76.3		3.8	1	26.5
	4		19.2	4.3		22.1		28.9		53.8	5	24.0
7 days post-nephrectomy	1		7.2	4.8		31.1		96.2		1.7	1	22
	2		4.0	5.5		24.9		119.1		3.0	1	23.0
	3		6.4	4.4		34.2		127.3		5.8	5	22.0
	4		18.9	4.3		55.9		71.9		37.2	5	22.0
	5		9.4	4.6		36.1		88.1		22.8	5	21.5
Mean			9.2	4.7		36.4		100.5		14.1		

I refers to intact kidney, *R* to remnant kidney.

TABLE III

Potassium Excretion at Two Levels of Sodium Excretion by the Remnant Kidney of Five Uremic Dogs in Which the Intact Kidney Had Been Removed

Dog	GFR		$U_{Na}V$		U_KV	
	A	B	A	B	A	B
	ml/min		*μEq/min*		*μEq/min*	
1	15.5	16.6	12.2	16.6	50.7	34.2
2	14.5	16.4	50.1	118.7	51.4	65.4
3	8.7	11.3	9.2	38.4	44.0	62.8
4	5.5	7.3	22.0	29.0	35.2	26.9
5	11.8	12.8	31.7	92.8	47.2	41.8
Mean	11.2	12.9	25.0	59.1	45.7	46.2

A refers to the period of lower sodium excretion, *B* to the period of increased sodium excretion. Each group of studies (*A* vs. *B*) was done after the salt and potassium intake had been maintained constant for at least 4 days.

The relationship between the rate of potassium excretion and the concurrent rate of sodium excretion is shown in Table III for a group of five dogs in which the potassium intake was held constant at 50 mEq/day, but the sodium intake was varied. On the low sodium diet, sodium excretion averaged 25 μEq/min; on the higher salt intake, the excretion rate of sodium averaged 59 μEq/min. Under both circumstances, however, the mean potassium excretion rates were virtually identical.

In order to examine further the relationship between sodium excretion and potassium excretion, the effects of renal artery constriction were studied in six dogs in which only the remnant kidney contributed to renal function. The results of these studies are shown in Fig. 2. Before constricting the renal artery, GFR averaged 7.7 ml/min (range 5.4–11.0 ml/min). After constriction, GFR fell to a mean value of 5.5 ml/min (range 3.9–6.8 ml/min). Sodium excretion fell from a mean of 84 μEq/min before constriction to 36 μEq/min

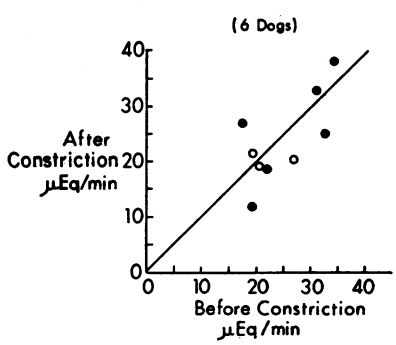

FIGURE 2 The effect of renal artery constriction on potassium excretion in dogs in which the control kidney had been removed at least 7 days before study. The details of these studies are reported in the text.

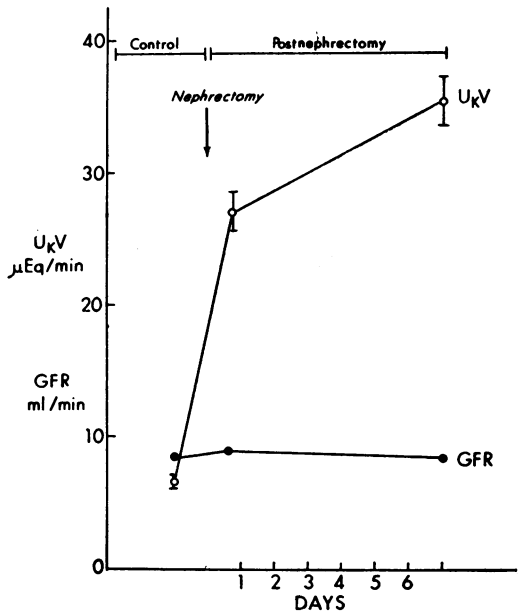

FIGURE 3 The rate of potassium excretion by the remnant kidney in 18 dogs maintained on a constant potassium intake is plotted against GFR for the remnant kidney before and after removal of the contralateral intact kidney.

after constriction. However, potassium excretion rates were the same before and after renal artery constriction. With additional constriction in two animals, GFR fell further but potassium excretion rates increased slightly in one and decreased slightly in the other. Thus, renal artery constriction failed to blunt the acquired kaliuresis per nephron.

The relationship between GFR in the remnant kidneys and their rate of potassium excretion before and after removal of the intact kidney is shown in Fig. 3 for 18 dogs. GFR remained essentially constant for the group both during the 1st day postnephrectomy and 7 days postnephrectomy.[1] The increase in potassium excretion rate thus is not dependent upon a concurrent increase in GFR.

In nine dogs, potassium excretion was measured at hourly intervals for 5 hr after administering 25 mEq of potassium by gastric tube. These studies were performed initially in the presence of the intact kidney and were repeated at least 7 days after the intact kidney had been removed. The data are shown in Table IV. Potassium excretion by the remnant plus intact kidneys in the initial studies averaged 6.84 mEq in the 5 hr. After removal of the intact kidney and after administra-

[1] The reason why an adaptive increase in GFR did not occur in the remnant kidneys postnephrectomy is not obvious. However, one possible explanation is that the synthetic diet on which the animals were maintained contained only 18% protein.

TABLE IV

Plasma Potassium Concentration and Potassium Excretion Hourly for 5 hr after an Oral Potassium Load of 25 mEq

	Control		1 hr		2 hr		3 hr		4 hr		5 hr	
	PK	U_KV	PK	U_KV	PK	U_KV	PK	U_KV	PK	U_KV	PK	U_KV
	mEq/liter	*mEq/hr*	*mEq/liter*	*mEq/hr*	*mEq/liter*	*mEq/hr*	*mEq/liter*	*mEq/hr*	*mEq/liter*	*mEq/hr*	*mEq/liter*	*mEq/hr*
Prenephrectomy												
Mean	3.76	0.75	3.34	0.84	3.75	1.27	3.83	1.69	4.04	1.69	4.12	1.35
SE	±0.15	±0.08	±0.12	±0.14	±0.11	±0.22	±0.08	±0.24	±0.09	±0.32	±0.10	±0.29
Postnephrectomy												
Mean	3.83	1.30	3.50	1.38	3.79	1.60	4.13	2.13	4.52	2.59	4.32	2.49
SE	±0.17	±0.19	±0.24	±0.11	±0.19	±0.16	±0.16	±0.26	±0.18	±0.22	±0.13	±0.22
P value prenephrectomy vs. postnephrectomy	>0.5	<0.01	>0.4	<0.02	>0.8	<0.1	>0.1	>0.2	<0.001	<0.05	>0.1	<0.02

Studies were performed before (prenephrectomy) and (postnephrectomy) removing the intact kidney in nine dogs. Potassium excretion rates shown for the prenephrectomy study are combined values for control plus remnant kidneys. Values for the postnephrectomy state are for the remnant kidneys only. The cumulative 5-hr excretion rates after administration of the loading dose (ie. excluding the control values) are 6.84 mEq in the prenephrectomy studies and 10.2 mEq in the postnephrectomy studies.

tion of the same oral load of potassium, the remnant kidneys excreted an average of 10.2 mEq in the same 5 hr period. Thus, during the first 5 hr after administration of a constant load of potassium, the small population of residual nephrons in the remnant kidneys excreted substantially *more* potassium than the remnant plus intact kidney had excreted after the administration of the same amount of potassium. In four of the five hourly periods, plasma potassium was not significantly greater in the postnephrectomy than in the prenephrectomy state.

Potassium excretion was measured during successive 2-hr intervals in three dogs for 24 hr before and again after removing the intact kidney. 25 mEq of potassum were administered in the morning and in the evening during the course of each study. The results of these studies are shown in Table V. When the intact kidney was present the excretion of potassium varied more from period to period than when only the remnant kidney was present. However, for the full 24 hr, the average rate of excretion by the remnant kidney was 87% of that by the remnant plus intact kidneys and 93.1% of the intake of potassium.

The relationship between potassium excretion and the concurrent rate of phosphate excretion by two dogs maintained on two different potassium intakes (50 and

TABLE V

24 hr Potassium Excretion by three Dogs before and after Removal of the Intact Kidneys

	Prenephrectomy				Postnephrectomy			
Period	Dog A	Dog B	Dog C	Mean ±SE	Dog A	Dog B	Dog C	Mean ±SE
1	1.57	0.99	1.37	1.31 ±0.17	3.12	2.51	2.91	2.85 ±0.18
2	2.16	3.07	1.27	2.17 ±0.52	3.26	3.97	2.34	3.19 ±0.47
3	6.58	6.20	3.71	5.50 ±0.90	5.31	5.09	3.71	4.70 ±0.50
4	5.33	3.28	6.66	5.09 ±0.99	5.11	4.82	4.21	4.72 ±0.26
5	3.19	4.04	3.95	3.73 ±0.27	3.88	4.10	3.67	3.89 ±0.13
6	3.99	9.68	4.27	4.98 ±1.85	3.28	4.55	3.69	3.84 ±0.37
7	19.58	2.80	8.56	10.32 ±4.92	6.35	7.09	4.72	6.05 ±0.70
8	5.02	3.32	2.63	3.65 ±0.71	5.88	5.78	4.82	5.49 ±0.34
9	3.22	4.29	4.62	4.04 ±0.42	4.07	5.44	3.87	4.46 ±0.50
10	2.10	4.17	4.89	3.72 ±0.84	3.77	3.83	3.77	3.79 ±0.02
11	2.72	3.36	6.03	4.04 ±1.01	3.58	3.14	2.80	3.17 ±0.22
12	2.55	2.27	3.46	2.75 ±0.36	3.26	2.51	2.43	2.73 ±0.27
Total: mEq/24 hr	58.0	47.5	51.4	52.3	50.9	52.8	46.7	48.9

Values are expressed as mEq/2 hr. Total potassium intake during the 24 hr was 50 mEq. 25 mEq of potassium were given by gastric tube with half of the daily diet before collections 2 and 6.

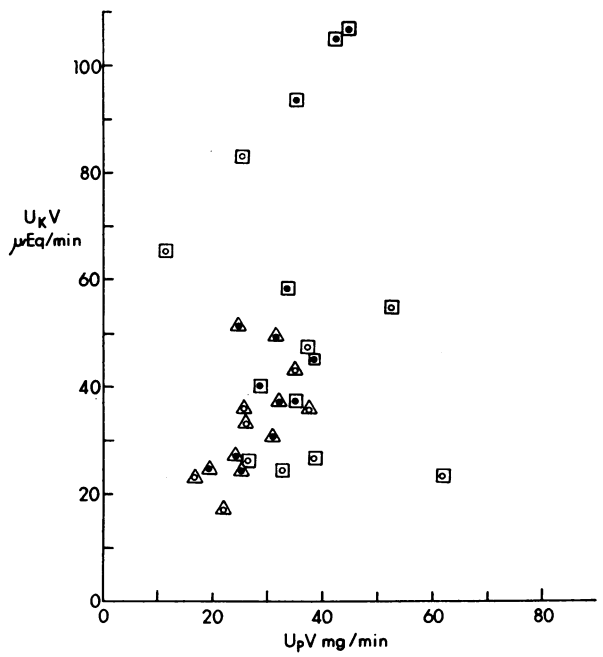

FIGURE 4 Correlation between potassium excretion and phospate excretion. Closed circles refer to dog 1, open circles to dog 2. Triangles indicate a potassium intake of 25 mEq twice daily; boxes indicate a potassium intake of 40 mEq twice daily. Two control urine collections were obtained after which either 25 or 40 mEq of potassium was administered by gastrict tube; urine then was collected at hourly intervals for 5 hr. Each point represents the value for a single urine sample.

80 mEq/day) is shown in Fig. 4. In each study, two control urine collections were made, half of the total amount of potassium was then administered by gastric tube, and urine was collected hourly for 5 hr. While there appears to be some correlation between potassium and phosphate excretion on the lower potassium intake, potassium excretion increased appropriately on the higher potassium intake without a concomitant rise in phosphate excretion.

DISCUSSION

Patients with chronic progressive renal disease who ingest a normal diet with an average content of potassium are not afflicted with progressive hyperkalemia until the end stages of their disease. Potassium balance thus is maintained in the face of advancing nephron destruction over periods that may extend to many years in duration. While increased gastrointestinal excretion of potassium may contribute in part to this capacity to preserve potassium balance (4), the principle mechanism underlying the phenomenon is a progressive increase in potassium excretion per nephron. The present studies were designed to examine certain of the characteristics of this adaptation using an experimental model in which nephron mass was decreased markedly. The data demonstrate clearly the capacity of the residual nephrons to increase their rate of potassium excretion strikingly and appropriately. They do not, however, reveal which, if any, of the events currently known to influence potassium excretion is responsible for the acquired kaliuresis.

The potassium control system has several known effector elements which contribute to the regulation of the renal excretion of potassium. These include mineralocorticoid hormone activity, plasma and intracellular potassium concentration, sodium delivery to the distal convoluted tubule, hydrogen ion secretion rate, and the anion composition of the tubular fluid. In the present experiments an attempt was made to control or quantify the contribution of as many of these variables as possible while simultaneously initiating a stimulus requiring a substantial increase in potassium excretion per nephron. The stimulus consisted of reducing the total number of nephrons markedly while holding the intake of potassium constant. Potassium excretion per nephron increased by fourfold within 18 hr of nephron reduction, and by 7 days there was a sixfold increase in the average excretion rate per nephron. The excretion rate of potassium by the small population of residual nephrons was appropriate for the continued maintenance of potassium balance and normokalemia. An increase in fecal excretion of potassium might also have occurred as part of the adaptive process (4), although in the animals in which potassium excretion was measured over a full 24 hr period, the rate of renal excretion averaged 93% of the intake with only the remnant kidney present.

The adaptation in renal excretion took place during the administration of large doses of supplemental mineralocorticoid hormone; it also occurred in adrenalectomized animals given only enough DOCA (0.5 mg/day) to maintain life. Thus, regulated *changes* in mineralocorticoid hormone activity do not seem essential for the adaptive kaliuresis. Nor was a persistent elevation of plasma potassium necessary for the sustained kaliuresis per nephron. Plasma potassium concentrations increased within the 1st day after nephron reduction and may have contributed to the initial kaliuretic response. However, in the 18 dogs shown in Fig. 1, the mean value for plasma potassium concentration decreased to control levels within 7 days; yet the striking increase in potassium excretion rate per nephron continued. It is possible that intracellular potassium concentrations in the renal tubular epithelial cells increased with nephron reduction despite the absence of a progressive rise in plasma potassium concentration and contributed to the acquired kaliuresis per nephron. No data in the present paper allow evaluation of this possibility. However, if the intracellular activity of potassium increases

with nephron reduction, there would have to be a slow and continuous rise over a period of many years in patients with slowly advancing renal disease to account for the continuing increase in potassium excretion per nephron. If this is a major element in the adaptation, it would still be necessary to explain the capacity of patients (or animals) with a reduced population of nephrons to *modulate* potassium excretion in accordance with day-to-day variations in potassium intake.

The adaptation in potassium excretion was observed to occur on a low salt diet as well as on a 3 or 5 g salt intake; potassium excretion rates thus were the same when sodium excretion rate averaged 25 μEq/min as when it averaged 59 μEq/min. Moreover, when sodium excretion (and presumably sodium delivery to the distal segments of the nephrons) was decreased by constriction of the renal artery of the remnant kidneys in six animals in which the intact kidney had been removed, no consistent decrease in potassium excretion was observed. Very likely, the distal delivery of sodium was sufficiently large so as not to be rate limiting for potassium secretion under any of the circumstances of the present studies; nevertheless, the data suggest that the absolute rate of distal sodium delivery and/or of sodium excretion did not modulate the rate of potassium excretion.

The rate of hydrogen ion secretion by the cells of the distal nephron is thought to vary reciprocally with potassium excretion under many circumstances. However, when the nephron population is reduced, hydrogen ion secretion per nephron must increase rather than decrease. For example, ammonia excretion per nephron averages about 0.2 mEq/ml GFR per day in a normal individual and may equal over 5 to 10 times that amount in a patient with advanced chronic renal disease. Titratable acid excretion per nephron also increases strikingly as GFR falls in chronic renal disease. Thus, a reduction in hydrogen ion secretion would not seem to provide an explanation for the acquired kaliuresis per nephron seen with nephron reduction.

An additional determinant of potassium excretion is the concentration of impermeant anions in the tubular fluid (5, 6). No correlation was observed between the absolute rate of potassium excretion and that of phosphate excretion when the intake of potassium was increased from 50 to 80 mEq/day. Moreover on *a priori* grounds, it seems obvious that the precise rate of potassium excretion must be attuned to the rate of acquisition of potassium rather than to the rate of excretion of any other solutes including impermeant anions. Nevertheless, an increased concentration of poorly reabsorbable anions in the tubular fluid could certainly contribute, perhaps importantly, to an increased rate of potassium excretion per nephron.

A further possibility that must be considered is that, in the presence of a reduced population of nephrons, there might be a delay in excretion of an administered load of potassium. This could lead to a more prolonged stimulation of the afferent limb of the control system in the presence of nephron reduction. However, when the hourly excretion rate of potassium was measured for 5 hr after the administration of 25 mEq of potassium by gastric tube before and after removing the intact kidney, the excretion rate was actually greater by the remnant kidney alone after nephrectomy than by both kidneys before the nephrectomy. Moreover, in 24-hr excretion studies, where potassium excretion rates were measured every 2 hr, no delay in excretion could be detected by the remnant kidneys functioning alone.

The phenomenon of potassium adaptation in the face of nephron reduction resembles in some ways the phenomenon of potassium adaptation described by Alexander and Levinsky (7). In their studies rats fed a high potassium diet for several days survived an acute load of potassium that was lethal to animals maintained on a normal potassium intake. They also found that adapted nephrectomized animals maintained a lower potassium concentration in blood after an acute potassium load than did the control animals fed a regular diet. Berliner, Kennedy, and Hilton (8) previously had found that dogs maintained on a high potassium intake excreted an intravenous load of potassium more rapidly than control animals given the same amount of potassium. Hyperaldosteronism is believed to be important in at least the extrarenal component of the adaptation induced by the continued administration of increased quantities of potassium (7); however, it is difficult to invoke this mechanism in the present studies in that mineralocorticoid hormone levels were maintained constant throughout the studies either at a high level, or at a very low level in adrenalectomized animals.

None of the determinants of potassium excretion which was examined in the present studies appears to account entirely for the adaptive increase in potassium excretion per nephron that attended reduction in total nephron population. Whether a heretofore undefined control factor contributed to the acquired kaliuresis per nephron remains to be determined.

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