

# WATER EXCRETION IN POTASSIUM-DEFICIENT MAN \*

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Kaliopenic nephropathy is now a well recognized entity in which diminished ability to concentrate urine is a prominent clinical feature (1-4). Most instances are reported in patients with an aldosterone-producing tumor or chronic diarrhea (5), and the defect in urine concentrating ability was well established when potassium deficiency was recognized. Usually the magnitude and duration of the potassium deficit could be only indirectly inferred.

Most studies of renal anatomy and function during potassium deficiency have been performed in animals, but it is generally assumed that man behaves similarly, and *a*) anatomic lesions in the collecting ducts and inner medulla cause the functional incapacity (3), *b*) the severity of these lesions reflects the magnitude of potassium depletion (2, 3, 6), and *c*) the functional and possibly the anatomic aberration is reversible if potassium is repleted (1, 3, 5).

Extrapolation of data obtained in the rat to limited experience in man is uncertain. The anatomic lesions of the kidney seem quite different in rats (7-11) and men (2, 12-14). Human lesions are often maximal in the proximal convolution rather than in the collecting system, and the vacuolated renal tubular epithelium usually seen in man (and dog) may be absent or minimal in the rat. Secondly, because potassium deficiency and the circumstances which cause it threaten health, serial study of the same untreated patient is usually precluded, and correlation of renal functional studies with the potassium deficit is of limited utility. Finally, focal scarring occurs in kidneys of animals maintained for even brief periods in the potassium-depleted state (15-17), and the reversibility of function with potassium repletion has been questioned (3, 13, 18).

The studies reported herein describe certain

experiences with experimental potassium depletion in man; they attempt to quantify in time the extent of the alteration in renal concentrating ability during progressive potassium depletion and its resolution during potassium replenishment. A temporal dissociation between the ability to concentrate the urine maximally during hydropenia, and the ability to conserve water during acute solute loading was found. Although permanent impairment of renal function was not observed in these studies, it is felt that this was fortuitously related to the relatively limited magnitude or duration of potassium depletion, and in view of the rat experience reported after these studies were instituted (17), which indicates that permanent renal scarring may result from even brief potassium depletion, we would hesitate to induce again severe potassium depletion in man.

## METHODS

Nine male patients participating in these studies were convalescent from orthopedic procedures, and free of cardiovascular, renal and endocrine disease by history, physical examination and the usual laboratory screening procedures. Experimental potassium depletion was produced by feeding a constant liquid diet, adequate in calories, protein and vitamins, but containing less than 0.1 mEq of potassium per kg body weight. Since the diet was made up of natural foods, it is likely that other trace elements were not seriously deficient. The diet could maintain nitrogen balance in adult man, and with added KCl, could promote normal growth in young rats. Sodium intake was kept constant, generally at 1 mEq per kg of body weight, but in certain studies was modified by protocol design. In some studies protein intake was kept low during the initial period of potassium depletion, then quadrupled without increasing potassium intake. Cumulative losses of potassium were monitored from analyses of urine and feces only, and are minimal rather than precise estimates of degree of potassium depletion. Their magnitude was again estimated during repletion, and in each instance was confirmatory within 15 per cent. Measured amounts of distilled water were given *ad libitum*.

Each subject was first observed for 1 week on the metabolic ward. KCl, 1.0 mEq per kg body weight, was given

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with the potassium-depletion diet during this period, and control studies of concentrating ability during dehydration, water reabsorption during mannitol diuresis, the response to a water load, and vasopressin sensitivity were performed. The test diet was then continued without potassium supplements for 20 to 35 days, and these studies were repeated at intervals. Serial concentration tests twice weekly were feasible in six subjects throughout the depletion and repletion periods; observation was less complete in the others. Three or more mannitol infusions were performed in five potassium-depleted subjects; in three others only a control study and a single study during potassium depletion were performed. Similarly, serial weekly studies of water diuresis were feasible in only four of the subjects, although several studies during the potassium-depletion period were performed in the others.

Urinary concentrating ability was assessed after overnight dehydration both with and without Pitressin (vasopressin). Although a more concentrated urine can be achieved by normal men by prolonging or intensifying the period of dehydration, or by increasing the protein content of the diet (19, 20), this simple technique gives closely reproducible results in any single individual (average variation from the mean of two or more tests: normals, 4.2 per cent; renal disease with hyposthenuria, 6.9 per cent). Water reabsorption was examined during osmotic diuresis produced by infusing 10 per cent mannitol during dehydration. Dehydration tests and osmotic diuresis were usually performed in tandem; i.e., after two or three hourly urines were collected, the mannitol infusion was started and infusion rate slowly raised until maximal urine flow was achieved. Sufficient vasopressin was added to the infusion (in excess of 200  $\mu$ U per hour) to insure maximal antidiuretic hormone (ADH) activity. Maximal water reabsorption ( $T^*H_2O$ , the difference between osmolar clearance and urine flow) was arbitrarily selected as the average value obtained in three to five collection periods agreeing within  $\pm 10$  per cent. These generally were obtained at intermediate rates of solute excretion ( $C_{osm}$ , 15 ml per minute), for with more rapid rates of mannitol infusion  $T^*H_2O$  appeared to decrease irregularly.

Water diuresis was produced by giving 20 ml per kg of tap water, or by giving a sustained load of 1.0 L. The adequacy of diuresis after a water load was evaluated from time course and magnitude of peak urine flow, minimal urine osmolality, and gross water balance after 2 and 3 hours. Often minimal urine osmolality was also observed during sustained water loads. The reproducibility of such data even in the same subject on constant diet was less than ideal, reflecting undoubtedly the uncontrolled differences in antecedent bodily hydration and fluctuating renal hemodynamics. At least 2 days separated tests of dilution and concentration.

Sensitivity to exogenous vasopressin was examined at intervals during progressive potassium depletion. Each subject was titrated by determining the minimal amount of vasopressin given intravenously during water diure-

sis which could induce urine to become more concentrated than plasma. Then twice this amount of vasopressin was administered in successive studies using a fresh ampule of the same lot for each study to obviate the problem of deterioration after dilution. Two different lots were used which differed by cross assay in normal man by 50 per cent, so that cited dosage administered is only a rough approximation.

All urines were collected by spontaneous voiding. Urinary sediment was examined at frequent intervals. In five subjects, quantitative sediment counts were performed daily on overnight specimens. Fleeting mild albuminuria or increased cellular elements were seen in most cases, but rarely in consecutive specimens. Three subjects who had increased numbers of white cells in their urinary sediment on several occasions were studied more intensively, but repeated urine cultures revealed no significant bacilluria.

Chemical methods employed have been previously described (21). Osmolality of plasma and urine was estimated with a Fiske osmometer by comparing the freezing point depression to that of standard solutions of sodium chloride.

## RESULTS

Potassium-restricted subjects lost their ability to concentrate urine normally (Figure 1). Significant hyposthenuria was apparent as early as the fourth day in one subject and common to all the subjects by the second week. Generally the impairment of concentrating ability was slight until approximately 200 mEq of potassium had been lost. After approximately 3 weeks of potassium restriction (deficit, 350 mEq), the degree of hyposthenuria became relatively constant although potassium restriction continued, and even in the most severe potassium depletion, 24-hour urine

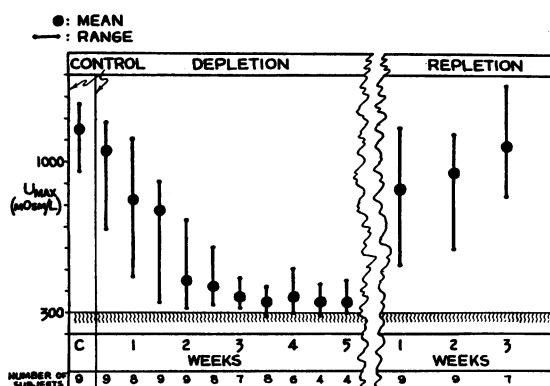


FIG. 1. URINE CONCENTRATION DURING HYPORENIA IN POTASSIUM DEPLETION. The mean and range of maximal urine concentration examined in 9 subjects is depicted. The mean  $U_{max}$  is significantly ( $p < 0.05$ ) different from control by the tenth day.

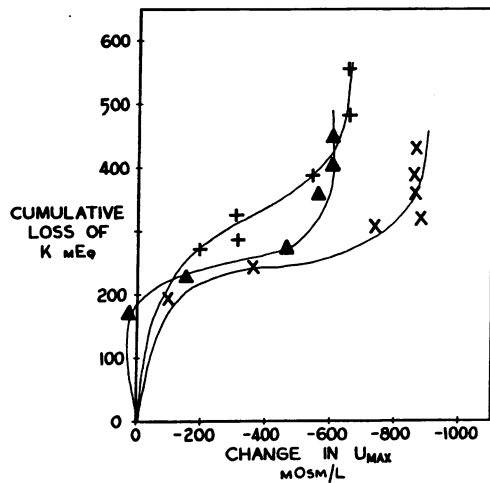


FIG. 2. RELATIONSHIP BETWEEN URINE CONCENTRATING ABILITY AND THE MAGNITUDE OF THE POTASSIUM DEFICIT.

was generally more concentrated than plasma. Linear correlation of the loss of urine concentrating ability with the cumulative loss of potassium was low ( $R = 0.55$ ,  $p > 0.1$ ), and such correlation seemed appropriate only in the range of potassium deficit of 200 to 400 mEq. At values above and below these limits, changes in potassium balance were little reflected in changes in maximal urinary concentration ( $U_{\max}$ ). The diphasic curves shown in three subjects (Figure 2) were typical.

Maximal water reabsorption during osmotic diuresis fell abruptly as potassium was withdrawn from the diet (Figure 3, Table I). The concen-

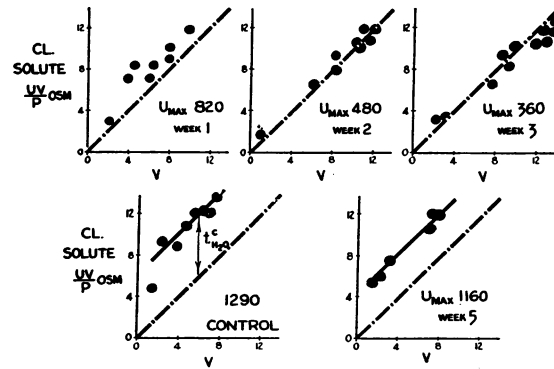


FIG. 3. WATER REABSORPTION DURING OSMOTIC DIURESIS IN PROGRESSIVE POTASSIUM DEFICIENCY. Serial studies in a single individual are depicted. The  $U_{\max}$  refers to concentration during hyponatremia obtained before starting the mannitol infusion. The study during Week 5 was performed after repletion; external balance of potassium was +80 mEq.

trating defect was prominent at high rates of solute excretion in subjects who retained considerable concentrating ability during simple dehydration when the rate of solute excretion was low. Thus two subjects could concentrate urine to 800 mOsm per L during dehydration, but maximal  $T^cH_2O$  was  $< 3.0$  ml per minute; four subjects who could concentrate urine to twice plasma osmolality could not reabsorb 1 ml per minute  $T^cH_2O$ .

As the potassium deficit was increased further, the  $U/P$  osmotic gradient during hyponatremia could be maintained only when the rate of solute excretion was low. After more than 300 mEq of

TABLE I  
Water reabsorption in potassium-depleted subjects \*

Control	Week	Potassium depletion				Recovery	
		1	2	3	4	2	4+
$U_{\max} 1,140 \pm 80$ (mOsm/L) [9]		$801 \pm 110$ [9]	$410 \pm 40$ [8]	$340 \pm 20$ [6]	$328 \pm 18$ [5]	$960 \pm 42$ [9]	
Max. $T^cH_2O 5.6 \pm 0.9$ (ml/min) [9]		$1.2 \pm 0.8$ [8]	$0.2 \pm 0.6$ [5]	$-0.8 \pm 0.9$ [6]	$-0.1 \pm 0.4$ [3]	$0.9 \pm 1.2$ [4]	$5.3 \pm 1$ [5]
K balance (mEq)		$-210 \pm 62$ [9]	$-295 \pm 32$ [9]	$-354 \pm 60$ [8]	$-428 \pm 26$ [3]	$60 \pm 15$ [9]	

\* The values reported (mean  $\pm$  standard deviation) are arbitrarily grouped by weeks of depletion. When more than one study was performed during a single week the values obtained were averaged. The number of patients studied in each period is shown in brackets. The numerical values assigned to  $T^cH_2O$  during potassium restriction are arbitrary and conceptually artifactual, since in most studies no apparent plateau was achieved and urine often became progressively less concentrated as solute load was raised. The calculated  $T^cH_2O$  values that were observed at the same range of solute excretion rates obtained in the control study were averaged. This is better depicted in Figure 3 and discussed further in the text. The repletion studies are timed from the onset of repletion. Although potassium was given at different rates and retention of potassium varied, all subjects had a calculated net positive balance of potassium by 2 weeks.

TABLE II  
Parameters of water diuresis compared in seven subjects at approximately equivalent deficits of potassium (250 to 300 mEq) \*

	Control		Deficit 250-300 mEq						
	Mean	Range	Subject no.: Day of study: I 16	II 18	III 20	IV 21	V 22	VI 26	VII 28
Maximal flow (ml/min)	14.2	10.6-22.3	13.8	8.3†	14.7	16.2	21.9	9.4†	11.1
Minimal osmolality (mOsm/L)	69	60-89	72	120†	65	60	64	71†	88
"Lag time" (min)	60	35-110	48	80†	90	75	93	65†	
% Excreted at 2 hrs	81†	62-106		82				60†	

\* The day of study is shown to give some estimate of the rate of development of potassium deficiency. "Lag time" refers to the time elapsed between water load and peak urine flow. Excretion at 2 hours was not corrected for insensible losses of about 50 ml/hour. All data were obtained during sustained water loading except those designated by † to denote a single water load. The data demonstrate normal water diuresis at a time when urine concentrating ability was severely reduced.

potassium had been lost, maximal water reabsorption in three of six subjects in whom an osmotic diuresis was induced was actually "negative." Although urine during hydropenia was in each instance at least 20 per cent more concentrated than coincident plasma, the osmotic gradient was rapidly lost with increasing solute excretion, and urine became more dilute than plasma. Potassium replenishment caused a prompt return in the ability to concentrate urine during hydropenia. This was not true of water reabsorption during mannitol loading and maximal  $T^cH_2O$  was severely reduced when  $U_{max}$  had already returned to normal (Table I). Two of the five subjects studied 1 month after repletion still had a low  $T^cH_2O$  (3.2 and 3.6 ml per minute). Three months later, the opportunity to re-examine one of these subjects and two of the others revealed no abnormalities of renal function.

Water diuresis was little affected by moderate potassium deficiency and a seemingly normal response to ingested water was obtained in subjects whose capacity for urine concentration had already deteriorated (Table II). When potassium deficiency progressed beyond 350 mEq, ab-

normal water excretion became evident (Table III). The response to intravenous loads of a dilute fructose solution was also abnormal at this time, indicating that impaired intestinal absorption was not the decisive factor. The abnormal water diuresis was not improved by salt loading except in a subject whose previous sodium intake had been restricted parallel to potassium restriction, and who never achieved a normal response to water loading even in the first week. Although consistent changes in creatinine clearance were not found during potassium deficiency, significant changes in glomerular filtration were not ruled out.

Increasing resistance to vasopressin became evident as potassium deficiency progressed. Yet this did not always closely parallel loss of concentrating ability, and two of the subjects who could still concentrate their urine to 400 to 500 mOsm per L during dehydration continued to excrete very dilute urine during water diuresis despite vasopressin administration (Figures 4 and 5). While it is attractive to consider that these data would substantiate a dual process of water reabsorption (25, 26), one partly independent of ADH action, creatinine clearance and

TABLE III  
Abnormal water diuresis in three of five subjects studied when the potassium deficit exceeded 350 mEq

	Deficit (mEq): 351 Subject: III	382 I	396 VII	422 VII	461 VI	524 V
Maximal flow (ml/min)	6.2	11.8	2.4	1.4	19.2	1.6
Minimal osmolality (mOsm/L)	185	82	232	201	76	206
"Lag time" (min)	80	75			45	
% Excreted at 2 hrs	22	92	8	10	102	11

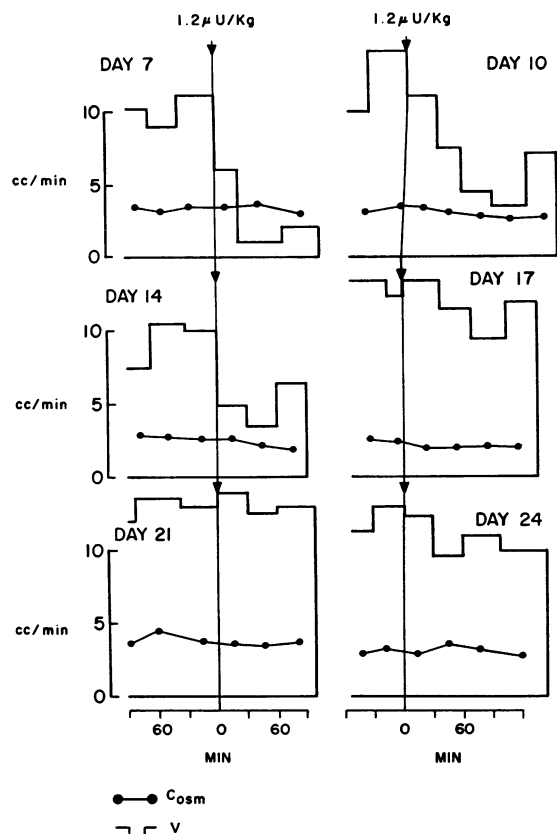


FIG. 4. VASOPRESSIN RESPONSIVENESS IN POTASSIUM DEFICIENCY. The measured potassium deficit was approximately 200 mEq by Day 10 and 320 mEq by Day 21. The study on Day 24 was performed after 200 mEq had been given, replacing more than half the cumulative deficit. This lot of vasopressin had probably lost considerable activity. See text.

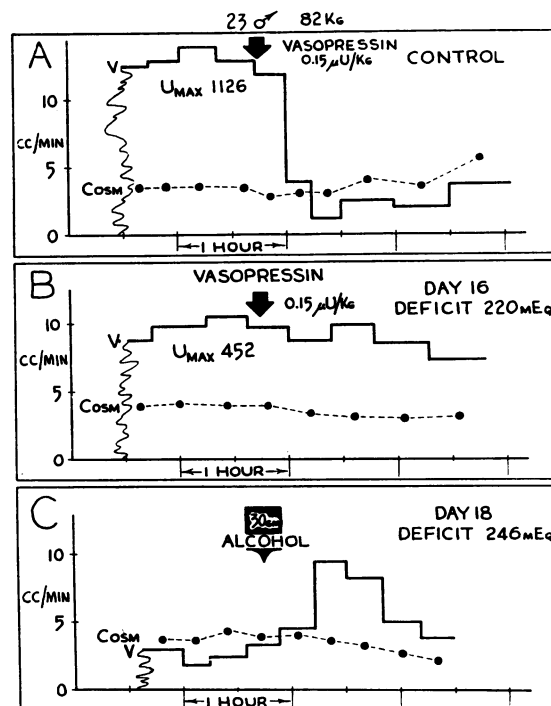


FIG. 5. "WATER TYPE" DIURESIS AFTER ETHYL ALCOHOL INGESTION IN A POTASSIUM-DEPLETED SUBJECT RESISTANT TO VASOPRESSIN. Free water clearance is depicted as the difference between  $C_{osc}$  and  $V$ .

hence probably glomerular filtration rate invariably increased during mannitol infusion, and it is difficult to explain the effect of ethyl alcohol in the moderately potassium-depleted subject (Figure 5). The "water-type" diuresis evident after

TABLE IV

Effect of urea on  $T^{\circ}H_2O$  in potassium-depleted dogs \*

	Rate of solute excretion		
	1,000-2,000	2,000-3,000	3,000+
	$\mu Osm/min$	$\mu Osm/min$	$\mu Osm/min$
Normal	3.6 to 4.2	3.9 to 4.4	3.4 to 5.2
Normal + urea	2.9 to 4.6	3.8 to 5.2	4.7 to 6.5
K-depleted	-0.1† to 0.3	-1.2† to 0.5	-1.1† to 0.4
K-depleted + urea	-0.4† to 0.5	-1.0† to 0.1	-1.2† to 0.1

\* Range of  $T^{\circ}H_2O$  during osmotic diuresis in the same dogs studied before and after potassium depletion. The potassium-deficient diet was fed for 5 weeks prior to study. Cumulative negative balance was in excess of 90 mEq (approximately  $\frac{1}{3}$  normal body content) and moderate hypokalemic alkalosis was present. The infusion rate of 10% mannitol was increased until urine flow exceeded 10 ml/min for three successive periods. Then 50 g of urea was instilled into the stomach and rate of mannitol infusion slowly reduced to observed  $T^{\circ}H_2O$  over a wide range of solute loads. The post-urea periods are limited to those in which urea excretion had increased more than twice. The data from 3 dogs are amalgamated.

† A negative  $T^{\circ}H_2O$  indicates urine was more dilute than plasma.

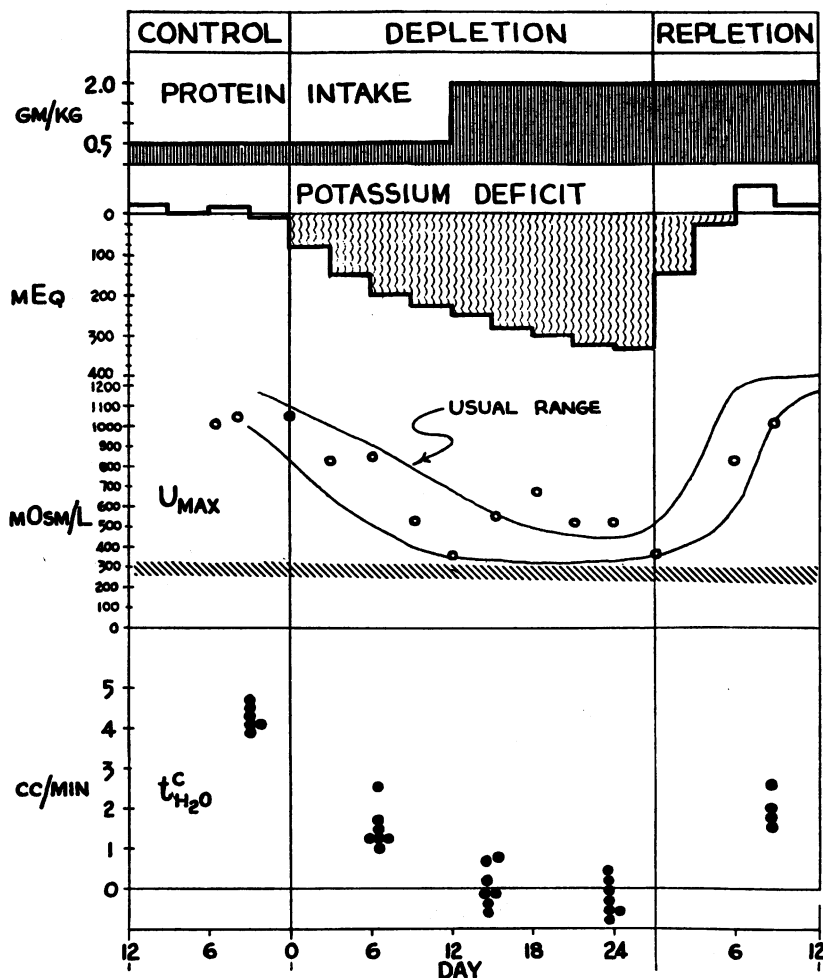


FIG. 6. EFFECT OF PROTEIN FEEDING ON WATER CONSERVATION DURING POTASSIUM DEFICIENCY. Not shown is the balance of nitrogen and phosphorus which became positive. The relative potassium deficit was probably aggravated (see text). Serum potassium fell from 3.8 to 2.6 mEq per L when protein intake was quadrupled in this subject, but remained unchanged in a similar study on another subject.

alcohol suggests that some ADH was previously present and acting on the renal tubule, since the main action of alcohol on water balance seems to be inhibition of ADH release (22). This is further implied by the absence of hypotonic polyuria which might be expected if total insensitivity to ADH was present (23, 24).

Protein feeding or urea administration may increase apparent urine concentrating ability both in normal subjects and in some patients with hyposthenuria due to renal disease (25). The effect of increased loads of urea on the hyposthenuria of potassium deficiency was examined in three subjects. In a subject whose dietary protein was

increased while potassium restriction continued, maximal urinary concentration was more than 100 mOsm per L higher on the high protein intake, although the degree of potassium depletion had increased 100 mEq (Figure 6). A second subject, more severely depleted of potassium, similarly increased  $U_{max}$ , but in another subject with hyposthenuria and potassium depletion of over 300 mEq, 3 days of urea feeding did not appreciably alter concentrating ability. Feeding urea during mannitol infusion, which increases apparent maximal water reabsorption in normal dogs, and, under special circumstances, in man (25, 26), did not increase water reabsorption in

potassium-depleted dogs (Table IV), or in a potassium-depleted subject.

#### DISCUSSION

The inability to concentrate urine normally that attends potassium depletion had two main characteristics: 1)  $U_{\max}$  fell slowly and reached a minimum only when considerable potassium had been lost from the body; yet at the extreme deficits of this study, urine could be concentrated to levels higher than plasma osmolality. 2)  $T^cH_2O$  deteriorated abruptly when potassium was restricted and, even with mild potassium deficits, increasing solute load abolished the U/P osmotic gradient despite maximal ADH activity. While massive solute loading may induce a progressive fall in negative free water clearance and even hypotonic urine in dehydrated dogs, such occurrence in man is unusual, and was unexpected with this moderate degree of solute loading. Similar mannitol infusions in isosthenuric patients with advanced renal disease have not, in our experience, induced urine more dilute than plasma.

A readily demonstrable defect in renal tubular function occurred with degrees of potassium depletion tolerated by other body cells with apparent impunity (27–29). This may be ascribed to an apparent critical vulnerability of the renal tubular epithelium to potassium deficiency; however, comparable techniques to examine other body cells are lacking. Urine concentrating ability was invariably compromised while serum potassium concentration remained within the normal range. The failure of serum concentration of potassium consistently to reflect body stores has been frequently pointed out (2, 30–32) and is probably related at least in part to the level of sodium intake (33, 34).

The intensity and significance of a given potassium deficit must undoubtedly include a temporal factor so that the length of time a given potassium deficit is maintained and the rate at which it developed must probably qualify the pathophysiologic response (22–24, 30). We have tried to induce a mild but acute potassium depletion by reducing potassium content of the dialysis bath of a patient being hemodialyzed for barbiturate poisoning. Water reabsorption was measured during continuous mannitol diuresis. A measured de-

pletion of over 250 mEq of potassium failed to alter water reabsorption acutely.

The mechanism by which the defect is produced is not entirely clear but certain possibilities can be considered. 1) Osmotic diuresis. The inability to concentrate adequately is common to many types of anatomic injury which reduce effective renal mass. Fewer nephrons processing a given solute load produce urine similar to that obtained during osmotic diuresis. The hyposthenuria of potassium depletion cannot be readily ascribed to increased osmotic load per nephron unit, as filtration rate was relatively unimpaired, and the concentrating defect was evident even when the solute load was reduced by feeding a diet restricted in sodium or protein as well as in potassium. 2) Animal studies indicate that there is a lessened hypertonicity of tissue samples taken from the region of the papilla in potassium-depleted animals (35). This may indicate either that less solute has been reabsorbed from the tubular urine or that less solute has been retained *in situ* by the countercurrent system of the medullary vascular bundles. These data indicate that kaliopenic isosthenuria can not be attributed *solely* to ADH refractoriness, unless it is assumed that the permissive action of ADH on water diffusion indirectly regulates medullary blood flow and hence solute retention. A reduced solute concentration in the medulla may prevent efficient operation of the countercurrent multiplier system of the loops of Henle and the collecting ducts by reducing the rate of transfer of water across the tubular cell (36–39).

Even if one assumes that solute reabsorption is altered in potassium deficiency, the source of medullary solute remains unclear. In potassium-deficient rats unable to concentrate urine normally, micropuncture samplings from the distal convolution failed to show altered concentration (38, 40). While this may localize the final concentrating defect in potassium-deficient rats to a more terminal segment of the nephron, possibly the collecting ducts, the possibility that reduced reabsorption of sodium occurred in the loop of Henle or even in the proximal convolution is not entirely negated. Perhaps flow rate rather than concentration of tubular urine was altered. Restrained diffusion of water could have maintained normal plasma/tubular fluid osmotic gradients even while

flow rate was increased so that the volume of water reaching the collecting ducts may have been in excess of concentrating capacity.

The subjects of this report could normally dilute their urine at a time when their concentrating ability had already deteriorated, implying that solute reabsorption during water diureses (presumably the ascending limb of Henle's loop) was adequate for the normal genesis of free water. The redistribution of body fluids with sodium retention, especially the increased extracellular volume that attends potassium deficiency (27-29) if sodium is not restricted, could be expected to alter the excretion of a water load. Extrarenal factors, such as production and renal responsiveness to aldosterone and changes in body fluid volumes, may be produced by potassium depletion and may exert unknown effects on these experiments. Furthermore, extrapolation from water diuresis to hydropenic states may not be valid.

It is attractive to consider the proximal reabsorption of sodium as critical to the diminished concentrating ability in potassium deficiency, for such a concept would not relegate to insignificance the distinct anatomic alterations in the proximal convolution; but, although phenol red and para-aminohippurate are poorly excreted in potassium deficiency, evidence for other "proximal" dysfunction is meager. Salt wastage during rigid sodium restriction might be expected if proximal solute reabsorption were seriously impaired in potassium deficiency, but this is not usual in potassium-depleted states. We would suspect that the defect is a consequence of diminished reabsorption of sodium rather than of impaired equilibration of water. That the hydropenic potassium-deficient subject could still concentrate urine when solute load was kept low implies that the countercurrent system was operating effectively (albeit at limited capacity) and that the countercurrent function must be to some degree independent of the tonicity within the medulla. Reduction in the osmotic gradient between urine and interstitial fluid of the medulla may be adequate to establish a relatively high urine concentration during dehydration when flow rate is very low, but might be inadequate to maintain an effective gradient during osmotic diuresis when flow rate is greatly increased.

Both reduction in volume of filtrate and estab-

lishment of a high osmotic ratio define the conservation of urinary water. The retention of the latter capability at low solute loads may reflect the methodologic inadequacy wherein high solute loads are needed to "unmask" the altered equilibration of water. It was not possible within such protocol to compare widely different rates of solute excretion at identical filtration rates, and the temporal "dissociation" may be an unavoidable artifact reflecting renal hemodynamic changes.

Increased retention of nitrogen and phosphorus that occurred with protein feeding implies storage of protoplasmic nitrogen without potassium, so that the potassium deficiency may have been aggravated at the cellular level, and the somewhat greater concentrating ability that obtains with protein feeding becomes even more significant. It appears that the increased contribution of urea to the peritubular osmolality may overcome in part the deficit in medullary tonicity and hence increases the concentration attained by the final urine.

The effect of urea on the concentrating process may be qualified by the coincident osmotic load, since we were unable to increase water reabsorption by giving urea to potassium-depleted dogs at the height of mannitol diuresis. The failure of urea feeding, which should have increased urea excretion without altering relative potassium deficiency, is unexplained.

#### SUMMARY

Serial studies of urine concentrating ability were performed in man during progressive potassium depletion. A temporal dissociation between the ability to concentrate urine during hydropenia and the capacity to reabsorb water during osmotic diuresis was found.  $U_{\max}$  was resistant to potassium depletion until about 200 mEq of potassium had been lost, progressively fell as the potassium deficit was doubled, and then reached a threshold hypertonic to plasma despite continuing potassium depletion. Free water reabsorption during mannitol diuresis fell abruptly with potassium restriction, and approached zero at a time when appreciable concentrating ability was retained. With more severe potassium deficiency, urine became hypotonic to plasma with solute loading. The capacity to dilute urine after water loading was retained. Some considerations of the

mechanism whereby potassium deficiency may alter water conservation are discussed.

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