in 22 clearance periods in 3 experiments; the ratios reached at least 1.15 in each dog. It is worthy of note that after preparation with oral KCl high rates of potassium excretion were attained with only minimal elevation of the plasma potassium concentration (Table III).

Discussion. The excess of excreted potassium over filtered load was well beyond the limits of experimental error. There is no reason to believe that the filtration rate actually exceeded the creatinine clearance, especially since the inulin and creatinine clearances were the same.

It should be noted that the amount of potassium filtered has been calculated simply as the product of creatinine clearance and plasma potassium. Correction of the filtered potassium for the Donnan equilibrium would lower the filtered load by about 5% and increase the excess of excreted potassium observed in these experiments.

The data obtained constitute evidence for the existence of a mechanism for the addition of potassium to the tubular urine.§ The coexistence of tubular mechanisms for both reabsorption and secretion of a single substance has not previously been demonstrated. Tubular secretion of a number of substances generally considered to undergo only filtration and reabsorption, including potassium, has been suggested by Barclay, Cooke and Kenney,[6] but the evidence on which this conclusion is based is not presented in the published abstract.

Summary and Conclusions. A constant rate of potassium excretion, dissociated from filtered load, occurring after salyrgan administration suggested a tubular secretory mechanism located, presumably, in the distal tubule. The presence of such a mechanism has been demonstrated by the intravenous administration of hypertonic KCl solutions which yielded rates of potassium excretion considerably above the rates of filtration of potassium at the glomerulus.

§ Doctors Mudge, Foulks, and Gilman[5] inform us that they have similarly concluded that potassium is secreted by the renal tubules on the basis of observations during forced osmotic diuresis.

[5] Mudge, G. H., Foulks, J. G., and Gilman, A., personal communication.

[6] Barclay, J. A., Cooke, W. T., and Kenney, R. A., XVII Internat. Physiol. Congress, Abstracts of Communications, 1947, p. 58.

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The Renal Excretion of Potassium.*

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The potassium (K) excreted in the urine under normal circumstances can be accounted for by the tubular rejection of approximately 10% of the calculated filtered K. This has been accepted as evidence that K is excreted by the process of filtration and incomplete reabsorption. The possibility of tubular secretion has been suggested by isolated observations. McCance and Widdowson[1] reported a case of alkalosis and dehydration with a low filtration rate and a K clearance greater than the inulin clearance. Keith, King and Osterberg[2] noted similar K : Inulin clearance

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[1] McCance, R. A., and Widdowson, E. M., *Lancet*, 1937, **2**, 247.

[2] Keith, N. M., King, H. E., and Osterberg, A. E., *Arch. Int. Med.*, 1943, **71**, 675.

ratios in normal subjects receiving KCl, but gave no experimental data and did not mention possible K secretion in subsequent reports.[3] Barclay, Cooke and Kenney[4] stated that K, urea and phosphorus were excreted by the triple process of filtration, reabsorption and secretion, but gave no experimental results. Winkler and Smith[5] observed a maximum excretion of 35% of filtered K in dogs, but noted no evidence of tubular secretion. This preliminary report is submitted because in experiments on dogs we have repeatedly observed K clearances greater than the simultaneously determined filtration rates. In studies on trained dogs infused with KCl, Berliner and Kennedy[6] have also independently observed K excretion in excess of the calculated amount filtered.

Methods. Mongrel dogs were studied under light pentobarbital anesthesia. Conventional clearance techniques and analytical procedures were employed. Creatinine or thiosulfate clearances were used as a measure of the glomerular filtration rate. K was determined by an improved type internal standard flame photometer with an accuracy of ± 1%. K clearances were calculated without correction for the Donnan equilibrium or protein binding.

Results. In studies on the electrolyte excretion associated with urea diuresis, K clearances increased from 5-10% of the creatinine clearance at normal rates of urine flow to 80-90% of the creatinine clearance during marked diuresis with minute urine volumes of 18 to 35 cc and at creatinine U/P ratios of approximately 2. At lower creatinine U/P ratios the C_K/C_{cr} ratio exceeded 1 by as much as 0.36 without the administration of exogenous K. Under these circumstances the urea clearance/creatinine

TABLE 1.
Effect of Urea Diuresis on the U/P Ratios of Creatinine and Potassium.

Elapsed time, min.	KCl infusion rate, mEq/min.	Urine vol., cc/min.	Serum K, mEq/L	Serum urea, mOsM/L	C urea / C_{Cr}	U/P Cr	U/P K	U/P K / U/P Cr
10	0	1.7	4.4	2.9	.58	27.9	2.4	.09
20	KCl infusion started.							
160	.450	8.2	10.3	2.3	.72	7.6	4.6	.60
161	50% urea infusion started at 12.5 mOsM/min.							
180	.450	9.2	10.4	15.8	.66	5.02	3.7	.74
235	.350	—	10.6	—	—	1.41	1.53	1.09
255	.163	22.5	7.3	276	.88	1.82	2.37	1.30
275	.300	12.2	6.9	247	.81	2.15	2.99	1.39
295	.300	14.4	8.9	326	.85	1.33	1.60	1.20
310	.500	—	10.6	—	—	1.34	1.50	1.12

[3] Keith, N. M., and Osterberg, A. E., *J. Clin. Invest.*, 1947, **26**, 773.

[4] Barclay, J. A., Cooke, W. T., and Kenney, R. A., *XVII Internat. Physiol. Congress, 1947, Abstracts*, page 58.

[5] Winkler, A. W., and Smith, P. K., *Am. J. Physiol.*, 1942, **138**, 94.

[6] Berliner, R. W., and Kennedy, J. P., personal communication.

TABLE II
Effect of $NaHCO_3$ on the Renal Clearance of Potassium and Thiosulfate.

Elapsed time, min.	Urine vol., cc/min.	Serum K, mEq/L	Urine pH	Clearance S_2O_3 cc/min.	Clearance K cc/min.	$\frac{C_K}{C_{S_2O_3}}$
—143	Start of constant infusion .375 mEq KCl/min., maintained during entire experiment.					
0-20	3.8	7.3	5.6	56.8	67.5	1.19
40-60	1.8	6.9	5.6	55.7	53.4	.96
80-100	2.0	5.8	5.4	52.7	49.4	.94
120-140	2.6	6.3	5.6	51.2	46.8	.92
150-170	3.1	6.7	5.6	53.1	47.7	.90
	I.v. infusion of 200 mEq $NaHCO_3$ in 1 L. in 35 min.					
210-230	15.7	5.0	7.8	54.0	65.8	1.22
235-255	8.5	4.7	7.8	52.6	67.3	1.28
260-280	6.6	4.7	8.1	55.5	60.3	1.09

clearance ratios averaged .83 and never exceeded 1.0. In the sample protocol (Table I) both K and urea were infused and due to ECG changes the K infusion rate was not constant and therefore "spot" U/P ratios were taken.

Because of the elevation of urine pH occurring during marked urea diuresis and because of the observation of Darrow[7] that alkalosis is associated with K depletion when renal function is normal, the effect of alkalosis was studied in dogs receiving KCl by intravenous infusion. Under these conditions K clearances greater than filtration rates were also demonstrated (Table II).

C_K/C_{cr} ratios above 1 were observed in 7 different dogs with filtration rates varying from 23 to 75 cc per minute. K excretion in excess of filtration was not observed in every experiment. Factors which favored C_K/C_{cr} ratios greater than 1 were: (1) a moderate, rather than marked elevation of serum K when KCl was infused, (2) a decline in filtration rate which usually accompanied extreme urea diuresis, and (3) the duration of the KCl infusion. The first two factors would help reveal a secretory mechanism in the face of partial reabsorption of K. The third may represent a physiological adjustment.

Discussion and Conclusions. K clearances in excess of creatinine or thiosulfate clearances, under the conditions of these experiments, are interpreted as evidence that all of the K excreted in the urine cannot be accounted for by the filtration-reabsorption theory alone, but that tubular secretion of K also occurs. In the experiments on urea diuresis, urea clearances never exceeded creatinine clearances, and the ratios agreed with the observations of Shannon.[8] It is a reasonable hypothesis that during urea diuresis the secretion of K becomes apparent because its normal tubular reabsorption is hindered. The present data are insufficient to define the mechanisms involved in the secretory process or to demonstrate the relative magnitude of the processes of filtration, reabsorption and secretion in the renal excretion of K. Further work is in progress.

[7] Darrow, D. C., *J. Clin. Invest.*, 1946, **25**, 324.

[8] Shannon, J. A., *Am. J. Physiol.*, 1938, **122**, 782.