Renal Tubular Secretion of Magnesium in Dogs.* (25063)

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The mechanism for renal excretion of magnesium has not been determined. Since Bieter(1) demonstrated that magnesium is excreted by the aglomerular fish kidney, the possibility of tubular excretion of magnesium by the mammalian kidney has remained an open question despite several previous studies utilizing conventional clearance technics(2,3,4). Development of the "stop flow" technic for localization of transtubular transport along the nephrons(5,6) has afforded a new approach for study of this problem in animals.

Method. Six female dogs were anesthetized with intravenous pentobarbital in doses not in excess of 30 mg/kg. The right ureter was cannulated with polyethylene tubing which was advanced to just below the junction of ureter and pelvis and tied securely. The other ureter was cannulated and allowed to drain freely. A priming dose of creatinine (0.08 g/kg) was given intravenously over a period of one minute. 20% mannitol in 0.8% sodium chloride and 0.2% creatinine was administered intravenously by means of a constant infusion pump at a rate of 10 ml per minute. An equilibration period of 45 minutes was allowed. The ureteral catheter was clamped for a period of 6 to 8 minutes. Two minutes prior to release of the clamp a solution containing 150 mg para-amino hippurate (PAH), 1 g inulin, and 6.3 to 25.0 μc magnesium 28 (Mg^{28}) (125 to 500 mg $Mg(OH)_2$) was injected over a period of 2 minutes. The ureteral clamp was then released and serial urine samples of approximately 0.6 ml were collected. Volume, radioactivity, PAH, inulin, creatinine, sodium and potassium concentrations and pH were determined on all urine samples and on three 3-minute additional control samples prior to and following the occluded periods. Blood samples were collected just prior to and immediately following the occluded interval for plasma magnesium, creatinine, sodium and potassium concentrations. Creatinine U/P ratios were used to correct for water reabsorption along the nephrons. PAH was determined according to Smith(7), creatinine by the method of Bonsnes and Taussky (8) and inulin according to Schreiner(9). Sodium and potassium were analyzed with a Baird internal standard flame photometer, and radioactivity was counted utilizing a well type scintillation counter. Volume of the serial urine samples was determined by weight.

Results. Fig. 1 illustrates an example typical of the 6 experiments and the drawing at the top of the figure represents interpretation of its significance. Mg^{28} appeared in the fourth urine sample and radioactivity gradually increased until the filtered samples began to appear, whereupon the radioactivity showed a second pronounced rise. Mg^{28} appeared just proximal to the sharp peaks in pH change and in potassium change, 8 samples prior to the appearance of PAH, and 16 samples prior to the appearance of inulin. The variable level of plasma magnesium obtained in our 6 experiments (1.79 to 4.53 meq/l) did not influence the apparent site at which Mg^{28} appeared in the urine samples. All experiments yielded similar results (Table I).

Discussion. Renal magnesium excretion by a secretory process has been demonstrated in the aglomerular fish by the high content of magnesium in the urine(1,10). Whether or not such a process exists in the mammalian kidney has been a more difficult problem, although suggested by Hirshfelder(11) as early as 1934. Previous observations in normal men and in patients with chronic renal disease(2,3) were inconclusive. Experimental observations in dogs with magnesium loading revealed that in some dogs a ratio of slightly above unity (1.1) was attained for magnesium excreted over magnesium filtered when the amount of magnesium filtered was calculated from the ultrafiltrable concentration of mag-

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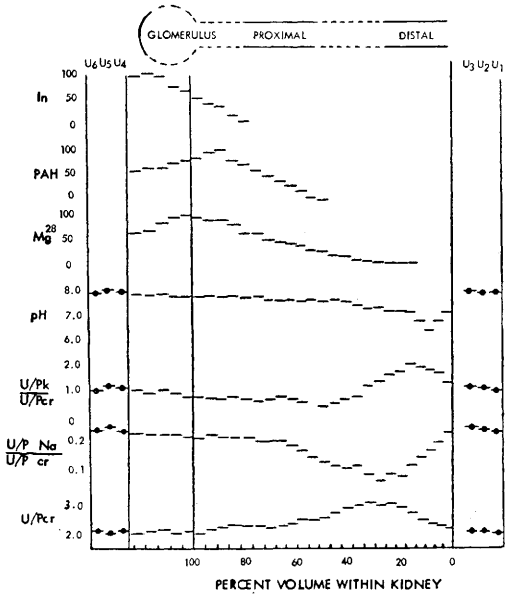

FIG. 1. Results of "stop-flow" analysis using magnesium-28. Magnesium-28 counts, inulin, and PAH are recorded in % of maximum excreted. Urine volume is recorded in % within the kidney using all samples distal to 50% maximal inulin excretion.

nesium in plasma(4). These data suggested, but were inconclusive evidence of, renal tubular secretion of magnesium. Recently Robinson *et al.*(12) have also stated that nonfiltered Mg^{28} can enter the renal tubule.

The pitfalls of the present technic are: nephrons are of variable lengths and have variable transit times; there is necessarily some mixing of fluid from the various nephrons at site of the renal pelvis; the nephrons are subjected to a highly abnormal, marked osmotic diuresis; the column of fluid is acted upon under a static condition; and, the more proximal fluid must pass through the more distal tubule and thereby has been acted upon by the more distal tubular epithelium. Nevertheless, the samples follow an orderly and characteristic pattern resulting in an informative degree of localization of tubular function.

TABLE I. Results Obtained in 6 Dogs Using "Stop-Flow" Analysis and Magnesium-28. Values given represent % level in nephron where the various substances appear.

Dog	Magnesium-28	PAH	Inulin
1	20	56	79
2	17	55	77
3	19	57	72
4	16	47	74
5	19	52	75
6	14	47	76
Mean & S.D.	17.50 ± 2.06	52.33 ± 4.11	75.50 ± 2.22

We consistently found that Mg^{28} appeared in the tubular urine distal to excretion of inulin and PAH. This is strongly suggestive that magnesium is secreted by the distal tubule.

Summary. Excretion of magnesium has been studied in dogs utilizing the "stop-flow" technic and Mg^{28}. The evidence indicates that magnesium is secreted by the distal tubule.

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