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Effect of Probenecid on Urate Excretion in the Cat Kidney

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= ABSTRACT =

The characteristics of probenecid effect on renal urate excretion in the cat were studied by clearance method and compared with those in the rabbit. In the cat GFR was 3.03±0.09 ml/min·kg, and endogenous plasma urate concentration was 1.12±0.57 μg/ml, which is less than that in the rabbit (3.33±0.46 μg/ml). In the rabbit, FE_{Ur} was 1.76±0.08 and net urate secretion was observed, while, in the cat FE_{Ur} was 0.70±0.02 and net reabsorption was observed. In the cat FE_{Ur} was dependent on urine flow and independent of plasma urate concentration. In the rabbit FE_{Ur} was suppressed by infusion of probenecid (30 mg/kg - 0.6 mg/kg·min) into femoral vein. In the cat the same dose of probenecid increased FE_{Ur}, and concomitantly increased urine flow. Thus, an increase in FE_{Ur} by probenecid could be considered to be resulted from a change in urine flow. In the cat infusion of probenecid (2.5 mg/kg·min) into renal artery markedly suppressed FE_{PAH}, but the effects on FE_{Ur} and urine flow were similar to those when probenecid was infused into femoral vein. These results indicate that in the cat kidney urate filtered through glomerulus is reabsorbed by a probenecid-insensitive mechanism with no evidence for net secretion.

Key Words: Uric acid, *p*-Aminohippuric acid, Probenecid, Cat kidney.

INTRODUCTION

Urate is filtered by the glomerulus and transported bidirectionally in renal tubules (Weiner, 1979; Roch-Ramel & Weiner, 1980). Thus, the urate appearing in the final urine results from a complex modification of filtration, tubular reabsorption and secretion.

It has been known that the relative importance of reabsorption and secretion of urate is different from species to species (Weiner, 1979). Zins and Weiner (1968) have developed a classification of renal urate transport based on types of tubular activity. In the first group, birds and reptiles, urate is secreted strongly with reabsorption being minimal or absent. In the second group represented by Dalmantian coach hound and guinea pig, secretion usually predominates, but reabsorp tion may be observed by inhibiting secretion pharmacologically. In the third group examplified by the rabbit, either net reabsorption or net secretion is seen with about equal frequency. The fourth group is one in which tubular reabsorption normally predominates but secretion may be demonstrable under certain circumstances. This includes man, some of the other primates, and rat.

p-Aminohippurate (PAH) inhibits competitively the urate excretion in the rabbit (Møller, 1967a; Møller, 1967b), pig (Roch-Ramel et al, 1980; Schali & Roch-Ramel, 1981), but no effect in man, chimpanzee (Fanelli et al, 1970; Weiner & Tinker, 1972), snake (Dan-

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tzler, 1970), dog (Perez-Gonzalez & Weiner, 1983; Russel et al, 1988) and guinea pig (Perez-Gonzalez & Weiner, 1983). Probenecid has uricosuric effect in the species that reabsorption is predominant, while it has inhibitory effect on urate excretion in the species that secretion is predominant. Thus, there is species difference in response of urate excretion by other organic anions, suggesting that mechanism of the tubular transport of urate is different from that of PAH in some species.

Owing to the diversity of the renal handling of urate, the tubular transport of urate was extensively studied in various species. Until now, little has been known, however, about the handling of urate by the cat kidney. The only data on the cat are the report of Mudge (1965) who found slightly proximal reabsorption without evidence for secretion but was unble to show convincing durg effects.

This study thus was designed to investigate characteristics of renal urate excretion in the cat and compare with those of the rabbit.

METHODS

Clearance experiments

Experiments were performed on the cat and New Zealand White rabbit of both sexes ranging in body weight from approximately 1.5 to 2.5 kg.

Cats were anesthetized with thiopental sodium (25 mg/kg) by intravenous injection and maintained anesthetic state throughout the study by giving 5 mg/kg of thiopental sodium intravenously every thirty minutes. Rabbits were anesthetized with ketamine (10 mg/kg) and xylazine (4 mg/kg) given by intravenous and intramuscular injection, respectively.

Solutions were infused through femoral vein, and blood was sampled by femoral artery. The bladder was catheterized through a suprapubic incision for urine sampling. In experiments for infusion of probenecid into the renal artery, the catheter was inserted upwardly from the low abdominal aorta for its tip to be located slightly below the both renal arteries, and abdominal aorta with catheter was tied with silk above the superior mesenteric artery.

In experiments for a gradual increase in plasma urate concentration, infusion solution contained lithium urate from 0.25 mg/ml to 3 mg/ml.

A priming dose of urate (5 mg/kg) or PAH (10 mg/kg) was injected and followed by a sustaining infusion of saline containing 3% mannitol and urate (0.5 mg/ml) or PAH (0.2 mg/ml) at a rate of 1 ml/min. After an equilibrium period of approximate 1 hour, urine was collected during four 10-min control clearance periods and blood was sampled at the midpoint of each period.

When the effect of probenecid was examined, a priming dose of 30 mg/kg of probenecid after the control periods was infused through the femoral vein and followed by a sustaining infusion of a dose of 0.6 mg/kg·min. After infusion of probenecid, five 10-min collections of urine and blood were made. In experiments for the renal arterial infusion, probenecid was given as a dose of 2.5 mg/kg·min.

Analytical method

PAH in plasma and urine was determined by the method of Smith et al (1945). Urate and creatinine concentration in plasma and urine were analyzed with Atron chemicals kit, using a uricase method and a picric acid method, respectively. Lithium urate was prepared by mixing uric acid and lithium carbonate.

Data handling and analysis

Glomerular filtration rate (GFR) was calculated by creatinine clearance (C_{Cr}). PAH clearance (C_{PAH}), PAH fractional excretion (FE_{PAH}) were calculated in the general manner.

Difference between experimental means determined by Student's *t*-test. A probability level less than 0.05 was accepted as signifi-

cant.

RESULTS

Control values for renal function in the cat and rabbit

Control values for various parameters of renal function in the cat and rabbit are presented in Table 1. Endogenous plasma urate concentration in the cat was 1.12±0.57 μg/ml but in some cases were not detectable, which was lower than that in the rabbit (3.33±0.46 μg/ml) and lower by about 1 order of magnitude than those reported in most common laboratory mammals (Roch-Ramel & Peters, 1978). Since the activity of uricase in the cat has been known to be lower than that of dog and similar to other laboratory animals (Truszkowski & Goldmanowna, 1933), this value is very impressive.

GFR in the cat was 3.03±0.09 ml/min·kg, which is similar to that reported by other investigators (Friedman & Roch-Ramel, 1977; Kim et al, 1982) and less than that obtained in the rabbit (4.08±0.19 ml/min·kg). During exogenous infusion of urate, urate clearance and FE_{Ur} were 2.12±0.10 ml/min·kg and 0.70 ±0.02, respectively, indicating that approximately 70% of filtered urate was excreted. These values in the rabbit were 6.75±0.27 ml /min·kg and 1.76±0.08, respectively, which reflects net secretion of urate, in agreement with data reported by others (Poulsen & Praetorius, 1954; Donoso & Grantham, 1986). During all experimental periods after exogenous infusion of urate in this study, plasma urate concentration in the cat was maintained in the range of 5 to 20 μg/ml (molar concentration of approximate 30 to 120 μM). Ratio of urine to plasma urate concentration in the cat was 12.66±0.74, which

Table 1. Summary of control values for renal function in the cat and rabbit

Parameter	Cat		Rabbit	
	Mean ± SE (Range)	n[a]	Mean ± SE (Range)	n[a]
GFR(ml/min·kg)	3.03 ± 0.09 (1.65 − 5.22)	22	4.08 ± 0.19 (1.40 − 7.47)	10
C_{Ur}(ml/min·kg)	2.12 ± 0.10 (1.03 − 4.07)	22	6.75 ± 0.27 (3.53 −12.26)	10
FE_{Ur}	0.70 ± 0.02 (0.31 − 1.16)	22	1,76 ± 0.08 (1.12 − 4.07)	10
$(U/P)_{Ur}$	12.66 ± 0.74 (4.06 −33.89)	22	27.21 ± 1.90 (14.75 −67.54)	10
Endogenous P_{Ur}(μg/ml)	1.12 ± 0.57 (N.D.[b] − 5.90)	11	3.33 ± 0.46 (0.79 − 5.24)	8
C_{PAH}(ml/min·kg)	12.90 ± 0.49 (10.38 −19.54)	4	15.30 ± 1.25 (11.54 −22.41)	4
FE_{PAH}	3.94 ± 0.22 (2.72 − 6.65)	4	4.12 ± 0.76 (2.54 − 6.87)	4

Values are means±SE of n animals.

Abbreviations used: GFR, glomerular filtration rate; C_{Ur}, urate clearance; FE_{Ur}, fractional urate excretion; $(U/P)_{Ur}$, urine/plasma ratio of urate concentration; P_{Ur}, plasma urate concentration;C_{PAH}, PAH clearance; FE_{PAH}, fractional PAH excretion.

[a] Number of observations.

[b] N.D., not detectable.

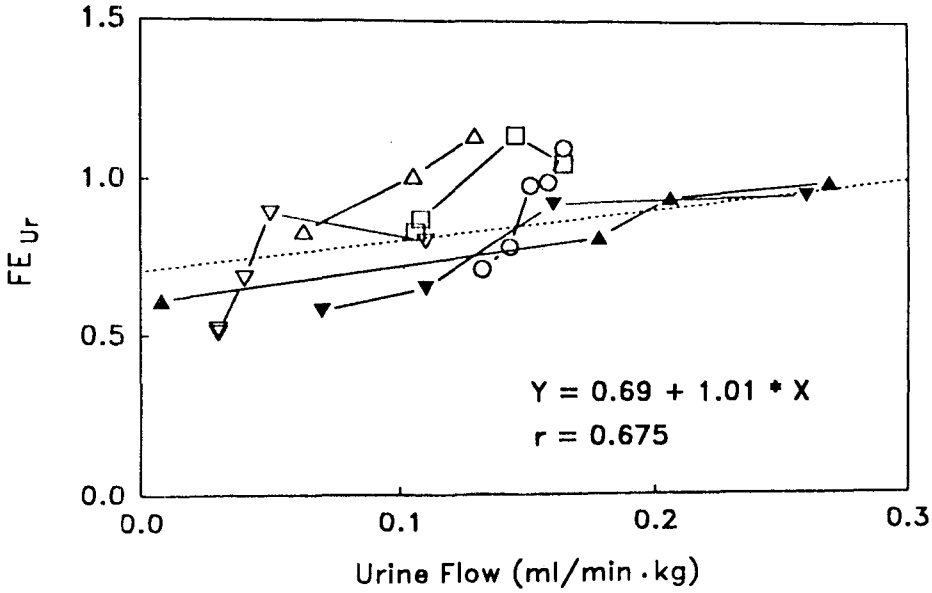

Fig. 1. Relationship between urine flow and FE_{Ur} in the cat. Dashed line is the regression line calculated by the method of least squares. Data are obtained from six animals. Each symbol and line is the result from different subject.

was significantly less than that in the rabbit (27.21±1.90).

PAH clearance and FE_{PAH} for the cat obtained from this study were 12.90±0.49 ml/min·kg and 3.94±0.22, respectively, and similar to those of rabbit (15.30±1.25 ml/min·kg and 4.12±0.76). These values for the cat were in agreement with those reported by other workers (Friedman & Roch-Ramel, 1977; Kim et al, 1982; Eggleton & Habib, 1950).

Effect of urine flow on urate excretion in the cat

The relationship between FE_{Ur} and urine flow in the cat was presented in Fig. 1. The urinary excretion of urate was dependent on urine flow, showing significant increase in FE_{Ur} with increased urine flow ($P<0.01$). This result is similar to those reported in man (Gutman et al, 1959; Gutman & Yü, 1960), mongrel dog (Kessler et al, 1959) and rat (Lang et al, 1974) in which urate reabsorption is predominant.

Fig. 2 shows the relationship between urine flow and plasma urate concentration When plasma urate concentration increased from endogenous level to 400μg/ml by continuous infusion of lithium urate, the urine flow was decreased dependently.

Effect of plasma urate concentration on urate excretion in the cat

Fig. 3 shows the relationship between FE_{Ur} and plasma urate concentration ranging from endogenous level to 100 μg/ml at which plasma urate has not an effect on urine flow. FE_{Ur} were independent of plasma urate concentration, unlike the rabbit in which FE_{Ur} was increased dependently by elevating plasma urate concentration (Donoso & Grantham, 1986).

In the cat renal urate excretion and reabsorption rates as a function of plasma urate concentration are presented in Fig. 4. The rate of urate excretion was linearly increased with increased plasma urate concentration. The amount of urate excreted was less than that filtered in most cases, suggesting the net

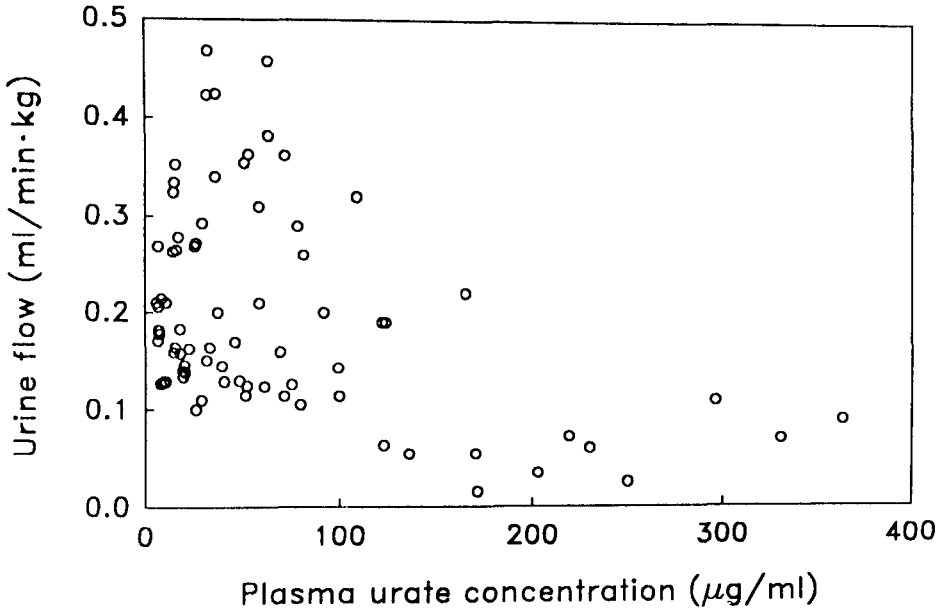

Fig. 2. Relationship between plasma urate concentration and urine flow in the cat. Data are obtained from nine cats.

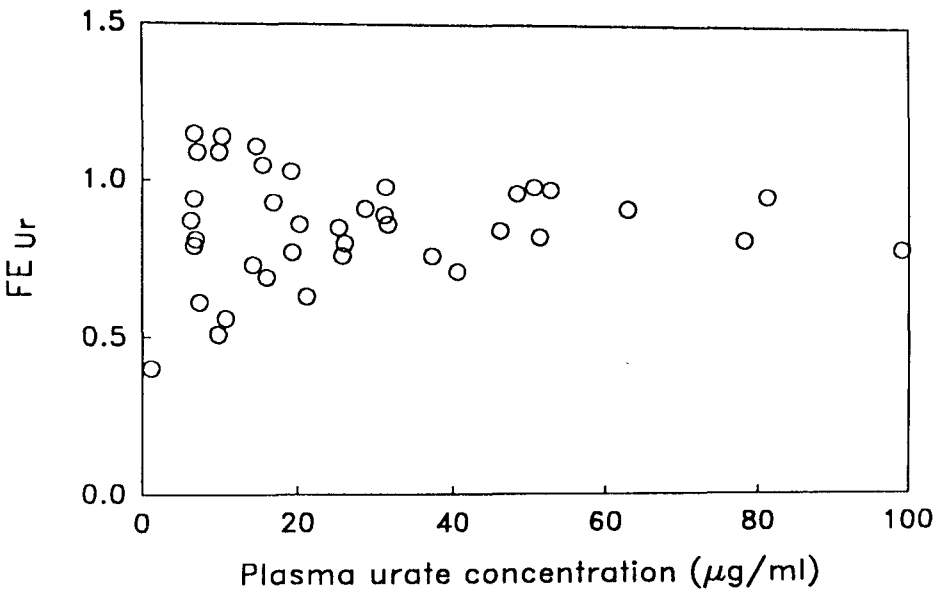

Fig. 3. Relationship between plasma urate concentration and FE_{Ur} in the cat. Data are obtained from nine cats.

tubular reabsorption. In contrast, the amount of urate excretion in the rabbit was larger than that filtered, indicating the net tubular secretion (Fig. 4).

Changes in urate excretion during systemic infusion of probenecid

In next series of experiments, effect of probenecid on urate excretion was examined in the cat and rabbit. As shown in Table 2 and Fig. 5, administration of probenecid in the cat resulted in slightly but a significant increase in FE_{Ur}. However, the urine flow was concomitantly increased after infusion of probenecid.

It is thus considered that an increase in

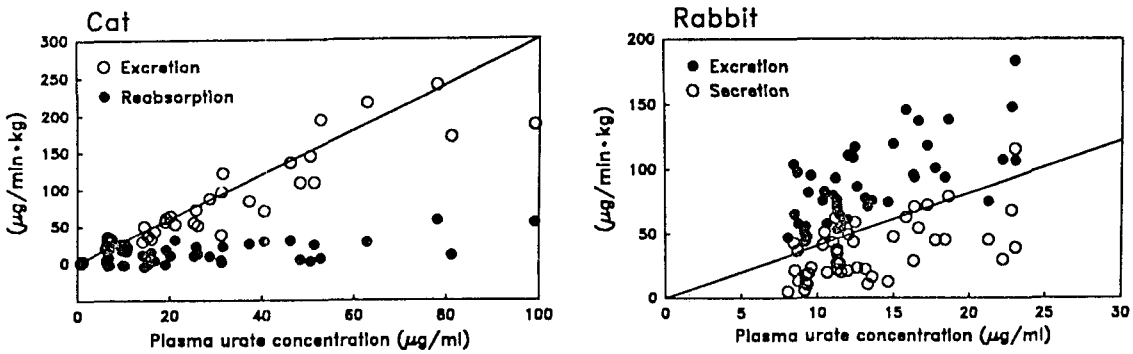

Fig. 4. Renal fitration, excretion, and reabsorption or secretion of urate, plotted as a function of plasma urate concentration in the cat (upper) and rabbit (lower). .Solid line is filtered urate load. Reabsorption and secretion were calculated from difference of filtered urate load and excretion rate of urate. Data for cat and rabbit are obtained from nine and eleven animals, respectively.

Table 2. Effect of probenecid on urate excretion in the cat

Time (min)	V (ml/min·kg)	P_{Ur} (μg/ml)	GFR (ml/min·kg)	$(U/P)_{Ur}$	C_{Ur} (ml/min·kg)	Ur excreted (μg/min·kg)	FE_{Ur}
0	Priming infusion: urate(5 mg/kg)						
40	Sustaining infusion: saline containing mannitol(30 mg/ml) and urate(0.25 mg/min·kg)						
60~ 70	0.174±0.037	13.83±3.25	3.775±0.459	15.35±1.54	2.652±0.480	31.53±4.64	0.70±0.09
70~ 80	0.174±0.038	15.01±3.01	3.248±0.346	12.11±1.05	2.185±0.385	27.30±3.40	0.65±0.09
80~ 90	0.191±0.049	13.63±2.07	3.292±0.486	12.21±1.60	2.297±0.469	26.67±4.52	0.65±0.07
90~100	0.195±0.047	11.90±0.99	3.515±0.317	11.55±1.88	2.600±0.266	30.22±3.18	0.71±0.03
	Probenecid infusion: priming dose; 30 mg/kg, sustaining dose; 0.6 mg/min·kg						
100~110	0.275±0.076	12,67±2.24	3.328±0.613	9.88±1.35	2.287±0.377	24.78±3.54	0.69±0.03
110~120	0.279±0.069	11.96±2.26	3.348±0.347	10.50±1.23	2.609±0.252	28.82±3.25	0.79±0.05
120~130	0.278±0.061	12.46±2.41	3.411±0.332	10.08±1.27	2.506±0.140	30.48±5.54	0.76±0.06
130~140	0.253±0.046	13.35±2.90	3.239±0.315	9.41±1.00	2.222±0.121	28.66±5.42	0.71±0.05
140~150	0.266±0.059	15.32±3.39	3.288±0.359	9.80±1.18	2.371±0.237	32.04±2.84	0.73±0.06

Data are the mean±SE of six animals.

Abbreviations used: V, urine flow; Ur, urate; P_{Ur}, plasma urate concentration; $(U/P)_{Ur}$, urine/plasma ratio of urate concentration; C_{Ur}, urate clearance; FE_{Ur}, fractional urate excretion

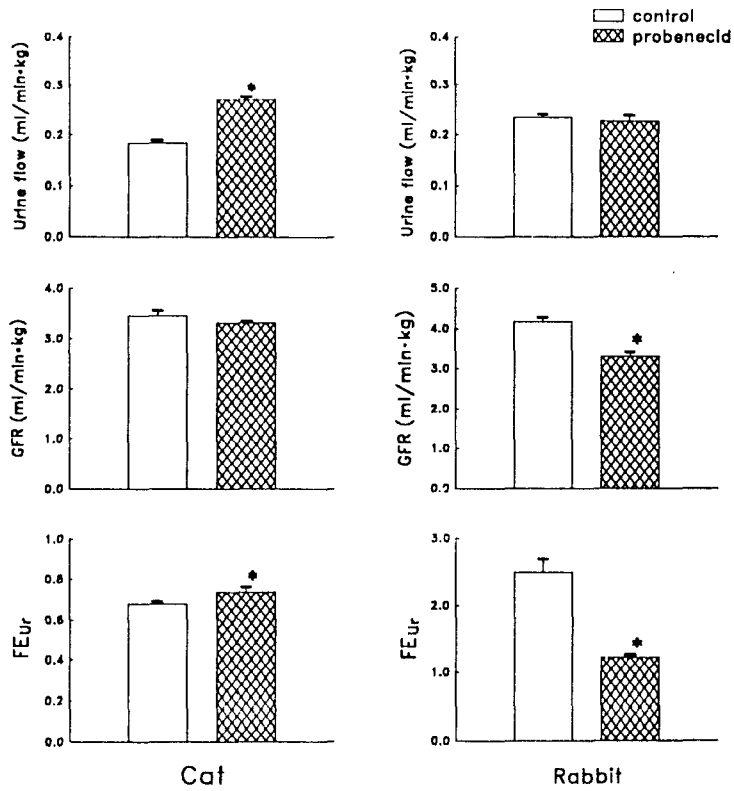

*Fig. 5. Effects of systemic infusion of probenecid on urate excretion in the cat and rabbit. Experimental conditions were the same as table 2 and 3. All data are obtained from 4 animals. *P<0.05, vs. control.*

Table 3. Effect of probenecid on urate excretion in the rabbit

Time (min)	V (ml/min·kg)	P_{Ur} (μg/ml)	GFR (ml/min·kg)	$(U/P)_{Ur}$	C_{Ur} (ml/min·kg)	Ur excreted (μg/min·kg)	FE_{Ur}
0	Priming infusion: urate(5 mg/kg)						
40	Sustaining infusion: saline containing mannitol(30 mg/ml) and urate(0.25 mg/min·kg)						
60~ 70	0.23±0.05	11.15±2.41	4.16±0.34	42.35± 9.28	8.10±1.06	82.92±17.40	2.08±0.47
70~ 80	0.25±0.04	11.03±2.24	4.40±0.33	42.50±10.06	9.32±1.64	89.21±13.75	2.28±0.61
80~ 90	0.24±0.03	11.36±2.43	4.03±0.36	39.54± 9.45	8.73±1.79	82.79±13.04	2.41±0.77
90~100	0.21±0.02	7.92±2.23	4.09±0.59	52.95± 0.88	11.29±1.25	78.34±15.28	3.20±0.77
	Probenecid infusion; priming dose; 30 mg/kg, sustaining dose; 0.6 mg/min·kg						
100~110	0.22±0.03	12.01±3.34	3.63±0.30	23.26±5.10	4.48±0.54	47.94± 9.75	1.26±0.19
110~120	0.23±0.05	11.43±2.64	3.45±0.28	21.91±4.93	4.24±0.48	45.36± 9.05	1.24±0.14
120~130	0.21±0.04	11.53±2.74	3.28±0.38	22.56±4.66	4.05±0.26	46.81±10.84	1.30±0.17
130~140	0.20±0.03	12.22±2.57	3.00±0.46	20.31±4.86	3.56±0.57	47.48±12.36	1.18±0.03
140~150	0.27±0.04	9.85±2.49	3.19±0.57	15.94±4.44	3.59±0.58	41.11±14.63	1.14±0.02

Data are the mean±SE of six animals.
Abbreviations used: the same as table 2.

FE_{Ur} by probenecid results from increase in urine flow rather than a direct inhibition of urate tubular reabsorption.

In contrast, the same dose of probenecid in the rabbit inhibited significantly FE_{Ur} from 2.49±0.21 to 1.22±0.03, without an effect on urine flow (Table 3 and Fig. 5). This means that urate secretion was strongly sup-

Table 4. Effect of probenecid infusion into the renal artery on urate excretion in the cat

Time (min)	V (ml/min·kg)	P_{Ur} (μg/ml)	GFR (ml/min·kg)	$(U/P)_{Ur}$	C_{Ur} (ml/min·kg)	Ur excreted (μg/min·kg)	FE_{Ur}
0	Priming infusion: urate(5 mg/kg)						
40	Sustaining infusion: 0.6 ml/min saline containing mannitol(30 mg/ml) and urate(0.25 mg/min·kg)						
60~ 70	0.22±0.06	10.56±1.62	3.03±0.26	8.16±0.57	1.81±0.50	18.58±4.73	0.56±0.10
70~ 80	0.23±0.05	11.36±1.64	3.11±0.22	7.50±0.49	1.66±0.33	18.52±3.61	0.53±0.08
80~ 90	0.25±0.05	12.10±1.32	3.19±0.29	6.97±0.59	1.66±0.32	19.94±3.93	0.51±0.07
90~100	0.27±0.06	11.82±1.36	3.01±0.26	7.36±0.85	1.79±0.36	20.36±3.47	0.58±0.07
	Probenecid infusion: 0.6 ml/min saline containing probenecid(2.5 mg/min·kg)						
100~110	0.28±0.05	9.90±1.88	3.13±0.28	6.35±0.83	1.69±0.30	16.80±3.89	0.54±0.08
110~120	0.32±0.06	9.20±2.03	2.92±0.28	6.15±1.10	1.77±0.33	15.61±3.65	0.61±0.09
120~130	0.33±0.07	8.58±2.26	2.98±0.42	5.90±1.19	1.83±0.59	15.72±5.28	0.61±0.15
130~140	0.35±0.07	9.51±1.86	2.85±0.28	5.12±0.84	1.69±0.45	16.05±4.73	0.57±0.10
140~150	0.32±0.06	8.79±2.06	2.68±0.18	5.76±1.44	1.81±0.55	13.82±3.16	0.69±0.22

Data are the mean±SE of six animals.

Abbreviations used: the same as table 2.

Table 5. Effect of probenecid infusion into the renal artery on PAH excretion in the cat

Time (min)	V (ml/min·kg)	P_{Ur} (μg/ml)	GFR (ml/min·kg)	$(U/P)_{Ur}$	C_{Ur} (ml/min·kg)	Ur excreted (μg/min·kg)	FE_{Ur}
0	Priming infusion: PAH(10 mg/kg)						
40	Sustaining infusion: 0.6 ml/min saline containing mannitol(30 mg/ml) and PAH(0.1 mg/min·kg)						
60~ 70	0.36±0.11	45.56±1.92	3.39±0.27	55.23±14.38	14.25±0.70	646.7±28.18	4.34±0.47
70~ 80	0.34±0.08	37.95±1.46	3.45±0.09	42.37± 9.04	12.07±0.47	457.4±22.59	3.51±0.17
80~ 90	0.33±0.05	32.02±2.61	3.46±0.14	42.59± 9.44	12.09±0.42	384.2±25.75	3.53±0.23
90~100	0.31±0.05	27.08±2.57	3.28±0.05	43.06± 7.47	12.11±1.12	319.7±19.74	3.72±0.40
	Probenecid infusion: 0.6 ml/min saline containing probenecid(2.5 mg/min·kg)						
100~110	0.34±0.08	40.13±2.39	3.39±0.21	16.16±3.93	4.46±0.31	176.2±5.68	1.36±0.17
110~120	0.35±0.08	42.79±3.38	3.11±0.20	14.69±4.41	3.89±0.46	160.3±7.36	1.30±0.23
120~130	0.38±0.09	50.32±3.16	3.11±0.21	9.80±1.84	3.05±0.12	153.6±11.20	1.00±0.09
130~140	0.39±0.09	54.38±3.89	3.10±0.29	10.85±2.99	3.25±0.28	173.3±9.98	1.09±0.15
140~150	0.38±0.08	56.96±4.69	2.97±0.32	9.16±1.82	2.92±0.25	166.5±20.74	1.00±0.07

Data are the mean±SE of six animals.

Abbreviations used: V, urine flow; P_{PAH}, plasma PAH concentration; $(U/P)_{PAH}$, urine/plasma ratio of PAH concentration; C_{PAH}, PAH clearance; FE_{PAH}, fractional PAH excretion

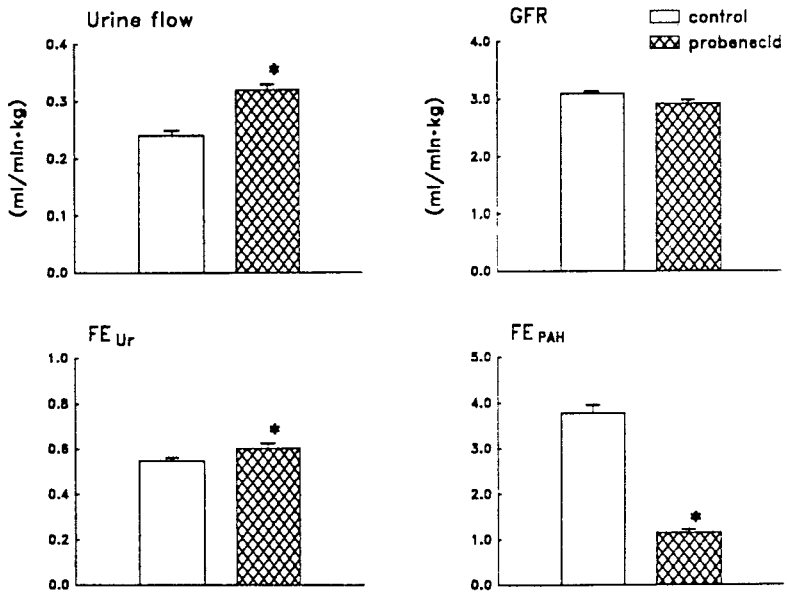

*Fig. 6. Effects of renal artery infusion of probenecid on urate and PAH excretion in the cat. Experimental conditions were the same as table 4 and table 5. All data are obtained from 4 animals. *P<0.05, vs. control.*

pressed by probenecid in the rabbit..

Changes in urate excretion during renal artery infusion of probenecid

To further clarify the effect of probenecid on urate excretion in the cat, probenecid (2.5 mg/min·kg) was infused into renal artery. As shown in Table 4 and Fig. 6, probenecid increased significantly both urine flow and FE_{Ur}, similarly to that presented by systemic infusion of probenecid (Fig. 5).

In order to test whether probenecid concentration used in this study affects excretion of other organic acid in the cat, the effect of the same dose of probenecid on PAH excretion was studied (Table 5 and Fig. 6). As expected, FE_{PAH} was remarkably reduced from 3.78 ± 0.19 to 1.15 ± 0.07 by infusion of probenecid. This reveals that the dose of probenecid used in this study for the cat is sufficient for blocking the transport system of organic anion such as PAH.

DISCUSSION

Although the urate excretion in mammalian kidney has been extensively studied (Weiner, 1979; Møller & Sheikh 1983), little information is available on the renal handling of urate in the cat. This study provides information about the characteristics of urate excretion in the cat.

General pattern of urate excretion

FE_{Ur} is highly variable among species (Weiner, 1979; Roch-Ramel & Weiner, 1980). In this study FE_{Ur} measured in 22 cats was 0.70 ± 0.02, indicating that approximate 30% of filtered urate amount was reabsorbed by the renal tubule. This result is similar to the report of Mudge (1965) who found a slight reabsorption in the cat. FE_{Ur} in the rabbit was 1.76 ± 0.08 similar to those reported in other studies (Donoso & Grantham, 1986), indicat-

ing net secretion.

Since solutes impermeable to renal tubular epithelium would not be reabsorbed by the nonionic diffusion, their renal excretion have been known to be independent on the urine flow (Steele & Rieselbach, 1976). Most of urate with pKa of 5.75 would be present as a dissociation form in the proximal tubular lumen, and urate also has a low solubility in organic lipophilic solvents. Therefore, it was expected that the renal excretion of urate would be independent on the urine flow in the cat. But in this study urate excretion was highly dependent to urine flow (Fig. 1). This result suggests, but not proved, that a small amount of diffusion may occur from urine of high urate concentration in the most distal portion of the nephron, the collecting duct, or the pelvis, ureter, or bladder.

Probenecid effect of urate excretion

Probenecid has been known to be a very potent competitive inhibitor of urate transport and effective in plasma and luminal sides in mammalian kidney (Mudge et al, 1973; Weiner, 1973). Probenecid causes uricosuria by inhibition of urate reabsorption in species showing net reabsorption, such as human (Mudge, 1965; Dayton et al, 1963; Sirota et al, 1952), chimpanzee (Fanelli et al, 1971), Cebus monkey (Fanelli et al, 1970) and rat (Knight et al, 1979). On the other hand, probenecid inhibits urate secretion in species showing net secretion, such as pig (Simmonds et al, 1976), Dalmatian dog (Kesseler et al, 1959), Guinea-pig (Mudge et al, 1968) and rabbit (Donoso & Grantham, 1986).

In this study it was determined whether the urate excretion by the cat kidney was susceptible to probenecid. When probenecid (30 mg/kg) was infused through the femoral vein, urate excretion was not altered (Table 2, Fig. 5). In other series of experiments, changes in urate excretion by the cat kidney was also not appeared by probenecid infused into the renal artery (Table 4, Fig. 6). When the same concentration of probenecid was infused into renal artery, PAH excretion was remarkably inhibited (Table 5, Fig. 6). These results indicate that urate is reabsorbed by a probenecid-insensitvie mechanism and that renal tubular transport of urate is different from that of other organic anions such as PAH and probenecid. On the contrary to the cat, in the rabbit GFR was decreased significantly by systemic infusion of probenecid (Fig. 5). The underlying mechanism of decreased GFR by probenecid was not clear at present.

Attempts to obtain an evidence for saturable process of urate reabsorption by the cat kidney was excluded because the infusion of high concentration of urate produced a decrease in urine flow, presumably by the intrarenal precipitation of urate due to its limited solubility. Thus it is unclear in the cat that urate is reabsorbed by a carrier-mediated mechanism in the kidney.

In this study, only urate reabsorption in the cat was observed with no evidence of net secretion. Up to date, it has not been known whether an evidence for bidirectional transport of urate by the cat kidney under some other experimental conditions can be obtained.

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