Associations between dry dietary factors and canine calcium oxalate uroliths

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Objective—To identify factors in dry diets associated with the occurrence of calcium oxalate (CaOx) uroliths in dogs.

Animals—600 dogs with CaOx uroliths and 898 dogs without urinary tract diseases.

Procedure—Univariate and multivariate logistic regression were performed.

Results—Compared with diets with the highest concentrations of sodium, dry diets with the lowest concentrations of sodium, phosphorus, calcium, chloride, protein, magnesium, or potassium were linearly associated with increased risk of CaOx urolith formation. Significant nonlinear associations between increased occurrence of CaOx uroliths and urine acidifying potential and low moisture content were observed. Significant nonlinear associations between decreased occurrence of CaOx uroliths and carbohydrate and fiber contents were observed. A significant association between the occurrence of CaOx uroliths and dietary fat was not observed.

Conclusions and Clinical Relevance—Results suggest that dry diets formulated to contain high concentrations of protein, calcium, phosphorus, magnesium, sodium, potassium, and chloride may minimize formation of CaOx uroliths. In addition, comparison of risk and protective factors of various diet ingredients fed to dogs with CaOx uroliths suggests that although similar findings were observed in canned and dry formulations, in general, greater risk is associated with dry formulations. However, before these hypotheses about dietary modifications are adopted by food manufacturers, they must be investigated by use of appropriately designed clinical studies of dogs with CaOx urolithiasis. (*Am J Vet Res* 2002;63:330–337)

During the past 20 years, there has been a dramatic increase in the number of canine **calcium oxalate (CaOx)** uroliths submitted to the **Minnesota Urolith Center (MUC)**. In the year 2000, 38% (7,895/21,008) of the uroliths contained primarily CaOx. Medical protocols for dissolution of these uroliths have not been developed, partially because of incomplete knowledge about the cause of this disease.[1] Although surgery usually provides effective short-term treatment if all uroliths are removed, persistence of underlying causes of urolith formation often results in their recurrence.

Identification and elimination of risk factors associated with CaOx urolith formation in dogs would likely improve detection, treatment, and prevention of uroliths. Therefore, we have directed our efforts toward evaluation of the epidemiologic features of naturally occurring disease. Results of epidemiologic studies[a] of CaOx urolithiasis in dogs indicate that diet-related factors in manufactured canned foods may increase or decrease the risk of CaOx urolithiasis. Although results of similar epidemiologic studies have not been reported in dogs consuming dry diets, we have recommended commercial canned diets over dry formulations to minimize CaOx urolithiasis in dogs on the basis of empirical clinical experience.[1] The purposes of the epidemiologic study reported here were to identify factors in dry diets associated with increased and decreased risk of CaOx urolithiasis in dogs and compare them with risk factors identified in canned diets.

Materials and Methods

Case selection—Cases consisted of records of dogs with uroliths composed of at least 70% CaOx. Uroliths were submitted to the MUC for analyses between 1990 and 1992. Only uroliths retrieved from dogs residing in the United States and Canada were included. To enhance the opportunity for staff of veterinary hospitals to submit uroliths, analysis was provided without charge. Quantitative analysis of uroliths was performed with the aid of optical crystallography and, when necessary, infrared spectroscopy.

Control selection—Controls consisted of records of dogs evaluated at the same veterinary hospital as the CaOx urolith-forming dogs. Appointments with veterinarians for these dogs were made just prior to and immediately following the CaOx urolith-forming dogs.

Exclusion criteria—Dogs fed canned, semimoist, or combinations of canned, semimoist, and dry diets were not evaluated in this study. To evaluate the long-term effects of diets, dogs that consumed primary brands of dry diets for < 6 months were excluded from this study. To minimize confounding effects associated with recent treatment for urinary tract diseases, dogs with a history of any type of upper and lower urinary tract disease were also excluded. Likewise, dogs consuming therapeutic diets for urinary tract diseases were excluded. Because the composition of diets fed to

Received Aug 29, 2001.
Accepted October 23, 2001.
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immature dogs commonly changes during their growth, and because CaOx uroliths affect < 1% of CaOx urolith-forming dogs,[2] records of dogs < 1 year of age were also excluded.

Questionnaire design and administration—After CaOx uroliths were received at the MUC, a content-validated[3] multiple-choice questionnaire[b] designed to collect information about each dog's signalment, diet (brands, quantities, types, and duration of consumption), and medical history (present illness, previous illnesses, treatments, and therapeutic diets) at the date of urolith detection was mailed to owners with the permission of primary care veterinarians. The same questionnaire was also mailed to the owners of control dogs. If the owners did not respond, they were mailed reminder cards or contacted by telephone.

Diet evaluation—The questionnaire allowed the owner to designate 1, 2, or a combination of 3 brands of commercial dry diets consumed by the dog. The owners were asked to specify the quantity of each brand of diet fed to each dog. On the basis of this information, the dry diet fed in the largest quantity was designated as the primary brand. When equal amounts of 2 or more brands were fed or the amount fed was unknown, the first dry diet listed by the owner was designated as the primary brand. The owner's recall of how much dry diet was fed was not used to determine the quantity of dry diet consumed by each dog; instead, to minimize recall bias, the estimated quantity of dry diet consumed by each dog was based on the daily adult maintenance caloric requirement.

Information about urine pH values after feeding the dry diets and the quantity of each dry dietary component (protein, carbohydrate, fat, fiber, calcium, phosphorus, magnesium, sodium, potassium, chloride, and moisture) was supplied for diets formulated during the study period by their manufacturers. The means of dietary components and urine acidifying potential were used. When a range of values for dietary components and urine acidifying potential were reported by manufacturers instead of mean values, the midrange values were used. The typical nutrient analysis of dry dietary components was expressed as grams per 100 kcal for protein, carbohydrate, fat, and fiber and milligrams per kilocalorie for calcium, phosphorus, magnesium, sodium, potassium, and chloride. Moisture was expressed as percentage of water in the diet.

Statistical evaluation—On the basis of the dog's caloric requirement, the typical nutrient quantity of each dry dietary component fed to case and control dogs was compared by use of the *t*-test for 2 independent samples method.[4] Correlations among dry dietary components were performed by use of the Pearson correlation method.[5] On the basis of guidelines recommended by Newton and Rudestam,[6] we interpreted correlation coefficients as follows: 0 to +0.29 and 0 to –0.29 = no correlation, +0.3 to +0.69 and –0.3 to –0.69 = weak correlation, and +0.7 to +1 and –0.7 to –1 = strong correlation.

To calculate crude **odds ratios (OR)** and 95% **confidence intervals (CI)**, dry dietary components fed to case dogs and control dogs were grouped into quartiles and analyzed as categoric variables by use of univariate logistic regression analysis with the logarithmic approximation (Woolf) method.[7] Because only 4 diets were designed to produce a urine pH > 7, and because > 50% of dry diets were designed to produce a urine pH 7, data for the third and fourth pH quartile were combined. In this context, the highest quartile for each dry dietary component and urine acidifying potential was used as a basis for comparison.

Because it was impractical for participating veterinarians to match breed, age, sex, neutering, and body condition of each case dog with a corresponding control dog, the multivariate logistic regression technique was used for each dietary component. Odds ratios and 95% CI for each dietary component adjusted for breed, age, sex, neutering, and body condition were calculated by including these covariates in the multivariate logistic regression model. Additionally, the χ^2 test for trend of OR was computed to evaluate a linear association across quartiles of dry dietary components.[8] Multivariate logistic regression incorporating multiple dietary components adjusted for the aforementioned covari-

Table 1—Differences in dietary components and urine acidifying potential associated with dry diets fed to dogs without urinary tract diseases (controls) and dogs with calcium oxalate urolithiasis (cases)

	Controls			Cases				
Component	**No.**	**Mean**	**SD**	**No.**	**Mean**	**SD**	***t* test**	***P* value**
Protein (g/100 kcal)	898	6.33	1.02	600	6.01	1.36	4.88	< 0.001
Carbohydrate (g/100 kcal)	898	13.41	3.10	599	13.93	2.83	–3.32	< 0.001
Fat (g/100 kcal)	898	3.36	0.80	600	3.30	0.78	1.61	0.107
Fiber (g/100 kcal)	898	0.99	1.47	600	1.36	2.12	–3.72	< 0.001
Calcium (mg/kcal*)	898	3.05	0.85	600	2.75	1.01	6.10	< 0.001
Phosphorus (mg/kcal)	898	2.33	0.57	600	2.11	0.71	6.45	< 0.001
Magnesium (mg/kcal)	883	0.36	0.10	598	0.34	0.10	3.07	0.002
Sodium (mg/kcal)	898	0.98	0.34	600	0.90	0.33	4.69	< 0.001
Potassium (mg/kcal)	883	1.78	0.53	598	1.69	0.60	3.10	0.002
Chloride (mg/kcal)	845	1.58	0.77	581	1.52	0.80	1.54	0.123
Moisture (%)	898	9.28	1.79	600	9.11	1.69	1.89	0.059
Urine acidifying potential† (pH)	221	6.77	0.24	233	6.76	0.31	0.29	0.770

*mg/kcal ÷ 10 = g/100 kcal. †Urine pH expected after consumption of the diet; values were supplied by diet manufacturers.

Table 2—Pearson correlation coefficients for dietary components and urine acidifying potential associated with dry diets fed to 1,498 dogs

Variable	Protein	CHO	Fat	Fiber	Ca	P	Mg	Na	K	Cl	Moisture	pH
Protein	1											
CHO	–0.24	1										
Fat	0.32	–0.61	1									
Fiber	0.30	0.35	–0.36	1								
Ca	0.41	–0.22	–0.00*	–0.01*	1							
P	0.46	–0.25	0.08	–0.07	0.94	1						
Mg	0.41	0.51	–0.20	0.41	0.45	0.45	1					
Na	0.48	–0.29	0.09	0.03*	0.63	0.57	0.32	1				
K	0.35	0.26	–0.16	0.33	0.50	0.42	0.77	0.57	1			
Cl	0.35	–0.17	0.01*	0.04*	0.48	0.36	0.28	0.80	0.68	1		
Moisture	–0.14	0.12	–0.32	–0.13	0.18	0.12	0.26	0.33	0.49	0.54	1	
pH	0.02*	0.09*	0.23	–0.58	0.25	0.17	0.04*	–0.06*	–0.13	0.15	–0.05*	1

*All coefficients were significantly ($P < 0.05$) different from 0, except for those marked with an asterisk. CHO = Carbohydrate. Ca = Calcium. P = Phosphorus. Mg = Magnesium.Na = Sodium. K = Potassium. Cl = Chloride. pH = Urine pH associated with diets.

ates was not evaluated because of multicollinearity between dietary components and because of insufficient sample size. For multivariate analyses, the highest quartile for each dry dietary component and urine acidifying potential was used as the primary basis for comparison. In addition, to facilitate comparison of our results with the results of a parallel study[a] designed to evaluate associations between canned dietary factors and canine calcium oxalate uroliths, we also used the lowest levels of dietary contents as a reference.

The estimation of OR was considered significant if 95% CI for OR did not include 1.0.[9] On the basis of recommendations by Lilienfeld and Stolley,[10] we classified significant OR between 1.1 and 1.9 or between 0.5 and 0.9 as weak associations. Likewise, we interpreted significant OR that were > 2 (ie, risk) or < 0.5 (ie, protective) as clinically (biologically) important and requiring further experimental or prospective studies to support causality.

Results

Overall, 1,717 questionnaires were sent to owners of dogs with CaOx uroliths, and 2,852 questionnaires were sent to owners of dogs without urinary tract disease. Response rate was 85% (1,454/1,717) for owners of dogs with uroliths and 75% (2,147/2,852) for owners of dogs without urinary tract diseases. On the basis of exclusion criteria and availability of information about components of dry diets, 600 dogs with CaOx uroliths and 898 dogs without urinary tract diseases were included for statistical analysis.

Compared with control dogs, dogs with CaOx uroliths were fed dry diets with either less protein, calcium, phos-

Table 3—Odds ratios (OR) and 95% confidence intervals (CI) for quartile values for dry dietary components in dogs with calcium oxalate uroliths, compared with dogs without urinary tract diseases

Components and range	Median concentration in diets	Univariate crude OR	95% CI	Multivariate adjusted OR*	95% CI
Protein (g/100 kcal)					
1.90–5.88	4.76	2.30	1.71–3.10	1.84	1.32–2.57
5.89–6.11	5.89	0.95	0.71–1.29	0.98	0.70–1.37
6.12–6.85	6.36	1.07	0.79–1.44	1.03	0.74–1.43
6.86–9.66	7.31	1.00	Reference	1.00	Reference
P for trend		< 0.001		< 0.001	
Carbohydrate (g/100 kcal)					
6.23–11.15	9.94	0.48	0.35–0.66	0.66	0.46–0.95
11.16–13.41	12.59	0.76	0.57–0.99	1.02	0.75–1.40
13.42–15.64	14.95	0.59	0.44–0.79	0.72	0.52–0.99
15.65–20.12	17.30	1.00	Reference	1.00	Reference
P for trend		< 0.001		0.251	
Fat (g/100 kcal)					
1.71–2.70	2.65	1.41	1.07–1.85	1.12	0.82–1.53
2.71–3.17	2.92	0.94	0.71–1.24	0.81	0.59–1.10
3.18–3.69	3.58	1.25	0.91–1.71	1.12	0.79–1.60
3.70–5.80	4.35	1.00	Reference	1.00	Reference
P for trend		0.072		0.996	
Fiber (g/100 kcal)					
0.18–0.46	0.34	0.57	0.43–0.76	0.74	0.53–1.02
0.47–0.55	0.56	0.63	0.45–0.87	0.73	0.51–1.05
0.56–0.73	0.70	0.57	0.44–0.74	0.70	0.52–0.94
0.74–9.45	1.36	1.00	Reference	1.00	Reference
P for trend		< 0.001		0.110	
Calcium (mg/kcal)					
0.80–2.19	1.70	2.20	1.64–2.95	2.11	1.52–2.93
2.20–2.89	2.89	0.78	0.52–1.16	0.74	0.48–1.15
2.90–3.69	3.30	0.80	0.61–1.05	0.68	0.51–0.92
3.70–4.70	4.00	1.00	Reference	1.00	Reference
P for trend		< 0.001		< 0.001	
Phosphorus (mg/kcal)					
0.30–1.69	1.50	2.29	1.72–3.05	2.20	1.60–3.03
1.70–2.19	2.19	1.36	0.95–1.94	1.07	0.72–1.60
2.20–2.79	2.40	0.70	0.53–0.92	0.63	0.47–0.85
2.80–4.00	3.00	1.00	Reference	1.00	Reference
P for trend		< 0.001		< 0.001	
Magnesium (mg/kcal)					
0.07–0.27	0.27	1.80	1.33–2.43	1.82	1.30–2.56
0.28–0.33	0.29	0.70	0.51–0.96	0.94	0.66–1.33
0.34–0.38	0.38	1.15	0.87–1.52	1.25	0.91–1.70
0.39–0.71	0.50	1.00	Reference	1.00	Reference
P for trend		0.012		0.004	
Sodium (mg/kcal)					
0.20–0.69	0.60	2.67	1.88–3.78	2.31	1.57–3.41
0.70–0.99	0.80	1.03	0.77–1.38	0.91	0.65–1.26
1.00	1.00	1.00	0.75–1.34	0.94	0.68–1.30
1.01–2.60	1.40	1.00	Reference	1.00	Reference
P for trend		< 0.001		< 0.001	
Potassium (mg/kcal)					
0.80–1.49	1.20	1.51	1.12–2.03	1.62	1.16–2.27
1.50–1.59	1.50	0.63	0.46–0.87	0.86	0.60–1.24
1.60–1.99	1.80	1.05	0.80–1.39	1.16	0.85–1.57
2.00–3.20	2.60	1.00	Reference	1.00	Reference
P for trend		0.130		0.021	
Chloride (mg/kcal)					
0.30–1.09	1.00	2.17	1.57–3.00	1.94	1.35–2.78
1.10–1.49	1.30	1.14	0.88–1.49	1.08	0.80–1.45
1.50–1.59	1.50	0.77	0.56–1.06	0.80	0.56–1.13
1.60–4.70	2.00	1.00	Reference	1.00	Reference
P for trend		< 0.001		< 0.001	
Moisture (%)					
7.4–7.9	7.5	1.07	0.78–1.46	1.31	0.93–1.86
8.0–8.9	8.0	1.64	1.24–2.17	1.74	1.27–2.37
9.0–10.4	9.0	1.59	1.19–2.14	1.71	1.23–2.37
10.5–16.6	11.1	1.00	Reference	1.00	Reference
P for trend		0.325		0.065	
Urine acidifying potential (pH)					
6.25–6.59	6.25	2.33	1.25–4.36	2.62	1.33–5.13
6.60–6.99	6.60	0.50	0.33–0.75	0.68	0.42–1.10
7.00–7.40	7.00	1.00	Reference	1.00	Reference
P for trend		0.443		0.135	

*Adjusted odds ratio for purebred (purebred/mixed breed), age (> 8 years old/≤ 8 years old), sex (male/female), reproductive status (neutered/sexually intact), and overweight (yes/no).

phorus, sodium, or potassium and with more carbohydrate or fiber (**Table 1**). However, caution must be used in interpreting these results, because correlations were detected between several dry dietary components (**Table 2**). Unfortunately, there were insufficient data to perform multivariate regression analyses with the goal of further defining the importance of these dietary correlations.

Results of univariate logistic regression analyses for crude OR of dry dietary components and urine acidifying potential of dry diets expressed as quartiles indicated a linear increase in risk for CaOx urolith formation (*P* for trend < 0.05) in dogs fed dry diets with low quantities of protein, calcium, phosphorus, magnesium, sodium, or chloride (**Table 3**). On the other hand, a linear increase in risk for CaOx urolith formation was observed in dogs fed dry diets with high quantities of carbohydrate and fiber. We did not observe a significant linear association between CaOx urolith formation and dry dietary fat, potassium, moisture, and urine acidifying potential.

Because significant demographic differences in pure versus mixed breed, age, sex, reproductive status, and body condition were observed between case and control dogs, multivariate logistic regression adjusted for these potential confounding variables was performed (**Tables 3** and **4**). By use of the highest concentrations of dry dietary contents as reference points, dogs fed dry diets with either lower concentrations of protein, calcium, phosphorus, magnesium, sodium, potassium, or chloride had increased risk for CaOx urolith formation (*P* for trend < 0.05). Significant linear associations between CaOx urolithiasis and dry dietary carbohydrate, fat, fiber, moisture, and urine acidifying potential were not observed. Increased risk for CaOx urolithiasis was associated with diets lowest in sodium (OR, 2.3), lowest in phosphorus (OR, 2.2), and lowest in calcium (OR, 2.1). Additionally, diets lowest in chloride (OR, 1.9), lowest in protein (OR, 1.9), lowest in magnesium (OR, 1.8), and lowest in potassium (OR, 1.6) were also associated with increased risk of CaOx urolithiasis.

The lowest levels of dietary contents were used as reference points to facilitate comparison of our results pertaining to dry foods to a parallel study[a] of canned dietary components that used low rather than high concentrations of dietary components as reference ranges. In this context, dogs fed dry diets with either higher quantities of protein, calcium, phosphorus, magnesium, sodium, potassium, or chloride had decreased risk for CaOx urolith formation (*P* for trend < 0.05). Significant linear associations between the CaOx urolithiasis and dry dietary carbohydrate, fat, fiber, moisture, and urine acidifying potential were not observed (**Table 5**).

Table 4—Patient and demographic characteristics of 600 dogs with calcium oxalate uroliths (cases) and 898 dogs without urinary tract diseases (controls)

Characteristics	No. of cases	No. of controls	OR	95% CI
Breed				
Pure	531	655	2.9	2.1 to 3.8
Mixed	69	243	1	Reference group
Age				
> 8 years old	339	622	2.9	2.4 to 3.6
≤ 8 years old	261	276	1	Reference group
Sex				
Male	438	439	2.8	2.3 to 3.5
Female	162	457	1	Reference group
Neutering				
Neutered	511	702	1.6	1.2 to 2.1
Sexually intact	89	194	1	Reference group
Body condition				
Overweight	178	166	1.9	1.5 to 2.4
Not overweight	422	732	1	Reference group

Table 5—Summary of magnitude of associations between dry and canned dietary factors and dogs with calcium oxalate uroliths

	Dry diets		Canned diets[a]	
Factor (highest quartile*)	Risk*	Odds ratio	Risk*	Odds ratio
Protein	1.8 times less likely	0.54†	4.8 times less likely	0.21†
Carbohydrate	1.5 times more likely	1.5‡	2.6 times more likely	2.6†
Fat	NS	NS	4.0 times less likely	0.25†
Fiber	NS	NS	2.4 times less likely	0.41‡
Calcium	2.1 times less likely	0.47†	6.7 times less likely	0.15†
Phosphorus	2.2 times less likely	0.45†	8.3 times less likely	0.12†
Magnesium	1.8 times less likely	0.55†	3.2 times less likely	0.31†
Sodium	2.3 times less likely	0.43†	5.6 times less likely	0.18†
Potassium	1.6 times less likely	0.62†	5.3 times less likely	0.19†
Chloride	1.9 times less likely	0.52†	4.2 times less likely	0.24†
Moisture	NS	NS	6.3 times less likely	0.16†
Urine alkalinizing potential	2.6 times less likely	0.37‡	NS	NS

*Comparison of the highest quartile to the lowest quartile. †A significant (*P* for trend < 0.05) linear association was observed. ‡A significant (*P* for trend ≥ 0.05) linear association was not observed.
NS = No significant association (*P* > 0.05).

Discussion

When the highest concentrations of dietary components were used as reference points, results of our study indicated that dry diets lower in either protein, calcium, phosphorus, magnesium, sodium, potassium, or chloride were linearly associated with increased risk for CaOx urolith formation in dogs. Although significant associations between higher dietary carbohydrate, fiber, and diets formulated to maximize urine acidity and increased risk for CaOx urolith formation were observed, they were not linear. Likewise, a significant but nonlinear association was observed between high dietary moisture and reduced risk of CaOx urolith formation.

Consumption of high-protein diets has been reported to increase the risk for CaOx urolith formation in humans[11] by promoting acidosis and subsequent hypercalciuria. A similar phenomenon has been proposed to occur in dogs.[2] Therefore, our observation that dogs fed dry diets highest in protein were 1.8 times less likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in protein, was unexpected. However, in a parallel study,[a] dogs fed high-protein canned diets were approximately 5 times less likely to develop CaOx uroliths, compared with dogs fed canned diets with lower quantities of protein. In cats, high concentrations of dietary (canned and dry) protein were also associated with decreased risk (OR, 0.5) for CaOx urolithiasis.[a]

Results of a study[12] in healthy adult cats provide 1 plausible mechanism that may explain, at least in part, why CaOx uroliths formed less frequently in dogs fed dry diets high in protein. In that study, consumption of a high-protein diet (14 g/100 kcal) by cats increased water consumption and urine volume, compared with cats that consumed less protein (8 g/100 kcal). The urinary excretion and urinary concentration of calcium did not increase during consumption of high protein diets, but the urinary excretion and urinary concentration of phosphorus doubled. Increased urinary phosphorus excretion could conceivably reduce the risk for CaOx urolithiasis by enhancing the urine concentration of pyrophosphate (a CaOx crystal inhibitor)[13] and by reducing production of calcitriol by the kidney.[14]

Dogs fed dry diets highest in carbohydrate were 1.5 times more likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in carbohydrate; however, we did not observe a linear association between quantities of carbohydrate in the diet and risk of CaOx urolithiasis. Similarly, in a parallel study,[a] dogs fed canned diets highest in carbohydrate were 3 times more likely to develop CaOx uroliths than were dogs fed canned diets lowest in carbohydrate.

In humans, consumption of high carbohydrate diets may increase the risk of CaOx urolithiasis by increasing calcium excretion.[15] In healthy dogs[16] and humans,[17] a transient hypercalciuric response to dietary carbohydrates has been observed. Postprandial increases in plasma insulin, which in turn impair proximal renal tubular reabsorption of calcium, were suggested as 1 plausible explanation of this phenomenon.

In this study, we did not observe an association between dietary fat and CaOx urolithiasis. In a parallel study,[a] dogs fed canned diets highest in fat were 4 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in fat. The explanation of these differences may be related, at least in part, to the fact that the highest concentrations of fat in dry diets would be interpreted as the moderate to low concentrations of fat in canned diets.

Although a significant association between higher dietary fiber and increased risk for CaOx urolith formation was observed, it was not linear. Likewise, an association between fiber in canned canine diets and CaOx urolith formation was not detected.[a] However, results of a study[18] of healthy humans suggested that physical and chemical properties of different types of bran in diets had different effects on urinary calcium and oxalic acid excretion. Our study was not designed to identify quantities of specific types fiber fed to urolith-forming and control dogs.

The prevailing consensus of opinion has been that restriction of dietary calcium would reduce urinary calcium excretion and, therefore, reduce CaOx urolith formation.[11,19,20] However, results of recent epidemiologic studies[20,21] in humans revealed that restriction of dietary calcium was a risk factor for CaOx urolith formation. Humans who consumed high quantities of dietary calcium had reduced risk for CaOx urolithiasis. It was postulated that consumption of high dietary calcium increased formation of nonabsorbable CaOx in the intestinal lumen, resulting in reduced urinary oxalic acid excretion.

Results of our epidemiologic study support these findings in that dogs fed dry diets highest in calcium were approximately 2 times less likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in calcium. In a parallel study[a] of canned diets, a similar but more pronounced trend was observed. Dogs fed canned diets highest in calcium were approximately 7 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in calcium. In cats, low and high concentrations of dietary (canned and dry) calcium were also associated with increased risk for development of CaOx uroliths, compared with midrange calcium concentrations.[a]

The hypocalciuric effect of dietary phosphorus is well established in humans.[22] In fact, humans with CaOx uroliths are often given neutral phosphate supplements to reduce urinary calcium excretion, CaOx crystalluria, and recurrence of CaOx uroliths.[23,24] In addition,salts of orthophosphate enhance urinary excretion of pyrophosphate sand citrate.[25,26] Pyrophosphates and citrate are CaOx crystallization inhibitors. In contrast, diets deficient in phosphorus may stimulate calcitriol production, which in turn promotes intestinal absorption of calcium and phosphorus.[22] Also, diets deficient in phosphorus may enhance intestinal absorption of calcium that has not combined with phosphorus to form an insoluble salt.[2]

Our results are consistent with these observations in that dogs fed dry diets highest in phosphorus were approximately 2 times less likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in phosphorus. In a parallel study[a] of canned diets, a similar but more pronounced trend was observed. Dogs fed canned diets highest in phosphorus were approximately 8 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in phosphorus. In cats, low and high concentrations of dietary (canned and dry) phosphorus were associated with increased risk for development of CaOx uroliths, compared with midrange phosphorus concentrations.[a]

Magnesium has been hypothesized to be an inhibitor of CaOx urolithiasis on the basis of several lines of evidence.[27-29] Our results are consistent with this hypothesis in that dogs fed dry diets highest in magnesium were approximately 2 times less likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in magnesium. In a parallel study,[a] dogs fed canned diets highest in magnesium were approximately 3 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in magnesium. However, these observations should be cautiously interpreted, because consumption of excessive magnesium may also be a risk factor for CaOx urolith formation by causing hypercalciuria. For example, when 6 clinically normal dogs consumed a canned diet with 2.5 mg of magnesium/kcal, urinary calcium excretion was 5 times as high as that observed when the same dogs consumed the same diet with only 0.2 mg of magnesium/kcal.[c] In cats, lowest and highest concentrations of dietary (canned and dry) magnesium were associated with increased risk for development of CaOx uroliths, compared with midrange magnesium concentrations.[a] In addition, oral administration of magnesium oxide to humans with CaOx uroliths was associated with increased urinary calcium excretion.[30]

For the past decade, the prevailing consensus of opinion of veterinary urologists has been that dietary restriction of sodium would reduce the risk of CaOx urolith formation.[1,31-33] This opinion was substantially influenced by the observation that in healthy adult dogs[c] and humans,[20,34,35] high dietary sodium consumption promoted hypercalciuria. However, our results indicated that dogs fed dry diets highest in sodium were approximately 2 times less likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in sodium. In a parallel study[a] of canned diets, a similar but more pronounced trend was observed. Dogs fed canned diets highest in sodium were approximately 6 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in sodium. Also in cats, high concentrations of dietary (canned and dry) sodium were associated with decreased risk (OR, 0.5) for development of CaOx uroliths.[a]

In a recent crossover study of 6 healthy adult dogs performed at the University of Minnesota, we confirmed that urinary sodium and calcium excretion significantly increased when they consumed high sodium (0.5 mg/kcal) diets, compared with when they consumed low sodium (2.5 mg/kcal) diets. However, during consumption of the high sodium diets, the urine calcium concentration decreased, compared with that measured when they consumed the low sodium diets. These results emphasize the need to be cautious about formulating generalizations regarding the effects of dietary sodium on urinary calcium concentration and urinary calcium concentration. Although increased dietary sodium does enhance urine calcium excretion, it may decrease urine calcium concentration by increasing urine volume. Conceivably, urinary oxalic acid concentration could also be reduced.[36] Even if the total quantity of urinary calcium excretion per day increased, CaOx urolith would not be expected to form in urine unless it was oversaturated with calcium and oxalic acid.[37] Appropriately designed studies in CaOx urolith-forming dogs are required to test the hypothesis that consumption of increased dietary sodium will also result in enhanced calcium excretion but reduced calcium and oxalic acid concentration.

Dogs fed dry diets highest in potassium were approximately 1.5 times less likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in potassium. In a parallel study,[a] a similar but more pronounced trend was observed. Dogs fed canned diets highest in potassium were approximately 5 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in potassium. Also in cats, high concentrations of dietary (canned and dry) potassium were associated with decreased risk (OR, 0.4) for development of CaOx uroliths.[a] Reduced risk of CaOx urolith formation associated with increased dietary potassium may be related to potassium-induced alterations in urinary calcium excretion. Results of a study[34] in healthy adult humans revealed that reducing dietary potassium by substitution of KCl with NaCl, or substitution of $KHCO_3$ with $NaHCO_3$, was accompanied by increased urinary calcium excretion. If a similar effect occurs in CaOx urolith-forming dogs, it would provide a plausible explanation of why dry diets with high potassium concentrations were associated with decreased risk of CaOx urolithiasis.

In our study, dogs fed dry diets highest in chloride were approximately 2 times less likely to develop CaOx uroliths, compared with dogs fed dry diets lowest in chloride. In a parallel study,[a] a similar but more pronounced trend was observed. Dogs fed canned diets highest in chloride were approximately 4 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in chloride. Because several different types of chloride salts (ie, sodium, potassium, calcium, choline [vitamin B_4], and pyridoxine [vitamin B_6]) are commonly used in many commercial diets,[38] associations between chloride and CaOx urolithiasis may be confounded. For example, in our study the quantity of dietary chloride was directly correlated with the quantity of dry dietary sodium ($r = 0.8$), which was also associated with decreased risk for CaOx urolith formation.

A significant association between high and low amounts of moisture in dry diets and CaOx urolith formation was not observed in our study. The explanation for this association is unknown to us. However, these results should not be interpreted to indicate that there is not an association between dietary moisture and CaOx urolith formation. For example, results of a parallel study[a] indicated that dogs fed canned diets highest in moisture were approximately 6 times less likely to develop CaOx uroliths, compared with dogs fed canned diets lowest in moisture. Also, in cats, high amounts of dietary (canned and dry) moisture were associated with decreased risk (OR, 0.3) for development of CaOx uroliths.[a] These findings are consistent with the observation that increased water consumption associated with increased volume and decreased urine concentrations of minerals has been an effective strategy to minimize formation of canine uroliths.[1] Consumption of high moisture diets by clinically normal cats has also been associated with production of greater volumes of less concentrated urine, compared with consumption of low-moisture diets.[39-41]

In this study, dogs fed dry diets formulated to maximize urine acidity were approximately 3 times more likely to develop CaOx uroliths, compared with dogs that were fed diets formulated to produce neutral or alkaline urine. Although this association was significant, it was not linear. In a parallel study,[a] we did not observe a significant association between dogs fed canned diets designed to maximize urine acidity and increased risk for CaOx urolithiasis. We attributed this finding to the small sample size available for analysis (38 control dogs and 52 case dogs). However, cats fed diets (canned and dry) formulated to maximized urine acidity (pH, 6.0 to 6.2) were approximately 3 times more likely to develop CaOx uroliths, compared with cats fed diets formulated to produce urine pH values between 6.5 and 6.9.[a]

The association between acidemia, aciduria, and CaOx urolithiasis may be related, at least in part, to acidemia that promotes mobilization of bone calcium and hypercalciuria.[42-44] In addition, induction of metabolic acidosis in dogs, humans, and rats resulted in hypocitraturia.[45] Hypocitraturia may increase the risk of CaOx urolithiasis, because citrate is an inhibitor of CaOx crystal formation.

It is apparent that several dietary ingredients may play a substantial role in development of CaOx uroliths in dogs. For example, on the basis of results of our epidemiologic study, we hypothesize that dry diets formulated to contain high levels of protein, calcium, phosphorus, magnesium, sodium, potassium, and chloride may minimize formation of CaOx uroliths. In addition, comparison of risk and protective factors of various diet ingredients fed to dogs with CaOx uroliths suggests that although similar trends were observed in canned and dry formulations, in general, greater risk is associated with dry formulations. Results of our epidemiologic studies suggest that greater reduction in risk for CaOx urolithiasis in canned diets may be associated with several factors. For example, compared with dry diets, the canned diets evaluated in a previous study contained greater quantities of dietary components (protein, fat, sodium, potassium, chloride, and moisture) associated with decreased risk of CaOx urolithiasis.

Because our study was not designed to identify underlying mechanisms by which various components in dry diets, singly or in combination, promote or prevent CaOx urolithiasis, associations that we identified should not be interpreted as proof of cause and effect relationships. Before these hypotheses about dietary modifications are adopted by food manufacturers, they must be investigated by appropriately designed clinical studies of dogs with CaOx urolithiasis. To minimize confounding effects, such controlled studies should be designed to match CaOx urolith-forming dogs for breed, age, sex, reproductive status, and body condition.

[a]Lekcharoensuk C. *Epidemiology of urolithiasis in cats and dogs*. PhD Thesis, Department of Small Animal Clinical Sciences, University of Minnesota, St Paul, Minn, 2001.

[b]Questionnaire upon request to Carl A. Osborne, Department of Small Animal Clinical Sciences, 1352 Boyd Ave, St Paul, MN 55108.

[c]Lulich JP. *Canine calcium oxalate urolithiasis: etiology, pathophysiology, and therapy*. PhD Thesis, Department of Small Animal Clinical Sciences, University of Minnesota, St Paul, Minn, 1991.

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