Evaluation of trends in urolith composition and characteristics of dogs with urolithiasis: 25,499 cases (1985–2006)

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Objective—To evaluate trends in urolith composition and urolithiasis in dogs during the past 21 years.

Design—Retrospective case series.

Sample Population—25,499 uroliths and the dogs from which they were obtained.

Procedures—Database of the Gerald V. Ling Urinary Stone Analysis Laboratory was searched from January 1985 through December 2006. All uroliths from dogs and the accompanying submission forms were evaluated. Age, sex, breed, and urolith location were recorded.

Results—Minerals identified in uroliths included struvite, calcium oxalate (CaOx), urate, apatite, brushite, cystine, silica, potassium magnesium pyrophosphate, sulfa drug, xanthine, and newberyite. Although more struvite-containing uroliths were submitted during this period, a significant decrease in the proportion of struvite-containing uroliths submitted as a percentage of all uroliths submitted was detected. Also, a significant increase in the proportion of CaOx-containing uroliths submitted over time was detected. There was a significant nonlinear decrease in submission of urate-, silica-, and cystine-containing uroliths. The CaOx-, cystine-, and silica-containing uroliths were obtained significantly more often from male dogs; struvite- and urate-containing uroliths were obtained significantly more often from female dogs.

Conclusions and Clinical Relevance—An increase in the proportion of CaOx uroliths submitted over time was detected. Reasons for long-term changes in this trend were likely multifactorial and could have included alterations in diet formulations and water consumption and possibly the fact that people favor ownership of breeds more prone to developing CaOx-containing uroliths. The decrease in metabolic uroliths could have been related to better breeding practices and increased awareness of results of genetic studies. (*J Am Vet Med Assoc* 2010;236:193–200)

Urolithiasis is a common and often recurrent problem in dogs. Surgery or other techniques[1–3] are usually necessary to remove uroliths so that they can be submitted for quantitative crystallographic analysis. The 2 most common mineral types reported in uroliths of dogs are CaOx and struvite. Our laboratory group has reported[4] that the proportion of struvite-containing uroliths decreased significantly and the proportion of CaOx-containing uroliths increased significantly during the period from 1981 to 2001. In that report,[4] CaOx-containing uroliths were the most common type; however, other mineral types were not addressed. General trends for the most common uroliths of dogs, as determined by the use of descriptive statistics, have also been reported in other studies.[5,6] In one of those studies,[6] > 16,000 uroliths from dogs were examined and struvite was the most common mineral detected.

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Abbreviations

CaOx	Calcium oxalate
CI	Confidence interval
OR	Odds ratio

The purpose of the study reported here was to determine the various types of minerals that were contained in uroliths obtained from dogs and submitted to our laboratory for cystallographic analysis. Trends for mineral composition of uroliths and age, breed, sex, and other risk factors for development of uroliths in dogs during the past 21 years were evaluated.

Materials and Methods

Case selection—A computer-assisted search of the records of the Gerald V. Ling Urinary Stone Analysis Laboratory at the School of Veterinary Medicine, University of California-Davis, was conducted to identify all submissions of uroliths obtained from dogs.

Medical records review—Records were searched to detect all uroliths obtained from dogs and submitted for analysis from January 1985 through December

2006. Information from the database had been obtained from a submission form that accompanied each urolith; the uroliths and forms were received from veterinarians, various universities, and private veterinary practices across the United States. Age, breed, sex, mineral composition of the urolith, year of urolith submission, and location of the urolith within the urinary tract were recorded. Furthermore, the numbers of the common breeds of dogs that were examined at the William R. Pritchard Veterinary Medical Teaching Hospital at the University of California-Davis were also tabulated for use as a reference population for calculating ORs for breed predispositions.

Mineral analysis—To determine the mineral composition of uroliths, each visibly distinct layer of each urolith was initially analyzed by use of the oil-immersion method of optical crystallography[7] with polarizing light microscopy. Infrared spectroscopy, x-ray diffractometry, high-pressure liquid chromatography, scanning electron microscopy that used energy-dispersive x-rays, and electron probe microanalysis were used as adjunctive analytic methods when needed to obtain a definitive identification of the minerals or elements in a urolith.

For purposes of this study, CaOx included CaOx monohydrate, CaOx dihydrate, or both, and urate included uric acid and the salts of uric acid (eg, ammonium urate). For each urolith, each mineral that was present in any amount was recorded, and the percentage of each mineral within each layer was estimated by calculating a mean value for the crystal counts obtained by microscopic examination of 5 to 10 microscopic slide preparations by use of the oil-immersion method of optical crystallography. The amount of specific minerals in the individual uroliths varied from 1% to 100%. For uroliths with distinct layers and variations in the thickness of each distinct layer, it was not possible to accurately designate a single mineral as being predominant. For the purpose of consistency in the reporting technique for our laboratory, uroliths composed of a mixture of 2 or more minerals, whether the multiple mineral components were contained in distinct layers or uniformly scattered throughout the urolith, were reported as containing that mineral component; in the compilations reported here, they were counted once for each mineral detected. Because of overlap of minerals, this method of tabulation of minerals detected in uroliths resulted in totals > 100%.

Statistical analysis—Nonparametric tests were used to evaluate associations between categorical variables. These included χ^2 tests of homogeneity to compare groups (eg, sex, age, and urolith location) with respect to the distribution of nominal variables (eg, urolith type), Kruskal-Wallis tests to compare groups with respect to the distribution of ordinal variables (eg, age), and Cochran-Armitage trend tests to examine changes in proportions of individual urolith types over successive time periods. Logistic regression analysis was used to examine breed predilection by comparing breed distributions in dogs with individual urolith types with breed distributions of 2 groups (dogs with other urolith types and dogs examined at the veterinary medical teaching hospital at the University of California-Davis during the same period as the study). Results were reported as ORs and 95% CIs. Values of $P < 0.05$ were considered significant.

Results

Sample population—From 1985 through 2006, 25,499 uroliths obtained from dogs were analyzed at the Gerald V. Ling Urinary Stone Analysis Laboratory. Of these 25,499 samples, 18,633 (73.1%) were uroliths composed of mixtures of 2 or more mineral substances as a combination of minerals within layers or as single minerals in distinct layers. Those uroliths were removed from both the upper (ie, kidneys and ureters) and lower (ie, bladder and urethra) urinary tract of dogs. The most common minerals identified in the various uroliths were struvite, CaOx, urate, apatite, brushite, cystine, and silica. Less common uroliths reported were potassium magnesium pyrophosphate, sulfa drug, xanthine, and newberyite (**Table 1**). Uroliths were removed from all areas of the urinary tract.

Struvite and CaOx—Of the 25,499 uroliths submitted, 13,625 (53.4%) contained struvite and 10,699 (42.0%) contained CaOx. Even though more struvite-containing uroliths were submitted during this period, there was a significant ($P < 0.001$) decrease in the proportion of struvite-containing uroliths identified as a percentage of all uroliths submitted over time and a significant ($P < 0.001$) increase in the proportion of CaOx-containing uroliths identified as a percentage of all uroliths submitted over time (**Figure 1**). The CaOx-containing and struvite-containing uroliths were submitted in approximately equal proportions by 1997, and then the number of CaOx-containing uroliths continued to increase slightly, whereas the number of struvite-containing uroliths decreased. The most common location for both types of uroliths was the bladder. When evaluating uroliths voided during urination, struvite-containing uroliths were identified significantly more often than were uroliths containing other minerals (**Figure 2**). When evaluating uroliths removed from the upper urinary tract, CaOx-containing uroliths were found more

Table 1—Association between the mineral detected in a urolith and sex of dogs for 25,499 uroliths.

	Males		Females		Total	
Mineral	No.	%	No.	%	No.	%
Struvite*	3,181	23.4	10,394	76.6	**13,575**	**100**
CaOx*	7,365	69.0	3,308	31.0	**10,673**	**100**
Apatite	2,156	22.4	7,472	77.6	**9,628**	**100**
Urate	2,739	45.4	3,293	54.6	**6,032**	**100**
Silica*	1,501	88.8	189	11.2	**1,690**	**100**
Brushite	148	45.5	177	54.5	**325**	**100**
Cystine*	313	97.8	7	2.2	**320**	**100**
Xanthine	114	96.6	4	3.4	**118**	**100**
Sulfa drug	20	48.8	21	51.2	**41**	**100**
Newberyite	2	50.0	2	50.0	**4**	**100**
Potassium magnesium pyrophosphate	1	100	0	0	**1**	**100**
Unknown	65	51.6	61	48.4	**126**	**100**

*Values differed significantly ($P < 0.001$) between male and female dogs.

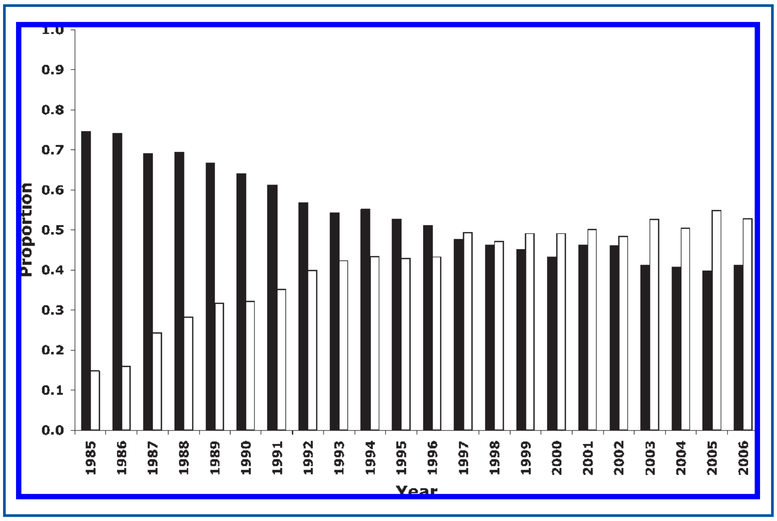

Figure 1—Proportion of CaOx-containing (white bars) and struvite-containing (black bars) uroliths obtained from dogs and submitted for analysis from 1985 through 2006. The ratio of CaOx-containing uroliths to struvite-containing uroliths increased significantly ($P < 0.001$) during the study period.

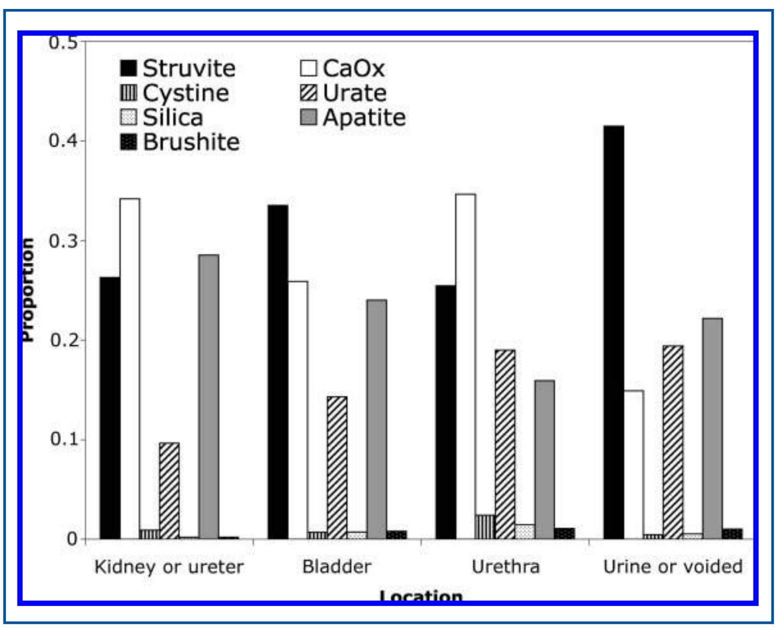

Figure 2—Proportion of the most common urolith types categorized on the basis of location. For uroliths that were voided, struvite-containing uroliths were identified significantly ($P < 0.001$) more often, compared with the proportion of uroliths containing other minerals. Notice that CaOx-containing uroliths were removed from the upper urinary tract (ie, kidney or ureter) more commonly than were other urolith types.

commonly than were other urolith types; however, a significant ($P < 0.001$) decrease in CaOx- and struvite-containing uroliths removed from the upper urinary tract was detected over time **(Figure 3)**.

Struvite-containing uroliths were submitted significantly ($P < 0.001$) more often for younger dogs; 7,524 of 13,625 (55.2%) struvite-containing uroliths were submitted for dogs < 7 years old, whereas only 2,651 of 10,699 (25.0%) CaOx-containing uroliths were submitted for dogs of this age group. Struvite-containing uroliths were submitted significantly ($P < 0.001$) more often for female dogs than for male dogs (10,394 [76.3%] vs 3,181 [22.3%] respectively). A significant ($P < 0.001$) association was detected between sex and urolith type for struvite-containing uroliths, compared with the association for all other urolith types. In contrast, a significantly ($P < 0.001$) higher proportion of CaOx-containing uroliths were submitted for males than for females (69.0% vs 31.0%, respectively).

Four breeds were considered clinically to be at a substantially higher risk (OR > 4.0; $P < 0.001$) of developing struvite-containing uroliths, compared with the risk for mixed-breed dogs (reference group) of developing struvite-containing uroliths. Those 4 breeds were the Bichon Frise (OR = 15.1; 95% CI, 13.5 to 17.0), Miniature Schnauzer (OR = 8.0; 95% CI, 7.5 to 8.7), Shih Tzu (OR = 7.4; 95% CI, 6.8 to 8.1), and Pekingnese (OR = 85.3; 95% CI, 4.5 to 6.1). Six breeds were considered clinically to be at a substantially lower risk (OR < 0.25; $P < 0.001$) of developing struvite-containing uroliths, compared with the risk for mixed-breed dogs of developing struvite-containing uroliths. Those 5 breeds were the Australian Cattle Dog (OR = 0.008; 95% CI, 0.001 to 0.056), Rottweiler (OR = 0.14; 95% CI, 0.11 to 0.18), Boxer (OR = 0.16; 95% CI, 0.11 to 0.23), Border Collie (OR = 0.21; 95% CI, 0.15 to 0.30), and Standard Poodle (OR = 0.21; 95% CI, 0.14 to 0.34).

Nine breeds were considered clinically to be at a substantially higher risk (OR > 4.0; $P < 0.001$) of developing CaOx-containing uroliths, compared with the risk for mixed-breed dogs of developing CaOx-containing uroliths. Those 9 breeds were the Bichon Frise (OR = 23.6; 95% CI, 20.8 to 26.8), Miniature Schnauzer (OR = 21.6; 95% CI, 19.9 to 23.4), Shih Tzu (OR = 10.2; 95% CI, 9.2 to 11.3), Lhasa Apso (OR = 10.1; 95% CI, 9.2 to 11.2), Pomeranian (OR = 7.2; 95% CI, 6.3 to 8.2), Cairn Terrier (OR = 7.3; 95% CI, 5.8 to 9.1), Yorkshire Terrier (OR = 6.5; 95% CI, 5.9 to 7.2), Maltese (OR = 5.2; 95% CI, 4.4 to 6.0), and Keeshond (OR = 4.6; 95% CI, 3.5 to 5.8). Of the most common breeds, 9 were considered clinically to be at a substantially lower risk (OR < 0.25; $P < 0.001$) of developing CaOx containing uroliths, compared with the risk for mixed breed dogs of developing CaOx-containing uroliths. Those 9 breeds were the German Shorthair Pointer (OR = 0.06; 95% CI, 0.02 to 0.18), Great Dane (OR = 0.04; 95% CI, 0.01 to 0.17), Rottweiler (OR = 0.05; 95% CI, 0.03 to 0.09), Australian Cattle Dog (OR = 0.08; 95% CI, 0.03 to 0.19), Labrador Retriever (OR = 0.10; 95% CI, 0.08 to 0.13), Boxer (OR = 0.10; 95% CI, 0.06 to 0.19), German Shepherd Dog (OR = 0.15; 95% CI, 0.11 to 0.21), Border Collie (OR = 0.15; 95% CI, 0.08 to 0.28), and Bull Mastiff (OR = 0.20; 95% CI, 0.09 to 0.45).

Apatite—The number of apatite-containing uroliths submitted was 9,699 (38.0%). No significant ($P = 0.093$) changes in trends were evident over time. Of these 9,699 apatite-containing uroliths, 3,162 (32.6%) were submitted for middle-aged dogs (4 to 6 years old) and 2,162 (22.3%) were submitted for dogs 7 to 9 years old. A significantly (P < 0.001) higher proportion of apatite-containing uroliths were submitted for female dogs than for male dogs (77.6% vs 22.4%, respectively).

Five breeds were considered clinically to be at a substantially higher risk (OR > 4.0; P < 0.001) of developing apatite-containing uroliths, compared with the risk for mixed-breed dogs of developing apatite-containing uroliths. These 5 breeds were the Bichon Frise (OR = 19.7; 95% CI, 17.3 to 22.1), Miniature Schnauzer (OR = 9.5; 95% CI, 8.8 to 10.4), Shih Tzu (OR = 8.6; 95% CI, 7.8 to 9.5), Pekingese (OR = 5.5; 95% CI, 4.6 to 6.5), and Lhasa Apso (OR = 4.1; 95% CI, 3.7 to 4.6). Of the most common breeds, 6 were considered clinically to be at a substantially lower risk (OR < 0.25; P < 0.001) of developing apatite-containing uroliths, compared with the risk for mixed-breed dogs of developing apatite-containing uroliths. Those 6 breeds were the Rottweiler (OR = 0.05; 95% CI, 0.03 to 0.09), Dalmatian (OR = 0.09; 95% CI, 0.04 to 0.17), Great Dane (OR = 0.09; 95% CI, 0.04 to 0.2), Boxer (OR = 0.07; 95% CI, 0.03 to 0.13), German Shorthaired Pointer (OR = 0.08; 95% CI, 0.03 to 0.19), and Golden Retriever (OR = 0.20; 95% CI, 0.16 to 0.24).

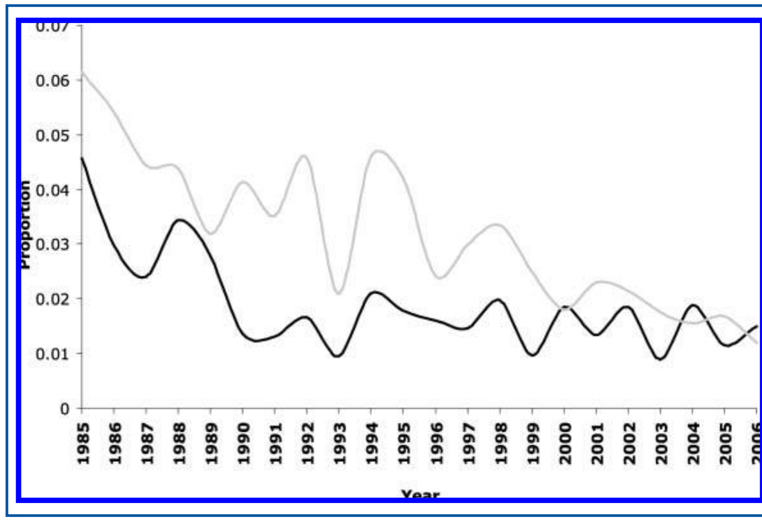

Figure 3—Proportion of CaOx-containing (gray line) and struvite-containing (black line) uroliths submitted that were obtained from the upper urinary tract of dogs. A significant (P < 0.001) decrease in these urolith types was detected during the study period.

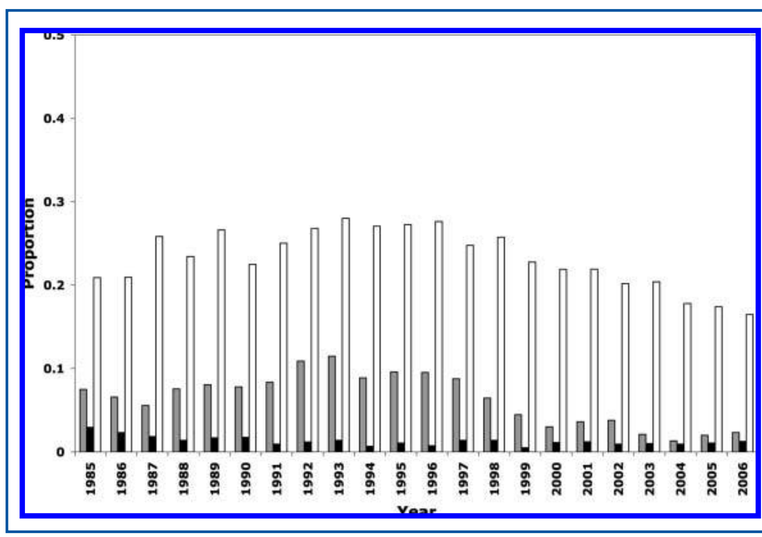

Figure 4—Proportion of silica-containing (gray bars), cystine-containing (black bars), and urate-containing (white bars) uroliths obtained from dogs and submitted for analysis from 1985 through 2006. A significant (silica, P < 0.001; cystine, P = 0.006; and urate, P < 0.001) nonlinear decrease for all 3 urolith types was detected during the study period.

Urate—The number of urate-containing uroliths identified during the study was 6,062 (23.8%). A significant (P < 0.001) trend was detected for urate-containing uroliths (**Figure 4**). During the study period, the proportion of urate-containing uroliths submitted to the laboratory decreased; however, the trend was not linear. Although an initial increase in the number of urate-containing uroliths was detected, the number of urate-containing uroliths submitted had decreased by the latter half of the 1990s. Urate-containing uroliths were submitted significantly (P < 0.001) more often for younger dogs; 3,927 (64.8%) of all urate-containing uroliths submitted were obtained from dogs < 7 years old, and 1,700 (28.0%) were obtained from dogs < 3 years old. A significantly (P < 0.001) higher proportion of urate-containing uroliths were submitted for female dogs than for male dogs (54.6% vs 45.4%, respectively).

Six breeds were considered clinically to be at a substantially higher risk (OR > 4.0; P < 0.001) of developing urate-containing uroliths, compared with the risk for mixed-breed dogs of developing urate-containing uroliths. Those 6 breeds were the Dalmatian (OR = 32.0; 95% CI, 29.0 to 35.3), Miniature Schnauzer (OR = 12.5; 95% CI, 11.3 to 14.0), English Bulldog (OR = 4.1; 95% CI, 3.3 to 5.2), Bichon Frise (OR = 10.7; 95% CI, 8.9 to 12.8), Pekingese (OR = 7.2; 95% CI, 5.8 to 9.0), and Scottish Terrier (OR = 4.2; 95% CI, 3.2 to 5.5). Furthermore, 1,142 of 1,428 (80.0%) urate-containing uroliths obtained from Dalmatians and 57 of 83 (68.7%) urate-containing uroliths obtained from English Bulldogs were composed of 100% urate. Breeds considered clinically to be at a substantially lower risk (OR < 0.25; P < 0.001) of developing urate-containing uroliths included the Australian Cattle Dog (OR = 0.03; 95% CI, 0.01 to 0.18), German Shorthaired Pointer (OR = 0.10; 95% CI, 0.03 to 0.30), Great Dane (OR = 0.24; 95% CI, 0.11 to 0.50), Border Collie (OR = 0.20; 95% CI, 0.10 to 0.40), and Doberman Pinscher (OR = 0.22; 95% CI, 0.13 to 0.36).

Silica—The number of silica-containing uroliths analyzed at the laboratory during the study was 1,697 (6.7%). There was a significant decrease in the number of silica-containing uroliths submitted over time, compared with the numbers of all other uroliths submitted (P < 0.001; Figure 4); however, this trend was not linear. Submissions of silica-containing uroliths increased until 1993 and then began to decrease. A significantly ($P < 0.001$) higher proportion of silica-containing uroliths were submitted for male dogs than for female dogs (88.8% vs 11.2%, respectively).

Five breeds were considered clinically to be at a substantially higher risk (OR > 4.0; $P < 0.001$) of developing silica-containing uroliths, compared with the risk for mixed-breed dogs of developing silica-containing uroliths. Those 5 breeds were the Miniature Schnauzer (OR = 10.1; 95% CI, 8.4 to 12.2), Lhasa Apso (OR = 6.7; 95% CI, 5.3 to 8.4), Samoyed (OR = 4.2; 95% CI, 2.6 to 6.6), Bichon Frise (OR = 9.7; 95% CI, 7.1 to 12.3), and Pekingese (OR = 4.4; 95% CI, 2.8 to 7.0). Three breeds were considered clinically to be at a substantially lower risk (OR < 0.25; $P < 0.001$) of developing silica-containing uroliths. Those breeds were the Australian Cattle Dog (OR = 0.17; 95% CI, 0.04 to 0.68), German Shorthaired Pointer (OR = 0.10; 95% CI, 0.01 to 0.75), and Great Dane (OR = 0.22; 95% CI, 0.05 to 0.88).

Cystine—The number of cystine-containing uroliths analyzed at the laboratory during the study was 322 (1.3%). The trend for submission of cystine-containing uroliths was similar to that for urate-containing uroliths, whereby there was a significant ($P = 0.006$) decrease in submission of cystine-containing uroliths, compared with submission of all other urolith types; however, this trend was not linear (Figure 4). Significantly ($P < 0.001$) more cystine-containing uroliths were obtained from dogs < 7 years old, compared with all other urolith types; 249 (77.3%) of all cystine-containing uroliths were obtained from dogs < 7 years old. A significantly ($P < 0.001$) higher proportion of cystine-containing uroliths were submitted for male dogs than for female dogs (97.8% vs 2.2%, respectively). Six breeds were considered clinically to be at a substantially higher risk (OR > 4.0; $P < 0.001$) of developing cystine-containing uroliths, compared with the risk for mixed-breed dogs of developing cystine-containing uroliths. Those 6 breeds were the English Bulldog (OR = 44.2; 95% CI, 29.0 to 67.3), Newfoundland (OR = 12.6; 95% CI, 6.9 to 22.6), Dachshund (OR = 7.6; 95% CI, 4.8 to 11.8), Chihuahua (OR = 5.6; 95% CI, 3.0 to 10.7), Miniature Pinscher (OR = 9.3; 95% CI, 4.0 to 22.0), and Welsh Corgi (OR = 5.0; 95% CI, 2.0 to 12.7). Two breeds were significantly overrepresented with respect to developing cystine-containing uroliths (Bull Mastiff [OR = 52.2; 95% CI, 34.2 to 79.8] and Scottish Deerhound [OR = 70.1; 95% CI, 26.6 to 184.7]); however, these breeds of dogs were relatively uncommon in the population of the veterinary medical teaching hospital. Two breeds were considered clinically to be at a substantially lower risk (OR < 0.25; $P < 0.001$) of developing cystine-containing uroliths, compared with the risk for mixed-breed dogs of developing cystine-containing uroliths. Those 2 breeds were the Labrador Retriever (OR = 0.24; 95% CI, 0.08 to 0.67) and Cocker Spaniel (OR = 0.18; 95% CI, 0.02 to 1.30).

Discussion

Evaluation of trends in urolith submissions to our laboratory revealed several important findings. Similar to results in another study[4] in which our laboratory group detected a significant increase in the proportion of CaOx-containing uroliths by 2001, this trend was continued in the study reported here whereby CaOx was the most common mineral detected in uroliths submitted by veterinarians to our laboratory. A significant reciprocal decrease in struvite-containing uroliths was also apparent. These changes in trends were not independent of sex, breed, and age, and 1 factor may influence another.[4]

Reasons for the long-term changes in this trend were likely multifactorial and could have included demographic and nutritional changes during the period of the study. Factors may include feeding a more acidified diet, changes in mineral content of diets, an increase in obesity in dogs, and, possibly, a trend for people to favor owning breeds more prone to formation of CaOx-containing uroliths. Five of the 9 breeds predisposed to CaOx-containing uroliths (Miniature Schnauzer, Shih Tzu, Pomeranian, Yorkshire Terrier, and Maltese) were ranked in the top 20 of the most common dog breeds in the United States on the basis of information from the American Kennel Club.[8] Although other geographic locations may differ with regard to the most common breeds of dogs, other investigators have reported[5,6] a similar predilection for CaOx-containing uroliths in small-breed dogs. When evaluating metropolitan areas specifically, small-breed dogs are even more common. The only larger breed of dog at risk for CaOx urolithiasis was the Keeshond; this breed is predisposed to primary hyperparathyroidism,[9] which could lead to increases in serum calcium concentrations (a risk factor for developing CaOx-containing uroliths). Obesity has been associated with CaOx urolithiasis in humans,[10,11] but to our knowledge, no evidence has been published to indicate that this relationship exists in dogs. However, it has been reported that obesity in dogs has increased dramatically since the mid-1980s,[12] and studies are needed to determine the correlations, if any, that exist between these 2 variables.

The CaOx-containing uroliths were submitted significantly more often for males than for females. This has been reported in a variety of species, including dogs,[5,6] humans,[13] and cats.[14] The reasons are not clear, but it has been reported that in humans, males have a higher urine osmolality, which could lead to higher supersaturation of minerals.[13] A genetic linkage has also been postulated in humans.[15] No studies in dogs have been conducted to prove or disprove these theories. Given the retrospective nature of the present study, we were unable to evaluate diet and other environmental or genetic factors, which were beyond the scope of the study.

When evaluating uroliths removed from the upper urinary tract, CaOx-containing uroliths were more commonly identified than were uroliths containing other minerals. Results in other studies[14,16] revealed a significant increase in submissions of CaOx-containing uroliths from the upper urinary tract of cats. Although extremely rare in cats, struvite-containing uroliths have been detected in the kidneys and ureters of dogs. Limited information is available on the prognosis of dogs with CaOx- or struvite-containing uroliths located in the upper urinary tract; however, a small case series of 16 dogs with ureteral uroliths revealed favorable outcomes for most of the dogs.[17] Of these 16 dogs, approximately half had CaOx-containing uroliths and the other half had struvite-containing uroliths. Dogs with struvite ureterolithiasis had significantly higher preoperative WBC counts, which were associated with staphylococcal infections.[17]

The reason for the significant decreases in CaOx- and struvite-containing uroliths in the upper urinary tract is unknown, but we hypothesize that there have been changes in recommendations regarding surgical removal of uroliths during the study period. In more recent years, clinicians have often only recommended surgical removal of uroliths located in the upper urinary tract when they are causing obstruction or are contributing to recurrent infections. Uroliths in the renal pelvis often are only monitored via sequential imaging evaluations. Furthermore, renal uroliths composed of struvite can potentially be removed by treatment in accordance with dissolution protocols.

Struvite uroliths in dogs develop primarily as a result of urease-producing bacterial urinary tract infections.[18] In the study reported here, female dogs had significantly more struvite-containing uroliths than did male dogs. A strong association between female sex and increased risk of struvite urolithiasis was reported in another study[19] conducted by our laboratory group. Because most struvite uroliths in dogs develop as a result of urease-producing bacterial infections, it is not surprising that the majority (10,394/13,625 [76.2%]) of these uroliths developed in female dogs. Because of the retrospective nature of the present study, we were not consistently provided information with regard to results of bacterial culture of urine samples for the dogs. In contrast to CaOx-containing uroliths, struvite-containing uroliths may be amenable to dissolution; thus, they may not require surgical removal and subsequent submission to a laboratory for analysis. It is possible that increased awareness about this treatment option and the availability of diets for dissolution may have led to fewer struvite-containing uroliths being submitted to our laboratory for analysis and may have contributed to the reciprocal relationship that was detected between CaOx- and struvite-containing uroliths. However, our findings differ from those in another report[6] in which struvite was still the most common type of urolith detected at another laboratory. The authors of that report[6] commented that struvite uroliths in dogs may be more difficult to dissolve, compared with dissolution of struvite uroliths in cats, and surgical removal may be more likely.

The numbers of other common urolith types submitted to our laboratory, such as silica, cystine, and urate, also have decreased. Only apatite-containing uroliths had no significant change in trends during the past 21 years. The trends for the metabolic uroliths (urate and cystine) as well as silica were extremely similar. Urate-containing uroliths were the fourth most common mineral type detected at our laboratory during the study period. Dalmatians had the highest OR for developing this particular urolith type, and most urate uroliths obtained from Dalmatians contained 100% urate. Dalmatians have been reported[20,21] to be at risk for development of uroliths because of a genetic defect that results in hyperuricosuria, which is caused by a defect in uric acid transport in the kidneys and liver.[22,23] Hyperuricosuria and hyperuricemia are controlled by a simple autosomal recessive trait for which all Dalmatians are homozygous.[24,25] The SLC2A9 transporter has been identified as the cause of the change in uric acid metabolism by Dalmatians, as determined via positional cloning by use of an interbreed backcross.[26]

In the study reported here, we also detected an increase in the OR for English Bulldogs with regard to development of urate-containing uroliths. Some members of that breed as well as the Black Russian Terrier were also homozygous for the same mutation in SLC2A9.[25] We hypothesize that increased awareness of owners and breeders has contributed to the decrease in the number of urate-containing uroliths that have been submitted recently. However, it is possible that owners and veterinarians presumed that uroliths identified for these breeds were likely urate and chose not to submit them for analysis.

In addition to the aforementioned genetic defect, other breeds typically develop urate-containing uroliths as a result of liver disease, namely portosystemic shunts. The other breeds listed as having a significantly higher OR were likely detected because these dogs are from breeds that appeared to be overrepresented[27–29] or that have an increased risk[30,31] for portosystemic shunts. This could explain why some of these breeds had increased ORs with regards to developing urate-containing uroliths. However, because of the retrospective nature of the study, we were unable to obtain records to determine whether these dogs had any underlying pathological conditions of the liver. Urate-containing uroliths were submitted more often for female dogs than for male dogs, which contradicts the literature, particularly when discussing Dalmatians.[32] Although male Dalmatians were reported to be at a higher risk of developing uroliths in another study,[21] the risk was not significantly different from that for female dogs. This contradiction could have resulted because we reported all dogs that had uroliths containing urate. Furthermore, urate can also be found quite commonly in dogs with struvite urolithiasis, and struvite-containing uroliths are significantly more common in female dogs.

Silica-containing uroliths were identified in 6.6% of the uroliths analyzed. Similar to results in another report,[33] a significant predisposition for males was detected. These types of uroliths have been reported to develop significantly more often in German Shepherd Dogs and Old English Sheepdogs.[33] Although we did not find that German Shepherd Dogs had an OR > 4.0, compared with the OR for the mixed-breed dogs, the OR for German Shepherd Dogs was 1.7 (95% CI, 1.3 to 2.1; $P < 0.001$). Old English Sheepdogs constituted too few submissions to be included in our statistical analyses. Of the 5 breeds found to have a significantly higher OR for the development of silica-containing uroliths, 4 were small-breed dogs. Silica is often found in conjunction with CaOx- and struvite-containing uroliths. For example, silica could act as a nidus for a subsequent staphylococcal urinary tract infection, which could lead to struvite deposition in the outer portion of the urolith. The association of CaOx and silica within a single urolith may be attributable to the possibility of epitaxy associated with silica and CaOx urolithiasis.[34]

Cystine-containing uroliths constituted only 1.3% of the uroliths analyzed during the study period. Similar findings have been reported by investigators at the Minnesota Urolith Center,[35] but much higher prevalences of cystine-containing uroliths have been reported by laboratories in Europe.[36] Similar to results in other studies,[19,36] we found that cystine-containing uroliths developed more often in younger male dogs. Similar to the situation for urate-containing uroliths, a genetic mutation in dogs with cystinuria has been reported.[25] Mutations in the canine SLC3A1 gene can predispose dogs to developing cystinuria and cystine uroliths.[37] A test for this mutation in Newfoundlands has been available for several years, which may have contributed to the decrease in cystine-containing uroliths observed during the past 10 years. As genetic studies continue, breeders can identify dogs that are clinically normal carriers and choose not to mate pairs that could yield affected offspring. Genetic mutations in other breeds have also been investigated.[36,38]

A similar mutation in the SLC3A1 gene has been reported[25] in cystinuric Labrador Retrievers, and this defect resembles the phenotype described for Newfoundlands. However, we determined that Labrador Retrievers have a significantly lower OR of developing cystine-containing uroliths, compared with the OR for mixed-breed dogs. In support of our data, Labrador Retrievers were not listed as 1 of the 67 breeds affected by cystine uroliths at another laboratory.[35] Although the mutation is present in Labrador Retrievers, they do not appear to develop cystine uroliths that are submitted to laboratories as commonly as the other described breeds.

Because we analyzed too few uroliths that contained newberyite, xanthine, brushite, or potassium magnesium pyrophosphate, it was difficult to assess clinically important trends that would affect management of dogs with uroliths of these mineral compositions. The characterization of new mineral types contained in uroliths, such as potassium magnesium pyrophosphate[39] and uric acid monohydrate,[40] makes it possible to more accurately identify the minerals contained within a urolith, some of which may have remained unidentified prior to the characterization of these minerals.

Of the 25,499 uroliths submitted to our laboratory during the study period, 18,614 (73.0%) contained > 1 mineral. In data compiled for our study, all minerals were counted in each layer of every urolith. The advantage of data compilations in which each mineral type is counted, irrespective of the amount contained in the urolith, is that each mineral component in uroliths (with or without distinct layers) will be included. The disadvantage of compiling data in this manner is the possible overlap of different mineral components in a urolith and inclusion of components that are present in smaller percentages. This could explain why some of our data differ slightly from that of other laboratories and why some of the breed predispositions, such as those for silica-containing uroliths, appeared to contradict information in other reports. However, when tailoring prevention strategies for a dog with these types of uroliths, it is clinically helpful to know the mineral composition of the various layers contained in the urolith, which is the reason that most laboratories provide reports of each mineral in this manner.

Several variables must be taken into account when evaluating data in this report. To be included in the statistical analysis, an affected dog had to develop a urolith and the owners had to seek veterinary care. If the urolith was removed, it also had to be submitted to our laboratory to be counted in the statistical analysis. Despite these limitations, potentially valuable patterns emerged from analysis of the data, and this information in regard to potential risk factors for the development of certain types of uroliths can be helpful for veterinarians, breeders, and owners.

In the study reported here, CaOx-containing uroliths continued to be the primary urolith type submitted to our laboratory, whereas the number of struvite-containing uroliths submitted has decreased. Other urolith types, such as urate, silica, and cystine, had a significant change in trend that was not linear, which resulted in a decrease in the number of these types of uroliths submitted. Although these trends may not always accurately represent the distribution of uroliths in the canine population, they do provide guidance for areas of urolithiasis in need of further research. Evaluation of pet foods as well as continued genetic studies will be necessary to help prevent recurrent urolithiasis in dogs.

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From this month's *AJVR*

Effect of changes in number of doses and anatomic location for administration of an *Escherichia coli* bacterin on serum IgG1 and IgG2 concentrations in dairy cows

Ronald J. Erskine et al

Objective—To determine effects of injection site on antibody response to J5 *Escherichia coli* bacterin.

Animals—28 adult Holstein cows.

Procedures—Cows were randomly assigned as control cattle (n = 4 cows), not administered J5 *E coli* bacterin; 3X (8), administered 3 doses of bacterin SC in the left side of the neck; 5XN (8), administered 5 doses of bacterin SC in the left side of the neck; or 5XSR (8), administered 5 doses of bacterin SC sequentially in the left side of the neck, right side of the neck, right side of the thorax, left side of the thorax, and left side of the neck. Blood samples were collected from the cows to determine anti-J5 *E coli* IgG1 and IgG2 concentrations.

Results—Vaccinated cows had higher mean serum anti-J5 *E coli* IgG1 concentrations than did control cows. The 5XN and 5XSR cows had higher mean serum anti-J5 *E coli* IgG1 concentrations than did 3X cows. Additionally, 5XSR cows had higher mean serum anti-J5 *E coli* IgG1 concentrations than did 5XN cows. Vaccinated cows had higher mean serum anti-J5 *E coli* IgG2 concentrations than did control cows. The 5XN and 5XSR cows had higher mean serum anti-J5 *E coli* IgG2 concentrations than did 3X cows. The 5XSR cows had higher mean serum anti-J5 *E coli* IgG2 concentrations than did all other groups at 84 days after the fifth vaccination.

Conclusions and Clinical Relevance—Sequential doses of core-antigen bacterins administered at different anatomic locations may improve antibody response in dairy cattle. (*Am J Vet Res* 2010;71:120–124)