


STANDARD ARTICLE

Urolithiasis in cats: Evaluation of trends in urolith composition and risk factors (2005-2018)

Lucy Kopecny¹  | Carrie A. Palm¹  | Gilad Segev²  | Jennifer A. Larsen³ |
 Jodi L. Westropp¹ 

¹Department of Veterinary Medicine and Epidemiology, University of California Davis, Davis, California

²Koret School of Veterinary Medicine, The Robert H. Smith Faculty of Agriculture, Food and Environment, Hebrew University of Jerusalem, Rehovot, Israel

³Department of Molecular Biosciences, University of California Davis, Davis, California

Correspondence

Jodi L. Westropp, University of California, Davis, School of Veterinary Medicine, One Garrod Drive, Davis, CA 95616.
 Email: jlwestropp@ucdavis.edu

Abstract

Background: Urolithiasis is an important upper and lower urinary tract disease in cats that results in morbidity and mortality.

Objective: To describe trends in composition of uroliths in cats and evaluate risk factors related to age, breed, sex, urolith location, and bacterial urolith cultures.

Sample Population: A total of 3940 uroliths and the cats from which they were obtained.

Methods: The database of the UC Davis Gerald V. Ling Urinary Stone Analysis Laboratory was searched for all urolith submissions from cats between January 2005 and December 2018. Mineral type, age, breed, sex, and urolith location and culture results were recorded. Trends were evaluated and variables compared to evaluate risk factors.

Results: A significant decrease in the proportion of calcium oxalate (CaOx)-containing uroliths occurred over time ($P = .02$), from 50.1% (204/407) of all submissions in 2005 to 37.7% (58/154) in 2018. In contrast, the proportion of struvite-containing uroliths increased significantly ($P = .002$), from 41.8% (170/407) in 2005 to 54.5% (84/154) in 2018. The proportion of CaOx-containing uroliths in the upper urinary tract was significantly higher compared to the proportion of other urolith types in the upper urinary tract. Urate-containing uroliths were the third most common type (361/3940, 9.2%). Overall, sex and age predispositions were similar to those reported previously.

Conclusions and Clinical Importance: The decrease in the proportion of CaOx-containing uroliths and increase in the proportion of struvite-containing uroliths warrants investigation. Further education regarding the efficacy of medical dissolution of struvite-containing uroliths is recommended.

KEYWORDS

calcium oxalate, feline, struvite, urate, urolithiasis

Abbreviations: 95% CI, 95% confidence interval; CaOx, calcium oxalate; DMH, domestic medium hair; DSB, dried solidified blood; DSH, domestic shorthair; MUC, Minnesota Urolith Center; OR, odds ratio.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Journal of Veterinary Internal Medicine* published by Wiley Periodicals LLC on behalf of American College of Veterinary Internal Medicine.

1 | INTRODUCTION

Urolithiasis is an important disease in cats, particularly because of its occurrence within both the lower and upper urinary tract, which can result in clinically important morbidity and mortality. Calcium oxalate (CaOx) and struvite historically have been the most common mineral types reported in cats, but the relative proportion of these uroliths has varied over time. The proportion of CaOx-containing uroliths was higher than the proportion of struvite-containing uroliths from 1993 to 2004 at the Gerald V. Ling Urinary Stone Analysis Laboratory at the School of Veterinary Medicine, University of California, Davis, but a gradual increase in struvite-containing uroliths was noted in the later years of that study.¹ Calcium oxalate uroliths also were the most common type reported from the Canadian Veterinary Urolith Centre between 1998 and 2014.² A report from the Minnesota Urolith Center (MUC) identified struvite as the most common urolith type submitted to that laboratory in 2007 (49% struvite compared to 41% CaOx) and 2019 (52% struvite compared to 35% CaOx).³

An increasing number of veterinary therapeutic diets for the management of urinary disease in cats has become available and could impact the numbers and types of uroliths ultimately submitted for analysis because dissolution or urolith prevention is feasible, but affected by urolith type. Dietary influences on urine composition also may result in shifts in urolith risk and composition that can be documented at the population level. Breed, age, and sex are recognized as predisposing factors to certain types of uroliths in cats. For example, CaOx urolithiasis occurs more commonly in male than in female cats.^{1,2}

Trends in submission also can be influenced by changes in treatment approaches to urolithiasis, particularly because just over 70% of 2445 nephroureteroliths in cats were composed of CaOx between 1981 and 2003.³ The number of CaOx-containing uroliths from the upper urinary tract increased significantly in submissions to our laboratory between 1985 and 2004.¹ However, the development of renal decompressive procedures for ureteral obstruction in which ureteroliths are not removed (eg, ureteral stent and subcutaneous ureteral bypass system placement) could affect this trend.^{4,5}

These changing trends in urolithiasis emphasize the importance of ongoing evaluation, including evaluation of risk factors for specific urolith types. Our study aimed to describe the composition of uroliths from cats submitted to the Gerald V. Ling Urinary Stone Analysis Laboratory between 2005 and 2018. We also aimed to evaluate risk factors for urolithiasis in cats, including age, breed, sex, urolith location, and bacteria cultured from submitted uroliths.

2 | MATERIALS AND METHODS

2.1 | Study population

A computer-assisted search of the records of the Gerald V. Ling Urinary Stone Analysis Laboratory at the University of California, Davis was performed to identify all urolith submissions from cats between

January 1, 2005 and December 31, 2018. Information in the database was obtained from a standard form submitted with each urolith. Year of urolith submission, mineral composition of the urolith, age, breed, sex, and location of the urolith within the urinary tract were recorded. Individual cats may have had >1 urolith submission during this time period and each urolith submission was considered separately.

2.2 | 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, with polarizing light microscopy and infrared spectroscopy as previously described.¹ X-ray diffractometry and high pressure liquid chromatography were utilized if necessary. For each urolith, each mineral present in any amount was recorded. 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 minerals, whether multiple mineral components were contained in distinct layers or uniformly distributed throughout the urolith, were reported as containing that mineral component. In our study, they were counted once for each mineral detected in the urolith and as a result, totals of minerals detected in uroliths is higher than the number of uroliths.

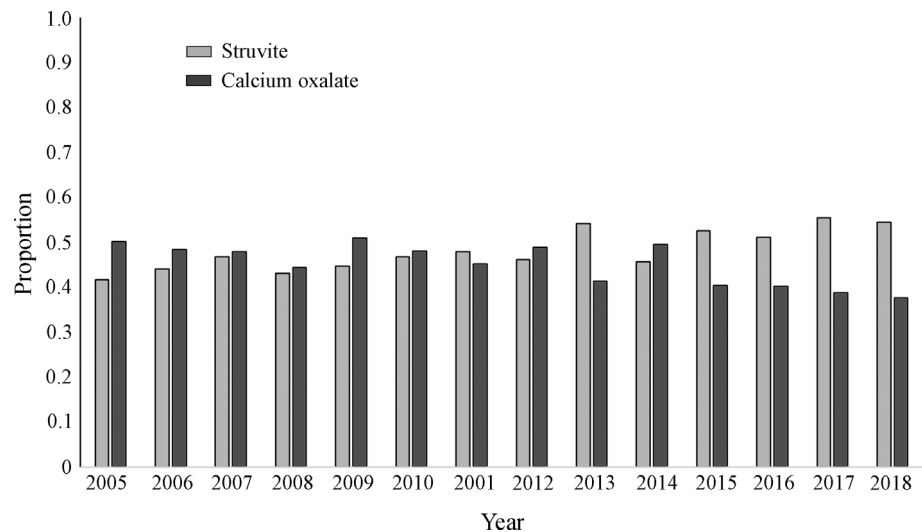
In our study, CaOx included CaOx monohydrate, dihydrate, or both, and urate included uric acid and its salts (eg, ammonium urate). For location, the upper urinary tract was considered to include the kidney and ureter and lower urinary tract included the bladder and urethra. Voided uroliths were considered separately. Because uroliths were retrieved from >1 location in some cats, totals of location may be higher than the total number of uroliths containing each mineral type.

Urolith cultures were performed as previously described when requested by the submitting veterinarian.⁶ Briefly, uroliths were washed 4 times with 50 mL of sterile saline for 10 seconds. The uroliths then were cracked using sterile rongeurs and the core was scraped into a sterile mortar. One milliliter of sterile saline was added to this sample and a 0.2 mL aliquot was cultured for aerobic bacteria.

2.3 | Statistical analysis

Descriptive statistics were used for individual urolith types for age group, breed, sex, location, and urolith culture results. Age groups were determined a priori based on a previous publication from our laboratory to enable comparisons.¹ Because totals of minerals

FIGURE 1 Proportion of calcium oxalate- and struvite-containing uroliths (of all urolith types) each year from 2005 to 2018. There was a significant nonlinear decrease and significant nonlinear increase in the proportion of CaOx-containing ($P = .02$) and struvite-containing ($P = .002$) uroliths respectively over time



detected in uroliths were higher than the number of uroliths submitted, the totals for age, sex, and breed sum to >100% when all mineral types are considered. The χ^2 test was used to compare association between categorical variables (age group, breed, sex, urolith location, and urolith bacterial culture) for each urolith type. For breed analysis, domestic shorthair (DSH) was used as the reference breed. Cats for which breed was unknown or listed as mixed were excluded from breed analysis. Breeds for which there were <10 cats of that breed in the database over the time period evaluated were not reported because of small numbers. The χ^2 tests for trend were used to evaluate trends in urolith composition over time and trends in age groups for individual urolith types. Results were reported as odds ratios (ORs) and 95% confidence intervals (95% CIs). P values <.05 were considered significant.

3 | RESULTS

A total of 3940 urolith submissions from cats were analyzed at the Gerald V. Ling Urinary Stone Analysis Laboratory between January 2005 and December 2018. Submissions were from various academic and private veterinary practices almost exclusively within the United States. Of 3940 uroliths from cats, 3187 (80.9%) uroliths were composed of a single mineral type.

For 9 urolith submissions, data regarding sex of the cat were missing. For 63 urolith submissions, data on the age were missing. For 33 urolith submissions, data regarding breed were missing.

3.1 | Calcium oxalate- and struvite-containing uroliths

Of 3940 urolith submissions from cats, 1820 (46.2%) were CaOx-containing uroliths and 1856 (47.1%) were struvite-containing uroliths. Of 1820 CaOx-containing uroliths, 56.6% were composed of CaOx monohydrate only, 0.9% of CaOx dihydrate only, and 42.6%

contained both CaOx monohydrate and dihydrate. A significant nonlinear decrease in the proportion of CaOx-containing uroliths occurred over time ($P = .02$) from 50.1% (204/407) in 2005 to 37.7% (58/154) in 2018. In contrast, the proportion of struvite-containing uroliths increased significantly in a nonlinear fashion over this period ($P = .002$) from 41.8% (170/407) in 2005 compared to 54.5% (84/154) in 2018 (Figure 1).

Of CaOx-containing uroliths, 64% (1168/1814) were from male and 36% (646/1814) were from female cats. The proportion of CaOx-containing uroliths among male cats (1168/2344; 49.8%) was significantly higher compared with the proportion of CaOx-containing uroliths among female cats (646/1587; 40.7%; OR, 1.5; 95% CI, 1.3-1.7; $P < .001$). Of cats with struvite-containing uroliths, 47.1% (873/1852) were submitted from female cats and 52.9% (979/1852) were from male cats. The proportion of struvite-containing uroliths among female cats (873/1587; 55.0%) was significantly higher than the proportion of struvite-containing uroliths among male cats (979/2344; 41.8%; OR, 1.7; 95% CI, 1.5-1.9; $P < .001$).

Approximately 2/3 of CaOx-containing uroliths (1180/1775; 66.5%) were submitted from cats between 7 and 15 years of age. The proportion of CaOx-containing uroliths was significantly higher in cats ≥ 7 years of age (1289/2280; 56.5%) compared to the proportion of CaOx-containing uroliths in cats <7 years of age (486/1557; 31.2%; OR, 2.9; 95% CI, 2.5-3.3; $P < .001$). Struvite-containing uroliths most often were submitted from cats between 4 and 10 years of age (63.1% of 1821). The proportion of struvite-containing uroliths among cats <7 years of age (954/1557; 61.3%) was significantly higher compared to the proportion of struvite-containing uroliths from cats ≥ 7 years of age (867/2280; 38.0%; OR, 2.6; 95% CI, 2.3-3.0; $P < .001$) (Figure 2).

Breeds at higher risk of developing CaOx-containing uroliths compared to the DSH were Burmese (OR, 5.3; 95% CI, 1.1-35.7; $P = .02$) and Persian (OR, 1.7; 95% CI, 1.06-2.9; $P = .02$). The domestic medium hair (DMH) was the only breed at significantly higher risk of developing struvite-containing uroliths compared to the DSH (OR, 1.4; 95% CI, 1.1-1.7; $P = .003$). Several breeds were at lower risk of

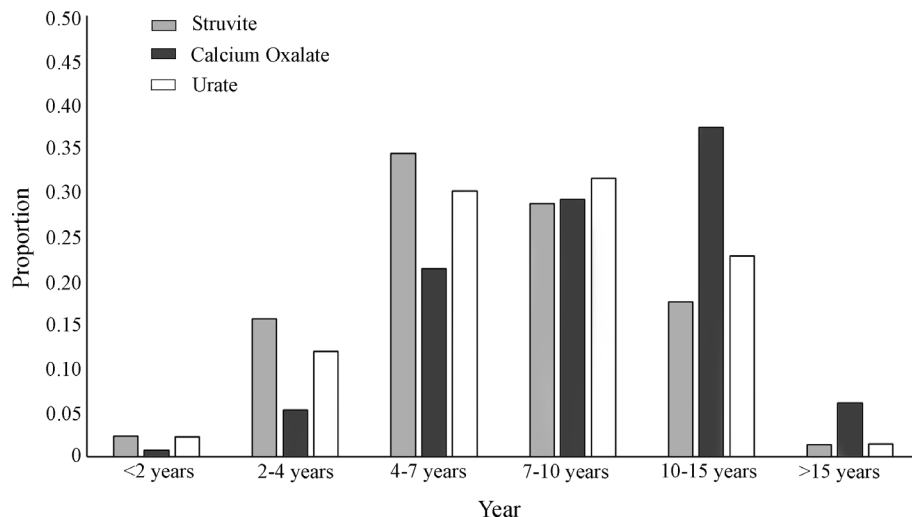


FIGURE 2 Age distribution of cats with struvite-, calcium oxalate-, and urate-containing uroliths submitted for analysis from 2005 to 2018. Proportions represent the proportion of cats with each the mineral type within the age grouping

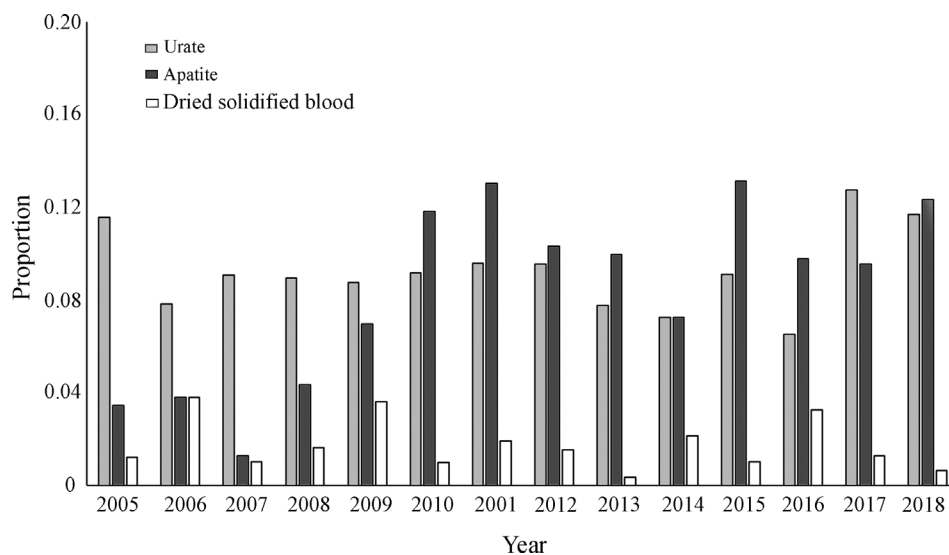


FIGURE 3 Proportion of urate-, apatite-, and dried solidified blood-containing uroliths in cats between January 2005 and December 2018

developing struvite-containing uroliths compared with the DSH, including Bengal (OR, 0.2; 95% CI, 0.02-0.7; $P = .004$), Ocicat (OR, 0.2; 95% CI, 0.02-0.7; $P = .02$), and Persian (OR, 0.6; 95% CI, 0.3-0.9; $P = .02$).

3.2 | Urate-containing uroliths

Urate-containing uroliths represented 361/3940 (9.2%) of all urolith submissions from cats. Of urate-containing uroliths, 186/361 (49.3%) were composed solely of urate. Of mixed urate-containing uroliths (118/175; 67.4%), the following minerals were also noted: struvite (57/175; 32.6%), CaOx (10/175; 5.7%), apatite (3/175; 1.7%), silica (3/175; 1.7%), and dried solidified blood (DSB; 1/175; 0.6%). No significant change in the proportion of urate-containing urolith submissions was found over time ($P = .6$; Figure 3).

No sex predisposition was found for urate-containing uroliths, with 44.6% (161/361) from female and 55.4% (200/361) from male cats ($P = .09$). Urate-containing uroliths most often were submitted

from cats between 4 and 10 years of age, representing 217/352 (61.6%) of urate-containing uroliths (Figure 2). No significant difference was found in the proportion of urate-containing uroliths between cats <7 years of age and ≥ 7 years of age ($P = .1$). The Ocicat was the only breed at significantly higher risk of urate-containing uroliths compared to the DSH (OR, 8.3; 95% CI, 2.5-27.8; $P < .001$).

3.3 | Apatite-containing uroliths

In total, 293 apatite-containing uroliths were submitted, representing 7.4% of 3940 urolith submissions from cats. Of these, 12 (4.1%) were pure and the remainder mixed. Coprecipitates in mixed apatite-containing uroliths were struvite (202/281; 71.9%), CaOx (83/281; 29.5%), urate (10/281; 3.6%), DSB (8/28; 2.8%), and silica (2/281; 0.7%). A significant nonlinear increase in the proportion of apatite-containing uroliths was observed between 2005 and 2018 ($P < .001$), with apatite-containing uroliths constituting 3.4% of all urolith submissions in 2005 and 12.3% in 2018 (Figure 3).

TABLE 1 Proportion of upper (kidney and ureter), lower urinary tract, and voided uroliths in cats for each mineral type

| Urolith type | Upper urinary tract (%) | Lower urinary tract (%) | Voided (%) |
|------------------------|-------------------------|-------------------------|---------------|
| Calcium oxalate | 140/1996 (7.0) | 1834/1996 (91.9) | 22/1996 (1.1) |
| Struvite | 2/1929 (0.1) | 1909/1929 (99.0) | 18/1929 (0.9) |
| Urate | 3/372 (0.8) | 368/372 (98.9) | 1/372 (0.3) |
| Apatite | 11/292 (3.8) | 278/292 (95.2) | 3/292 (1.0) |
| Silica | 0/19 (0) | 15/19 (89.5) | 2/19 (10.5) |
| Dried solidified blood | 10/73 (13.7) | 60/73 (82.2) | 3/73 (4.1) |

Of 290 cats with apatite-containing uroliths for which sex was known, 144 (49.7%) were females and 146 (50.3%) were males. The proportion of apatite-containing uroliths in female cats (144/1587; 9.1%) was significantly higher compared with the proportion of apatite-containing uroliths in male cats (146/2344; 6.2%; OR, 1.5; 95% CI, 1.2-1.9; $P = .001$). The proportion of apatite-containing uroliths in cats ≥ 7 years of age (189/2280, 8.3%) was significantly higher than the proportion of apatite-containing uroliths in cats < 7 years of age (93/1557; 6.0%; OR, 1.4; 95% CI, 1.1-1.9; $P = .007$). Apatite-containing uroliths most often were submitted from cats between 7 and 10 years of age (99/282; 35.1%). No breed predispositions were identified.

3.4 | Dried solidified blood-containing uroliths

Seventy-two uroliths (1.8% of 3940 submissions from cats) were composed of DSB. No significant change in the proportion of DSB-containing urolith submissions over time was observed ($P = .2$; Figure 3).

Of all cats with DSB-containing uroliths, 15.3% (11/72) were female and 84.7% (61/72) were male. The proportion of DSB-containing uroliths in male cats (61/2344; 2.6%) was significantly higher compared with the proportion of DSB-containing uroliths in female cats (11/1587; 0.7%; OR, 3.8; 95% CI, 2.0-7.7; $P < .001$). The mean age of cats with DSB-containing uroliths was 10.6 (± 4.3) years; 45.6% (31/68) of submissions were from cats between 10 and 15 years of age, followed by cats between 7 and 10 years of age (14/68; 20.6%). The proportion of DSB-containing uroliths in cats that were ≥ 7 years of age (54/2280; 2.4%) was significantly higher than the proportion of DSB-containing uroliths in cats that were < 7 years of age (14/1557; 0.9%; OR, 2.7; 95% CI, 1.4-5.0; $P = .001$).

Three breeds of cats were at significantly higher risk of DSB-containing uroliths than the DSH: Bengal (OR, 9.6; 95% CI, 1.5-47.1; $P < .001$), Persian (OR 3.9, 95% CI, 1.1-11.8; $P = .007$) and domestic longhair (OR, 2.1; 95% CI, 1.1-4.0; $P = .02$). No cat breed had a decreased risk of DSB-containing uroliths.

3.5 | Silica-containing uroliths

Only 20 (0.5%) submitted uroliths contained silica. Of these, 6 (30%) were from female and 14 (70%) were from male cats. No significant

differences were noted with respect to sex and age when comparing the proportion of silica-containing uroliths to other urolith types. This mineral most often was present in uroliths submitted from DSH cats (13/20, 65%). Because of the limited number of silica-containing uroliths, too few breeds were available to perform statistical comparisons. The breeds represented included 13 DSH, 2 DMH, 2 Persian, 1 Himalayan, 1 Siamese, and 1 Burmese.

3.6 | Others

The following minerals were noted infrequently: potassium magnesium pyrophosphate (8), xanthine (6), brushite (5), cystine (2), and newberyite (1). Mineral type could not be identified in 5 instances.

3.7 | Urolith location

Table 1 describes urolith location. The proportion of CaOx-containing uroliths in the upper urinary tract was significantly higher compared to the proportion of other stone types in the upper urinary tract (OR, 11.0; 95% CI, 6.3-20.0; $P < .001$). The mean age of cats with CaOx-containing uroliths removed from the upper urinary tract was 8.7 (± 3.8) years and from the lower urinary tract was 8.9 (± 3.6) years. In addition to CaOx-containing uroliths, the proportion of DSB-containing uroliths from the upper urinary tract was significantly higher than for other urolith types (OR, 4.5; 95% CI, 2.1-9.1; $P < .001$).

3.8 | Urolith bacterial culture results

Of all submissions, aerobic bacterial culture was performed on 1007 uroliths (25.6%), of which 89 (8.8%) were positive. The most frequently cultured bacteria were *Staphylococcus* spp. (44/89; 49.4%), *Enterococcus* spp. (21/89, 23.6%), and *Escherichia coli* (17/89, 19.1%). Struvite-containing uroliths were more likely to have positive culture results (55/503; 10.9%) compared with all other mineral types (OR, 1.7; 95% CI, 1.1-2.7; $P = .02$). Of 55 struvite-containing uroliths with a positive urolith culture, 30 (54.5%) cultured *Staphylococcus* spp. Other urease-producing bacteria cultured in association with struvite-containing uroliths were *Proteus* spp. (2/55) and *Corynebacterium urealyticum* (3/55). Of CaOx-containing uroliths

cultured, 34/468 (7.3%) were positive. Of urate-containing and DSB-containing uroliths that were cultured, 1/84 (1.3%) and 2/15 (13.3%), respectively, were positive.

4 | DISCUSSION

Evaluation of trends in urolith composition over time identified several important findings. Between 2005 and 2018, the proportion of CaOx-containing uroliths decreased and the proportions of struvite- and apatite-containing uroliths increased. No change in the frequency of urate-containing uroliths was noted over this time period. Age and sex predispositions were overall similar to those reported previously.^{1,2}

The decrease in the proportion of CaOx-containing uroliths with an increase in the proportion of struvite-containing uroliths is in contrast to what our laboratory reported from 1985 to 2004, where 52.8% of uroliths from cats contained CaOx and 43.4% contained struvite, with the proportion of CaOx-containing uroliths increasing significantly during that time period. However, we noted a gradual decrease in the proportion of CaOx-containing uroliths from 2001 to 2004, suggesting an emerging trend,¹ which appears to have continued based on the present study. These findings are similar to data from the MUC from 2004 to 2007.³ Whereas sex predisposition for CaOx- and struvite-containing uroliths did not change, some changes in breed risk were apparent.¹ The Persian breed continued to have an increased risk for CaOx-containing uroliths,¹ and an increased risk for the Burmese breed was also found, in agreement with reports from several urolith laboratories.^{1,2,7} Such breed predispositions could suggest an underlying genetic predisposition to CaOx urolithiasis in combination with dietary and environmental factors. Heritability in humans with CaOx nephrolithiasis has been reported.⁸ Genome-wide association and candidate gene studies have identified genes associated with hyperoxaluria and calcium-based nephrolithiasis.⁹ Because breed associations continue to be reported for CaOx, studies evaluating the genetics in cats with naturally occurring disease could be relevant to other species. The DMH was the only breed at increased risk of developing struvite-containing uroliths. The Manx and Siamese breeds were at increased risk based on previous data from our laboratory as well as data from the Canadian Veterinary Urolith Centre during a more recent time period.^{1,2}

Environmental and dietary influences likely have contributed to the reciprocal change in trend reported for CaOx- and struvite-containing uroliths. It is hypothesized that widespread use of highly acidified diets for cats (target urine pH <6.2) accounted for the increase in the proportion of CaOx-containing uroliths and decrease in the proportion of struvite-containing uroliths, particularly in the early 1990s.¹⁰ The solubility of struvite increases with decreasing urinary pH, but acidifying diets can promote release of calcium carbonate and calcium phosphate from bone, possibly resulting in hypercalciuria.¹¹ Although CaOx uroliths may develop in a wide range of urinary pH, highly acidic urine can alter concentrations of potentially important inhibitors of calcium oxalate crystallization such as

magnesium, pyrophosphates, and Tamm-Horsfall mucoprotein.^{12,13} Because of this concern, as well as market demands, most veterinary therapeutic diet formulations were altered to address both struvite prevention and dissolution as well as CaOx prevention. As such, some of these therapeutic diets now promote more moderate urine pH (up to pH 6.5) and incorporate other strategies such as increased sodium or moisture content to help achieve a urinary environment that still remains under the saturation threshold for struvite crystallization.¹⁴ Improved preventative management (possibly including dietary strategies) could have resulted in the decrease in the proportion of CaOx-containing uroliths noted in our current study, although dietary and medical histories were not available to enable assessment of any associations. A recent observational study from cat and dog owners in 5 countries indicated that feeding unconventional diets such as raw or homemade diets appears more prevalent.¹⁵ The effect of these diets on mineral types in cats with urolithiasis is uncertain. Prospective long-term diet studies are needed to fully characterize the role of diet and risk of CaOx-containing uroliths (or any urolith type). Despite clinical trial data demonstrating efficacy of struvite dissolution with currently available veterinary therapeutic diets,¹⁶⁻¹⁹ the proportion of struvite-containing urolith submissions has increased over time. Further education regarding noninvasive treatment for suspected struvite urolithiasis is needed to promote dietary dissolution as the first therapeutic approach.

Apatite-containing uroliths significantly increased over the study period. Because this mineral is often a coprecipitate with other mineral types, this change in trend likely is a reflection of the changes in minerals that coprecipitate with apatite. In the present study, the change could be related to the increase in struvite-containing uroliths. Previously, we reported a significant decrease in apatite-containing uroliths, and not surprisingly a significant decrease in struvite-containing urolithiasis also was noted.¹ Although the presence of apatite within struvite uroliths has been reported to be a reason for dissolution failure, particularly in dogs,²⁰ over 1600 struvite uroliths did not contain apatite in urolith submissions from cats during our current study. Moreover, studies evaluating struvite dissolution protocols in cats reported no apatite mineral content in the uroliths from the majority of nonresponders; apatite content in responders cannot be evaluated.¹⁷⁻¹⁹ Our data suggest that further education regarding noninvasive treatment for suspected struvite urolithiasis is needed to promote dietary dissolution as the first therapeutic approach.²¹ If dietary treatment fails, urolith removal and accurate histories should help elucidate reasons for failure.

Approximately 57% of CaOx-containing uroliths were CaOx monohydrate, 43% were mixed and rarely were uroliths comprised of purely the dihydrate form. This finding is in contrast to what has been reported for dogs in which just under 20% of 6690 uroliths reported by European urolith laboratories were mixed CaOx monohydrate and dihydrate.²² In dogs in France, 56.3% of CaOx uroliths were CaOx monohydrate and 43.7% were CaOx dihydrate, but the proportion of mixed CaOx monohydrate and dihydrate uroliths was not reported.²³ In humans, CaOx dihydrate and CaOx monohydrate may be associated with various metabolic abnormalities: CaOx monohydrate urolith

formers have a higher incidence of hyperoxaluria and hypocitraturia whereas CaOx dihydrate urolith formers tend to be hypercalciuric.²⁴ Calcium oxalate dihydrate can transform into CaOx monohydrate in vitro²⁵ and shifts between these subtypes could occur as the crystal lattice is exposed to a changing urine environment.²⁶ Investigating potential metabolic abnormalities in cats with CaOx urolithiasis could be considered for further study.

Although CaOx and DSB-containing uroliths were more likely to be removed from the upper urinary tract compared to other urolith types, the proportion submitted from this location was lower than previously reported.¹ Between 1985 and 2004, 21.0% of CaOx-containing urolith submissions were from the upper urinary tract,¹ whereas only 7.0% were from the upper tract in the present study. The proportion of DSB-containing uroliths from the upper urinary tract also decreased. Between 1986 and 2003, 39.6% of DSB-containing uroliths submitted from cats were from the upper urinary tract, whereas only 13.7% were from the upper urinary tract in our present study.²⁷ Previously, ureterotomy frequently was performed for ureterolithiasis in cats.²⁸ With newer renal decompressive procedures in which ureteral stents and subcutaneous ureteral bypass systems are placed without ureterolith removal,^{4,5} a decrease in the proportion of CaOx- and DSB-containing uroliths removed from the upper tract likely has occurred, despite the disease still being prevalent. It is unknown whether cats in our study with CaOx-containing and DSB-containing uroliths submitted from the lower urinary tract also had these uroliths in the upper urinary tract that were not removed because this information is not captured on the submission form, and removal of upper urinary tract uroliths is not recommended unless clinical abnormalities such as ureteral obstruction or perceived patient pain are identified.¹⁹ Based on the overall proportion removed from the upper urinary tract, it is unlikely that the decrease in the proportion of CaOx-containing urolith submissions is solely because of the lack of removal of upper urinary tract uroliths. Uroliths retrieved from the lower urinary tract also could have formed in the upper urinary tract and developed further in the bladder.

Urate urolithiasis continues to be uncommon in cats.^{1,2,29} Several purebred cat breeds previously have been associated with predisposition to urate urolithiasis, but only the Ocicat, a breed previously reported to be predisposed, was identified as having a higher risk of urate-containing uroliths in our current study.^{2,29} This finding differs from what we reported previously, where the Siamese breed had increased risk.¹ A genetic cause of urate urolithiasis is recognized in many dog breeds including the Dalmatian and Bulldog,^{30,31} but little information regarding the pathogenesis of urate urolithiasis in cats exists. Portosystemic shunts appear to be uncommon in most cats with urate urolithiasis, particularly if these uroliths are documented in a middle-aged cat.³² Genetic evaluation of the Ocicat and other previously identified predisposed breeds should be considered to evaluate potential genetic mutations leading to hyperuricosuria and subsequent development of urate-containing uroliths. When urate-containing uroliths occurred as mixed uroliths, they most often were associated with struvite. The coprecipitation of urate and struvite could reflect a development of urease producing bacterial infection

secondary to initial urate urolith formation within the urinary tract, similar to what occurs in some dogs.³³

Few DSB-containing uroliths were submitted. Similar to our previous data, a male predisposition was noted,^{1,27} but, reasons for this association remain unclear. The mean age of cats with DSB-containing uroliths previously has been reported as 9 years.²⁷ This finding is similar to our current data in which mean age was 10.5 years. Microscopic or macroscopic hematuria are thought to be predisposing factors in some cats with DSB uroliths. Although a predisposition for the Persian and Bengal breeds has not been recognized previously, the Bengal and Persian breeds are predisposed to other urolith types, and predisposition to DSB-containing uroliths could reflect a predisposition to development of urolithiasis in general.^{1,2,29}

Although struvite-containing uroliths were more likely to be associated with a positive bacterial urolith culture, only 10.9% of all struvite-containing uroliths that underwent bacterial culture were positive. Of these, 64.8% yielded urease-producing bacteria. The low proportion of positive struvite-containing urolith cultures is similar to a prior study⁶ and consistent with this mineral type most often being sterile in cats rather than infection-associated, as typically noted in dogs.^{6,19} Because the most common bacteria cultured were *Staphylococcus* spp., struvite-containing uroliths in cats can be infection-associated. Interpretation of urolith cultures should be tailored to the individual patient and antimicrobials often are not warranted if clinical signs are no longer present after the urolith is removed.³⁴ Based on the low proportion of positive cultures associated with struvite-containing uroliths and the need to improve antimicrobial stewardship, the clinical utility of urolith cultures in cats is low and not recommended in most cases.

Data for cats in our study were from the Gerald V. Ling Urinary Stone Analysis Laboratory and, as a result, might not be representative of all urolith types, ages, breeds, and sex across the United States, with submissions from various academic and private veterinary hospitals. In addition, because of the reporting methods of the laboratory, the proportion of each mineral within uroliths varied, and in some cases, represented <50% of the overall urolith composition. The advantage of data compilations in which each mineral type is counted, regardless of the amount contained in the urolith specimen, is that each mineral component in the calculi, with or without distinct layering, will be included. The disadvantage of compiling data in this manner is the possible overlap of different mineral components in a calculus and inclusion of components that are present in lesser percentages. Finally, recurrent urolith episodes could not reliably be documented and as such, some uroliths included might represent recurrent uroliths from the same cat.

5 | CONCLUSIONS

The proportion of CaOx-containing uroliths decreased and a reciprocal increase in the proportion of struvite-containing uroliths occurred, which warrants investigation. Further education regarding struvite dissolution is recommended. Similar to previous studies, urate-containing uroliths were the third most common mineral type in this

population and the trends in submission have not changed. Overall, sex and age predispositions were similar to those reported previously.

ACKNOWLEDGMENT

No funding was received for this study.

CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

ORCID

Lucy Kopecny  <https://orcid.org/0000-0002-6935-9463>

Carrie A. Palm  <https://orcid.org/0000-0003-1445-5113>

Gilad Segev  <https://orcid.org/0000-0003-4714-3159>

Jodi L. Westropp  <https://orcid.org/0000-0003-1287-3979>

REFERENCES

- Cannon AB, Westropp JL, Ruby AL, Kass PH. Evaluation of trends in urolith composition in cats: 5,230 cases (1985-2004). *J Am Vet Med Assoc.* 2007;231:570-576.
- Houston DM, Vanstone NP, Moore AEP, Weese HE, Weese JS. Evaluation of 21,426 feline bladder urolith submissions to the Canadian Veterinary Urolith Centre (1998-2014). *Can Vet J.* 2016;57:196-201.
- Osborne CA, Lulich JP, Kruger JM, Ulrich LK, Koehler LA. Analysis of 451,891 canine uroliths, feline uroliths, and feline urethral plugs from 1981 to 2007: perspectives from the Minnesota Urolith Center. *Vet Clin North Am Small Anim Pract.* 2009;39:183-197.
- Berent AC, Weisse CW, Todd K, Bagley DH. Technical and clinical outcomes of ureteral stenting in cats with benign ureteral obstruction: 69 cases (2006-2010). *J Am Vet Med Assoc.* 2014;244:559-576.
- Berent AC, Weisse CW, Bagley DH, Lamb K. Use of a subcutaneous ureteral bypass device for treatment of benign ureteral obstruction in cats: 174 ureters in 134 cats (2009-2015). *J Am Vet Med Assoc.* 2018;253:1309-1327.
- Perry LA, Kass PH, Johnson DL, Ruby AL, Shiraki R, Westropp JL. Evaluation of culture techniques and bacterial cultures from uroliths. *J Vet Diagn Invest.* 2013;25:199-202.
- Lekcharoensuk C, Lulich JP, Osborne CA, et al. Association between patient-related factors and risk of calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc.* 2000;217:520-525.
- Goldfarb DS, Avery AR, Beara-Lasic L, Duncan GE, Goldberg J. A twin study of genetic influences on nephrolithiasis in women and men. *Kidney Int Rep.* 2019;4:535-540.
- Sayer JA. Progress in understanding the genetics of calcium-containing nephrolithiasis. *J Am Soc Nephrol.* 2017;28:748-759.
- Lekcharoensuk C, Osborne CA, Lulich JP, et al. Association between dietary factors and calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc.* 2001;219:1228-1237.
- Dibartola SP. Chapter 10: Metabolic acid-base disorders. In: Dibartola SP, ed. *Fluid, Electrolyte and Acid-Base Disorders in Small Animal Practice.* 4th ed. St Louis, MO: Elsevier Saunders; 2012:251-283.
- Hess B, Nakagawa Y, Parks JH, Coe FL. Molecular abnormality of Tamm-Horsfall glycoprotein in calcium oxalate nephrolithiasis. *Am J Physiol.* 1991;260:F569-F578.
- Kirk CA, Ling GV, Franti CE, Scarlett JM. Evaluation of factors associated with development of calcium oxalate urolithiasis in cats. *J Am Vet Med Assoc.* 1995;207:1429-1434.
- Queau Y. Nutritional management of urolithiasis. *Vet Clin North Am Small Anim Pract.* 2019;49:175-186.
- Dodd S, Cave N, Abood S, Shoveller AK, Adolphe J, Verbrugghe A. An observational study of pet feeding practices and how these have changed between 2008 and 2018. *Vet Rec.* 2020;186:643-651.
- Houston DM, Weese HE, Evason MD, Biourge V, van Hoek I. A diet with a struvite relative supersaturation less than 1 is effective in dissolving struvite stones in vivo. *Br J Nutr.* 2011;106:S90-S92.
- Lulich JP, Kruger JM, Macleay JM, et al. Efficacy of two commercially available, low-magnesium, urine-acidifying dry foods for the dissolution of struvite uroliths in cats. *J Am Vet Med Assoc.* 2013;243:1147-1153.
- Torres-Henderson C, Bunkers J, Contreras ET, Cross E, Lappin MR. Use of Purina Pro Plan Veterinary Diet UR Urinary St/Ox to dissolve struvite cystoliths. *Top Companion Anim Med.* 2017;32:49-54.
- Tefft KM, Byron JK, Hostnik ET, et al. Effect of a struvite dissolution diet in cats with naturally occurring struvite urolithiasis. *J Feline Med Surg.* 2021;23(4):269-277. <https://doi.org/10.1177/1098612X20942382>.
- Dear JD, Larsen JA, Bannasch M, et al. Evaluation of a dry therapeutic urinary diet and concurrent administration of antimicrobials for struvite cystolith dissolution in dogs. *BMC Vet Res.* 2019;15:273.
- Lulich JP, Berent AC, Adams LG, Westropp JL, Bartges JW, Osborne CA. ACVIM small animal consensus recommendations on the treatment and prevention of uroliths in dogs and cats. *J Vet Intern Med.* 2016;30:1564-1574.
- Hesse A, Frick M, Orzekowsky H, Failing K, Neiger R. Canine calcium oxalate urolithiasis: frequency of whewellite and weddellite stones from 1979 to 2015. *Can Vet J.* 2018;59:1305-1310.
- Blavier A, Sulter A, Bogey A, et al. Results of infrared spectrophotometry analysis of 1131 canine urinary stones, collected in France from 2007 to 2010. *Eur J Companion Anim Pract.* 2013;47:7-16.
- Bamberge JN, Blum KA, Kan KM, et al. Clinical and metabolic correlates of calcium oxalate stone subtypes: implications for etiology and management. *J Endourol.* 2019;33:755-760.
- Hesse A, Berg W, Schneider HJ, Hienzsch E. In vitro experiments concerning the theory of the formation of whewellite and weddellite urinary calculi. *Urol Res.* 1976;4:157-160.
- Domingo-Neumann RA, Ruby AL, Ling GV, Schiffman PS, Johnson DL. Ultrastructure of selected calcium-oxalate containing urinary calculi in dogs. *Am J Vet Res.* 2001;62:237-247.
- Westropp JL, Ruby AL, Bailiff NL, Kyles AE, Ling GV. Dried solidified blood calculi in the urinary tract of cats. *J Vet Intern Med.* 2006;20:828-834.
- Kyles AE, Hardie EM, Wooden BG, et al. Management and outcome of cats with ureteral calculi: 153 cases (1984-2002). *J Am Vet Med Assoc.* 2005;226:937-944.
- Albasan H, Osborne CA, Lulich JP, Lekcharoensuk C. Risk factors for urate uroliths in cats. *J Am Vet Med Assoc.* 2012;240:842-847.
- Bannasch D, Safra N, Young A, et al. Mutations in the SLC2A9 gene cause hyperuricosuria and hyperuricemia in the dog. *PLoS Genet.* 2008;4:1-8.

31. Karmi N, Brown EA, Hughes SS, et al. Estimated frequency of the canine hyperuricosuria mutation in different dog breeds. *J Vet Intern Med.* 2010;24:1337-1342.
32. Dear JD, Shiraki R, Ruby AL, Westropp JL. Feline urate urolithiasis: a retrospective study of 159 cases. *J Feline Med Surg.* 2011;13:725-732.
33. Caporali EHG, Phillips H, Underwood L, et al. Risk factors for urolithiasis in dogs with congenital extrahepatic portosystemic shunts: 95 cases. *J Am Vet Med Assoc.* 2015;264:530-536.
34. Weese JS, Blondeau J, Boothe D, et al. International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats. *Vet J.* 2019;247:8-25.
35. Minnesota Urolith Center, University of Minnesota. 2019 global urolith data. <https://www.vetmed.umn.edu/sites/vetmed.umn.edu/files/globaldata.pdf>. Accessed December 3, 2020.

How to cite this article: Kopecny L, Palm CA, Segev G, Larsen JA, Westropp JL. Urolithiasis in cats: Evaluation of trends in urolith composition and risk factors (2005-2018). *J Vet Intern Med.* 2021;35:1397-1405. <https://doi.org/10.1111/jvim.16121>