
Allison B. Cannon, DVM; Jodi L. Westropp, DVM, PhD, DACVIM; Annette L. Ruby, BA; Philip H. Kass, DVM, PhD, DACVP

Objective—To determine trends in urolith composition in cats.

Design—Retrospective case series.

Sample Population—5,230 uroliths.

Procedures—The laboratory database for the Gerald V. Ling Urinary Stone Analysis Laboratory was searched for all urolith submissions from cats from 1985 through 2004. Submission forms were reviewed, and each cat’s age, sex, breed, and stone location were recorded.

Results—Minerals identified included struvite, calcium oxalate, urates, dried solidified blood, apatite, brushite, cystine, silica, potassium magnesium pyrophosphate, xanthine, and newberyite. During the past 20 years, the ratio of calcium oxalate stones to struvite stones increased significantly. When only the last 3 years of the study period were included, the percentage of struvite stones (44%) was higher than the percentage of calcium oxalate stones (40%). The most common location for both types of uroliths was the bladder. The number of calcium oxalate-containing calculi in the upper portion of the urinary tract increased significantly during the study period. The number of apatite uroliths declined significantly and that of dried solidified blood stones increased significantly, compared with all other stone types. No significant difference in the number of urate stones was detected.

Conclusions and Clinical Relevance—The increasing proportion of calcium oxalate uroliths was in accordance with findings from other studies and could be a result of alterations in cats’ diets. However, the decreased percentage of calcium oxalate calculi and increased percentage of struvite calculi observed in the last 3 years may portend a change in the frequency of this type of urolith. (J Am Vet Med Assoc 2007;231:570–576)

Urolithiasis accounts for approximately 15% to 21% of the diagnoses in cats with clinical signs of disease in the lower portion of the urinary tract.1,2 Uroliths in the upper portion of the urinary tract can lead to serious problems such as ureteral obstruction, acute renal failure, and death. Surgical removal has been the principal treatment modality for calculi, although medical dissolution, voiding urohydropropulsion,3 and lithotripsy4 can be used in cats with uroliths composed of certain minerals. In a recent descriptive study5 from a stone laboratory in Canada, the most common minerals contained in uroliths from cats were struvite and calcium oxalate. Moreover, calcium oxalate appears to be the most common mineral component in calculi derived from the upper portion of the urinary tract in cats.6,7 Although struvite and calcium oxalate are the 2 primary minerals contained in uroliths from cats, additional components include urate (sodium or ammonium salt), xanthine, apatite, brushite, silica, DSB, cystine, potassium magnesium pyrophosphate, and newberyite. General trends determined by use of descriptive statistics in the most common feline uroliths and urethral plugs found at another urolith center have been reported.8,9

The purpose of the present study was to determine the various types of minerals that were contained in uroliths obtained from cats and submitted for crystallographic analysis to the Gerald V. Ling Urinary Stone Analysis Laboratory at the University of California, Davis. Age, breed, sex, other risk factors, and certain changes in mineral trends that have developed during the past 20 years in cats with urolithiasis were evaluated.

Criteria for Selection of Cases
A computer-assisted search of records from the Stone Analysis Laboratory from January 1985 through Decem-

<table>
<thead>
<tr>
<th>ABBREVIATION</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSB</td>
<td>Dried solidified blood</td>
</tr>
</tbody>
</table>

Figure 1—Number of uroliths from cats submitted to the UC Davis Gerald V. Ling Urinary Stone Analysis Laboratory from 1985 to 2004.
ber 2004 was used to compile information regarding urinary calculi specimens from cats. Records surveyed were those of all urinary calculi from cats submitted for analysis during that interval. Information from this database was obtained from completed questionnaires submitted along with the urinary calculi by veterinarians from various universities and private practices in the United States. Age, breed, sex, mineral composition of the calculus, year of calculus submission, and location of the calculus within the urinary tract were recorded. For the purposes of the study, no distinction was made between urethral plugs and urethral calculi.

Procedures

Mineral analysis—To determine mineral composition, each visibly distinct layer of each specimen was initially analyzed by the oil immersion method of optical crystallography; polarizing light microscopy,10,11 infrared spectroscopy, x-ray diffractometry,11 high-pressure liquid chromatography;11 scanning electron microscopy with energy dispersive x-rays,12 and electron probe microanalysis14 were used as adjunctive analytic methods when needed to definitively identify minerals in the specimen.

For purposes of this study, the term calcium oxalate includes calcium oxalate monohydrate, calcium oxalate dihydrate, or both. The term urate includes uric acid and salts of uric acid (eg, ammonium urate). For each specimen, each mineral that was detected in any amount was recorded, and the percentage of each mineral in each layer of the specimen was estimated by obtaining a mean crystal count from microscopic examination of 5 to 10 microscopic slide preparations by use of the oil immersion method of optical crystallography. Minerals detected in individual specimens varied from 1% to 100%. For calculi with distinct layering and with variations in the thickness of each layer in the calculus, it was not possible to accurately designate a single mineral as being predominant. For the purpose of consistency in the reporting technique for this laboratory,15,16 calculi composed of a mixture of ≥2 minerals, whether the mineral components were contained in distinct layers or distributed uniformly throughout the calculus, are reported for example as struvite-containing or calcium oxalate–containing and were counted once for each mineral present. Because of overlap of minerals, this method of tabulation of minerals detected in uroliths resulted in totals >100%.

Statistical analysis—Contingency table data were analyzed in 1 of 3 ways. Relationships between nominal variables (eg, stone type, breed, location, and sex) were evaluated with χ² tests of homogeneity. Ordinal variables (eg, age and year) were evaluated by use of the Kruskal-Wallis test for singly ordered contingency tables or the Jonckheere-Terpstra test for doubly ordered contingency table data. When χ² tests of homogeneity for doubly nominal contingency tables (eg, stone type vs breed) were significant, cells that contributed substantially to significance were identified by having components to the overall χ² statistics exceed 3.84, with attention given to cells with small observed and expected counts. For all comparisons, values of P < 0.05 were considered significant.

Table 1—Association between minerals analyzed and cats’ sex

<table>
<thead>
<tr>
<th>Mineral analyzed</th>
<th>No. (%) of males</th>
<th>No. (%) of females</th>
<th>Overall number of minerals analyzed</th>
</tr>
</thead>
<tbody>
<tr>
<td>CaOx</td>
<td>1,596 (58)</td>
<td>1,168 (42)</td>
<td>2,764</td>
</tr>
<tr>
<td>Struvite</td>
<td>977 (43)</td>
<td>1,293 (57)</td>
<td>2,270</td>
</tr>
<tr>
<td>Urate</td>
<td>249 (49)</td>
<td>258 (51)</td>
<td>507</td>
</tr>
<tr>
<td>Apatite</td>
<td>138 (47)</td>
<td>159 (53)</td>
<td>296</td>
</tr>
<tr>
<td>DSB</td>
<td>46 (77)</td>
<td>14 (23)</td>
<td>60</td>
</tr>
<tr>
<td>Brushite</td>
<td>5 (21)</td>
<td>19 (79)</td>
<td>24</td>
</tr>
<tr>
<td>Silica</td>
<td>11 (50)</td>
<td>11 (50)</td>
<td>22</td>
</tr>
<tr>
<td>Xanthine</td>
<td>2 (25)</td>
<td>6 (75)</td>
<td>8</td>
</tr>
<tr>
<td>Cystine</td>
<td>3 (43)</td>
<td>4 (57)</td>
<td>7</td>
</tr>
<tr>
<td>Potassium magnesium pyrophosphate</td>
<td>5 (71)</td>
<td>2 (29)</td>
<td>7</td>
</tr>
<tr>
<td>Newberyte</td>
<td>4 (100)</td>
<td>0 (0)</td>
<td>4</td>
</tr>
<tr>
<td>Unknown</td>
<td>15 (56)</td>
<td>12 (44)</td>
<td>27</td>
</tr>
</tbody>
</table>

Figure 2—Percentage of calcium oxalate– (black bars) and struvite-containing (dotted bars) uroliths from the same cats as in Figure 1. Notice that the ratio of calcium oxalate–containing stones to struvite-containing stones increased significantly (P < 0.001) during the past 15 years.

Figure 3—Number of calcium oxalate– (black bars) and struvite-containing (dotted bars) uroliths categorized by age group. Struvite-containing uroliths (*) were significantly (P < 0.001) more common than calcium oxalate–containing uroliths in younger cats (< 7 years of age).
Results

From 1983 through 2004, 5,230 specimens from cats were analyzed. Of those, 699 (13%) were composed of calculi containing ≥2 mineral substances arranged in combination within layers or singly in distinct layers.

The mixed calculus specimens were removed from both the upper (n = 34) and lower (665) portions of the urinary tract. Struvite, calcium oxalate, urates, DSB,17 apatite, brushite, cystine, silica, potassium magnesium pyrophosphate, xanthine, and newberyite were detected in various stones. A mineral type was not conclusively identified in 27 specimens, and these were listed as unknown. The number of uroliths analyzed each year was summarized (Figure 1).

Struvite and calcium oxalate—Changes in the percentages of struvite- and calcium oxalate–containing calculi were summarized (Figure 2). The numbers of struvite- and calcium oxalate–containing stones analyzed were 2,270 and 2,764, respectively. Struvite-containing stones were the predominant mineral type evaluated until 1993. During the past 20 years, the ratio of calcium oxalate stones to struvite stones increased significantly (P < 0.001). Although the increase in number of calcium oxalate stones was apparent in the mid 1990s, it appears that during the most recent 3 years of the study period (ie, 2002 through 2004), the percentage difference between these 2 types of calculi was only 14%, with calcium oxalate being the predominant mineral type. With regard to sex, an increase in calcium oxalate–containing calculi was detected in male cats, compared with female cats (P < 0.05), and the percentage of struvite-containing stones submitted from female cats in the past 15 years decreased significantly (P < 0.001; Table 1). Struvite was significantly (P < 0.001) more common than calcium oxalate in younger cats (Figure 3). The most common location for both types of uroliths was the bladder (Figure 4). A significant (P = 0.03) increase in the number of calculi in the upper portion of the urinary tract (eg, in the kidneys and ureters) was found for calcium oxalate–containing calculi (Figure 5). Struvite-containing calculi were rarely detected in the upper portion of the urinary tract, and most (n = 8) were recorded in the mid-1980s. Evaluation of breed predispositions revealed that domestic longhair cats had significantly more struvite- and calcium oxalate–containing calculi, Persian and Himalayan cats had significantly more calcium oxalate–containing calculi, and Manx and Siamese cats had significantly more struvite-containing calculi. Siamese cats had significantly fewer calcium oxalate–containing calculi, whereas Persian cats had significantly fewer urate-containing calculi. Less common breeds were not included.

![Figure 4](image4.png) Percentage of calcium oxalate- (black bars) and struvite-containing (dotted bars) uroliths categorized by location. Notice that the most common site noted on submittal forms for both types of stones was the bladder.

![Figure 5](image5.png) Number of calcium oxalate–containing stones in the upper portion of the urinary tract (kidneys and ureters) in cats. The increase in number of calcium oxalate–containing calculi was significant (P = 0.03).

Table 2—Minerals analyzed and association with the 8 most common feline breeds at the Gerald V. Ling Urinary Stone Analysis Laboratory. Significant (P < 0.001) associations between minerals analyzed and breed were found. Domestic longhair cats had significantly more struvite- and calcium oxalate–containing calculi, Persian and Himalayan cats had significantly more calcium oxalate–containing calculi, and Manx and Siamese cats had significantly more struvite-containing calculi. Siamese cats had significantly fewer calcium oxalate–containing calculi, whereas Persian cats had significantly fewer urate-containing calculi. Less common breeds were not included.

<table>
<thead>
<tr>
<th>Breed</th>
<th>Struvite</th>
<th>CaOx</th>
<th>Apatite</th>
<th>DSB</th>
<th>Urate</th>
<th>Cystine</th>
<th>K Mg</th>
<th>Brushite</th>
<th>Silica</th>
<th>Newberyite</th>
<th>Unknown</th>
<th>Xanthine</th>
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</thead>
<tbody>
<tr>
<td>DSH</td>
<td>1,370</td>
<td>1,728</td>
<td>168</td>
<td>38</td>
<td>287</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>18</td>
<td>11</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>DLH</td>
<td>346</td>
<td>313</td>
<td>51</td>
<td>10</td>
<td>57</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>DMH</td>
<td>131</td>
<td>115</td>
<td>15</td>
<td>0</td>
<td>26</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Siamese</td>
<td>174</td>
<td>132</td>
<td>14</td>
<td>3</td>
<td>44</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Persian</td>
<td>129</td>
<td>204</td>
<td>14</td>
<td>1</td>
<td>10</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Himalayan</td>
<td>94</td>
<td>212</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Manx</td>
<td>27</td>
<td>10</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Maine Coon</td>
<td>20</td>
<td>16</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

DSH = Domestic shorthair, DLH = Domestic longhair, DMH = Domestic medium hair, K Mg Pyrophosphate = Potassium magnesium pyrophosphate.
Similar to calcium oxalate–containing calculi, they occurred less commonly in young (ie, < 4 years of age) cats. No breed or sex predilections were found. The most common site for urolith removal was the bladder (71%), and 21% of uroliths were removed from the upper portion of the urinary tract.

**DSB**—The number of DSB-containing calculi analyzed was 60. A significant (P < 0.001) increase in the number of those calculi was detected during the past 15 years (Figure 7). A significant (P < 0.05) difference was identified regarding sex, with a predisposition for uroliths containing DSB in males (Table 1). No significant differences regarding location or age were found. Although there were some breeds that had a significant association with DSB calculi (ie, Ragdoll, Balinese, and Snowshoe), the number of those breeds was small.

**Urate**—Five hundred seven uroliths contained urate. The percentage of urate-containing calculi analyzed each year at the laboratory was summarized (Figure 8). During the study period, the mean percentage of stones analyzed each year that contained urate was 10% (range, 7% to 18%). Although more urate-containing calculi were detected in the late 1980s, no significant (P = 0.62) trends were detected in urate-containing urolith submissions. No significant difference in the frequency of urate-containing uroliths was found between sexes (Table 1). No significant trends were detected when the location of these uroliths or age of cats was evaluated. Siamese cats had significantly (P < 0.001) more urate-containing calculi, whereas Persian cats had significantly (P < 0.001) less. Other mineral types identified in the search were detected only in small numbers.

**Discussion**

Evaluation of trends in stone submissions to the authors’ laboratory revealed several important findings. In 1993, the percentages of calcium oxalate– and struvite-containing calculi were approximately equal, and substantial increases in calcium oxalate–containing uroliths continued thereafter. The Minnesota Urolith Center has reported similar findings in struvite and calcium oxalate epidemiologic data from 1981 to 1997, and recent data reported from that Center suggested a similar trend. This apparently reciprocal relationship in the prevalence of these 2 types of calculi was likely a result of overzealous use of acidifying and potentially magnesium-restricted diets. Research implicating magnesium as a potential cause of struvite urinary stones in cats seems to have led cat food manufacturers to restrict the magnesium content of diets and to add...
late nephrolithiasis in humans may occur in the vascular abnormalities (eg, hypertensive vascular injury or atherosclerosis) can lead to formation of Randall’s plaques (papillary lesions usually associated with calcium and phosphate or calcium oxalate). It has been hypothesized that the initiating event in calcium oxalate nephrolithiasis in humans may occur in the vascular bed at the tip of the renal papilla. Therefore, the primary site of calcium oxalate urolithiasis may be unrelated to urinary stasis, infection, or other secondary causes of urolithiasis. The pathophysiology of calcium oxalate formation is incompletely understood, and it is possible that formation of calcium oxalate–containing uroliths begins in the kidneys. Interestingly, cats of these two breeds are also predisposed to developing polycystic kidney disease. To the authors’ knowledge, no studies in which Randall’s plaques and renal formation of calcium oxalate uroliths were investigated in cats and dogs have been published.

Further evidence to support that calcium oxalate uroliths form in the kidney may be inferred from the fact that, in our study, only 7 struvite-containing calculi were confirmed to have been found in the upper portion of the urinary tract, and we detected a significant increase in the number of calcium oxalate–containing stones in the upper portion of the urinary tract in the past decade. Kyles et al reported on the increase in numbers of ureteral calculi that have been observed at several referral institutions. In those reports, most (87%) were calcium oxalate uroliths, and the others contained calcium phosphate. In the present study, postoperative complication and perioperative mortality rates were 31% and 18%, respectively. Lekcharoensuk et al also reported that the frequency of calcium oxalate upper urinary tract stones has significantly increased during the past 10 years. This trend is likely a result of several factors, including dietary alterations, increased awareness of the role of ureterolithiasis in chronic kidney disease, and an increase in the number of skilled surgeons performing more invasive stone removal surgeries in the upper portion of the urinary tract.

A significant decrease in the number of apatite-containing calculi, compared with other stones analyzed, was noticed. When these records were evaluated more closely, most apatite-containing calculi analyzed during that time period developed in association with struvite. Therefore, the decrease is likely secondary to the fact that acidifying diets helped decrease the formation of struvite-containing calculi. Apatite commonly coprecipitates with struvite.

A significant increase in the number of DSB-containing uroliths was also noticed during the past 20 years. The reasons for this are unclear, but may include factors similar to those described for the increase in calcium oxalate–containing stones in the upper portion of the tract. Increased awareness and better imaging techniques, particularly for DSB-containing stones in the upper portion of the tract, may have contributed to the increase in those submissions to our laboratory. Overall, only 60 stones submitted to our laboratory contained DSB, and only 49 were entirely composed of DSB. Too few breeds were represented for firm conclusions to be drawn regarding breed predilections. Significantly more males were involved, possibly because of anatomic differences and the potential for urethral obstruction with these calculi. For a complete review of DSB calculi, readers are referred to a recent publication in which these stones were investigated.

Although most urate-containing calculi in cats are ammonium urate, it can sometimes be difficult to iden-
ify what salt is present with the uric acid; we therefore refer to them as urate-containing stones. In the present study, no significant trend changes were observed in these calculi from 1985 to 2004. On the basis of our data, the frequency of urate-containing calculi did not appear to be influenced by the changes in diets during this time. The etiology of urate calculus formation has been investigated in Dalmatian dogs,\textsuperscript{11,12} but little information exists regarding the pathogenesis of these stones in cats. In non-Dalmatian dogs, a portovascular anomaly can often be detected. In our experience, cats with urate-containing calculi do not have portovascular anomalies or hepatopathies. However, the authors still recommend that cats with urate-containing calculi be screened for such diseases. Overall, the percentage of urate-containing calculi was approximately 9% of the total number of stones analyzed each year. This is slightly higher than findings at the Minnesota laboratory,\textsuperscript{13} where only 5.6% of total submissions were urate stones, but the trends appear to be similar. The difference in percentages between the 2 laboratories may reflect the manner of epidemiologic data reporting. In data compiled for our study, a calculus was counted as urate-containing if any percentage of urate was contained in the calculus. The advantage of data compilations in which each mineral type is counted, irrespective of the amount contained in the calculus specimen, is that each mineral component in calculus, 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. When data for epidemiologic studies at the Minnesota Urothel Center are compiled, uroliths are primarily categorized according to the predominant mineral content of the calculus (70% to 100% of the mineral present in a urolith when no distinct nucleus or shell was detected); in an earlier study,\textsuperscript{13} uroliths that did not contain at least 70% of a given mineral type were categorized as mixed without designating a mineral type, and uroliths that contained an identifiable nucleus and 1 or more surrounding layers of a different mineral type were categorized as compound uroliths without naming any mineral types. By compiling mineralogic data via this method, there is no overlap of mineral components in a calculus. The disadvantage of this type of data compilation is that all minerals in a specimen may not be included.

Because we analyzed too few stones that contained cystine, newberryite, xanthine, silica, brushite, or potassium magnesium pyrophosphate, it was difficult to assess clinically important trends that would affect management of cats with stones of these mineral compositions. The infrared spectrum for potassium magnesium pyrophosphate uroliths has only recently been identified,\textsuperscript{34} and it is therefore possible that some of our earlier unknown samples contained this mineral component. This possibility is being investigated.

In the present study, significantly more calcium oxalate stones were detected during the years analyzed; however, on the basis of the past 3 years, it is uncertain whether this trend will continue. Further data from our laboratory and others will help establish whether the trend will persist. Ureterolithiasis is a difficult disease to manage, and complete stone analyses and renal histologic analysis will hopefully augment our understanding of calcium oxalate uroliths and possibly DSB stone formation. Little change has occurred in urate-containing calculus during the past 15 years. Given the observation that changes in mineral composition in uroliths in cats have occurred, studies designed to evaluate the relationship of these changes to dietary modifications, medical management, and surgical techniques are warranted.

References


