

Analysis of 451,891 Canine Uroliths, Feline Uroliths, and Feline Urethral Plugs from 1981 to 2007: Perspectives from the Minnesota Urolith Center

Carl A. Osborne, DVM, PhD^{a,*}, Jody P. Lulich, DVM, PhD^a,
John M. Kruger, DVM, PhD^b, Lisa K. Ulrich, CVT^a, Lori A. Koehler, CVT^a

KEYWORDS

• Urolith • Calculi • Stone • Urolith analysis • Urethral plug
• Urolith trends

Urolithiasis is a general term referring to the causes and effects of stones anywhere in the urinary tract. Urolithiasis should not be viewed conceptually as a single disease with a single cause, but rather as a sequela of multiple interacting underlying abnormalities. Thus, the syndrome of urolithiasis may be defined as the occurrence of familial, congenital, or acquired pathophysiologic factors that, in combination, progressively increase the risk of precipitation of excretory metabolites in urine to form stones (ie, uroliths).

With the support of an Educational Grant from Hill's Pet Nutrition, the Minnesota Urolith Center (MUC) has performed quantitative analysis of uroliths retrieved from animals for more than 2.5 decades. During this period, the authors have observed dramatic shifts in urolith type. The following epidemiologic discussion is based on quantitative analysis of 350,803 canine uroliths (**Figs. 1–3, Tables 1 and 2**), 94,778 feline uroliths (**Figs. 4–6, Tables 3 and 4**), and 6,310 feline urethral plugs (**Figs. 7–9, Tables 5 and 6**) submitted to the MUC from 1981 to 2007.

^a Veterinary Clinical Sciences Department, Minnesota Urolith Center, College of Veterinary Medicine, University of Minnesota, 1352 Boyd Avenue, St. Paul, MN 55108, USA

^b Department of Small Animal Clinical Sciences, Michigan State University College of Veterinary Medicine, Room D208, Veterinary Teaching Hospital, East Lansing, MI 48824-1314, USA

* Corresponding author.

E-mail address: osbor002@umn.edu (C.A. Osborne).

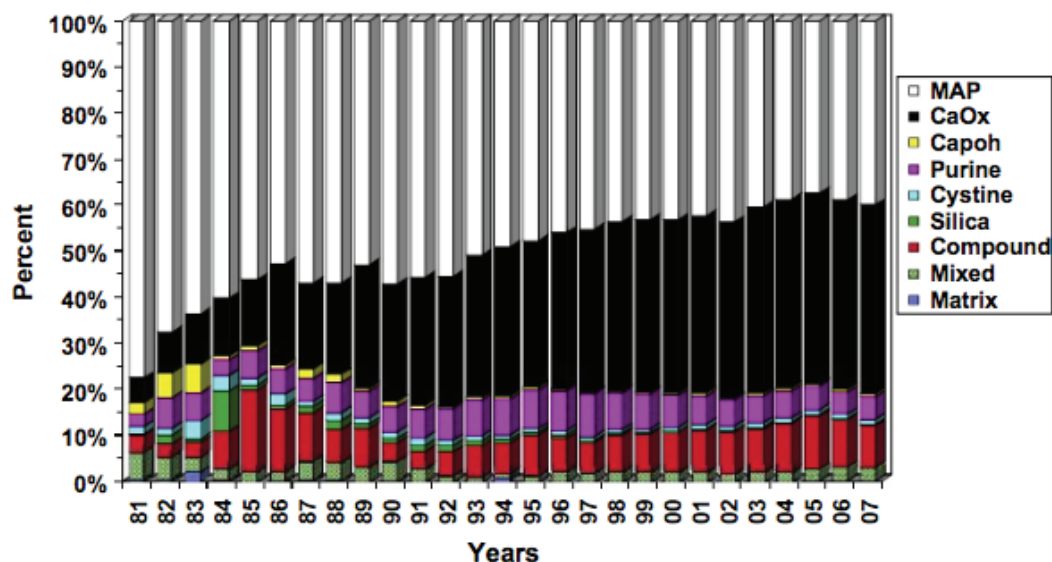


Fig.1. Canine urolith distribution: 1981 to 2007.

EPIDEMIOLOGY OF CANINE UROLITHS

In 1981, calcium oxalate was detected in only 5% of canine uroliths submitted to the MUC, whereas struvite (magnesium ammonium phosphate or MAP) was detected in 78%. However, evaluation of the prevalence of different types of minerals in canine uroliths during successive years revealed a gradual and consistent increase in occurrence of calcium oxalate uroliths, and a gradual and consistent decline in the occurrence of struvite uroliths (see Fig. 1). In fact, by 2003 the prevalence of calcium oxalate (41%) was approximately equal to struvite (40%). In 2004, calcium oxalate (41%) surpassed struvite (39%). In 2005, calcium oxalate was detected in 42% of the urolith submissions, while struvite was detected in (38%). In 2006, calcium oxalate was again detected in 41% of the canine urolith submissions, while struvite was detected in 39%. In 2007, 40% of the urolith submissions were struvite while calcium oxalate represented 41% (see Fig. 3 and Table 2). The total submission ($n = 40,612$) of canine uroliths in 2007 was 4,580 more than for the year 2006 ($n = 36,032$).

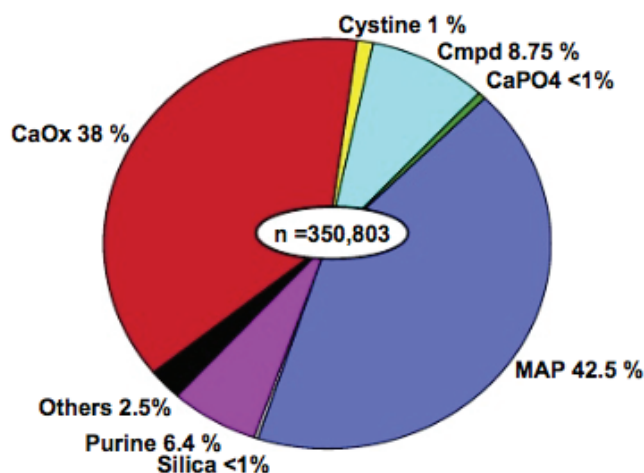


Fig. 2. Mineral composition of canine uroliths: 1981 to 2007.

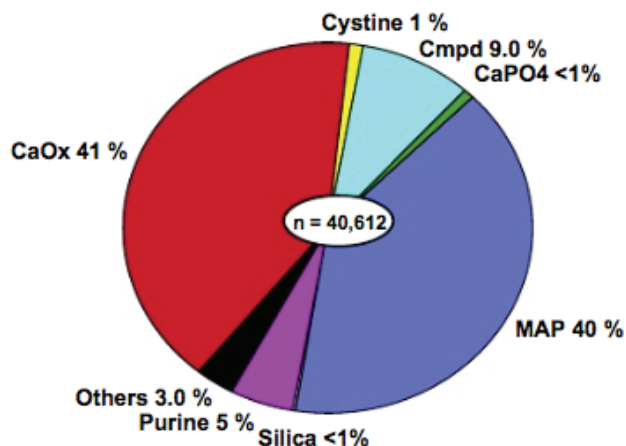


Fig. 3. Mineral composition of canine uroliths 2007.

EPIDEMIOLOGY OF FELINE UROLITHS

The change in frequency of feline calcium oxalate and struvite occurrence was even more dramatic than the occurrence of canine struvite and calcium oxalate uroliths during a similar period. In 1981, calcium oxalate was detected in only 2% of feline uroliths submitted to the MUC, whereas struvite was detected in 78% (see Fig. 4). However, beginning in the mid-1980s, a dramatic increase in the frequency of calcium oxalate uroliths occurred in association with a decrease in the frequency of struvite uroliths. In 2002, approximately 55% of the feline uroliths submitted to the MUC were composed of calcium oxalate, while only 33% were composed of struvite. During this

Table1 Mineral composition ^a of 350,803 canine uroliths evaluated at the MUC from 1981 to 2007		
Struvite	149,199	42.5%
Magnesium hydrogen phosphate	52	0.01%
Magnesium phosphate hydrate	4	<0.01%
Calcium oxalate	133,338	38.0%
Calcium phosphate	1801	0.5%
Purines	22,412	6.4%
Cystine	3402	1.0%
Silica	1414	0.4%
Calcium carbonate	6	<0.01%
Dolomite	1	<0.01%
Mixed ^b	8146	2.3%
Compound ^c	30,832	8.8%
Matrix	153	0.04%
Drug metabolite	19	<0.01
Other	24	<0.01
Total	350,803	100%

^a Analyzed by polarizing light microscopy or infrared spectroscopy.

^b Uroliths did not contain at least 70% of mineral type listed; no nucleus or shell detected.

^c Uroliths contained an identifiable nucleus and one or more surrounding layers of a different mineral type.

Table 2
Mineral composition^a of 40,612 canine uroliths evaluated at the MUC, 2007

Predominant Mineral Type	Number of Uroliths	%
Magnesium ammonium phosphate 6H ₂ O	16,124	39
Magnesium hydrogen phosphate 3H ₂ O	5	0.01
Magnesium phosphate hydrate	1	<0.1
Calcium oxalate	16,761	41.3
Calcium phosphate	273	0.7
Purines	2,020	5.0
Xanthine	43	0.1
Cystine	447	1.1
Silica	134	0.3
Other	1	<0.1
Calcium carbonate	2	<0.1
Mixed ^b	1,132	2.8
Compound ^c	3,698	9.1
Matrix	10	<0.1
Drug metabolite	4	<0.1
Date 2007	40,612	100

^a Analyzed by polarizing light microscopy or infrared spectroscopy.

^b Uroliths did not contain at least 70% of mineral type listed; no nucleus or shell detected.

^c Uroliths contained an identifiable nucleus and one or more surrounding layers of a different mineral type.

period, the decline in appearance of naturally occurring struvite uroliths associated with a reciprocal increase in calcium oxalate uroliths may have been associated with: (1) the widespread use of a calculolytic diet designed to dissolve struvite uroliths; (2) modification of maintenance and prevention diets to minimize struvite crystalluria (some dietary risk factors that decrease the risk of struvite uroliths increase the risk of calcium oxalate uroliths); and (3) inconsistent follow-up evaluation of efficacy of dietary management protocols by urinalysis and radiography.

In 2003, the trends in the occurrence in feline uroliths began to change again. The frequency of feline calcium oxalate uroliths declined to 47%, while the frequency of struvite uroliths increased to 42% (see **Fig. 4**). During 2004, the number of struvite uroliths (44.9%) submitted to the MUC nudged past those containing calcium oxalate (44.3%). In 2005, the number of struvite uroliths (48.1%) surpassed those containing calcium oxalate (40.6%) in frequency of occurrence (see **Fig. 6**). Of 10,093 feline uroliths submitted to the MUC in 2006, 5,001 (50%) were struvite and 3,914 (39%) were calcium oxalate. In 2007, of 11,174 uroliths submitted to the MUC, 5,432 (49%) were struvite, and 4,553 (41%) were calcium oxalate (see **Figs. 4** and **6**, **Tables 3** and **4**). The progressive decrease in occurrence of naturally occurring calcium oxalate uroliths during the past 5 years may be associated with reformulation of adult maintenance diets to minimize risk factors for calcium oxalate crystalluria, improvements in formulation of therapeutic diets designed to reduce risk factors for calcium oxalate uroliths, and increased use of therapeutic diets designed to reduce risk factors for calcium oxalate uroliths. The increase in appearance of naturally occurring struvite uroliths during the past 5 years may be associated with the reciprocal relationship between some dietary risk factors for calcium oxalate and struvite uroliths.^{1,2} For example, diets that reduce urine acidity and provide adequate quantities of magnesium reduce the risk of

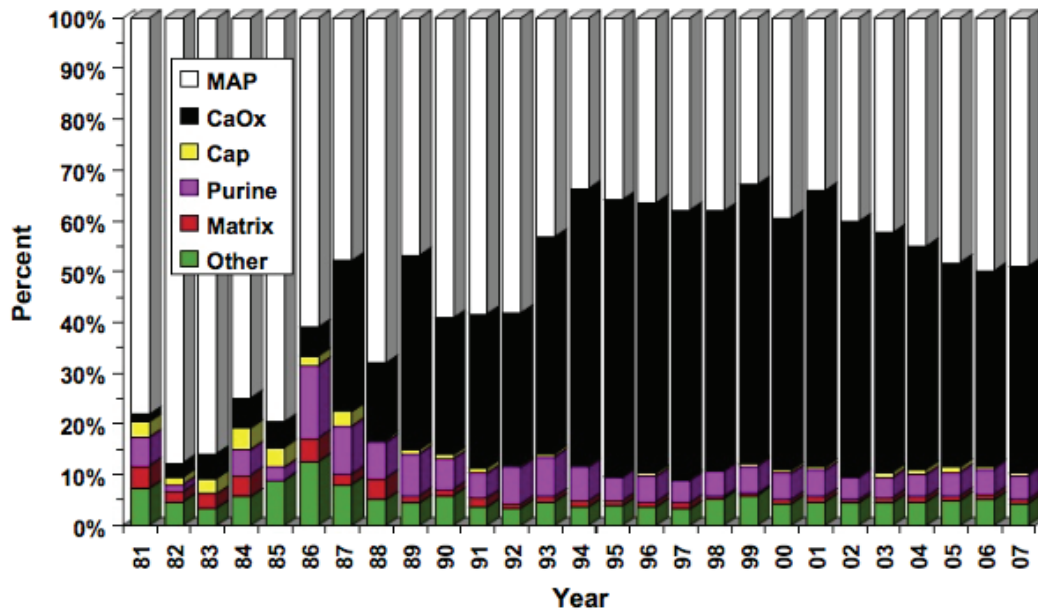


Fig. 4. Feline urolith distribution: 1981–2007.

calcium oxalate urolith formation, but increase the risk of struvite (magnesium ammonium phosphate) urolith formation. Whatever the reasons, it is likely that most of the 5,432 sterile struvite uroliths retrieved from cats and submitted to the MUC in 2007 could have been readily dissolved in 2 to 4 weeks by feeding a diet designed to promote formation of urine that is undersaturated with struvite.³

EPIDEMIOLOGY OF FELINE URETHRAL PLUGS

The team at the MUC has emphasized differences in the structure and composition between uroliths and urethral plugs.⁴ Urethral plugs contain varying quantities of minerals in proportion to large quantities of matrix (Figs. 10–13).

What would be an estimate of the occurrence of feline calcium oxalate urethral plug submissions to the MUC from 1981 to 2007? Unlike feline and canine stones, since 1981 struvite has consistently been the most common mineral identified in urethral plugs (see Figs. 7–9, Tables 5 and 6). The prevalence of calcium oxalate in urethral plugs always has been infrequent. Of 506 urethral plugs submitted to the MUC by veterinarians in

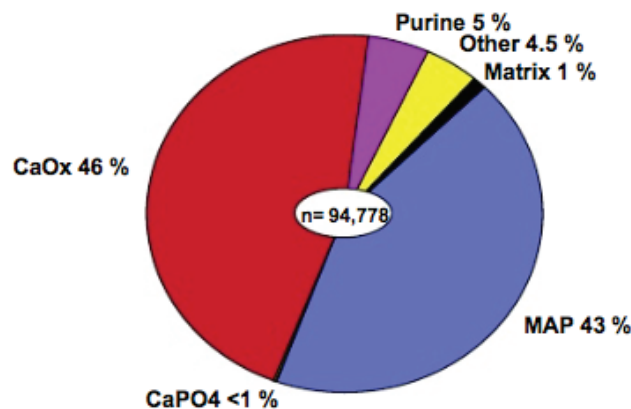


Fig. 5. Mineral composition of feline uroliths 1981–2007.

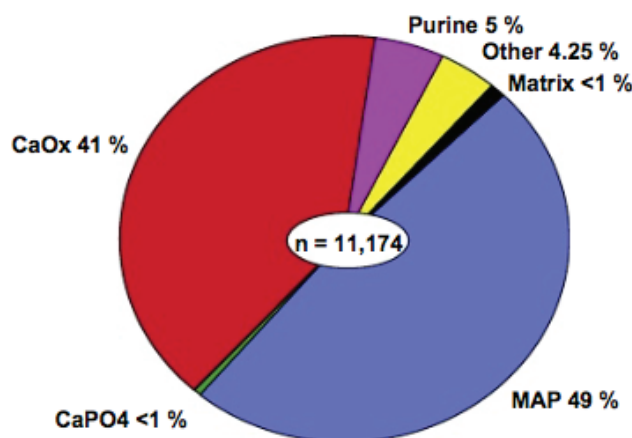


Fig. 6. Mineral composition of feline uroliths 2007.

2007, the mineral composition of approximately 92% was primarily struvite. Approximately 1% were composed of calcium oxalate (see Fig. 9 and Table 6).

The explanation as to why there have been significant shifts in the prevalence of calcium oxalate and struvite in feline uroliths during the past 25 years, while the prevalence of struvite and calcium oxalate in feline urethral plugs has not significantly changed, is not obvious. During the same time, the mineral composition of other types of uroliths has been associated with no obvious trend (see Figs. 1, 4 and 7; Tables 1, 3, and 5).

In a retrospective study of approximately 1,000 feline calcium oxalate uroliths evaluated at the MUC, only 3 were formed by cats less than 1 year of age.⁵ Of the cats affected with calcium oxalate uroliths, 97% were greater than 2 years of age. The greatest risk for developing calcium oxalate uroliths occurred in 10- to 15-year-old neutered male cats. These observations are of interest because it has been

Predominant Mineral Type	Number	%
Struvite	40,554	42.8
Magnesium hydrogen phosphate	93	0.1
Magnesium phosphate hydrate	189	0.2
Calcium oxalate	43,707	46.1
Calcium phosphate	338	0.4
Cystine	92	0.1
Silica	41	<0.1
Mixed ^b	928	1.0
Compound ^c	3,135	3.3
Matrix	925	1.0
Drug metabolite	5	0.0
Other	56	0.1
Total	94,776	100

^a Analyzed by polarizing light microscopy or infrared spectroscopy.

^b Uroliths did not contain at least 70% of mineral type listed; no nucleus or shell detected.

^c Uroliths contained an identifiable nucleus and one or more surrounding layers of a different mineral type.

Predominant Mineral Type	Number of Uroliths	%
Magnesium ammonium phosphate 6H ₂ O	5,432	48.6
Magnesium hydrogen phosphate 3H ₂ O	7	0.06
Magnesium phosphate hydrate	42	0.38
Calcium oxalate	4,553	40.8
Calcium phosphate	30	0.3
Purines	523	4.9
Xanthine	27	<0.1
Cystine	12	<0.1
Silica	8	<0.1
Other	10	<0.1
Mixed ^b	81	0.7
Compound ^c	356	3.2
Matrix	93	0.8
Date 2007	11,174	100

^a Analyzed by polarizing light microscopy or infrared spectroscopy.

^b Uroliths did not contain at least 70% of mineral type listed; no nucleus or shell detected.

^c Uroliths contained an identifiable nucleus and one or more surrounding layers of a different mineral type.

hypothesized that conditions promoting urine acidity are a risk factor for calcium oxalate urolithiasis. It has been reported however, that the urine pH of young cats is lower than that of adults consuming the same diet.⁶ One explanation advanced to explain this phenomenon is that growing animals synthesize bone mineral from calcium and phosphate in the blood. Phosphate circulates in the blood as HPO_4^{-2} and

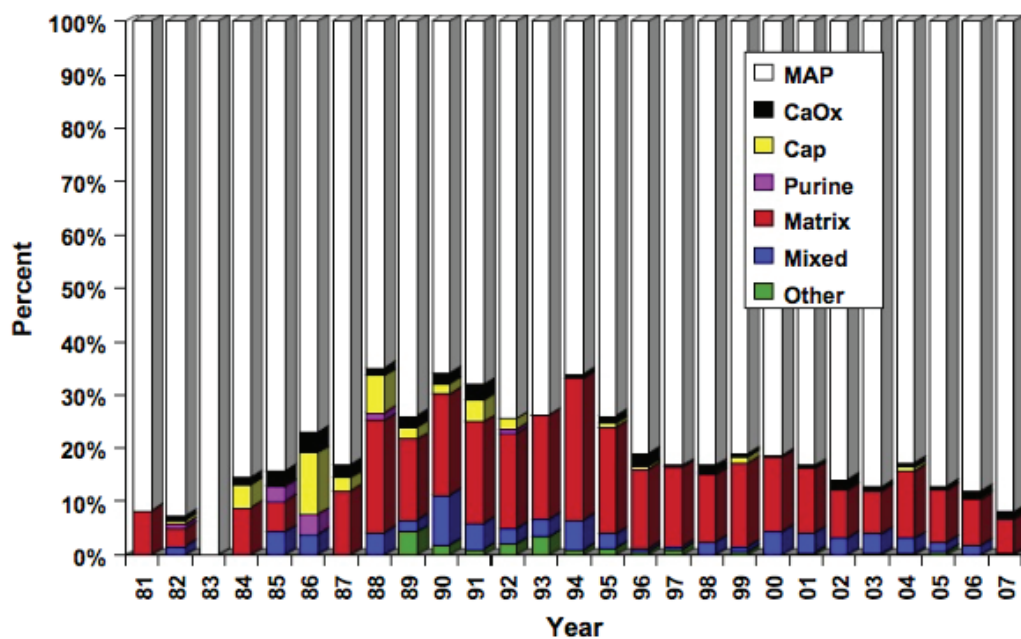


Fig. 7. Feline plug distribution: 1981–2007.

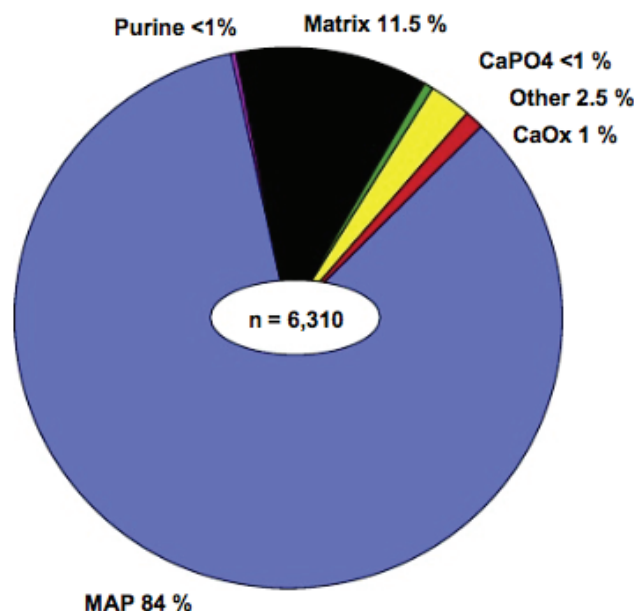


Fig. 8. Mineral composition of feline urethral plugs: 1981–2007.

H_2PO_4^- , and hydrogen ions are produced during bone mineralization and excreted in urine. If acidic urine is a risk factor for calcium oxalate urolithiasis, a reasonable question would be why calcium oxalate stones are uncommon in immature cats in which urine normally is acidic. The answer likely is related to a combination of risk factors associated with calcium oxalate urolithiasis, including the urine concentrations of minerals, nonmineral crystallization inhibitors and promoters, and the quantity of urine produced, in addition to acid-base balance. There likely is not a simple cause-and-effect relationship between risk factors (eg, urine pH) and calcium oxalate urolithiasis.

Why the prevalence of feline calcium oxalate uroliths are increased, while the prevalence of calcium oxalate in feline urethral plugs remained extremely low (see **Tables 1, 3, and 5**), is not obvious. This is especially true in light of the observation that male cats tend to be at higher risk for calcium oxalate uroliths and struvite urethral plugs than females. However, the very high prevalence of struvite in urethral plugs is of clinical significance in terms of dietary strategies designed to prevent their formation. The frequency of urethral obstruction of male cats with struvite plugs appears to have

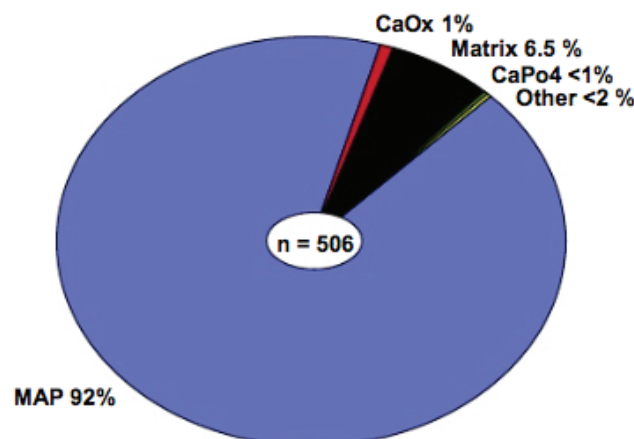


Fig. 9. Mineral composition of feline urethral plugs 2007.

Table 5
Mineral composition^a of 6,310 domestic feline urethral plugs evaluated at the MUC from 1981 to 2007

Predominant Mineral Type	Number	%
Struvite	5266	83.5
Magnesium hydrogen phosphate	48	0.8
Calcium oxalate	59	0.9
Calcium phosphate	37	0.6
Purines	8	0.1
Magnesium calcium phosphate carbonate	1	<0.1
Mixed ^b	154	2.4
Compound ^c	7	0.1
Matrix	727	1.5
Drug metabolite	1	0.0
Other	2	0.0
Total	6310	100

^a Analyzed by polarizing light microscopy or infrared spectroscopy.

^b Urethral plugs did not contain at least 70% of mineral type listed; no nucleus or shell detected.

^c Urethral plugs contained an identifiable nucleus and one or more surrounding layers of a different mineral type.

been declining during the past two decades. This decline, in all probability, resulted from widespread use of magnesium-restricted or acidifying diets. During the same time period, there has been a dramatic decline in the frequency with which perineal urethrostomies have been performed, and an associated decline in the undesirable sequela of perineal urethrostomies.⁷

A VIEW THROUGH THE RETROSPECTOSCOPE

In the early 1970s, the association between dry diets and feline lower urinary tract disease (LUTD) became a topic of intense discussion in England, Denmark, and the United States.⁸ Also in the early 1970s, and continuing sporadically for the next decade, several groups of investigators induced magnesium hydrogen phosphate

Table 6
Mineral composition^a for 506 feline urethral plugs analyzed at the MUC, 2007

Predominant Mineral Type	Number of Urethral Plugs	%
Magnesium ammonium phosphate 6H ₂ O	463	91.5
Magnesium hydrogen phosphate 3H ₂ O	2	0.4
Calcium oxalate	5	1.0
Calcium phosphate	2	0.4
Mixed ^b	1	0.2
Matrix	33	6.5
Total	506	100

^a Analyzed by polarizing light microscopy or infrared spectroscopy.

^b Urethral plugs did not contain at least 70% of mineral type listed; no nucleus or shell detected.

and then magnesium ammonium phosphate (struvite) uroliths in clinically normal cats by adding various types of minerals to their diets.^{8,9,10,11} The cats developed typical signs of LUTD, including urethral obstruction; however, they did not produce the struvite-matrix urethral plugs commonly encountered in cats with naturally occurring urethral obstruction (see **Figs. 10–13**). However, the general consensus of many investigators and clinicians was that consumption of dry diets with excessive magnesium was an important primary cause of lower urinary tract disease of cats.

Following development of dietary protocols to induce dissolution of naturally occurring struvite uroliths in dogs, in 1983, the authors developed dietary protocols to dissolve naturally occurring sterile struvite urocystoliths in cats.¹² Their effectiveness justified further clinical studies on development, detection, dissolution, and prevention of sterile struvite uroliths.

In 1985, results of studies of the effects of feeding diets containing alkalinizing and acidifying salts of magnesium to clinically normal cats were reported.¹³ These laboratory studies of induced uroliths shifted the focus of attention from dietary magnesium content to alkaline urine pH as a primary factor in development of struvite crystalluria. These studies had a profound effect on veterinarians and the pet food industry. Many adult feline maintenance diets eventually were modified to minimize struvite crystalluria. Because of dietary modifications, the prevalence of struvite uroliths and struvite urethral plugs began to decline in the mid-1980s, and unexpectedly, the occurrence of calcium oxalate began to increase.

THE CONTINUED PRESENCE OF CALCIUM OXALATE

The exact etiologic cascade of risk factors which lead to the increased prevalence of canine and feline CaOx uroliths remains unknown. However, results of epidemiologic studies support the hypothesis that diets designed to minimize MAP urolith formation may have inadvertently increased the occurrence of CaOx uroliths (see **Figs. 1, 4 and 7**). Several biologic phenomena provide plausible explanations for this association. (1) Whereas diet-mediated urine acidification enhances the solubility of MAP crystals in urine, dietary acids promote calcium oxalate crystalluria by inducing hypercalciuria.⁸ This association between aciduria, acidemia, and hypercalciuria may be explained by the fact that acidemia promotes mobilization of carbonate and phosphate from bone to buffer hydrogen ions. Concomitant mobilization of bone calcium may result in hypercalciuria. (2) Metabolic acidosis in dogs, human beings, and rats resulted in hypocitraturia. If consumption of dietary acid precursors is associated with hypocitraturia in cats, it may increase the risk of CaOx uroliths because citrate is an inhibitor of CaOx crystal



Fig. 10. Feline urethral plug composed of struvite crystals and a large quantity of matrix. (Compare with **Fig. 11.**)



Fig. 11. Sterile struvite urethral plug removed from an adult male cat with urethral obstruction (6 o'clock position). One end of the plug has been crushed with an index finger to illustrate its friable nature. (Compare with Fig. 10.) Two wafer-shaped sterile struvite uroliths retrieved from adult male cats are at 9 and 12 o'clock positions. A urocystolith associated with a urease positive urinary tract infection is positioned at the 3 o'clock position.

formation. (3) The widespread practice of feeding low moisture (dry) diets to companion animals resulted in the formation of concentrated urine.

THE AGE OF NEPHROURETEROLITHIASIS

The increase in occurrence of CaOx uroliths in cats has been associated with a parallel increase in occurrence of CaOx uroliths found in their kidneys and ureters (**Figs. 14** and **15**). In fact, there has been a 10-fold increase in the frequency of upper tract uroliths diagnosed in cats evaluated at veterinary teaching hospitals in North America during the past 20 years.¹⁴ Between 1981 and 2003, the MUC analyzed nephroureteroliths retrieved from 2,445 cats: 70% had uroliths composed of calcium oxalate. By contrast, only 8% were composed of MAP (see **Fig. 14**). This finding emphasizes the importance of CaOx prevention and control in cats to minimize potential

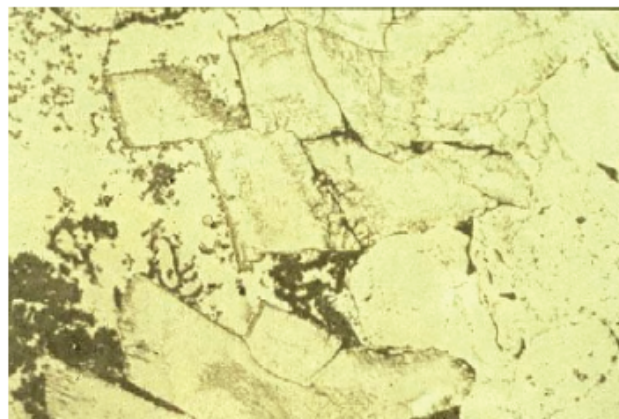


Fig. 12. Transmission electron micrograph of a sterile struvite stone illustrating a paucity of matrix. The clear spaces are areas where the crystals were located. Compare with Fig. 13.

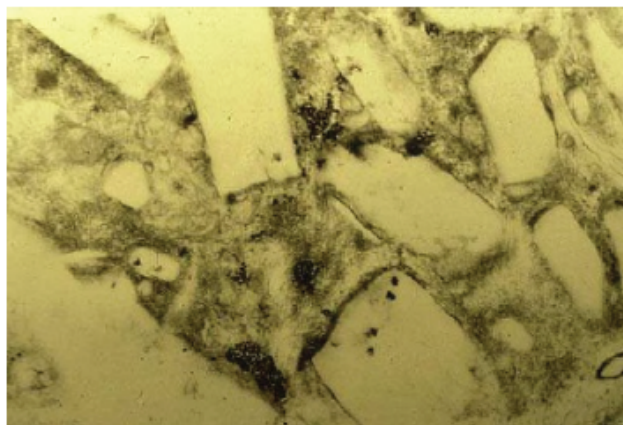


Fig. 13. Transmission electron micrograph of a matrix-crystalline struvite urethral plug retrieved from a cat. Notice the difference in the quantity of matrix between this plug and the stone described in Fig. 12.

life-threatening renal failure. The authors are unaware of a parallel increase in calcium oxalate nephroureteroliths in dogs.

Is there an etiologic link between kidney disease and calcium oxalate uroliths? Is kidney disease a cause or consequence of urolith formation? Hyperoxaluria may be the common link between these two processes. One group of investigators reported that excessive oxalic acid damages kidney tubules.^{15,16} It is also probable that high concentrations of urine oxalate would be a significant risk factor for the formation of calcium oxalate uroliths in cats. If these assumptions are correct, what is the source of oxalic acid? The answer to these questions likely can be found in the evaluations of various diets.

EPIDEMIOLOGY OF UROLITHIASIS IN HUMAN BEINGS

At the beginning of the twentieth century, the incidence of calcium oxalate uroliths in human beings living in the United States had also dramatically increased.¹⁷ Global distributions of urolithiasis in human beings indicate that calcium oxalate urolithiasis predominates in the United States and other industrialized, technologically advanced

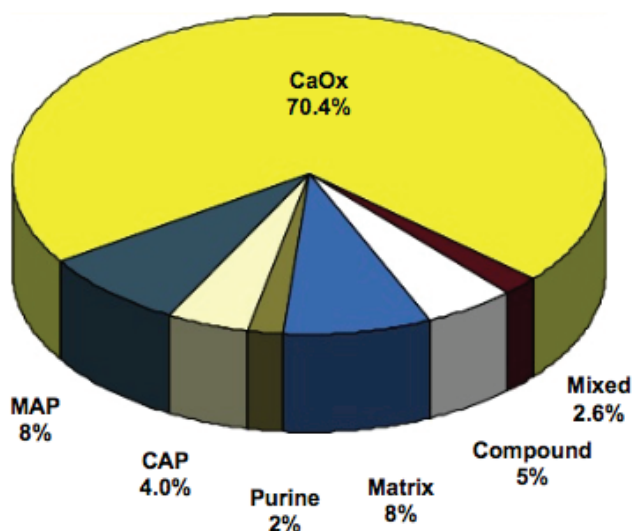


Fig. 14. Prevalence of the mineral types of 2,445 feline nephroureteroliths submitted to the Minnesota Urolith Center for analysis: 1981 to 2007.

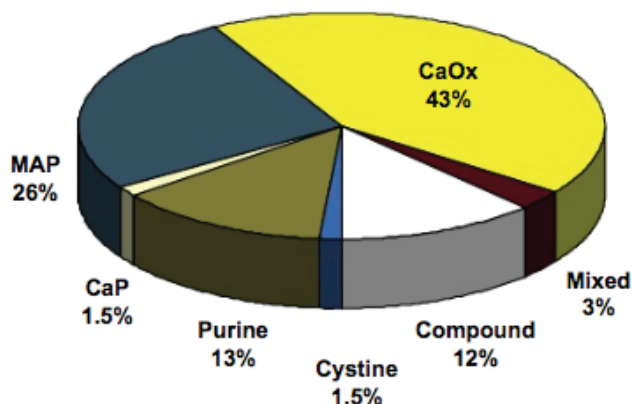


Fig.15. Prevalence of the mineral types of 5,591 canine nephroureteroliths submitted to the Minnesota Urolith Center for quantitative analysis: 1981 to 2007.

regions of the world. Although originally attributed to the sedentary lifestyle of inhabitants of such countries,¹⁸ the increased incidence of calcium oxalate uroliths now is believed to reflect the ability of these more affluent societies to spend disposable income for the consumption of animal protein, which leads to increased urinary excretion of calcium and oxalate.^{11,19} Regional environmental factors, such as water and soil quality, also may influence urolith formation. Because of the close relationship between human beings and their pets, it is logical to consider that risk factors contributing to the increased incidence of calcium oxalate uroliths in human beings also may influence the incidence of calcium oxalate uroliths in cats and dogs. Investigators need to explore the associations between strategies designed to improve nutrition and factors that increase over-nutrition and their relationship to formation of calcium oxalate uroliths.

RISK AND PROTECTIVE FACTORS

The reasons underlying such a dramatic change in the composition of canine and feline uroliths remains a topic of intense interest. Although several hypotheses have been proposed to explain this phenomenon, a cause-and-effect relationship has not yet been established. Not all risk and protective factors are of equal importance. In fact, each contributing risk or protective factor may play a limited or a significant role in the pathogenesis of different types of urolithiasis. The chance of developing a specific type of urolith when exposed to one or more risk or protective factors is often expressed in terms of numerical probabilities (so-called "odds" or "odds ratios").

When used in a qualitative (rather than quantitative) way, the significance of risk or protective factors should not be assigned an "all or none" or "always or never" interpretation.²⁰ In many situations, each risk factor alone contributes a limited role to the development of urolithiasis. In fact, in some situations, they may not play a role in every exposed patient. Furthermore, identifying one event in a chain of etiologic events is not the same as identifying the entire etiologic chain.

It is apparent that naturally occurring uroliths are affected by many risk factors, some of which are known and some of which are unknown. Some risk factors that influence urolith formation include breed, gender, age, anatomic and functional abnormalities of the urinary tract, abnormalities of metabolism, urinary tract infections, diet, urine pH, and body water homeostasis.

WHY IDENTIFY RISK AND PROTECTIVE FACTORS?

Our interest in recognizing the association of specific risk factors with urolithiasis is related to: 1) identifying healthy but susceptible populations of animals and trying to

minimize their exposure to these risk factors; 2) identifying healthy but susceptible populations and trying to enhance their exposure to protective factors; and 3) facilitating detection and treatment of subclinical urolithiasis that has already developed in susceptible patients. However, when several risk factors occur together, they may combine to put the patient at a higher risk than would be expected by the sum of each factor identified (eg, $1 + 1 + 1 = 5$). Recognition and control of lithogenic risk factors is the primary goal to prevent urolith formation and minimize their recurrence.

Because of the short time-span in which the change in the occurrence of mineral types of canine and feline uroliths has been recognized, breed, gender, and age are unlikely to have contributed substantially to this phenomenon. It is the authors' interpretation that changes in husbandry and nutrition represent significant contributing factors influencing this epidemiologic shift in urolith type.

FUTURE TRENDS: 10 PREDICTIONS DERIVED VIA THE CRYSTALLURIA BALL

What will be the trends associated with urolithiasis in the future? The authors predict the following advancements in the diagnosis, treatment, and prevention of various types of uroliths during the next decade.

Our understanding of the pathophysiology of calcium oxalate, sterile struvite, purine, cystine, silica, and calcium phosphate urolithiasis will expand. Their will be new insights into identification of genetic and acquired risk factors associated with this disorder, such that urolithiasis will be further divided into etiopathogenic subsets.

As techniques of preserving stone matrix are developed, the composition of matrix contained in different mineral types of uroliths will bring additional insights into stone formation.

Advances will be made in recognition and detection of urolith inhibitors and promoters found in urine. These advances will have diagnostic and therapeutic implications.

The role of various dietary constituents in the cause and treatment of urolithiasis will be further clarified, based on evidence derived from masked and controlled clinical trials.

Improvements in the resolution of imaging techniques (such as ultrasonography), and increased familiarity with their use, will allow detection and localization of all types of uroliths less than one millimeter in size.

Improvements will continue to be made in diagnostic imaging, facilitating identification of the mineral composition of uroliths *in vivo*.

Significant advances will be made toward identification of specific diagnostic markers of different types of uroliths in the urine of patients with urolithiasis.

There will continue to be a decline in the use of invasive therapeutic techniques, such as nephrectomies, nephrotomies, ureterotomies, urocystolithotomies, and urethrotomies. As the pathogenesis of different urolith types are discovered, and as molecular diagnostic strategies are developed and validated, early detection of uroliths will increase the development of medical dissolution and prevention strategies for all urolith types, including calcium oxalate.

Therapeutic use of minimally invasive types of therapy, such as lithotripsy, will become a standard of practice.

Veterinary medicine will lead the way in providing information about the causes, detection, and treatment of urolithiasis in animals that is of comparative value to human beings with various types urolithiasis.

REFERENCES

1. Kirk CA, Ling GV, Franti CE, et al. Evaluation of factors associated with development of calcium oxalate urolithiasis in cats. *J Am Med Assoc* 1995;207:1429–34.
2. Lekcharoensuk C, Osborne CA, Lulich JP, et al. Association between dietary factors and calcium oxalate and magnesium ammonium phosphate uroliths in cats. *J Am Vet Med Assoc* 2001;219:1228–37.
3. Osborne CA, Kruger JM, Lulich JP, et al. Medical dissolution of feline struvite urocystolithiasis. *J Am Vet Med Assoc* 1990;196:1053–63.
4. Osborne CA, Kruger JM, Lulich JP, et al. Feline matrix-crystalline urethral plugs: a unifying hypothesis of causes. *J Small Anim Pract* 1992;33:172–777.
5. Osborne CA, Lulich JP, Thumchai R, et al. Changing demographics of feline urolithiasis. In: August JR, editor. *Consultations in feline internal medicine*. 3rd edition. Philadelphia: WB Saunders; 1997. p. 349–60.
6. Buffington CAT. Effects of age and food deprivation on urine pH in the cat. In: *Proceedings of the 3rd Annual Symposium European Society Veterinary Nephrology Urology* 1988. p. 113–21.
7. Lekcharoensuk C, Osborne CA, Lulich JP. Evaluation of trends in frequency of urethrostomy for treatment of urethral obstruction in cats. *JAVMA* 2002;221:502–5.
8. Osborne CA, Kruger JM, Lulich JP, et al. Feline urologic syndrome; feline lower urinary tract disease; feline interstitial cystitis: what's in a name? *J Am Vet Med Assoc* 1999;214(10):1470–80.
9. Finco DR, Barsanti JA, Crowell WA. Characterization of magnesium-induced urinary disease in the cat and comparison with feline urologic syndrome. *Am J Vet Res* 1985;46:391–400.
10. Lewis LD, Chow FHC, Taton GF, et al. Effects of various dietary mineral concentrations on the occurrence of feline urolithiasis. *J Am Vet Med Assoc* 1978;172:559–63.
11. Rich LJ, Dysart I, Chow FC, et al. Urethral obstruction in male cats: experimental production by addition of magnesium and phosphate to the diet. *Feline Pract* 1974;4:44–7.
12. Osborne CA, Abdullahi S, Polzin DJ. Current status of dissolution of canine and feline uroliths. In: *Proceedings of the Kal Kan Symposium for treatment of small animal diseases*. 1983. p. 53–79.
13. Buffington CA, Rogers QR, Morris JG, et al. Feline struvite urolithiasis: magnesium effect depends on urinary pH. *Feline Pract* 1985;15:29–33.
14. Lekcharoensuk C, Osborne CA, Lulich JP, et al. Evaluation of the trends in the frequency of calcium oxalate uroliths in the upper urinary tract of cats. *J Am Anim Hosp Assoc* 2005;41:39–46.
15. Robertson WG, Peacock M, Hodgkinson A. Dietary changes and the incidence of urinary calculi in the UK between 1958 and 1976. *J Chronic Dis* 1979;32:469–76.
16. Turan T, Tuncay OL, Usubutun A, et al. Renal tubular apoptosis after complete urethral obstruction in the presence of hyperoxaluria. *Urol Res* 2000;28:220–2.
17. Lonsdale K. Human stones. *Science* 1968;159:199–207.
18. Mandel NS, Mandel GS. Urinary tract stone disease in the United States veteran population II. Geographical analysis of variations in composition. *J Urol* 1989;143:11516–21.
19. Robertson WG, Peacock M, Heyburn PJ. Should recurrent calcium oxalate stone formers become vegetarians? *Br J Urol* 1979;51:427–31.
20. Osborne CA, Lulich JP. Risk and protective factors for urolithiasis. What do they mean? *Vet Clin North Am Small Anim Pract* 1999;29(1):39–41.