

Calcium Oxalate Urolithiasis

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Abstract: Calcium oxalate (CaOx) uroliths are one of the most common urolith types in dogs, cats, and humans. Many factors predispose animals to CaOx uroliths, including breed, old age, obesity, male sex, being neutered, and certain diseases. Because there are no effective strategies for medical dissolution of these uroliths, management should focus on physical removal (by surgical or nonsurgical methods) and prevention, especially in patients with recurring uroliths, high-risk breeds, and animals with predisposing diseases. Prevention focuses on diet modification, primarily to increase water intake, and the appropriate use or avoidance of specific medications.

Calcium oxalate (CaOx) urolith formation depends on the degree of urine saturation with CaOx and the balance between urinary promoters and inhibitors of CaOx formation.¹

Promoters of Calcium Oxalate Formation

Hypercalciuria, which predisposes patients to CaOx urolithiasis, may be classified as absorptive, renal leak, or resorptive hypercalciuria. Absorptive hypercalciuria is characterized by increased intestinal absorption and renal excretion of calcium and oxalate and has been described in miniature schnauzers with urolithiasis.² Renal leak hypercalciuria is characterized by impaired renal tubular reabsorption of calcium. Resorptive hypercalciuria is characterized by parathyroid hormone-mediated mobilization of calcium from bone and is a result of primary hyperparathyroidism.^{3,4} Conditions associated with hypercalciuria include hypercalcemia; excessive dietary calcium, protein, sodium, vitamin D, or vitamin C intake; acidifying diets; urinary acidifiers; and certain drugs (e.g., glucocorticoids, loop diuretics) and diseases (e.g., hyperadrenocorticism).^{5,6}

Hyperoxaluria can occur with increased intake of dietary oxalate precursors, such as leafy green vegetables (e.g., spinach, rhubarb) or nuts (especially peanuts).⁷ Dietary calcium binds oxalic acid and inhibits its absorption; thus, calcium restriction enhances hyperoxaluria.⁷ Vitamin C (ascorbic acid) is metabolized to oxalate, and vitamin B₆ alters oxalate metabolism (FIGURE 1).⁷

Inhibitors of Calcium Oxalate Formation

Increases in serum phosphorus concentration decrease calcitriol production and enhance urinary excretion of a natural inhibitor of oxalate precipitation, pyrophosphate.⁷ Restricted dietary magnesium has been associated with CaOx formation because dietary magnesium complexes with oxalate and reduces oxalate binding with ionic calcium.^{8,9} Nephrocalcin is a substance in the urine that naturally inhibits CaOx uroliths and is less effective in patients that form CaOx uroliths.¹⁰ Other substances (e.g., Tamm-Horsfall mucoproteins, glycosaminoglycans) may inhibit CaOx formation in people, but their role in canine CaOx urolithiasis is unknown.

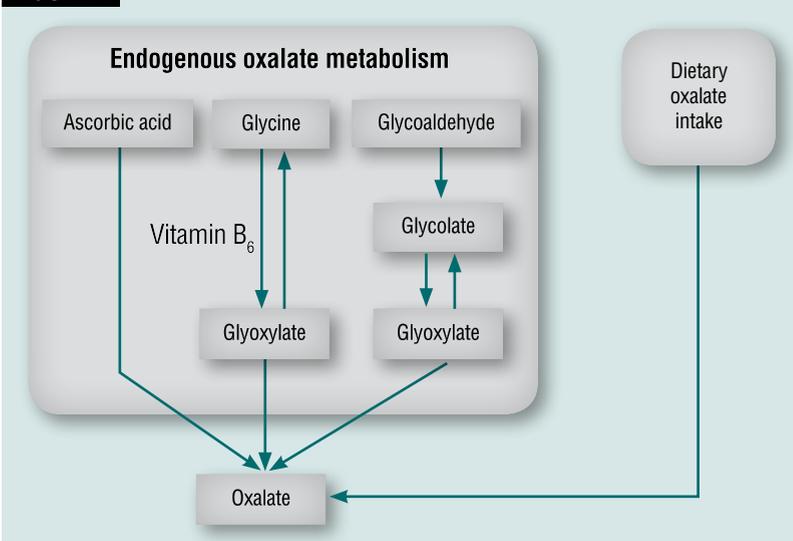
Signalment

Certain breeds of dogs and cats have been shown to have an increased or decreased incidence of CaOx urolithiasis (TABLES 1 and 2 and BOX 1).¹¹⁻¹³ Obesity and increasing age are risk factors for CaOx urolith formation in dogs and cats.¹¹⁻¹⁵ Cats are at the highest risk between 4 and 16 years of age, with a mean age of 7.3 years at diagnosis.^{12,16} In two studies,^{15,17} the mean age of dogs with CaOx uroliths was 7 and 8.4 years. CaOx uroliths are more common in male dogs (2:1 ratio) and male cats (1.5:1 ratio) than in females.^{11,15,17,18} Neutered dogs and cats are also at increased risk.^{11,18}

Incidence

CaOx is one of the most common substances in uroliths in dogs and cats.^{19,20} Over the past 21 years, the ratio of CaOx uroliths to struvite uroliths has increased significantly. The percentage of canine CaOx uroliths submitted for analysis increased from 7% in 1986 to 38% in 2000,^{8,11} and the percentage of feline CaOx uroliths submitted increased from 2% in 1984 to 55% in 2001.^{21,22} Increases in CaOx urolith formation may be related to dietary acidification and the increasing longevity of dogs and

FIGURE 1



Pathway of oxalate biosynthesis.⁷

cats, while decreases in struvite urolith submissions may be due to improved medical management.^{18,23,24} More recent information shows a plateau and possible decline in the incidence of CaOx uroliths.^{15,25}

TABLE 1 Canine Breeds With Increased Incidence of Calcium Oxalate Urolithiasis¹¹

Breed	Odds Ratio
Standard schnauzer	18.06
Miniature schnauzer	14.10
Lhasa apso	10.95
Parson Russell terrier	9.85
Papillon	9.85
Yorkshire terrier	6.64
Bichon frise	6.57
Keeshond	5.47
Pomeranian	4.93
Samoyed	4.69
Shih tzu	4.49
Chihuahua	3.88
Cairn terrier	3.69
Maltese	3.52
Miniature and toy poodle	3.32
West Highland white terrier	3.28
Dachshund	2.69

TABLE 2 Canine Breeds With Decreased Incidence of Calcium Oxalate Urolithiasis¹¹

Breed	Odds Ratio
Cocker spaniel	0.15
German shepherd	0.12
Golden retriever	0.069

QuickNotes

Breed, weight, age, and neuter status are all factors in developing CaOx uroliths.

BOX 1

Feline Breeds With Increased or Decreased Incidence of Calcium Oxalate Urolithiasis¹²

- | | |
|----------------------------|----------------------------|
| Increased Incidence | Decreased Incidence |
| ▶ Ragdoll | ▶ Birman |
| ▶ British shorthair | ▶ Abyssinian |
| ▶ Foreign shorthair | ▶ Siamese |
| ▶ Himalayan | ▶ Mixed breed |
| ▶ Havana brown | |
| ▶ Scottish fold | |
| ▶ Persian | |
| ▶ Exotic shorthair | |

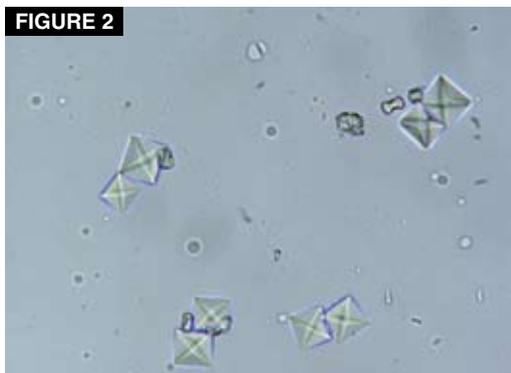


FIGURE 2
Microscopic image of calcium oxalate dihydrate crystals (400x magnification). Courtesy of Drs. Richard Luong and Andrew Loar, Animal Medical Center, New York.

QuickNotes

CaOx uroliths can develop secondary to metabolic acidosis, which leads to hypercalciuria.

Nephroliths and ureteroliths account for only 2% to 3% of urolith submissions from dogs and cats.^{26,27} In dogs, 31% to 39% of nephroliths and ureteroliths are composed of CaOx; 33% to 38% are composed of struvite.^{28,29} Most (80% to 99%) feline nephroliths and ureteroliths are composed of CaOx.^{28,30}

Diagnosis

Creation of acidic urine (pH <7.0) can predispose animals to CaOx urolithiasis by inducing increased excretion of calcium in the urine; however, CaOx solubility is not influenced by urine pH. Most CaOx uroliths form in sterile urine, either singly or as multiple stones. CaOx crystals can be found during urinalysis but do not necessarily correlate with urolith composition (FIGURE 2).



FIGURE 3
Lateral abdominal radiograph of a CaOx stone (arrow). Courtesy of Dr. Anthony Fischetti, Animal Medical Center, New York.

CaOx is the most radiopaque urolith substance (FIGURE 3). In an in vitro study,³¹ CaOx uroliths could be distinguished from struvite uroliths with 75% to 88% accuracy when computed tomography was used and uroliths were composed of a single mineral type. CaOx calculi are usually white and hard (FIGURE 4). Surface characteristics may vary, but they often have sharp, jagged edges. The gross appearance of any stone is never a replacement for stone analysis.

When radiopaque urinary calculi are found, a serum biochemistry panel, complete blood count, urinalysis, and urine culture should be evaluated for diseases associated with urolithiasis. Testing for hyperadrenocorticism should be considered if clinical criteria for this condition are met. A complete evaluation for hypercalcemia should be conducted if the ionized calcium level is elevated.

Treatment

The only effective treatment for CaOx stones is physical removal by any of the surgical or nonsurgical techniques that have been described in the literature.³² Guidelines on when to use surgical versus nonsurgical techniques have been published elsewhere.³²

Compared with other mineral types, canine CaOx uroliths are relatively easy to fragment with extracorporeal shock wave lithotripsy.³³ Feline CaOx uroliths are less susceptible to fragmentation with extracorporeal shock wave lithotripsy than canine CaOx uroliths.³⁴

Prevention

Diet

Diet is an important factor in the prevention of CaOx stones (TABLE 3). Canned diets high



FIGURE 4
A removed CaOx stone.

in fat, phosphorus, magnesium, potassium, chloride, and moisture have been associated with decreased risk of CaOx formation.^{9,24,35} Reducing dietary carbohydrate has reduced the risk of CaOx urolithiasis in dogs but not in cats.^{8,9} Dry diets with a high fiber content have been shown to be associated with an increased risk of urolithiasis in dogs.⁹ Diets formulated to maximize urine acidity are not proven to cause CaOx formation in dogs and cats.⁸ Acidemia may promote hypercalciuria and hypocitraturia, increasing risk of urolith formation.³⁶ The source of acidification plays a greater role than the urine pH achieved.

In one study in dogs,³⁵ Waltham Canine S/O Lower Urinary Tract Support Diet (Royal Canin USA) reduced CaOx relative supersaturation, a measure of the risk of CaOx formation, by 63%. For cats, Prescription Diet x/d Feline (Hill's Pet Nutrition) showed a 59% reduction in CaOx relative supersaturation in one study³⁷; this diet has since been replaced by Prescription Diet c/d Multicare Feline (Hill's Pet Nutrition).

Increasing water consumption (either through the use of canned food or through adding water to the diet) to achieve a urine specific gravity <1.020 in dogs and <1.025 in cats dilutes the urine concentration and decreases risk of stone recurrence.³⁸ In cats, the risk of CaOx urolith formation was one-third less when canned diets were fed than when other dietary formulations were consumed.⁷

Medications

If dietary therapy is not effective at preventing CaOx crystalluria, or if uroliths recur, potassium citrate can be administered orally. Citrate may form soluble salts with calcium, thereby decreasing the formation of less soluble CaOx crystals; however, an increase in the urine pH and metabolic alkalosis with resultant reduction in calciuria are the main proposed mechanisms of action.³⁹ The potassium citrate dose (50 to 75 mg/kg mixed with food q12h) is titrated to maintain urine pH between 7.0 and 7.5. If dietary therapy alone maintains the urine pH above 7.0, potassium citrate should not be added. Serum potassium should initially be monitored monthly and the dose reduced if hyperkalemia occurs.

Thiazide diuretics promote natriuresis in the distal tubules, which results in calcium reabsorption.⁴⁰ In dogs, urine calcium concen-

TABLE 3 Prevention of Calcium Oxalate Urolithiasis

Parameter	Goal	Method to Achieve
Diet	—	<ul style="list-style-type: none"> ▶ Feed a diet not restricted in magnesium and phosphorus ▶ Avoid foods with excess oxalate^a
Urine specific gravity	<1.020 in dogs <1.025 in cats	<ul style="list-style-type: none"> ▶ Feed canned food ▶ Add water to dry food ▶ Provide multiple water bowls ▶ Provide running water ▶ Provide flavored water ▶ Increase sodium in diet
Urine pH	7.0–7.5	<ul style="list-style-type: none"> ▶ Manage by diet ▶ Increase potassium citrate by supplementation
CaOx crystalluria	Minimize or eliminate	<ul style="list-style-type: none"> ▶ Control hypercalcemia ▶ Administer thiazide diuretic ▶ Increase vitamin B₆ by supplementation

^aSee the food lists at CompendiumVet.com.

tration was reduced by 34% with hydrochlorothiazide (2 mg/kg PO q12h).⁴¹ Patients should be monitored for dehydration, hypokalemia, and hypercalcemia.²⁸

Vitamin B₆ supplementation (2 to 4 mg/kg PO q24–48h) could be considered in patients consuming homemade diets.⁴²

Vitamins D and C enhance intestinal calcium absorption; therefore, excessive supplementation should be avoided. Steroids (e.g., prednisone) and furosemide also lead to calciuresis and should be avoided.

Monitoring Schedule

About 50% to 60% of CaOx uroliths recur within 3 years of surgical or nonsurgical removal; this incidence may be exaggerated by incomplete removal of calculi at the initial surgery.³⁸ Recommended monitoring to decrease recurrence after stone removal includes urinalysis, electrolyte evaluation if using thiazide diuretics, radiography, and/or ultrasonography at 2 to 4 weeks, 3 months, and every 6 months thereafter. If recurrent uroliths are identified while they are still small, nonsurgical removal techniques should be considered, along with reevaluation for underlying causes.³⁸

TO LEARN MORE



For a partial list of human foods to avoid feeding to dogs with CaOx urolithiasis, visit CompendiumVet.com. A list of foods that can be fed to dogs with CaOx urolithiasis is also available.

Conclusion

More research is necessary to understand how to prevent CaOx uroliths. Early screening and detection of uroliths (especially in high-risk breeds) are important to allow use of nonsurgical removal techniques and to start preventive measures. Increased water consumption is the best strategy to maintain good urinary tract health.³⁹ C

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- Which is not a mechanism of hypercalciuria?
 - increased gastrointestinal absorption
 - impaired renal tubular reabsorption
 - calcium mobilization caused by primary hyperparathyroidism
 - decreased urinary calcium excretion
- _____ is not a risk factor for CaOx urolithiasis formation in dogs and cats.
 - Weight
 - Age
 - Sex
 - Coat color/pattern
- What percentage of feline nephroliths and ureteroliths are CaOx?
 - 20% to 30%
 - 40% to 50%
 - 60% to 70%
 - 80% to 99%
- What type of urinary environment promotes formation of CaOx stones?
 - acidic (pH <7.0)
 - neutral (pH 7.0 to 7.5)
 - alkaline (pH >7.5)
 - all of the above
- Which uroliths are the most radiopaque?
 - calcium oxalate
 - urate
 - struvite
 - cystine
- Which diet has been shown to dissolve CaOx stones in dogs?
 - Hill's Prescription Diet Canine s/d
 - Hill's Prescription Diet Canine c/d
 - Waltham Canine S/O Lower Urinary Tract Support Diet
 - none
- Potassium citrate helps prevent CaOx stone formation by _____ urine pH and causing metabolic _____.
 - increasing; alkalosis
 - decreasing; acidosis
 - increasing; acidosis
 - decreasing; alkalosis
- Thiazide diuretics help prevent CaOx stone formation by promoting natriuresis in the _____ tubules, which results in calcium _____.
 - distal; reabsorption
 - distal; secretion
 - proximal; reabsorption
 - proximal; secretion
- Vitamin _____ could be added to a homemade diet in an effort to prevent CaOx stone formation.
 - D
 - B₆
 - C
 - K
- What percentage of surgically removed CaOx stones recur in 3 years?
 - 10% to 20%
 - 30% to 40%
 - 50% to 60%
 - 70% to 80%