

# Calcium Oxalate Uroliths

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## Making the Diagnosis and Decreasing Recurrence

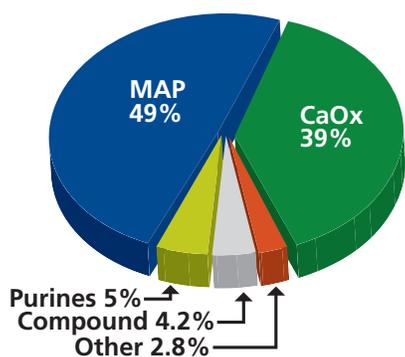
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## Key Points

- To efficiently verify, localize and diagnose underlying causes, a urinalysis and medical imaging should be performed on all cats with lower urinary tract signs.
- Survey radiography is a valuable diagnostic tool for cats with urethral disease (e.g., urethroliths, urethral plugs). However, remember to include the entire urethra.
- Survey radiography is a more reliable predictor of urolith composition than urinalysis findings.
- Measure serum concentration of ionized calcium to avoid missing the diagnosis of hypercalcemia in cats with calcium oxalate uroliths.
- Consider less urine acidifying, high moisture foods to decrease risk of recurrent calcium oxalate uroliths.



**Figure 1. Distribution of the mineral composition of 11,416 feline uroliths submitted to the Minnesota Urolith Center for quantitative analysis in 2008. (MAP = struvite; CaOx = calcium oxalate)**

Between 1981 and 2008, the Minnesota Urolith Center analyzed uroliths from over 106,000 cats. While uroliths composed of struvite predominated in the 1980s, there was a dramatic increase in the prevalence of calcium oxalate (CaOx) uroliths in the 1990s. Since 1981, the frequency of CaOx uroliths has increased more than 50-fold. In 2004, however, the rate of CaOx urolith submissions declined and for the first time in 12 years, struvite urolith submissions (44.9%) nudged above CaOx (44.3%). This reversion in urolith prevalence has continued. In 2008, 49% of feline urolith submissions were struvite compared with 39% composed of CaOx (**Figure 1**).

## Making the Diagnosis

A sage once said, “A well defined problem is half solved.”<sup>1</sup> This is especially appropriate when discussing diseases of the feline lower urinary tract where, in the majority of cases, a cause cannot be clearly defined. In addition, as a profession, we have created a myriad of synonyms for the unknown, as if a new name would produce clarity of cause or treatment. Of course, it has not, but we have learned much through the process and should continue to explore and question.

An efficient and cost-effective method of verifying history and physical examination findings, localizing disease, and establishing a diagnosis in cats with lower urinary tract signs is to routinely perform a urinalysis, with microscopic evaluation of urine sediment, and medical imaging during initial evaluation (**Table 1**). We also refrigerate a small aliquot of the urine sample in the event that a bacterial culture is needed to further refine our diagnosis. Based on the results of these initial tests, the status of the patient, and the frequency of recurrent signs, the need for additional tests to further evaluate the lower urinary tract and/or related organs can be determined. In most cats with lower urinary tract signs, results of complete blood cell counts and serum biochemistry profiles are usually not helpful unless the condition is complicated by concurrent illnesses.

## Urinalysis

The urinalysis is a simple and reliable test to confirm urinary tract disease and identify pathophysiologic mechanisms associated with the underlying cause. Despite the difficulty of obtaining samples from dysuric patients and the urgency to provide therapy, it is important to remember that accurate interpretation of results requires collection prior to therapy. The method of collection, the duration and method of storage, and the specific gravity are also essential to fully interpret results.

**Hematuria** (> 5 erythrocytes/hpf) is a common finding in cats with most causes of lower urinary tract disease, although to a lesser degree with behavioral periuria and urinary incontinence. The nonspecific diagnostic utility of this test may be confounded by the observation that cystocentesis, as well as manual bladder expression and transurethral catheterization, can result in significant hematuria in cats with or without urinary tract signs. Because cystocentesis-induced hematuria cannot be reliably distinguished from pathologic hematuria associated with naturally occurring lower urinary tract diseases, urine specimens for follow-up evaluations should be collected by spontaneous voiding into nonabsorbent litter or litter containing reagent pads for detecting blood.

**Pyuria** (> 3 to 5 leukocytes/hpf), in contrast to omnipresent hematuria, is rare in cats with feline idiopathic cystitis (FIC) (3%) or urine marking (2%).<sup>2,3</sup> This information is helpful in distinguishing FIC from other diseases of the lower urinary tract in which pyuria is more common. For example, approximately 60% of 20 cats with sterile struvite urocytoliths in one study had significant pyuria.<sup>4</sup> Similarly, pyuria is typically detected in cats with urinary tract infection and urethral obstruction. When monitoring pyuria, do not use results from leukocyte esterase reagent strips in lieu of results from microscopic evaluation of urine sediment. In cats, leukocyte esterase reagent pads are often positive (i.e., false positive) in the absence of leukocytes in feline urine.<sup>5</sup>

**Crystalluria** is abnormal because the urinary system is designed to eliminate wastes in liquid form (**Figure 2**). However, detection of crystals in the urine of cats that do not have or have never had uroliths or crystalline-matrix urethral plugs is likely to be clinically unimportant because crystals have not been shown to damage healthy urothelium and induce hematuria or dysuria. When is crystalluria clinically important? For the answer to this question, see **Table 2**.



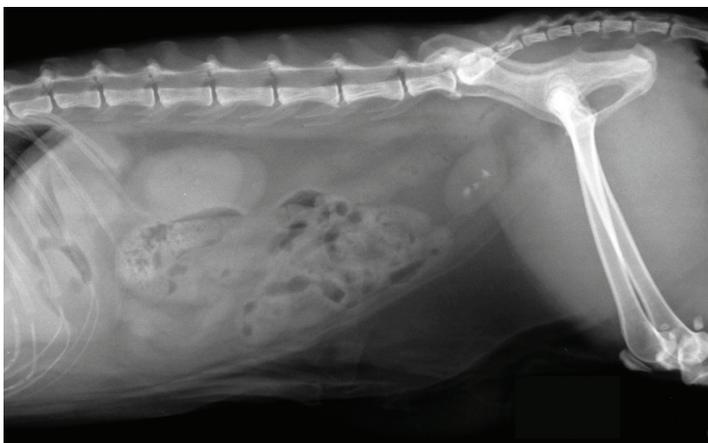
**Figure 2.** Urine sediment examination reveals calcium oxalate (CaOx) dihydrate crystals, which indicates increased risk for formation of CaOx uroliths.

**Table 1. Advantages and disadvantages of selecting survey radiography or ultrasonography for evaluating cats with lower urinary tract signs.**

Purpose	Survey Abdominal Radiographs	Abdominal Ultrasound
Diagnose and differentiate urethroliths from urethral plugs	Yes, if radiopaque	Poor
Diagnose uroliths in bladder	Yes, if radiopaque*	Yes
Accurately assess urolith characteristics (size, number, density, shape, laminations)	Yes	Poor
Accurately assess urinary bladder wall thickness	No	Yes, if urinary bladder is appropriately distended
Assess urinary bladder size	Yes	Yes
Differentiate blood clots from uroliths	No	Yes
Identify foreign material	Yes, if radiopaque	Yes, if radiopaque or radiolucent
Identify anatomical abnormalities	Usually no	Possible
Identify malformation of the spinal cord in Manx cats	Yes	No
Potential exposure to ionizing radiation	Yes	No

\*Radiopaque uroliths less than 2-3 mm in diameter are usually below the resolution of detection by survey radiography.

**Bacteriuria** detected in young cats (< 7 years) should arouse suspicion, because the prevalence of bacterial urinary tract infections in cats with adequately concentrated urine (> 1.035) is approximately 1% to 2% of patients.<sup>6</sup> In addition, coccoid bacteria are difficult to differentiate from fat droplets and other circular-shaped debris commonly present in urine. To avoid unnecessary treatment, first consider submitting a sample of urine for quantitative culture for aerobic bacteria. These generalities do not apply to cats with perineal urethrostomies or indwelling catheters, in which the risk of infection increases by greater than a factor of 10.<sup>7</sup>



**Figure 3. Lateral abdominal radiograph from an 11-year-old spayed female domestic shorthair cat with calcium oxalate uroliths.**

## Medical Imaging

Survey abdominal radiographs are helpful for identifying radiopaque uroliths, crystalline-matrix urethral plugs and foreign material. Because radiographs provide a global view of the abdomen, concurrent disorders involving the kidneys, ureters, bony pelvis and caudal spine may also be recognized. Survey radiographs are unremarkable in cats with FIC. However, negative results do not exclude radiolucent uroliths and foreign material (e.g., blood clots), neoplasia or anatomic abnormalities as potential causes for lower urinary tract signs. To exclude these possibilities, perform ultrasonography to evaluate the urinary bladder and/or contrast urethrocytography to evaluate the urethra and urinary bladder (**Table 1**).

Calcium oxalate uroliths are readily diagnosed on the basis of clinical and radiographic findings (**Table 3, Figure 3**). CaOx uroliths are typically more radiopaque and smaller than struvite uroliths (**Table 4**). Remember to include the entire urethra in the radiographic image so that distal urethroliths will not be overlooked (**Figure 4**). Although CaOx crystalluria is common, the absence of crystals or detection of struvite crystalluria is also possible in cats with CaOx uroliths. When the radiographic appearance of uroliths and crystalluria type are not in agreement, rely on the radiographic findings to more accurately predict mineral composition of uroliths.

**Table 2. Clinical significance of crystalluria.**

Significance	Explanation
Iatrogenic	To minimize in vitro or iatrogenic crystal formation, urine should be analyzed prior to administration of therapy (except when evaluating therapeutic response), analyzed within 2 hours of collection from the urinary bladder, and stored at room temperature in a container such that the surface of the urine sample is not exposed to air (eg, stored in a capped syringe).
Risk factor for urolith or crystalline-matrix plug formation	Crystal formation indicates that urine is sufficiently saturated such that it could support the formation and growth of uroliths of that respective mineral type. If sufficient numbers of crystals are present, with a concomitant inflammatory process, male cats are at risk for matrix-crystalline plug formation. Because crystals have not been demonstrated to cause lower urinary tract signs, crystalluria is an indicator to evaluate the patient for uroliths. However, uroliths can also be present in the absence of urine crystals.
Indication of disease	Crystals also form as a consequence of disease processes that alter urine composition. For example, calcium-containing crystals can be present in cats with hypercalcemia. Xanthine crystals may assist the diagnosis of hereditary xanthinuria. Urate crystals may indicate decreased hepatic function; however, increased blood concentrations of bile acids have not been demonstrated in most cats with urate urolithiasis.
Predict mineral composition of uroliths/plugs	Crystals in the urine of cats are often similar to the minerals identified in uroliths and urethral plugs of the corresponding patient. However, crystal identification is not an accurate substitute for quantitative mineral analysis.
Index of therapeutic response	Formation of crystals and uroliths are dependent on production of urine that is oversaturated for that particular mineral. One strategy to reduce urolith recurrence is to enhance the solubility of that mineral salt in urine. The presence of crystals consistent with the composition of previous uroliths indicates that urine saturation has not been sufficiently reduced.



**Figure 4.** Lateral abdominal radiograph from a 5-year-old neutered male domestic shorthair cat with an 11-month history of inappropriate urination. Note radiopaque uroliths in the distal urethra, which were composed primarily of calcium oxalate.

## Preventing Calcium Oxalate Urolith Formation and Recurrence

Because CaOx urolith formation is associated with a complex and incompletely understood sequence of events and causes, no treatment has been shown to completely prevent recurrence. For minimizing the risk of CaOx urolith reformation, the goals are to decrease urinary excretion of calcium and oxalate. This can be accomplished using medical, nutritional and pharmacological strategies (**Figure 5, Tables 5 and 6**).

### Reduce Urine Calcium Excretion

A key factor consistently distinguishes cats with CaOx uroliths — they are hypercalciuric compared with normal cats.<sup>8</sup> Therefore, preventing hypercalciuria is pivotal to minimize urolith recurrence. Veterinarians need to minimize hypercalciuria by recognizing and correcting hypercalcemia, avoiding over acidification of urine, increasing water consumption, modifying sodium intake, and avoiding excessive vitamin D supplementation (**Tables 5 and 6**).<sup>9</sup>

**Table 3.** Typical signalment, physical examination, urinalysis and radiographic findings for common lower urinary tract diseases in cats.

	Feline Idiopathic Cystitis	Urethral Obstruction	Struvite Urocystolith	Calcium Oxalate Urocystolith	Behavioral Periuria	Bacterial Urinary Tract Infection	Urinary Incontinence
Breed predisposition	None	None	None	Persian, Himalayan, Burmese, but also many breeds	None	None	Manx
Gender predisposition	None	Male	F > M	M > F	None	F > M	
Common age (years)	2 – 6	3 – 7	7 ± 3.5	7.3 ± 3.4		> 8 – 10	> 1
Neurologic abnormalities	Absent	Absent	Absent	Absent	Absent	Absent	Common
Urinary bladder size	Small	Large	Variable	Variable	Unremarkable	Variable	Variable
Urine pH	Acidic	Acidic	> 6.5	6.0 – 6.5	Unremarkable	Variable	Variable
Hematuria	Very frequent	Frequent	Frequent	Frequent	Variable	Frequent	Variable
Pyuria	Rare	Infrequent	Frequent	Frequent	Rare	Frequent	Absent
Crystals	Sometimes	MAP	MAP	CaOx	Rare	None	Variable
Bacteria	Absent	Absent	Variable	Absent	Absent	Variable	Variable
Survey radiography results	Small urinary bladder	Large urinary bladder, possible radiodense urethral plug or urolith	Moderately dense, round uroliths	Very dense, smooth or irregular small uroliths	Unremarkable	Unremarkable	Unremarkable to large urinary bladder

CaOx = calcium oxalate

F = female

M = male

MAP = magnesium ammonium phosphate (struvite)

## Reduce Urine Oxalate Excretion

Hyperoxaluria is an important risk factor for CaOx urolith formation. However, this may not be true for cats. Urolith-forming cats excrete similar quantities of oxalate as clinically healthy cats without uroliths.<sup>8</sup> Of particular interest is the observation that human patients with recurrent urinary tract infections excreted higher quantities of oxalate than urolith formers without urinary infections.<sup>10</sup> It was hypothesized that antibiotic control of urinary infections reduced intestinal *Oxalobacter*, the bacterium that consumes oxalate, reducing the quantity for absorption and ultimate urinary excretion. To prevent this from happening in cats, indiscriminate use of antibiotics should be avoided.

## Minimize Calcium Oxalate Precipitation on Sutures

Heterogeneous nucleation is the precipitation of crystals on a pre-existing surface other than CaOx. In a retrospective study of dogs and cats with uroliths associated with a suture nidus, eight cats had CaOx uroliths. Although seven of these cats had a history of CaOx uroliths, this study emphasizes that suture material may be a risk factor for urolith recurrence.<sup>11</sup> Therefore, when repairing the urinary bladder following surgical urolith removal, be careful not to place suture in the urinary bladder lumen. We have also observed heterogenous nucleation of CaOx uroliths over mineralized urinary bladder mucosa and other foreign material.

## Consider Thiazide Diuretics in Repeat Urolith Formers

Thiazide diuretics have been recommended to reduce the recurrence of calcium-containing uroliths in people because of their ability to reduce urinary calcium excretion. Although hydrochlorothiazide (1 mg/kg PO q12hr) administered to healthy cats decreased urine relative supersaturation for CaOx, reduction in urinary calcium excretion was minimal.<sup>12</sup> Because thiazide diuretics promote calcium retention, we do not recommend their use in cats with hypercalcemia. In addition, these agents have not been evaluated in cats with CaOx uroliths.

**Table 4. Predicting mineral composition of feline uroliths based on radiographic appearance.**

Mineral	Radiographic opacity compared to soft tissue	Surface contour	Shape	Usual Number	Approximate Size (mm)
CaOx monohydrate	+++ to +++++	Smooth, but occasionally resembling a cluster of grapes	Commonly round, but also rosette	>5	1 to 5
CaOx dihydrate	+++ to +++++	Rough to smooth	Rosettes	>3	1 to 7
Sterile MAP	++ to +++	Slightly rough	Round or discoid	Usually 1 to 3, occasionally many	3 to 10
Infection-induced MAP	+ to +++	Smooth to slightly rough	Round to faceted	Few to many	2 to >7
Urate	- to ++	Smooth	Round to ovoid	Usually 1, but up to 5	2 to 10
CaP	+++ to +++++	Rough	Too rare to comment	Too rare to comment	1 to 4
Cystine	- to +++	Rough	Round	Many, but some with few	1 to 4
Silica	++ to +++++	Too rare to comment	Too rare to comment	Too rare to comment	1 to 4
Xanthine	- to +	Smooth	Round to ovoid	1 to 3	1 to 5

CaOx = calcium oxalate    CaP = calcium phosphate    MAP = magnesium ammonium phosphate (struvite)

**Medical:**

- Hypercalciuria, a risk factor for CaOx urolithiasis has been associated with hypercalcemia, metabolic acidosis, high sodium consumption and vitamin D excess.
- The true prevalence of hypercalcemia is unknown; measure serum ionized calcium to accurately diagnose hypercalcemia.

**Nutritional:**

- Avoid calcium supplements and foods containing high quantities of oxalate (e.g., chocolate, peanuts, etc.)
- High moisture foods (e.g., canned) are more effective because increased water consumption is associated with decreased urine concentrations of calculogenic minerals.

**Pharmacological:**

- Consider potassium citrate if urine pH is consistently less than 6.2 or uroliths recur frequently.
- Consider vitamin B<sub>6</sub> (2 to 4 mg q 24-48 hr) in patients consuming primarily human food or diets with insufficient vitamin B<sub>6</sub>.
- Consider hydrochlorothizide (1-2 mg/kg q12hr) for highly recurrent urolithiasis in cats without hypercalcemia.

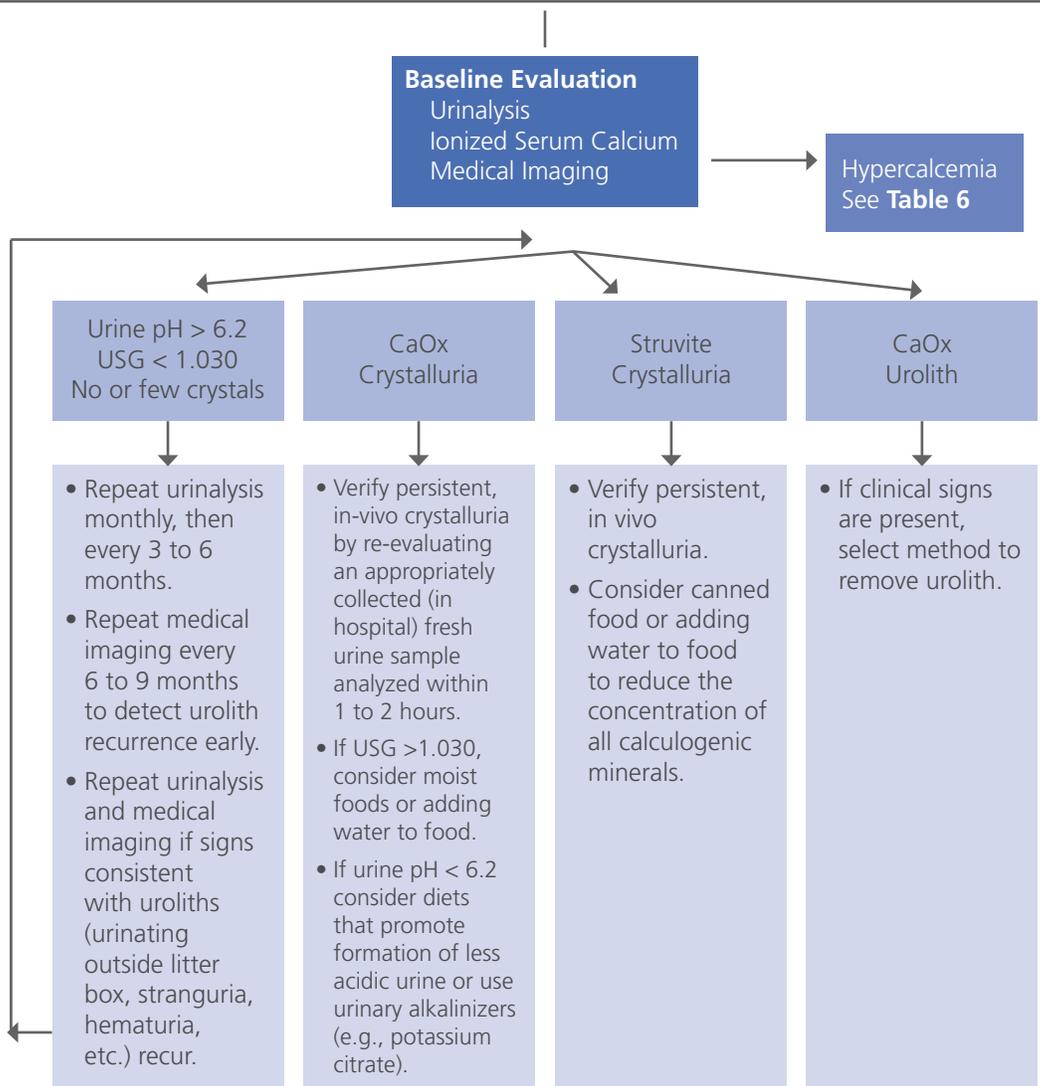


Figure 5. Approach for managing cats with calcium oxalate (CaOx) uroliths (USG = urine specific gravity).

**Table 5. Minimizing hypercalciuria in cats with calcium oxalate uroliths.**

Action	Rationale	Conclusion
Recognize and correct hypercalcemia	The quantity of calcium in blood is directly proportional to the amount filtered by the kidney. Epidemiological evaluation of feline patients revealed that 15 to 35% of CaOx urolith forming cats had hypercalcemia. In another study of 78 cats with ionized hypercalcemia, 64% would have been under-diagnosed if only total serum calcium content was measured. In most urolith-forming cats, hypercalcemia is idiopathic and mild.	Measure ionized calcium to identify hypercalcemia in cats with CaOx uroliths.
Avoid excessive aciduria	Consuming diets with ammonium chloride or magnesium chloride has been associated with increased urine calcium excretion in cats. Epidemiological studies in urolith-forming cats suggested that diets promoting urine pH less than 6.15 or 6.29 were associated with increased risk for CaOx urolith formation.	Avoid medications and diets that consistently result in urine pH values < 6.2.
Increase water consumption	Increasing water consumption is a safe and effective method to decreased urine concentration of calcium. Feeding moist food has been associated with an increase in urine volume and a decrease in urine specific gravity. Providing water fountains or flavored water may or may not be effective.	Provide moist food as the primary method of feeding. Check urine specific gravity to verify compliance (goal is urine specific gravity < 1.030)
Monitor sodium intake	Increasing sodium consumption increases urinary calcium excretion. In clinically healthy cats, increasing sodium content (1% Na, dry matter basis) of the food also promoted increased water intake, increased water excretion, and subsequent reduction in urine calcium concentration. However, the long-term adverse effects (kidney disease, negative calcium balance, hypertension) of higher dietary sodium fed to older cats or cats with CaOx uroliths have not been evaluated.	Avoid high sodium foods in older cats (> 10 years) or cats with kidney disease, heart disease or hypertension.
Avoid vitamin D supplementation	The minimum and maximum requirement for vitamin D in cat food is wide (a 20-fold difference). Therefore, some cat foods may contain high levels of vitamin D. Vitamin D can promote excessive absorption of calcium from the intestine and also promote release of calcium from bone.	Avoid excessive vitamin D intake. Measure serum vitamin D in hypercalcemic cats.

### Selecting a Diet to Minimize Urolith Recurrence

Results of experimental and clinical investigations have confirmed the efficacy of dietary modifications to alter urine saturation, which decreases the risk of CaOx urolith recurrence.<sup>8</sup> However, selection of an appropriate diet is challenging because: 1) the exact mechanisms underlying CaOx urolith formation are not completely known, 2) results of epidemiological studies of single dietary ingredients do not always match physiological response when the whole diet is consumed, and 3) diet efficacy has not been evaluated using clinically relevant endpoints (urolith recurrence) in urolith-forming cats. Epidemiological and clinical studies of data collected from 1990 to 1992 indicate that risk of recurrence of CaOx uroliths may be minimized by feeding a non-acidifying (urine pH greater than 6.15 to 6.29), high moisture diet (to promote urine specific gravity less than 1.030) formulated to avoid excessive protein, calcium, oxalate and sodium.<sup>13,14</sup> The diet should contain adequate quantities

**Table 6. Treatment strategies to correct idiopathic hypercalcemia.**

Strategy	Rationale
Increase dietary fiber	In one study, feeding foods with higher fiber restored normocalcemia in some cats with idiopathic hypercalcemia.
Feed less acidifying diets	Metabolic acidosis is associated with increased calcium mobilization from bone and increased filtered calcium by the kidneys
Avoid excessive vitamin D intake	Vitamin D promotes intestinal absorption of calcium. Vitamin D is not routinely available for all diets. However, you can contact the pet food manufacturer and ask for this information.
Glucocorticoids	Corticosteroids reduce intestinal calcium absorption, reduce bone resorption, and increase calcium excretion. Increasing calcium excretion is not ideal for cats with calcium oxalate uroliths, however.
Bisphosphonates	Bisphosphonates blunt osteoclastic bone resorption. Giving 10 mg of alendronate per cat per week has been effective for lowering serum calcium in a small number of cases. The medication should be given following a food fast. To avoid esophagitis, administer sufficient quantities of liquids to insure its complete passage out of the esophagus and into the stomach.

of phosphorus so as to minimize renal activation of vitamin D, adequate quantities of magnesium, and adequate quantities of vitamin B<sub>6</sub>, without excessive supplementation of vitamins C and D. Addition of citrate, an inhibitor of CaOx crystal formation, may be of value for some patients.

## Summary

For most cats with lower urinary tract signs, a diagnosis can be established after considering the clinical findings and results of urinalysis and medical imaging. Survey abdominal radiographs are a valuable diagnostic tool for cats with urethral disease; therefore, it is important to include the entire urethra in the field of view. Survey radiography may be more helpful for estimating mineral composition of uroliths than urinalysis findings. Results of complete blood cell count and serum chemistries usually are not helpful in cats with lower urinary tract signs unless there is concurrent illness (e.g., idiopathic hypercalcemia in cats with CaOx uroliths). The ideal treatment for preventing recurrence of CaOx uroliths is unknown; however, strategies that decrease risk of recurrence should be implemented after urolith removal (e.g., increased water intake, feeding high-moisture foods, avoiding excessive urinary acidification).

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