

UROLITHIASIS IN DOGS: Nutritional Management



UROLITHIASIS IS ONE OF THE MOST COMMON CANINE LOWER URINARY TRACT DISEASES

Urolithiasis has been reported in up to 3% of dogs and ranks as the third most common lower urinary tract disease, following urinary tract infection (UTI) and incontinence.¹⁻³ The two most prevalent mineral types found in canine uroliths are calcium oxalate (CaOx) and magnesium ammonium phosphate (struvite).⁵⁻¹¹ These uroliths may form in the upper urinary tract in addition to the lower urinary tract but are most commonly located in the bladder.^{8,12}

Clinical signs of CaOx and struvite urolithiasis may include hematuria, stranguria, pollakiuria, dysuria, and/or signs of pain on abdominal palpation.¹³⁻¹⁶ Systemic signs may be seen, particularly in cases of urinary obstruction. However, some affected dogs exhibit no clinical signs.

Nutritional intervention—feeding therapeutic urinary diets and increasing total daily water intake—is a key component of multimodal management for CaOx and struvite urolithiasis in dogs.⁴ Other urolith types that may respond to nutritional management include urate and cystine.^{4,17-20}

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WHAT ARE UROLITHS?

Uroliths have been defined as “solidified aggregates of mineral and nonmineral crystalloids that form in the urinary tract when urine becomes oversaturated with crystallogenic precursors.”²¹ Crystal and urolith formation involves the following processes:^{22,23}

- **Nucleation:** Precipitation begins, forming the first crystal nuclei.
- **Aggregation:** Crystal nuclei bind to each other.
- **Growth:** Additional mineral ions precipitate onto existing crystal nuclei.

A urolith may have up to four layers: a nidus—where crystals first precipitate, i.e., where the urolith starts to form—enclosed by a body (or stone) layer, which comprises the majority of the urolith, with a full outermost shell layer and/or an incomplete surface layer.^{21,24,25} A urolith may be comprised of one or more minerals. Multiple minerals in a single urolith may be interspersed throughout the urolith or occur in discrete layers.

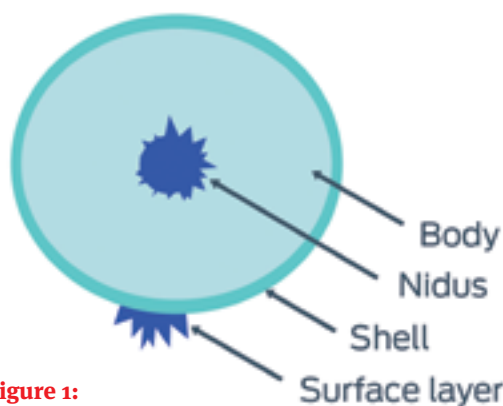


Figure 1:
Cross-section of a urolith

Common urolith minerals and location

CaOx and struvite account for the vast majority—72 to 97%—of canine uroliths submitted for laboratory quantitative analysis, similar to trends in cats.⁵⁻¹¹ CaOx has been reported in 27–47% of canine uroliths, and struvite in 36–54%.

Urolith submissions from different regions of the world may vary based on diet and environmental factors, which may affect reported prevalences.¹¹

Uroliths may occur anywhere in the urinary tract and may be found in multiple locations, particularly in male dogs.^{14,26,27} However, the majority of CaOx and struvite uroliths in dogs are located in the bladder.^{8,12} While most upper urinary tract uroliths in cats are composed of CaOx, struvite as well as CaOx are common minerals in upper urinary tract uroliths in dogs.^{12,16,27,28}

Also, unlike cats, in whom the majority of struvite uroliths are sterile,^{29,30} most struvite uroliths in dogs form secondarily to a UTI with a urease-producing bacteria.^{11,27,31}

Clinical signs

Although some dogs with urolithiasis do not show clinical signs, other dogs exhibit signs such as:^{13-16,32}

- Hematuria – blood in the urine.
- Pollakiuria – increased frequency of urination, usually of small amounts of urine.
- Dysuria – difficult and painful urination; may be associated with yelping or other vocalization.
- Stranguria – a type of dysuria characterized by slow, painful urination with straining; may pass only small amounts of urine.
- Signs of pain on abdominal palpation.
- Systemic signs, particularly in cases of urinary obstruction.

Diagnosis

Urinalysis, urine culture, and imaging are utilized for diagnosis in combination with patient signalment, clinical signs, history, and examination. Both CaOx and struvite appear radiopaque, but a positive urine culture revealing a urease-producing bacteria in addition to demographic factors (see Demographic risk factors) may raise the suspicion of struvite over CaOx.

Struvite crystals in the absence of a UTI in a dog are not considered pathologic nor does CaOx crystalluria necessarily indicate the presence of urolithiasis.^{2,33-35} Both types of crystals may be incidental findings in healthy animals, and treatment is not indicated in asymptomatic dogs with struvite or CaOx crystalluria. Crystals may also form as artifacts in urine samples that are not analyzed immediately after collection, i.e., those that are refrigerated or otherwise stored. Additionally, uroliths may be present in the absence of crystals. When both are detected, the type of crystal may not correspond to the mineral composition of the urolith.²

Recurrence and pseudorecurrence

Both CaOx and struvite uroliths may recur in dogs. Reported recurrence rates have varied widely.^{5,36-40} Rates may vary based on:

- Breed, i.e., high-risk versus low-risk breeds in the case of CaOx.
- Susceptibility to recurrent UTI, e.g., presence of endocrine disease or anatomic malformations, in the case of struvite.^{41,42}
- Diverse case populations.

Exposed suture material in the urothelium from previous cystotomies may act as a nidus leading to urolith recurrence. One study reported that 9.4% of recurrent canine uroliths submitted to a stone analysis laboratory between 1999 and 2006 had indications of having formed around a suture.⁴³ This finding supports the recommendation for minimally invasive techniques of urolith removal.⁴

There is also the possibility of **pseudorecurrence**, in which uroliths have not truly recurred but rather were not completely removed initially.⁴⁴ To avoid this, post-procedure imaging should be performed to confirm removal of all uroliths.

Clinical significance

The presence of urethrolith(s) may cause obstruction, which should be managed with appropriate emergency

care.⁴⁵⁻⁴⁷ Male dogs are at greater risk than females due to their narrower and longer urethra. Delayed treatment for a complete urethral obstruction may result in urethral or bladder rupture, uremia, electrolyte imbalances, and/or metabolic acidosis, even death.

Obstruction may also occur in the ureter(s) and, as with urethral obstruction, should be managed with appropriate emergency care.^{4,32}

Repeated obstruction or recurrence of clinical signs may significantly decrease the pet's quality of life and/or, especially with urination in the home or frequent requests to go outside, may damage the bond between the dog and owner, either of which may lead to relinquishment of the dog to a shelter or to elective euthanasia. Dogs reported by their owners to urinate in the home at least once per week for any reason were found to be at a 2–4x higher risk of being relinquished to a shelter than dogs who did not urinate in the house or did so less frequently.^{48,49}

FACTORS AFFECTING UROLITH FORMATION

The role of urine supersaturation

Whether crystals dissolve or, alternatively, precipitate, aggregate, and grow into uroliths is affected by, among other factors, the degree of urine saturation with the relevant mineral ions.^{22,23,50}

- In stable (or undersaturated) urine, crystals dissolve when chemically possible (dependent on composition) and do not precipitate, aggregate, or grow.
- In metastable (supersaturated) urine, new crystals are unlikely to form spontaneously. However, crystals and stones already present in a metastable solution may aggregate and grow and do not dissolve. Mineral ions may also precipitate onto other existing matter, such as sloughed epithelial cells or exposed sutures.

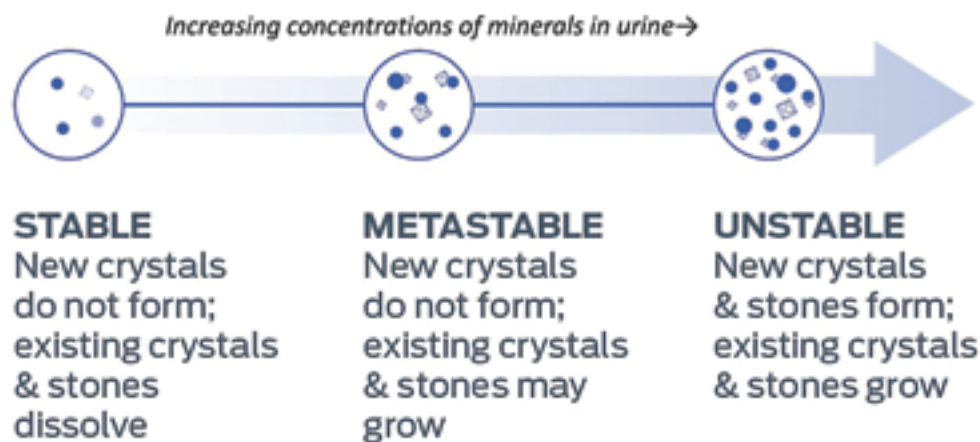


Figure 2:

Relationship between mineral concentration and urolith (stone) formation

- In unstable (or labile) supersaturated urine, new crystals form spontaneously. Crystals aggregate, grow, and do not dissolve.

The concentration at which an undersaturated solution becomes metastable is the thermodynamic solubility product.^{50,51} This measure is determined in pure water with pure crystals and is a fixed value at a specific temperature. The thermodynamic solubility product is used to calculate relative supersaturation (RSS), an indicator of the risk of urolith formation (see definition of RSS and further discussion under Evaluation of urolith risk). The concentration at which a metastable supersaturated solution becomes unstable is the thermodynamic formation product.

Other urinary factors

Urolith development is not dependent only on urine supersaturation but is also significantly influenced by the following urinary factors:

- **Urine pH.** Urease-producing bacteria alkalize the urine.^{33,52} Due to high solubility in acidic urine and lower solubility in alkaline urine, struvite uroliths tend to dissolve in acidic urine and form in alkaline urine.^{2,34,52}
- **Urine specific gravity (USG).** A higher USG, i.e., urine that is more concentrated, may increase the risk of urolith formation.⁵³ However, a more concentrated urine may also increase the concentration of urolith inhibitors and/or promoters.

- **Urolith inhibitors.** Urine contains hundreds of compounds, and their impact on urolith formation is not fully understood. Urolith inhibitors may block nucleation, aggregation, and/or growth.^{50,54}

- **Urolith promoters.** Similar to urolith inhibitors, urolith promoters, which are conditions or compounds that increase the likelihood of crystal formation and/or aggregation, fall into an area that has not been fully investigated. A urease-producing bacterial UTI, which increases the risk of struvite uroliths, is an example of a urolith promoter.^{50,54}

- **Noncrystalline matrix.** Other compounds such as sloughed cells may act as a nidus, or scaffolding, for crystal deposition.^{50,54}

- **Urine retention.** Prolonged urine retention in the bladder allows more time for crystals to precipitate and develop into uroliths.⁵⁴

Demographic risk factors

Based on submission data from urolith laboratories worldwide, the following demographic factors affect the likelihood for development of CaOx or struvite uroliths in dogs:

- **Sex and neuter status.** Male and neutered dogs are more likely to have CaOx uroliths, while female dogs are more likely to develop struvite.^{3,6-8,11,12,55-57} Female dogs are predisposed to struvite because they are more

prone to developing a UTI due to their shorter urethra (an ascending infection).^{1,2,24,31,58}

- **Age.** In general, older dogs are more likely to have CaOx uroliths and younger dogs to have struvite.^{8,11,12,26,59,60}
- **Breed.** Breed predispositions for CaOx and struvite urolithiasis have been identified.^{5-9,56,59,61} Most research has concluded that toy and small dog breeds are predisposed to CaOx urolithiasis, while larger breeds are more likely to have struvite uroliths.

Potentially factoring into a predisposition to CaOx urolithiasis, daily urine volume was significantly lower and urinary calcium concentration significantly higher (without hypercalcemia) in healthy Miniature Schnauzers, a small breed predisposed to formation of CaOx uroliths, than in healthy Labrador Retrievers, a large breed and a breed not predisposed to CaOx.⁶² The Miniature Schnauzers also urinated fewer times per day, extending urine retention time within the bladder.

Reported predispositions may differ among studies due to differences in breed popularity and diets fed around the world.¹¹

- **Weight.** Overweight/obesity has been reported as a risk factor for CaOx urolithiasis.^{6,58,63} One study found excess body weight was also associated with a lower risk for struvite uroliths in dogs.⁶
- **Genetics.** Genetics may contribute to the risk of CaOx urolithiasis:
 - **Hereditary CaOx urolithiasis.** Most cases of CaOx urolithiasis in English Bulldogs are caused by either a type I or type II genetic defect.⁶⁴ Type 1 has also been reported in the American Bully, American Staffordshire Terrier, Border Collie, Boston Terrier, Bullmastiff, Havanese, Rhodesian Ridgeback, Rottweiler, Sloughi, and Staffordshire Bull Terrier. Type 2 has also been reported in the American Bulldog, Basset Hound, Beagle, Bullmastiff, and English Mastiff.

- **Genetic defects in vitamin D receptors.** Genetic alterations in vitamin D receptors may increase the level of calcium excretion in the urine even with normal serum vitamin D and calcium levels.⁶⁵
- **Genetic defect in arachidonic acid metabolism.** A defect in metabolism of arachidonic acid in membrane phospholipids may contribute to development of hypercalciuria and hyperoxaluria in some dogs with CaOx urolithiasis.⁶⁶
- **Primary inherited hyperoxaluria.** A primary inherited type 1 hyperoxaluria resulting from elevated endogenous production of oxalate has been very rarely reported in puppies.⁶⁷

Dietary and other factors affecting risk of CaOx urolithiasis

The risk for CaOx urolithiasis is dependent upon urinary excretion of calcium and oxalate, the level of urolith inhibitors and promoters in the urine, and the presence of nutrients that alter urine volume/USG.^{54,68}

Urinary calcium excretion

The amount of calcium in the urine is the result of the complex metabolism of calcium in the body. Calcium balance in the body is regulated primarily by calcitriol and parathyroid hormone through their effects on the intestines, kidneys, and bone.⁶⁹⁻⁷¹ Calcium homeostasis is tied to that of phosphorus.^{69,72}

Hypercalciuria can occur due to:⁷³

- Excessive intestinal absorption of calcium from the diet, known as absorptive hypercalciuria.
- Decreased renal tubular calcium resorption, known as renal leak hypercalciuria.
- Excessive resorption of calcium from bone, known as resorptive hypercalciuria.

The mechanism leading to hypercalciuria may differ among breeds—those that are high risk versus low risk—and potentially within a breed.^{74,75}

The risk of CaOx formation is further influenced by how much calcium remains free in the urine to bind to oxalate. By forming a soluble complex with calcium, citrate reduces the availability of calcium to bind to oxalate, decreasing the risk of CaOx urolithiasis.^{50,54,76} Thus, the level of citrate in the urine is also a contributing factor.

Urinary oxalate excretion

Oxalate is produced endogenously and is available exogenously in the diet.^{77,78}

Endogenous oxalate production occurs predominantly in the liver via metabolism of glyoxylate.^{79–82} In health, glyoxylate primarily participates in other metabolic pathways, which serves to restrict oxalate production.^{80,82}

Glyoxylate originates from metabolism of sugars, hydroxyproline, and other amino acids.^{79–82} Hydroxyproline is found in the diet in animal proteins, especially collagen, or may be generated from collagen turnover in the body.^{79,80,82}

Excess supplementation with vitamin C, a precursor of hydroxyproline, may increase the risk of CaOx uroliths.⁸³ Dogs are able to produce vitamin C endogenously, and thus they have no mandatory dietary requirement for vitamin C.

Circulating oxalate, whether of endogenous or exogenous origin, is eliminated in the urine through glomerular filtration and, to some extent, via secretion in the proximal tubules.^{77,82,84}

Oxalate and the microbiome

Dietary oxalate cannot be metabolized by dogs or most other mammals.⁸¹ However, oxalate may be metabolized in the colon by *Oxalobacter formigenes* and other bacteria, including *Lactobacilli* and *Bifidobacterium*.^{85–87}

Oxalate that is not metabolized by colonic bacteria is available to be absorbed from the gut and ultimately

excreted in the urine. Prevalence of *Oxalobacter formigenes* was significantly lower in fecal samples from dogs with CaOx urolithiasis compared to healthy dogs from breeds without a predisposition to CaOx urolithiasis.⁸⁸

Various lactic acid bacteria and prebiotics have been demonstrated to influence oxalate degradation in vitro.^{85,87,89} Results have suggested that effects of probiotics are species- and strain-specific. However, whether administration of prebiotics and/or probiotics (or synbiotics and postbiotics) impacts oxalate degradation, intestinal absorption, and ultimately urinary excretion in dogs at risk of CaOx urolithiasis is not yet known.

Nutritional factors that affect urinary excretion of calcium and/or oxalate

Although researchers could not establish a direct cause-and-effect relationship, a survey of owners of 117 dogs with CaOx uroliths and 174 dogs without a history of urinary tract disease fed wet diets found the following associations between relative nutrient intake and risk of CaOx urolithiasis:⁹⁰

- **Higher moisture** (78–82%) versus lower moisture (70–73%) diets were associated with a **6.3x lower risk** of CaOx urolithiasis. A higher moisture diet may produce a less concentrated urine with a lower urinary excretion of calcium and oxalate.
- **Higher dietary calcium** (440–540 mg/100 kcal) versus lower calcium (50–170 mg/100 kcal) was associated with a **6.7x lower risk**. More calcium in the diet may lead to formation of CaOx complexes in the gut that are then eliminated in the feces, leaving less calcium and oxalate to be absorbed from the intestines and excreted in the urine.
- **Higher protein** (9.2–14.2 g/100 kcal) diets were associated with a **4.8x lower risk** compared to lower protein (1.5–6.3 g/100 kcal) diets. Researchers suggested two possible reasons for this result: 1) The higher protein diets were also higher in moisture. 2) The higher protein diets were higher in potassium. The survey found

higher potassium (240–420 mg/100 kcal) diets were associated with a **5.3x lower risk** of CaOx urolithiasis than lower potassium (60–160 mg/100 kcal) diets.

- **Higher phosphorus** (310–440 mg/100 kcal) compared to lower phosphorus (30–140 mg/100 kcal) diets were associated with an **8.3x lower risk** of CaOx urolithiasis.
- **Higher sodium** (250–510 mg/100 kcal) diets were associated with a **5.6x lower risk** than lower sodium (20–80 mg/100 kcal) diets.

In other research, while a small group of healthy adult Miniature Schnauzers had a significantly higher urinary calcium excretion ($\mu\text{mol/L/day}$) when fed a higher sodium diet (327 mg/100 kcal) than when fed a 67 mg sodium/100 kcal diet, urinary calcium and oxalate concentrations and CaOx RSS were significantly lower with the higher sodium diet,⁹¹ suggesting a lower risk and supporting the findings of the survey. Promotion of water intake and diuresis secondary to increased dietary sodium may counteract the increase in urinary calcium excretion.

A number of studies suggest that hypercalciuria plays a larger role in the risk of CaOx urolith formation than hyperoxaluria in high-risk dog breeds.^{37,38,70,84,92,93}

Urinary excretion of calcium and oxalate is influenced by dietary intake of calcium and oxalate. However, their intestinal absorption is complicated by the relative proportion of calcium to oxalate and the effects of other nutrients in the diet. In addition, the abundance of oxalate-degrading bacteria in the gut impacts how much oxalate remains to be absorbed.

It is not possible to understand the risk of a dog developing urinary stones on a specific diet simply by looking at the nutritional profile. How best to minimize urinary excretion of calcium and oxalate in order to lower the risk of CaOx urolithiasis remains an active area of research.

Factors affecting risk of struvite urolithiasis

The primary factor leading to formation of most struvite uroliths in dogs is the presence of a UTI, typically with a urease-producing bacteria, e.g., *Staphylococcus*.^{27,31,42,94,95} Of 23 dogs with suspected struvite urolithiasis that had a UTI confirmed by urine culture, *Staphylococcus* or *Proteus* accounted for nearly 90% of the infections.⁹⁵

Urease hydrolyzes urea to form ammonia, alkalinizing the urine, a condition in which struvite crystals are less soluble.^{3,33,96} By buffering free hydrogen ions, ammonia is then converted to ammonium, a component mineral ion of struvite.

EVALUATION OF UROLITH RISK

The effect of an individual diet on urolith risk can be assessed using various means, urine RSS being the most common. RSS is calculated with one of several computer software programs:

- After collection of urine samples from dogs fed the same diet, EQUIL programs utilize urine pH and urine concentrations of a urolith's constituent ions and other compounds (ammonium, magnesium, phosphate, calcium, oxalate, chloride, citrate, potassium, sodium, sulfate, urate, carbon dioxide, and pyrophosphate) to calculate RSS for a given type of urolith.^{51,97,98}
- The SUPERSAT program uses urine pH and urine concentrations of ammonium, magnesium, phosphate, calcium, oxalate, citrate, potassium, sodium, sulfate, uric acid, and chloride in its calculations.^{99,100} It is a proprietary program.

RSS may be used in the process of diet formulation. It is not used in a clinical setting to assess the risk of an individual dog forming uroliths.

NUTRITIONAL MANAGEMENT OF CaOx AND STRUVITE UROLITHIASIS IN DOGS

Calcium oxalate uroliths require removal by either noninvasive procedures, when available, or surgery.^{4,101} However, their recurrence may be lowered with nutritional management.

Unless urinary obstruction is present, nutritional intervention to dissolve struvite uroliths is advised over removal in dogs and presents a low risk of obstruction.⁴ However, antibiotics based on urine culture and sensitivity must also be administered to eliminate the causative UTI associated with struvite uroliths.^{4,54}

Recommended durations of antibiotic administration differ.^{15,102-104} The International Society for Companion Animal Infectious Diseases (ISCAID) guidelines for the diagnosis and management of bacterial urinary tract infections in dogs and cats acknowledges the rationale for continuing antibiotics throughout dissolution but questions whether the risk of failing to eliminate the infection is sufficient to outweigh the potential risks of antibiotic treatment, including long-term effects on the intestinal microbiome and development of antibiotic resistance.¹⁰⁴ The authors suggest short courses of antibiotics (3–7 days) but caution that additional research is needed.

The objectives of nutritional management of canine CaOx and struvite urolithiasis are to lower the concentration of minerals in the urine, to alter the chemical form of the ions in the urine by changing urine pH, and/or to influence the overall stability of the urine. Feeding of therapeutic urinary diets and increasing total daily water intake are the two modalities employed.

Therapeutic urinary diets

Therapeutic urinary diets are typically formulated to promote a urinary environment that is unsuitable for development of struvite and CaOx uroliths, targeting a specific urine pH while producing a urine in the undersaturated range for

struvite and the metastable range for CaOx uroliths. These diets help dissolve struvite uroliths and reduce the risk of CaOx and sterile struvite recurrence.

Lack of full compliance with a therapeutic urinary diet may lead to unsuccessful dissolution of struvite or to recurrence of CaOx uroliths (and struvite, if sterile).

Therapeutic urinary diets have been evaluated for dissolution of presumed struvite uroliths:

- Five of 10 dogs with suspected struvite urolithiasis secondary to a *Staphylococcus pseudointermedius* UTI fed a dry Purina therapeutic urinary diet and administered an antibiotic chosen based on urine culture and sensitivity showed complete urolith dissolution in a median of 31 days.¹⁰² Quantitative urolith analysis after removal in 4 of the 5 remaining dogs found minerals in addition to struvite.
 - Twenty-nine of 50 dogs with suspected struvite urolithiasis fed a wet therapeutic urinary diet and administered antibiotics (with one exception, apparently a case of sterile struvite) showed complete urolith dissolution on imaging at a median of 35 days.⁹⁵ Of the remaining 21 dogs, 7 dogs showed partial dissolution; 7 dogs showed no dissolution (quantitative analysis after removal revealed uroliths in 6 dogs contained at least 10% non-struvite minerals; the owner of the remaining dog was not fully compliant in feeding only the therapeutic diet); and the therapeutic diet was discontinued before the first recheck in 7 dogs.
- Urolith size and number did not significantly affect whether uroliths fully dissolved.
- Complete dissolution occurred in 6 female dogs with presumptive struvite upper tract urolithiasis that were fed a therapeutic urinary diet, administered an appropriate antibiotic to treat *Staphylococcus pseudointermedius* UTI, and encouraged to increase water intake.¹⁰³ Five dogs had a temporary or permanent ureteral stent placed. Median time to full dissolution was 3.9 months for ureteroliths and 5.3 months for nephroliths.

Therapeutic urinary diets have also been evaluated for their effects on urinary calcium and oxalate concentration and excretion, CaOx RSS, and recurrence of CaOx urolithiasis. Seventeen dogs with a history of CaOx urolithiasis fed a therapeutic urinary diet had a significantly lower mean CaOx RSS after 1 month.⁹² Mean urinary levels (mmol/L) of calcium and oxalate and mean calcium excretion (calcium-to-creatinine ratio on mmol basis) also significantly decreased after 3 months of feeding the therapeutic diet. The diet was continued for up to 11 months, and no recurrence was seen in the 13 dogs that completed the full study period.

Increased total daily water intake

The goal of increasing total daily water intake is to promote a more dilute urine.^{4,53} A more dilute urine may reduce RSS by reducing solute concentration, presumably lessening urolith risk.^{53,54} A higher urine volume may increase frequency of urination, helping eliminate calculogenic minerals and microscopic concretions before they can form larger uroliths.

The American College of Veterinary Internal Medicine (ACVIM) Small Animal Consensus Recommendations on the Treatment and Prevention of Uroliths in Dogs and Cats notes, “For all mineral types (except infection-induced struvite), feeding diets high in moisture is one of the cornerstones of urolith prevention strategies.”⁴ For CaOx uroliths, the Consensus Recommendations advises targeting a USG below 1.020 for dogs.

To achieve this in dogs, the primary recommendation is to feed a wet diet or add water to dry food.

MONITORING

CaOx

After removal of CaOx uroliths, long-term feeding of a therapeutic urinary diet or a therapeutic diet intended for another condition that has been RSS-tested is generally recommended to reduce the risk of recurrence, unless the dog should resume a different non-RSS-tested therapeutic

diet for management of a more urgent comorbidity.⁴ A wet diet is preferred, or water can be added to dry food to promote water intake. For pets that will not eat either of these options, feeding a diet with moderately increased sodium may help promote water intake.

Dogs with a history of CaOx urolithiasis should be actively monitored for recurrence. Urinalysis and radiographs are recommended every 4–6 months.⁵⁴

Struvite

In dogs with struvite urolithiasis managed with nutritional intervention, a urinalysis and radiographs are recommended every 4 weeks to monitor progression of dissolution. Uroliths that do not dissolve or do not fully dissolve may indicate:^{4,105}

- The presence of minerals other than struvite.
- Noncompliance with the therapeutic urinary diet and/or antibiotic regimen.
- Uncontrolled UTI. If the owner is administering antibiotics as directed but the UTI is not resolving, a repeat urine culture and sensitivity should be performed to ensure the appropriate antibiotic is being administered. The causative bacterial agent and/or sensitivity can change over time.¹⁰⁶
- Urolith(s) that is/are too large.

When uroliths do not completely dissolve or in dogs with continuing clinical signs, uroliths should be removed (see below for exceptions).^{15,102}

The ACVIM Small Animal Consensus Recommendations on the Treatment and Prevention of Uroliths in Dogs and Cats notes that there are exceptions to pursuing removal of bladder uroliths that do not dissolve. If clinical signs are absent and the urolith is sized or shaped in such a way that it is at low risk of causing a urethral obstruction, the dog can be monitored instead of having the urolith removed.⁴ The dog should remain on a therapeutic urinary diet in these cases, to help reduce the risk of further stone growth.

After successful dissolution of struvite uroliths associated with a UTI, feeding of a therapeutic urinary diet will not prevent struvite recurrence.⁴ In dogs prone to recurrent UTI or with an undiagnosed UTI, a therapeutic urinary diet may slow development of recurrent struvite uroliths. However, only prevention or early detection and treatment of UTI will prevent struvite recurrence. The ACVIM Small Animal Consensus Recommendations recommends a urine culture once a month up to 3 months and if negative, then to watch for return of clinical signs.⁴ Performing a urinalysis alone is not considered to be sensitive for detecting a UTI.

Dogs with recurrent UTI should be evaluated for the presence of contributing conditions, such as anatomical abnormalities, e.g., recessed vulva or ectopic ureters, and diseases including diabetes mellitus or Cushing's disease.^{4,42} A relapsing recurrent infection, i.e., one in which the causative bacteria has not changed, could indicate that the initial infection was not fully eliminated. This could result from administering an antibiotic to which the bacteria is not sensitive, insufficient treatment duration, or poor owner compliance with the treatment regimen.

In the rare case of sterile struvite urolithiasis in a dog, a therapeutic urinary diet is indicated for dissolution as well as long-term feeding to reduce the risk of recurrence.

THE RELATIONSHIP BETWEEN UPPER TRACT UROLITHIASIS AND CHRONIC KIDNEY DISEASE

As measured by submissions to urolith analysis laboratories, prevalence of upper urinary tract uroliths of any mineral type(s) is low, accounting for just 2–4% of all canine urolith submissions.^{1,26,27} Similarly, only 1–6% of CaOx urolith submissions and 1–4.5% of struvite submissions from dogs were upper tract uroliths.^{8,12}

Note, however, that these proportions likely do not represent true prevalence since renal uroliths are more commonly monitored rather than removed and submitted for analysis.

Obstructive nephroliths or ureteroliths may cause damage to the kidney(s). Damage may be reversible or may progress to chronic kidney disease (CKD) depending on severity (partial or complete obstruction), whether they are unilateral or bilateral, duration, and whether they recur.³²

In 16 dogs that had obstructive ureteroliths, 4 dogs had renal azotemia on presentation.¹⁶ After surgical removal of the obstruction, creatinine remained elevated in 3 of the 4 dogs, which may suggest the presence of CKD. However, researchers noted that further diagnostics and follow-up were needed for confirmation.

The ACVIM Small Animal Consensus Recommendations on the Treatment and Prevention of Uroliths in Dogs and Cats **does not advise removal of nephroliths** unless obstruction, pain, or recurrent infection are present, or the nephrolith is significantly compressing renal tissue.⁴ Urinalysis, urine culture, and imaging should be performed on a routine basis to detect if and when an “inactive” nephrolith begins to cause complications.¹⁰⁷ The ACVIM Small Animal Consensus Recommendations advises ureteral stenting procedures when obstructive ureteroliths occur.⁴

OTHER NUTRITION-RESPONSIVE UROLITHS

Although CaOx and struvite uroliths are the most common canine uroliths, urate and cystine uroliths also occur, may recur, and respond to dietary management.^{4,17-20}

Urate

As a percentage of canine urolith submissions, reported prevalence of urate uroliths typically ranges from 3.2–14.9%.^{6-8,11,56,108} Ammonium urate is the most common urate urolith.¹⁰⁹ Predisposed breeds for urate uroliths include Bichons Frises; American, English, and Old English Bulldogs; English Cocker Spaniels; Miniature Schnauzers; Pekingese; and Scottish Terriers.^{6,12,110,111} Dalmatians are at especially high risk.

Urate uroliths occur secondarily to a defect in metabolism of purines.^{17,83,109} Due to the defect, uric acid produced during purine metabolism is not converted to allantoin in the liver but instead accumulates in the circulation and then in the urine. Uric acid is less soluble in urine than allantoin leading to urate urolith formation. Hyperuricosuria can also occur with hepatic disease, e.g., portosystemic shunts.^{17,83}

Dalmatians have a defect in the SLC2A9 gene, causing faulty transport of uric acid into the liver and poor reabsorption in the renal tubules, resulting in hyperuricosuria.^{17,112,113} The gene defect has also been identified in urate urolith-forming dogs of other breeds.^{112,114} Genetic testing is available through commercial laboratories.

Dietary dissolution and reduction of the risk of recurrence have traditionally been achieved by feeding a reduced-protein, urine-alkalinizing diet and promoting water intake, preferably by feeding a wet diet, targeting a USG less than 1.020–1.025.^{4,17,19} Protein sources containing high concentrations of purines, e.g., shellfish, fish, organ meats, and some vegetables, e.g., asparagus, cauliflower, and legumes, should be avoided; low-purine protein sources include soy protein, egg, and dairy. A Purina crossover study showed that a soy protein hydrolysate diet (higher total protein but a low-purine source) was a comparable alternative to a traditional low-protein diet in the management of urate urolithiasis.¹¹⁵ Urinary excretion of uric acid, allantoin, and total purine, and RSS of ammonium urate and sodium urate were similar in male Dalmatians (including some with a history of urate urolithiasis) when fed either the soy protein hydrolysate diet or the low-protein diet.

When the gene defect is not present or the dog is a breed not known to have the gene defect, the dog should be assessed for liver disease and treated if liver disease is found.

Cystine

Reported prevalence of canine cystine uroliths based on urolith laboratory submissions ranges from 0.6–8%.^{7-9,11,56,108,116}

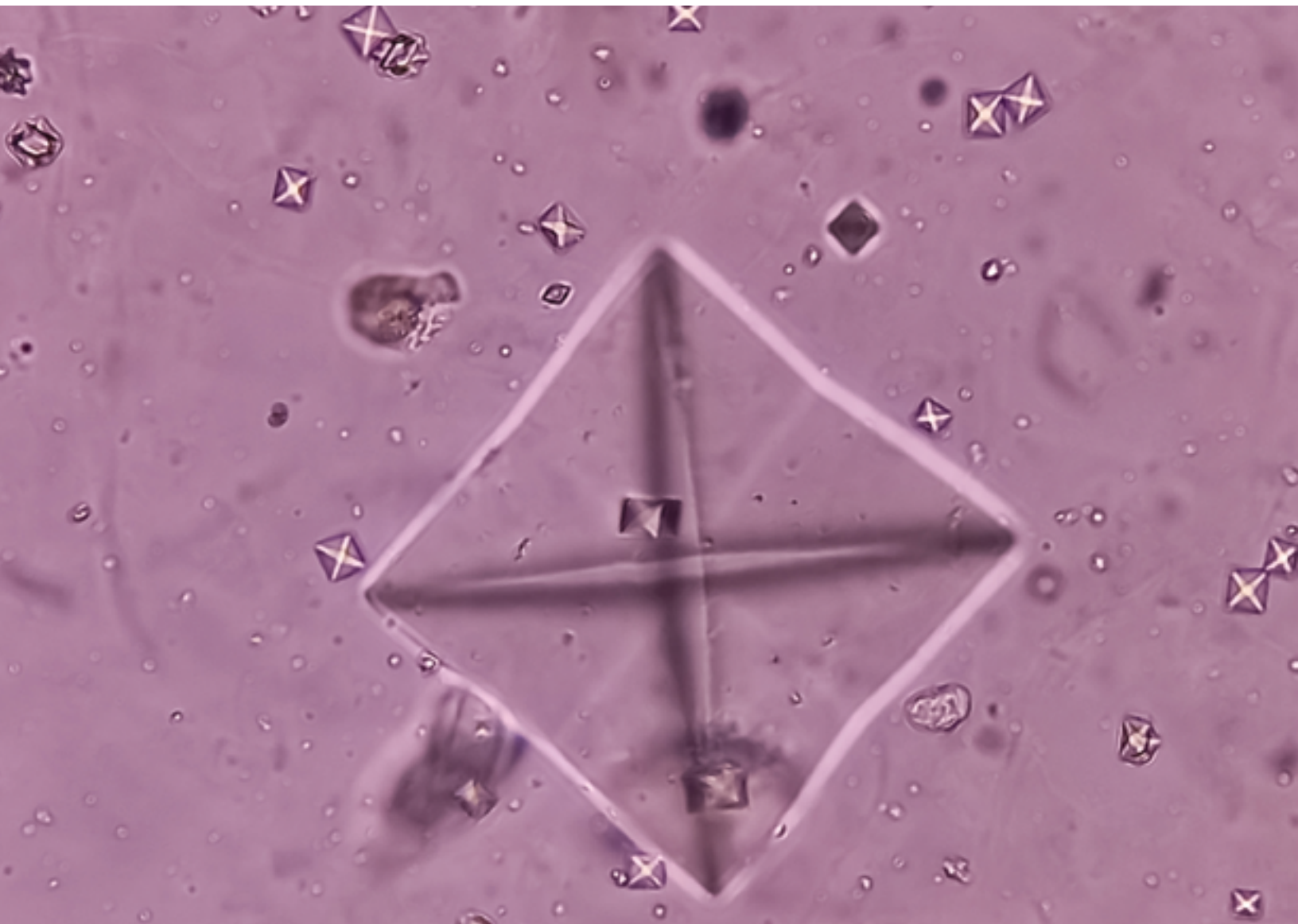
The English Bulldog is at particularly high risk as is the Miniature Pinscher.^{6,12} Other predisposed breeds include the American Staffordshire Terrier, Basset Hound, Chihuahua, Dachshund, French Bulldog, Newfoundland, Rottweiler, Staffordshire Bull Terrier, Welsh Corgi, and Yorkshire Terrier.^{6,12,116} Male dogs comprise nearly 100% of cystine urolith submissions, and many affected males are intact.^{6,12,116,117}

Cystine urolithiasis is associated with mutations affecting cystine transport.^{17,20,118} Several gene defects affecting the SLC3A1 gene and the SLC7A9 gene have been identified.¹¹⁸ An androgen-dependent sex-linked defect may promote formation of cystine uroliths in intact male dogs, although the gene has not been identified.^{18,116,118}

Genetic testing is available through commercial laboratories. Researchers have suggested that a given breed may be susceptible to more than one gene defect.¹¹⁶

Dietary dissolution and reduction of the risk of recurrence of canine cystine uroliths involve feeding a reduced-protein, urine-alkalinizing, moderate-sodium diet and promoting water intake, preferably by feeding a wet diet, targeting a USG less than 1.020–1.025.^{4,17,20,117} Animal-sourced proteins and proteins from nuts, wheat, and eggs should be avoided as they are high in methionine, a precursor to cystine. Commercial diets are available that manage the recurrence of both cystine and urate urolithiasis.

Since cystine urolithiasis is an inherited condition and may be due to a sex-linked defect, neutering of an intact dog with cystine urolithiasis is recommended.^{4,116}



CaOx and struvite are the two most common uroliths in dogs, as in cats, and are prone to recurrence. CaOx uroliths cannot be dissolved medically and must be removed, preferably using minimally invasive techniques. Struvite uroliths in dogs are usually associated with a UTI caused by urease-producing bacteria.

Nutritional management, combined with antibiotics based on urine culture and sensitivity, is the first-line approach to dissolution of struvite uroliths. Nutritional intervention is also indicated to help reduce the risk of recurrence of CaOx uroliths. Nutritional management comprises therapeutic urinary diets and increased total daily water intake.

While some dogs with urolithiasis show no clinical signs, others experience significant morbidity. Urolithiasis can adversely impact a dog's quality of life and strain the human-animal bond, in some cases leading to relinquishment or elective euthanasia, underscoring the importance of effective management.

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