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ACVIM Small Animal Consensus Recommendations on the Treatment and Prevention of Uroliths in Dogs and Cats

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In an age of advancing endoscopic and lithotripsy technologies, the management of urolithiasis poses a unique opportunity to advance compassionate veterinary care, not only for patients with urolithiasis but for those with other urinary diseases as well. The following are consensus-derived, research and experience-supported, patient-centered recommendations for the treatment and prevention of uroliths in dogs and cats utilizing contemporary strategies. Ultimately, we hope that these recommendations will serve as a foundation for ongoing and future clinical research and inspiration for innovative problem solving.

Key words: Calcium Oxalate; Lithotripsy; Stent; Struvite.

For the past century, treatment for urolithiasis in dogs and cats has been the province of the surgeon, but with the advent of new technologies, urolith management is evolving. Several minimally invasive procedures are performed daily in veterinary hospitals around the world. Not all management strategies are suitable for every patient or every situation. The challenge for clinicians is to move beyond traditional surgical care and consider less invasive alternatives. For clients to be properly educated and informed of their options, clinicians must understand these options and their associated indications and risks.

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Methodology

A panel of 6 specialists convened to formulate recommendations by constructing common clinical scenarios of dogs and cats with uroliths paired with suitable contemporary management strategies. The panelists were from different veterinary institutions around the country with various experiences and skill sets, although all are well versed in the management of urolithiasis. Each panelist cast an independent vote as to the appropriateness of the strategy. The panelists then met to conduct an iterative group discussion to reach consensus. During this discussion, the treatment decision for each clinical scenario was debated with the assumption that urolithiasis was the patient's primary problem. The committee recognized that not all veterinary care facilities have the technology or expertise to perform all minimally invasive procedures. This issue was not considered in the panelists' treatment decision; treatment decisions were selected in the patient's best interest as if all options were available. The committee recognized that cost and willingness to travel to centers of expertise affect treatment choices, but the panelists did not include these variables in proposing a standard of care. The committee recognized that exceptions to each recommendation always will exist, especially during emergency presentations. Therefore, the committee made its decisions on the assumption that any unexpected emergency situation would be sufficiently stabilized before urolith management.

It was requested that treatment justifications be supported by published research evidence when available. If published research was not available, then the panelists used research available from human medicine, as well as clinical expertise and experience. After the

iterative group discussion, a consensus recommendation was formulated. This recommendation was followed by a final vote of acceptance. Therefore, the panelists' collective personal experiences and interpretations of the published data constitute the basis for these guidelines.

The guidelines are divided into 3 sections: treatment of lower tract (bladder and urethra) uroliths, treatment of upper tract (kidney and ureter) uroliths, and urolith prevention (regardless of location). It was not the committee's goal to address every urolith type or combination of precipitating minerals, but to provide sufficient recommendations for the more common uroliths managed in practice. The less common clinical situations could be adequately addressed by extrapolation of a combination of this consensus statement, as well as by referring to the literature that has been published previously.

Part 1

Standards of Care for Dogs and Cats with Lower Urinary Tract Uroliths

Recommendation 1.1: Struvite Uroliths should be Medically Dissolved. Uroliths consistent with a composition of struvite (ie, moderately radiopaque uroliths in dogs with alkaline urine and a urinary tract infection caused by urease-producing bacteria (such as *Staphylococcus* spp), and moderately radiopaque uroliths in cats with approximately neutral urine pH) should be medically dissolved unless (1) medications or dissolution foods cannot be administered or are contraindicated, (2) the uroliths cannot be adequately bathed in modified urine (eg, urinary obstruction, large solitary urocystoliths occupying almost all of the urinary bladder), or (3) uncontrollable infection despite appropriate medical management and owner compliance. Most struvite cystoliths can be safely dissolved with minimal risk, including urinary obstruction (Table 1).

Rationale: Medical dissolution for both sterile and infection-induced struvite uroliths is highly effective and avoids the risks and complications of anesthesia and surgery. In many cases, dissolution is less expensive than surgery. Sterile struvite urocystoliths usually dissolve in less than 2–5 weeks.[1–6]

Avoiding cystotomy and closure of the bladder with sutures will eliminate the risk of suture-induced urolith recurrence, which may be responsible for up to 9% of urolith recurrences.[7,8] Although some believe that medical dissolution places the patient at high risk for urethral obstruction, this complication has not

Table 1. Summary of consensus recommendations for the treatment and prevention of uroliths in dogs and cats.

Recommendation 1.1: Struvite uroliths should be medically dissolved
Recommendation 1.2: Urocystoliths associated with clinical signs should be removed by minimally invasive procedures
Recommendation 1.2a Consider medical dissolution of urate uroliths before removal
Recommendation 1.2b Consider medical dissolution of cystine uroliths before removal
Recommendation 1.3: Nonclinical urocystoliths unlikely to cause urinary obstruction do not require removal
Recommendation 1.4: Nonclinical urocystoliths likely to cause urinary obstruction should be removed by minimally invasive procedures
Recommendation 1.5: Urethroliths should be managed by intracorporeal lithotripsy and basket retrieval
Recommendation 1.6: Urethral surgery to manage urolithiasis is discouraged
Recommendation 2.1: Only problematic nephroliths require treatment
Recommendation 2.2: Struvite nephroliths should be medically dissolved
Recommendation 2.3: Dissolution should not be attempted in cats with obstructive upper urinary tract uroliths
Recommendation 2.4: Problematic nephroliths should be removed by minimally invasive procedures
Recommendation 2.5: Hydronephrosis and hydroureter proximal to an obstructive lesion are sufficient to diagnose ureteral obstruction
Recommendation 2.6: Ureteral obstructions require immediate care
Recommendation 2.7: Medical treatment for obstructive ureterolithiasis is rarely effective, consider minimally invasive removal
Recommendation 2.8: Obstructive ureteroliths in cats should be managed by subcutaneous ureteral bypass or ureteral stenting
Recommendation 2.9: Obstructive ureteroliths in dogs should be managed by ureteral stenting
Recommendation 2.10: Ureterolith composition will affect management decisions
Recommendation 2.11: Routinely culture urine of dogs with ureteral obstruction and consider antimicrobial treatment
Recommendation 3.1: Prevent sterile struvite uroliths by feeding therapeutic maintenance foods with low magnesium and phosphorus that acidify urine
Recommendation 3.2: Primary prevention of infection-induced struvite uroliths is persistent elimination of urinary tract infection
Recommendation 3.3: To minimize calcium oxalate urolith recurrence, decrease urine concentration, avoid urine acidification, and avoid diets with excessive protein content
Recommendation 3.3a: Feeding high-sodium dry foods should not be recommended as a substitute for high-moisture foods
Recommendation 3.3b: Consider potassium citrate or other alkalinizing citrate salts for dogs and cats with persistently acidic urine
Recommendation 3.3c: Consider thiazide diuretics for frequently recurrent calcium oxalate uroliths
Recommendation 3.4: To minimize urate urolith recurrence, decrease urine concentration, promote alkaline urine, and limit purine intake
Recommendation 3.4.A: Consider xanthine oxidase inhibitors for dogs homozygous for genetic hyperuricosuria that have failed therapeutic diet prevention
Recommendation 3.5: To minimize cystine urolith recurrence, decrease urine concentration, limit animal protein intake, limit sodium intake, increase urine pH, and neuter
Recommendation 3.5.A: In recurrent cystine urolith formers, add 2-mercaptopropionylglycine (tiopronin, Thiola) to previously recommended prevention strategies to further lower cystine concentration and increase cystine solubility

been reported in the veterinary literature and is likely to occur with the same frequency or less frequently than when attempts at surgical removal are incomplete.[1–6]

Recommendation 1.2: Urocystoliths Associated with Clinical Signs should be Removed by Minimally Invasive Procedures. Urocystoliths small enough to pass through the urethra should be removed by medical dissolution, voiding urohydropropulsion, basket retrieval, or other extraction procedures that do not involve surgical intervention.

Rationale: Incision-less procedures are associated with shorter hospitalization, shorter anesthesia time, and faster patient recovery. Avoiding cystotomy and closure of the bladder with sutures will eliminate the risk of suture-induced urolith recurrence, which may be a primary causal factor in approximately 9% of recurrent urocystoliths.[7,8]

Urocystoliths too large to pass through the urethra should be removed by medical dissolution, intracorporeal laser lithotripsy, or percutaneous cystolithotomy instead of cystotomy. The committee recognizes that the urethras of small male dogs (eg, Yorkshire terriers, Maltese, Chihuahua) and almost all male cats may be too narrow to accommodate currently available cystoscopes, and the selection of which minimally invasive procedure to perform will depend on urolith type, experience of the operator, availability of equipment, urolith burden, and appropriateness of the patient to undergo a second procedure to completely clear the lower urinary tract of uroliths, if needed.

Rationale: Minimally invasive procedures are associated with shorter hospitalization, and perceived fewer adverse effects, fewer residual stones because of improved visualization, and possibly lower stone recurrence rates compared to surgical cystotomy.[9–13]

Recommendation 1.2a: Consider Medical Dissolution of Urate Uroliths before Removal. Hyperuricosuria, concentrated urine, and acidic urine are the predominant factors driving urate urolith formation. In most dogs and cats, uric acid, an intermediate product of purine metabolism, is transported to the liver where it is further metabolized by intracellular hepatic uricase to allantoin, an innocuous nitrogenous compound with relatively high water solubility. A defective uric acid transporter (ie, SLC2A9 genetic mutation) and hepatic porto-vascular anomalies have been identified as common causes for hyperuricosuria and subsequent urate urolithiasis. However, for some animals, especially cats, the cause for hyperuricosuria and urate urolith formation remains idiopathic. Dissolution may be attempted for urate uroliths unassociated with liver disease unless (1) medications or dissolution foods cannot be administered or tolerated, or (2) the urolith cannot be adequately bathed in modified urine (eg, urinary obstruction, urethroliths).

Rationale: Dissolution of urate uroliths in dogs usually is accomplished within 4 weeks by feeding a purine-restricted, alkalinizing, diuretic diet,[a] and administration of a xanthine oxidase inhibitor (ie, allopurinol: 15 mg/kg PO q12 h).[14,15] In 1 study, medical dissolution was effective in approximately 40% of Dalmatians, partial dissolution occurred in approximately 30%, and no dissolution occurred in approximately 30%.[16] Dissolution has not been possible in dogs and cats with uncorrected liver disease (ie, hepatic porto-vascular shunt). There are no data for the dissolution of urate uroliths in cats.

Recommendation 1.2b: Consider Medical Dissolution of Cystine Uroliths before Removal. Cystine uroliths form, in part, because of the decreased proximal tubular reabsorption of cystine. Dissolution is achieved by increasing cystine solubility and may be attempted in dogs unless (1) medications or dissolution foods cannot be administered or tolerated or (2) the urolith cannot be adequately bathed in modified urine (eg, urinary obstruction, urethroliths).

Rationale: In 1 study performed on cystinuric dogs, the consumption of a decreased protein, urine-alkalinizing, canned food[a] resulted in a 20–25% decrease in 24-hour urine cystine excretion compared with a canned maintenance food.[17] This same food with the addition of 2-mercaptopropionylglycine (Thiola®, tiopronin) at a dosage of 15–20 mg/kg PO q12 h successfully dissolved cystine stones in 18 of 18 episodes.[17] Cystine solubility increases with increasing urine pH.[18] In vitro studies that achieved a urine pH > 7.5 increased the efficacy of thiol-binding drugs to solubilize cystine in the urine from cystinuric humans.[19] Therefore, potassium citrate or other alkalinizing salts should be administered to dogs and cats with persistently acidic urine. The dosage should be gradually increased to achieve a urine pH of approximately 7.5, if possible. Studies showed that the administration of 2-mercaptopropionylglycine without modifying the diet is associated with dissolution.[17,20] Dissolution should be attempted cautiously in cats because of their perceived intolerance of 2-mercaptopropionylglycine.

In some forms of cystinuria, neutering has been associated with the decreases in urine cystine concentration as the result of a potential androgen-dependent effect, but this is not universal.[21] This uncertainty raises the question of whether or not neutering alone will result in urolith dissolution, or whether the combination of neutering and cystotomy is a medically economical approach for intact dogs with cystine uroliths.

Recommendation 1.3: Nonclinical Urocystoliths Unlikely to Cause Urinary Obstruction do not Require Removal. Dogs and cats without clinical signs but with nondissolvable uroliths too large to pass into the urethra or too irregular to cause urethral obstruction need only periodic monitoring and appropriate client education. With the onset of clinical signs (eg, hematuria, dysuria, urinary tract infection [UTI]), urolith removal should be considered. Imaging modalities including ultrasonography and radiology should be performed to assess urolith size and position as well as to predict mineral composition, as needed. Increasing stone size may limit the type of minimally invasive procedure that can be performed for future stone removal.

Rationale: Watchful waiting minimizes unnecessary intervention, especially for urolith types that are highly recurrent (eg, calcium oxalate, cystine, urate).[22] Client education about the clinical signs of urinary obstruction is essential so that clients seek timely and appropriate care in the event of obstruction.

Recommendation 1.4: Nonclinical Urocystoliths Likely to Cause Urinary Obstruction should be Removed by Minimally Invasive Procedures. Animals without clinical signs diagnosed with smooth uroliths that have a high likelihood of urethral obstruction (ie, diameter approximating the diameter of the urethral lumen) should have their uroliths removed or dissolved.

Rationale: Urolith removal is indicated as a precaution in patients that are likely to succumb to life-threatening urinary obstruction so that careful medical intervention can be implemented at the time of diagnosis as opposed to less carefully planned removal on an emergency basis. To minimize patient discomfort and unnecessary damage to healthy tissues, nonsurgical removal methods (eg, dissolution, basket retrieval, lithotripsy, percutaneous cystolithotomy) should be considered.

Recommendation 1.5: Urethroliths should be Managed by Intracorporeal Lithotripsy and Basket Retrieval. Whether causing urethral obstruction or not, urethroliths are quickly and safely managed by intracorporeal lithotripsy and basket retrieval.

Rationale: Intracorporeal lithotripsy was 100% effective in the removal of urethroliths.[23] The median time to complete initial evaluation, urethrolith removal, and postprocedural radiography was 36 minutes in dogs; no dog experienced adverse events. The committee recognizes that the urethra of small male dogs and most male cats may be too narrow to accommodate appropriate cystoscopes to manage urethroliths by minimally invasive procedures. In these situations, urethroliths can be urohydropropulsed retrograde back into the bladder and retrieved by percutaneous cystolithotomy or cystotomy.[24]

Recommendation 1.6: Urethral Surgery to Manage Urolithiasis is Discouraged. Urethrotomy and urethrostomy are salvage procedures that may result in permanent alterations in the anatomy and function of the urethra. Urethroliths should be repositioned (retrograde urohydropropulsion) into the urinary bladder and removed by minimally invasive procedures (eg, fragmented in the urethra by laser lithotripsy) and retrieved (by voiding urohydropropulsion, basket retrieval or percutaneous cystolithotomy if possible). Urethrostomy can be considered to minimize future urethral obstruction in highly recurrent stone-forming animals. Rigid adherence to strategies to prevent urolith recurrence, however, should be considered first.

Rationale: Because of the high frequency of morbidity and adverse effects associated with urethral surgery (eg, stricture, urine leakage, recurrent UTI, hemorrhage), urethral surgeries are discouraged except under few circumstances that go beyond the recommendations of sound medical judgment (eg, client inability to afford additional care with recurrent obstruction, inability for clients to access minimally invasive care, urethral stricture where alternative interventions are not an option).[25–27]

Part 2

Standard of Care for Dogs and Cats with Upper Urinary Tract Uroliths

Recommendation 2.1: only Problematic Nephroliths Require Treatment. Only those nephroliths contributing to outflow obstruction, recurrent infection, pain, and those enlarging to the point of causing renal parenchymal compression, should be considered for removal in dogs and cats. Dissolution only should be considered for nonobstructive nephroliths or if the obstruction can be concomitantly alleviated or bypassed (eg, urethral stenting).

Rationale: The presence of nephroliths in cats with chronic kidney disease did not significantly affect the progression of renal disease, and the same has been observed clinically in dogs.[13,28]

Recommendation 2.2: Struvite Nephroliths should be Medically Dissolved. Nephroliths and ureteroliths consistent with a composition of struvite (ie, moderately radiopaque uroliths in a dog with alkalinuria and a urinary tract infection with urease-producing bacteria (such as *Staphylococcus* spp.) should be medically dissolved. When ureters are obstructed, they should be stented to (1) improve kidney function, (2) allow medicated urine to reach the ureterolith, (3) allow antimicrobial access to eradicate bacteriuria, and (4) allow evacuation of bacteria and inflammatory debris. Treatment for other nephroliths potentially amenable to dissolution (eg, cystine, purine) should be addressed on a case-by-case basis considering the stability of kidney function and the likelihood of complete removal or dissolution.

Rationale: Approximately 20–30% of upper urinary tract uroliths in dogs are suspected to be struvite for which dissolution should be effective. Rapid control of infection while avoiding surgical urolith extraction should maximally preserve kidney function.[b,29] Dissolution requires that uroliths be bathed in appropriately medicated urine that is undersaturated for struvite. Obstructive uroliths are not surrounded by appropriate urine conditions unless a ureteral stent is placed concurrently.[b,30]

Recommendation 2.3: Dissolution Should not be Attempted in Cats with Obstructive Upper Urinary Tract Uroliths. *Rationale:* Over 90% of nephroliths and ureteroliths in cats are composed primarily of calcium oxalate. Calcium oxalate uroliths are not amenable to medical dissolution. Delaying appropriate care may contribute to an irreversible decrease in kidney function.[31–33]

Recommendation 2.4: Problematic Nephroliths should be Removed by Minimally Invasive Procedures. Nephroliths should be removed by (1) dissolution, (2) endoscopic nephrolithotomy (ie, for nephroliths too large for extracorporeal shock wave lithotripsy and for nephroliths in

cats), and (3) extracorporeal shockwave lithotripsy (for nephroliths in dogs only).[c]

Rationale: Minimally invasive urolith removal is less likely to adversely affect glomerular filtration rate. Extracorporeal shockwave lithotripsy has minimal effects on renal function, but is reserved for nephroliths ≤1.5 cm in diameter. Nephroliths >1–1.5 cm often require concurrent ureteral stent placement.[34,35] In human medicine, endoscopic nephrolithotomy is the most effective minimally invasive treatment option for large stone burdens and has the highest stone-free rate when compared to alternative therapies.[35] Endoscopic nephrolithotomy has been successfully performed in dogs and cats.[36]

Recommendation 2.5: Hydronephrosis and Hydroureter Proximal to an Obstructive Lesion are Sufficient to Diagnose Ureteral Obstruction. A diagnosis of a ureteral obstruction should be based on ultrasonographic findings of hydronephrosis and associated hydroureter proximal to an obstructive ureterolith regardless of the degree of the renal pelvic dilatation. If renal pelvic dilatation is <5 mm, careful imaging is needed to confirm obstruction unless it is associated with concurrent hydroureter proximal to an obstructive urolith. If no obstructive lesion is seen on ultrasound examination, abdominal radiography should be performed concurrently to evaluate for the presence of nephroureteroliths. If ureteroliths are not visualized, a ureteral obstruction is not necessarily excluded, because ureteral strictures are common (>25% of cats).

Antegrade contrast pyelography is not necessary for the diagnosis of ureteral obstruction if an obstructive ureterolith is seen at the distal termination of hydroureter. Likewise, advanced imaging studies such as computerized tomography and intravenous pyelography in patients with suspected ureteral obstruction do not typically provide more clinical information than that obtained from the combination of ultrasound examination and survey radiographs.

Rationale: In a study evaluating the causes of hydronephrosis, all renal pelves >13 mm were associated with ureteral obstruction and those >7 mm were likely associated with ureteral obstruction. Many <7 mm also were associated with ureteral obstruction. The cause of ureteral obstruction was not documented by ultrasonography alone in up to 25% of cats, which necessitated concurrent radiographic imaging and ureteropyelography.[33,37]

Recommendation 2.6: Ureteral Obstructions Require Immediate Care. Partial and complete ureteral obstructions should be managed as an emergency regardless of whether the obstruction is partial or complete. Decompression (eg, subcutaneous ureteral bypass, ureteral stent, traditional surgery) should be recommended when medical management fails or is contraindicated based on the severity of the patient's illness. Treatment only should be performed by those trained in the particular intervention to be used, and less invasive procedures should be recommended whenever possible.

Rationale: Experimental ureteral occlusion in healthy dogs is associated with a rapid and lasting decrease in renal function. A 35% permanent decease in glomerular filtration rate was noted after 7 days, 54% after 14 days and 100% after 40 days, but some studies support a return to normal function after 150 days.[38–41] Evidence-based data over the past 6 years support that interventional procedures, such as ureteral stents and subcutaneous ureteral bypass, have a lower morbidity and mortality rate for ureteral obstruction than do traditional surgical options in both dogs and cats, respectively.[b,30,33,42–47] Referral should be considered whenever possible for each patient if minimally invasive options cannot be performed locally. In animal models, renal function was maximized by relieving the obstruction of any functional kidney after it was partially obstructed for >8 weeks.[48,49] Over 80–90% of ureteral obstructions in cats are considered partial based on antegrade ureteropyelography.[33]

Data currently are not available to determine the amount of renal function that may return after the repair of complete or partial ureteral obstruction. Therefore, intervention to repair all obstructions appears justified at this time. Differential glomerular filtration rate studies in kidneys with ureteral obstruction are considered unreliable and should not preclude decompression. In cats, no imaging prognostic factors (eg, renal pelvis size, amount of renal parenchyma determined with ultrasound, renal tissue Doppler) have been found to predict the extent of renal recovery after decompression; the majority of kidneys seem to recover well.[43]

Recommendation 2.7: Medical Treatment for Obstructive Ureterolithiasis is Rarely Effective, Consider Minimally Invasive Removal. Medical management of stable obstructive ureterolithiasis can be considered for 24–72 hours. However, clients should be informed of the high rate of medical failure. Medical treatment should include fluid diuresis and mannitol continuous rate infusion treatment, if tolerated. Alpha adrenergic antagonists and tricyclic antidepressants also have been used with anecdotal reports of improvement in some cases and can be considered if not contraindicated. Medical treatment should not be continued in animals that are persistently oliguric or anuric, hyperkalemic, have progressive azotemia and progressive renal pelvic dilatation; minimally invasive urolith extraction or bypass is needed. Fluid treatment should be closely monitored to prevent overhydration. In dogs, in addition to propulsive treatment for uroliths, broad-spectrum antimicrobials IV (ideally for at least 24 hours before intervention) should be administered.

Ureterolith-induced ureteral obstructions should be monitored rather than decompressed when renal pelvic dilatation is ≤3–5 mm, and renal function is stable. Intervention only should be considered when an experienced operator is available.

Rationale: Medical management for the treatment of cats with ureteral obstructions is only reported to be effective in 8–13% of cases.[31] Because over 25% of ureteral obstructions in cats are associated with

concurrent ureteral strictures, success of medical management often is limited.[33] In dogs, 59% of all ureteral obstructions, and 85% of those with pyonephrosis, had evidence of UTI at the time of diagnosis, supporting the administration of antimicrobials.[b,30]

Higher complication rates are seen with less experienced operators. This may affect timing of surgical intervention, and waiting for a more experienced operator is ideal for the best possible outcome.

Recommendation 2.8: Obstructive Ureteroliths in Cats should be Managed by Subcutaneous Ureteral Bypass or Ureteral Stenting. Subcutaneous ureteral bypass or ureteral stenting for ureteral obstructions in cats should be considered the first choice for the best possible outcome. We emphasize that fluoroscopic imaging, proper training, and an experienced operator are needed to optimize the patient outcomes.

Recommendation 2.9: Obstructive Ureteroliths in Dogs should be Managed by Ureteral Stenting. Ureteral stents are the treatment of choice for ureterolith-induced ureteral obstructions in dogs if performed by a trained operator. This approach may be combined with subsequent extracorporeal shockwave lithotripsy if necessary.[13] Interventional options such as ureteral stent placement, extracorporeal shockwave lithotripsy, or both for the treatment of ureteral obstructions in dogs always should be considered and offered to clients.

Rationale: Ureteral stents are associated with the lowest short- and long-term morbidity and mortality rates when compared to all other reported treatment options.[b,30]

The morbidity and mortality rates (<2%) for ureteral stenting in dogs are lower than those reported for traditional surgery. A lower reobstruction rate (9%) and improvement in the severity of azotemia also have been reported after stent placement.[b,30] Extracorporeal shockwave lithotripsy has a low mortality rate (<2%), but requires retreatment in 15–50% of dogs. The placement of a concurrent ureteral stent for ureteral obstruction in dogs undergoing extracorporeal shockwave lithotripsy typically is recommended for dogs with ureteroliths and larger nephroliths.[13]

Recommendation 2.10: Ureterolith Composition will Affect Management Decisions. Careful assessment of urinalysis (eg, crystals, urine pH), urine culture results, radiographic appearance, and when possible, quantitative urolith analysis should always be performed. In dogs, suspected struvite ureteroliths should be stented and then dissolved as discussed in the lower urinary tract urolith section. Suspected obstructed calcium oxalate ureteroliths should be either stented for long-term treatment or stented with concurrent or subsequent extracorporeal shockwave lithotripsy, if necessary. Cystine and urate ureteroliths should be treated by a ureteral stent and concurrent medical and dietary treatment.

Rationale: Ureteral stents in dogs often can be placed endoscopically. This procedure can relieve an emergency situation both effectively and safely. Forty-four dogs that underwent ureteral stent placement had their stents in place for up to 1158 days, suggesting that long-term stent placement is possible.[b] Owners should be aware of the primarily reobstruction risks that are most often associated with concurrent ureteral stricture. If necessary, a ureteral stent exchange can be performed on an outpatient basis, but is not required for most dogs. Knowing the urolith composition will help by employing appropriate medical and dietary treatment to prevent stent encrustation and future urolith formation. If stenting fails, other options such as extracorporeal shock wave lithotripsy and subcutaneous ureteral bypass device placement, or traditional surgery, can be considered.

Recommendation 2.11: Routinely Culture Urine of Dogs with Ureteral Obstruction and Consider Antimicrobial treatment. Dogs with ureteral obstruction should have their urine cultured and should be given antimicrobial treatment at the time of diagnosis because of the high incidence of concurrent UTI and pyonephrosis.

Rationale: Fifty-nine percent of 44 dogs with ureteral obstructions had positive urine culture results at the time of diagnosis; 30% had a diagnosis of pyonephrosis and associated sepsis.[b]

Part 3

Urolith Prevention

Removal or bypass of uroliths will not alter the underlying conditions responsible for their formation. Therefore, it is logical to assume that additional therapeutic strategies are needed to prevent urolith recurrence. The most effective prevention strategies are those that eliminate the underlying cause. For cases in which a cause remains elusive or cannot be altered, minimizing pathophysiologic risk factors associated with formation should be considered.

Nutritional treatment remains a subject of much clinical interest and debate in the management of urolithiasis because of epidemiological and pathophysiological data associating nutrient intake with urine saturation and potential lithogenicity. For some urolith types, nutritional prevention plays a primary role (eg, sterile struvite uroliths), and for other urolith types, nutritional treatment plays a minor role (eg, infection-induced struvite and infection-induced calcium phosphate carbonate uroliths). For all mineral types (except infection-induced struvite), feeding diets high in moisture is one of the cornerstones of urolith prevention strategies.

Recommendation 3.1: Prevent Sterile Struvite Uroliths by Feeding Therapeutic Maintenance Foods with Low Magnesium and Phosphorus that Acidify Urine. Successful prevention of struvite uroliths is dependent on classifying them as sterile or infection-induced. To make this distinction, aerobic bacterial urine or urolith culture should be performed before antimicrobial treatment. Sterile struvite uroliths, which most often occur in cats, are best prevented by feeding therapeutic maintenance foods with low magnesium and phosphorus that acidify the urine.

Rationale: Struvite solubility is greatly increased by decreasing urolith precursors and acidifying the urine (pH <6.5).[2,4,50,51]

Recommendation 3.2: Primary Prevention of Infection-Induced Struvite Uroliths is Persistent Elimination of Urinary Tract Infection. Primary treatment for preventing infection-induced struvite uroliths, which is the most common struvite urolith in dogs, is early identification and elimination of UTI. Urine sediment evaluation and pH monitoring are not suitable diagnostic substitutes for aerobic bacterial urine cultures. Second tier treatment to manage infection-induced struvite uroliths includes therapeutic maintenance foods with low magnesium and phosphorus that acidify the urine.

Rationale: Urinary tract infection with urease-producing microorganisms is essential for the formation of infection-induced struvite uroliths. Eliminating these infections will prevent recurrence of infection-induced struvite uroliths. Therefore, structural and functional risk factors for UTI should be diagnosed and eliminated, and recurrent infection should be monitored in urine. Routine urinalysis is an insensitive marker for UTI.[52,53] Urine should be cultured monthly for 2–3 months and then as clinically indicated based on clinical signs and patient risk factors. Foods marketed to treat struvite urolithiasis will not prevent their recurrence but may delay or minimize, urolith burden in the presence of unrecognized UTI.

Recommendation 3.3: To Minimize Calcium Oxalate Urolith Recurrence, Decrease Urine Concentration, Avoid Urine Acidification, and Avoid Diets with Excessive Protein Content. Calcium oxalate urolithiasis in dogs and cats appears to be driven primarily by hypercalciuria in association with either hypercalcemia (eg, primary hyperparathyroidism, idiopathic hypercalcemia in cats) or normocalcemia.[54] Intrinsic risk factors should be evaluated in all patients that have been diagnosed with calcium oxalate uroliths (eg, evaluate serum ionized and total calcium concentrations, parathyroid hormone), and further diagnostic testing should be pursued if clinically indicated.

Selection of effective preventative treatment is challenging because (1) properly designed clinical trials evaluating urolith recurrence have not been published, (2) the exact mechanisms underlying calcium oxalate urolith formation are not completely understood, (3) associative factors identified in epidemiological studies have not been proven to result in disease, and (4) surrogate endpoints of therapeutic efficacy such as relative supersaturation are mathematical models that may not correlate well with calcium oxalate urolith formation.

Rationale: The high recurrence rate of calcium oxalate uroliths warrants a comprehensive approach and regular monitoring. High-moisture (>75% water) foods should be recommended. Alternatively, sufficient water can be added to dry kibble to increase moisture intake. Strive to achieve a urine specific gravity $\leq$1.020 in dogs and <1.030 in cats; additional water consumption to achieve lower urine concentrations of calcium oxalate theoretically provides more effective prevention. Short-term studies (ie, 12–19 days) in clinically normal dogs and cats indicated that foods containing high quantities of water (ie, 73% moisture) significantly decreased the relative supersaturation from 13 to 8 in dogs and from 2.3 to 1.1 in cats for calcium oxalate.[55–57]

Diets and medications designed to promote urine acidification (pH < 6.5) should be avoided. Diets that promote the formation of acidic urine in dogs (pH < 6.6) and cats (pH < 6.25) were associated with calcium oxalate urolith formation.[58–61] In a study of normal cats, calcium oxalate relative supersaturation linearly decreased with increasing urinary pH.[51]

Ingestion of foods that contain high quantities of animal protein (>10 g/100 kcal) contributes to calcium oxalate uroliths by increasing urine calcium excretion and decreasing urine citrate excretion. Increasing dietary protein from 35% to 57% (dry matter) increased urine calcium concentration by 35% and decreased urine citrate concentration by 45% in cats.[62]

In dogs and cats with hypercalcemia, correcting or controlling hypercalcemia aids in preventing calcium oxalate urolith recurrence. Doing so is difficult in cats with idiopathic hypercalcemia and no single treatment has been shown to be effective, including glucocorticoids, bisphosphonate administration, or dietary modification using a high-fiber diet with potassium citrate administration, but 5 cats with idiopathic hypercalcemia had normalization of blood calcium concentrations when treated with a high-fiber diet.[63]

Recommendation 3.3a: Feeding High-Sodium (>375 mg/100 kcal) Dry Foods should not be a Recommended as a Substitute for High-Moisture Foods. *Rationale:* High-sodium foods increase urinary water excretion, but the effects appear to be short-lived (ie, 3–6 months).[64–66] Although the extent of water intake and urine dilution achieved with increased dietary salt might not be similar to that observed with high-moisture foods, it can be considered in dogs and cats in which owners decline to feed high-moisture foods.

Recommendation 3.3b: Consider Potassium Citrate or Other Alkalinizing Citrate Salts for Dogs and Cats with Persistently Acidic Urine. Potassium citrate is an alkalinizing salt that when administered PO and metabolized promotes the excretion of more beneficial alkaline urine. Alkaline urine also enhances urinary citrate excretion, and citrate is a chelator of calcium ions.

Rationale: Oral administration of granular potassium citrate (150 mg/kg/d) was associated with variable increased urinary citrate concentration (3 ± 9 mmol/L) compared to a noncitrate control (0.1 ± 0.06 mmol/L).[67] This result may have occurred because the optimal dose of citrate has yet to be determined. In a summary of 5 studies with 283 human calcium oxalate stone formers, 97 (34%) reformed stones or had residual stones grow; this outcome occurred in 15% of patients receiving citrate salts compared to 52% of those not receiving citrate.[68] One in vitro study demonstrated that citrate, at a concentration similar to that achieved in urine (5 mmol/L), significantly dissolved and detached calcium oxalate monohydrate crystals from Madin-Darby canine kidney cells.[69]

Recommendation 3.3c: Consider Thiazide Diuretics for Frequently Recurrent Calcium Oxalate Uroliths. Thiazide diuretics enhance the renal tubular reabsorption

of filtered calcium. They also may indirectly affect intestinal calcium absorption and bone calcium deposition. Some recommend the concomitant administration of potassium citrate because thiazide diuretics contribute to urine acidification. We recommend monitoring urine pH first to assess whether or not potassium citrate is needed.

Rationale: A 55% decrease in urinary calcium concentration was reported in urolith-forming dogs that were treated with hydrochlorothiazide at a dosage of 2 mg/kg q12h.[70] A 65% decrease in urinary calcium oxalate relative supersaturation was reported in clinically normal cats receiving hydrochlorothiazide at a dosage of 1 mg/kg q12h.[71]

Recommendation 3.4: to Minimize Urate Urolith Recurrence, Decrease Urine Concentration, Promote Alkaline Urine, and Limit Purine Intake. Hyperuricosuria, concentrated urine, and acidic urine are the predominant factors driving urate urolith formation. In most dogs and cats, uric acid, an intermediate product of purine metabolism, is transported to the liver where it is further metabolized by intracellular hepatic uricase to allantoin, an innocuous nitrogenous compound with relatively high water solubility. Defective uric acid transporters (ie, SLC2A9 genetic mutation) and hepatic porto-vascular anomalies have been identified as common causes for hyperuricosuria and subsequent urate urolithiasis. However, in some animals, particularly cats, the causes for hyperuricosuria and urate urolith formation remain idiopathic.

For dogs with the SLC2A9 mutation (eg, Dalmatians, Bulldogs), urate urolith recurrence can be minimized by increasing fluid intake, promoting alkaline urine (pH $\geq$ 7), and limiting purine intake. In cats and dogs with porto-vascular anomalies (eg, Yorkshire terrier, Pug), correcting of the vascular anomaly should also be considered, if appropriate. Data in cats are limited, but purine restriction and urine alkalization are recommended and found to be effective.

Rationale: The high recurrence rate of urate uroliths warrants a comprehensive approach.[72] High-moisture (>75% moisture) foods should be recommended. Alternatively, sufficient water can be added to dry kibble to increase the moisture intake. Strive to achieve a urine specific gravity $\leq$1.020 in dogs and <1.030 in cats. Additional water consumption to achieve lower urine concentrations of uric acid provides more effective prevention.

Urate solubility increases with increasing urine pH. Although the solubility of ammonium urate is thought to plateau at pH $\geq$ 7.2, in vitro dissolution occurred a high rate at pH $\geq$ 8.0.[73]

Dietary purines are precursors of urate and found in virtually all foods. High-purine foods often are synonymous with high-protein foods, especially those containing organ meats and fish. Therefore, foods to prevent urate uroliths often are lower in protein. Decreasing dietary protein has been shown to decrease urinary saturation with ammonium urate in healthy dogs.[74] Higher-protein and lower-purine foods for dogs have also recently been marketed. Selecting an effective food may be difficult because properly controlled studies evaluating urolith recurrence are rare. In 1 study utilizing a crossover design, 6 client-owned, urolith-forming Dalmatians were evaluated monthly for urolith recurrence by double-contrast cystography.[d] After 6 months, 50% of dogs consuming the low-purine and low-protein prevention food[a] developed recurrent uroliths, whereas 87% developed recurrent uroliths while eating the maintenance diet (all recurrent stones were <2 mm in diameter and dogs did not have clinical signs). Preliminary results in 6 urate urolith-forming Dalmatians fed a higher-protein and low-purine dry diet[e] formulated with vegetable protein and eggs with additional water added to the food before feeding resulted in similar urinary purine excretion compared to lower-protein diets.[75] In the later study, dogs had bladder stones at the time of study entry and their urolith mass at 2 months appeared unchanged. Anecdotally, clinicians also have suggested vegetarian-based diets for purine urolith management. No published data exist as to the efficacy of this dietary management strategy.

Recommendation 3.4.a: Consider Xanthine Oxidase Inhibitors for Dogs Homozygous for Genetic Hyperuricosuria that have Failed Therapeutic Diet Prevention. *Rationale:* Urate urolith recurrence is common, especially in dogs with a genetic mutation in the urate transporter. Prevention may require more than dietary adjustments. The dosage of allopurinol to sufficiently prevent urate urolith recurrence without xanthine urolith formation is variable and influenced by the severity of disease, endogenous purine production, quantity of purines in the diet, urine pH, and urine volume. In a case series of 10 dogs with previous urate urolithiasis, allopurinol administration in excess of 9–38 mg/kg/d was associated with xanthine urolith formation.[76] This occurs because allopurinol inhibits the metabolism of xanthine to uric acid and because xanthine is less soluble in urine than is uric acid. Based on these observations, we recommend a dosage of 5–7 mg/kg q12–24 h to safely prevent urate uroliths.[14] The role and effectiveness of allopurinol and newer-generation xanthine oxidase inhibitors in patients with porto-vascular shunts are unknown.[77] Administration of xanthine oxidase inhibitors should be avoided in dogs that are not receiving decreased purine diets to minimize the risk of xanthine urolith formation. Xanthine oxidase inhibitors have not been formally investigated in cats.

Recommendation 3.5: To Minimize Cystine Urolith Recurrence, Decrease Urine Concentration, Limit Animal Protein Intake, Limit Sodium Intake, Increase Urine PH, and Neuter. Cystinuria is a rare genetic disease that is characterized pathophysiologically by the failure of renal tubular reabsorption of cystine (a poorly soluble amino acid) and phenotypically by highly recurrent cystine urolith formation. Newer classification systems for cystinuria have been published recently.[21] Few controlled studies have evaluated the prevention strategies. Lack of clinical information necessitates that therapeutic regimens be monitored frequently and individually adjusted to improve therapeutic efficacy and avoid adverse events.

Rationale: The relative insolubility of cystine in urine and the high recurrence rate warrant a comprehensive approach for urolith prevention. High-moisture (>75% moisture) foods should be recommended. Alternatively, sufficient water can be added to dry kibble to increase moisture intake. Strive to achieve a urine specific gravity ≤1.020 in dogs and <1.030 in cats; additional water consumption to achieve lower specific gravities and subsequently lower urine concentrations of cystine potentially improves prevention.

Cystine solubility increases with increasing urine pH.[18] In vitro studies that achieved a urine pH > 7.5 increased the efficacy of thiol drugs to solubilize cystine in the urine of cystinuric humans.[19] Therefore, potassium citrate or other alkalinizing citrate salts should be administered to dogs and cats with persistently acidic urine. The dosage should be gradually increased to achieve a urine pH of approximately 7.5.

Dietary methionine is a sulfur-containing amino acid that is precursor of cystine, another sulfur-containing amino acid. Methionine is common in many animal-derived nutrients and some plant-derived nutrients (eg, nuts, tofu, wheat). Diets for the prevention of cystine uroliths should be low in methionine and cystine precursors with adequate amounts of taurine and carnitine. Selecting an effective commercially prepared food may be difficult because controlled studies evaluating stone recurrence have not been reported. Feeding high-protein diets, particularly those rich in methionine, a cystine precursor, should be avoided in cystinuric dogs. However, the degree of protein restriction that is needed is controversial because protein quality and quantity may affect carnitine content. Carnitine deficiency and associated dilated cardiomyopathy were reported in 5 cystinuric dogs fed low-protein diets.[78] In 1 study performed on cystinuric dogs, the consumption of a decreased protein, urine-alkalinizing, canned food[a] resulted in a 20–25% decrease in 24-hour urine cystine excretion compared with a canned maintenance diet.[17] Canned foods of primarily plant origin also may be helpful in the management of cystine uroliths, but studies documenting the effects on urinary cysteine excretion, urolith prevention, or urolith dissolution are lacking.

In some forms of cystinuria, neutering has been associated with decreases in cystine concentration because of a suspected androgen-dependent effect, but this effect is not universal.[21] Nonetheless, neutering also would prevent unintentional genetic transmission of disease. The effect of neutering on urine cystine concentration in cats has not been investigated.

Recommendation 3.5.A: In Recurrent Cystine Urolith Formers, Add 2-Mercaptopropionylglycine (Tiopronin, Thiola) to Previously Recommended Prevention Strategies to Further Lower Cystine Concentration and Increase Cystine Solubility. *Rationale:* Thiol-binding drugs have been associated with adverse events (eg, fever, anemia, lymphadenopathy). Therefore, they are reserved for patients with more severe disease (nephrolithiasis) or for those with recurrent disease that is not adequately controlled by suitable nutritional and neutering strategies. Thiol-binding medications work by reducing cystine to 2 cysteine molecules. The thiol-cysteine product is 50 times more soluble than cystine. Urine alkalization potentiates the effect of thiol-binding medications.[19] Tiopronin is reported to have fewer adverse effects than d-penicillamine. Tiopronin dosages associated with prevention are 15 mg/kg PO q12h. Because 2-mercaptopropionylglycine sources are limited, compounding pharmacies have provided this medication for dogs. New compounds disrupting cystine crystal growth (L-cystine methyl esters) have been proposed.[77] Studies in dogs and cats with cystinuria are needed to insure that the efficacy and safety (eg, Fanconi syndrome, kidney failure) profile of these esters is better than that of the current thiol-binding drugs before their recommended use.

Footnotes

[a] Prescription Diet Canine u/d; Hills' Pet Products, Topeka, KS
[b] Pavia P, Berent A, Weisse C, et al. Canine Ureteral Stenting for benign ureteral obstruction in dogs. Abstract ACVS, 2014, San Diego, CA
[c] Berent A, Weisse C, Bagley D et al. Endoscopic nephrolithotomy for treatment of complicated nephrolithiasis in dogs and cats [abstract] ACVS, San Antonio TX, 2013
[d] Lulich J (abstract), Osborne C, Bartges J, Allen T, et al.: Effects of diets on urate urolith recurrence in Dalmatians. Journal of Veterinary Internal Medicine 1997; 11: 129
[e] Royal Canin Veterinary Diet Urinary U/C Low Purine Dry Dog Food

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Joseph Bartges serves as associate editor for the Journal of Veterinary Internal Medicine. He was not involved in review of this manuscript.

Larry Adams served as paid consultant related to the consensus statement topic for Hill's Pet Nutrition and sponsorship for continuing education lectures, sponsorship by Royal Canin for continuing education lectures, and sponsorship by Infiniti Medical for continuing education lectures. He conducted paid research for Akina 2010 through 2013, a research project for the development of new ureteral stents.

Carl Osborne in 2016 served as a book section editor of urinary system chapters for "The 5 Minute Veterinary Consult: Canine and Feline" by Larry P. Tilley and Francis W. K. Smith, Jr. He participated in multicenter studies evaluating the role of nutrition in the dissolution and prevention of struvite and calcium oxalate uroliths in cats.

Off-label Antimicrobial Declaration: The authors declare no off-label use of antimicrobials.

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