**Obstructed Path**

Urolithiasis is a general term referring to the presence of a stone anywhere in the urinary tract. It can be modified to indicate the location of the stone: nephrolith = kidney stone, ureterolith = stone within ureter, cystolith or cystic calculus = bladder stone, urethrolith = stone within urethra. Urolithiasis is a syndrome with multiple underlying etiologies.

**Pathogenesis of Stone Formation**

The initial step in stone formation is the precipitation of microcrystals in urine, which contains various salts, minerals, and other solutes. Normally, inhibitory mechanisms help prevent crystals, including undersaturation of solutes, inhibitory substances within urine, and lack of scaffolding matrix for precipitation.

Once microcrystals form, they can link together and increase in size to form macrocrystals and, eventually, a stone. Foreign material can serve as an excellent scaffold for crystal precipitation and subsequent stone formation. Absorbable suture (typically placed in the bladder wall following cystotomy) has been documented to play a causative role in the pathogenesis of some cystic calculi. Similarly, once a stone is formed it can become a scaffold for deposition of a different type of crystal. This typically results in a compound stone, in which the shell is made of a different substance than the nidus (FIGURE 1).

**History and Clinical Signs of Urolithiasis**

Clinical signs of cystic calculi may include hematuria, pollakiuria, stranguria, and dysuria, but these signs are also common with other diseases of the lower urinary tract. Small uroliths can cause partial or complete obstruction of the path.

**Managing Urolithiasis in Dogs**

*JD Foster, VMD, DACVIM*

Friendship Hospital for Animals, Washington, DC

*FIGURE 1. An example of a compound urolith. The calcium oxalate (CaOx) nidus serves as a scaffold for a bacterial urinary tract infection, leading to the deposition of struvite. The shell is also made of CaOx.*
Urinary obstruction of the urethra, leading to bladder distention, abdominal pain, paradoxical incontinence, stranguria, and signs of postrenal azotemia. Rarely, the bladder ruptures, resulting in uroabdomen.

Clinical signs of upper urolithiasis are different; they may be intermittent, or the patient may be asymptomatic. Microscopic or macroscopic hematuria may be present. Signs associated with ureteral calculi are usually caused by renal dysfunction from concurrent pyelonephritis or obstructive uropathy (postrenal azotemia). Abdominal pain may be present but does not seem to be common.3

Cystic calculi may be palpated during physical examination in some small patients. Rectal examination may allow for identification of uroliths within the bladder or pelvic urethra. Renomegaly or renal pain may be present with ureteral obstruction.

**DIAGNOSTIC TESTS**

The minimum database for patients presenting with lower urinary tract signs includes a complete blood count, serum biochemistry panel, urinalysis with culture, and diagnostic imaging. The major differentials for a dog with stranguria and pollakiuria are bacterial cystitis, urolithiasis, and neoplasia.

Urinalysis may allow for identification of crystals and infection as well as documentation of the pH and urine specific gravity (USG). Urine should be analyzed within 1 hour of collection to minimize temperature- and time-dependent changes in sediment. Refrigeration and prolonged storage time both may cause crystal precipitation that would not be observed in fresh, room-temperature urine.4 However, even in fresh urine, crystalluria is clinically insignificant (BOX 1).

Not all uroliths are radiopaque; therefore, it is recommended that diagnostic imaging consist of abdominal radiography (to include the urethra) and urinary ultrasonography. Radiographs may help provide some insight into stone type; however, there is significant overlap between types of stones.5 Ultrasonography can identify radiolucent stones such as urate, xanthine, and small cystine stones. Ultrasonography typically overestimates the size of a...

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**BOX 1 Crystalluria Is Not a Disease**

Crystalluria is not a disease and does not necessarily indicate the animal is at risk for urolithiasis. Treatment is not required unless a urolith or urethral plug is present or has previously formed. Some crystal types, such as cystine, xanthine, and urate, may suggest metabolic abnormalities and warrant further investigation even in the absence of uroliths. Struvite crystals may suggest the presence of urinary tract infection if bacteriuria and pyuria are concurrently observed.

**Key Points**

- Crystalluria is not a disease and does not necessarily indicate the animal is at risk for urolithiasis.
- Increased water intake is likely the most important factor to help prevent recurrence of calcium oxalate stones.
- Failure of uroliths to dissolve is common when urine targets are not met.
- For struvite stones, antibiotics should be administered throughout the entire dissolution period because live bacteria will be released as the stones dissolve.

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**FIGURE 2.** Canine cystoliths: (A) Struvite cystoliths; (B) calcium oxalate cystoliths.
stone by 68%, whereas radiographs are more accurate in helping predict stone size.6 Struvite stones are less radiopaque than calcium oxalate (CaOx) and tend to be larger, whereas CaOx typically accumulates as many small, irregular stones (FIGURE 2).

TYPES OF STONES
Calcium Oxalate

Risk Factors
The exact mechanism of CaOx stone formation is unknown and is likely a combination of genetic, dietary, and environmental factors. Systemic hypercalcemia can predispose animals to CaOx stones, as CaOx stones are commonly accompanied by hypercalciuria. Oxalate metabolism has also been proposed to be responsible; hyperoxaluria can occur from increased dietary intake or a loss of oxalate-degrading bacteria (Oxalobacter formigenes) in the colon.

Magnesium, phosphate, and citrate are inhibitors of CaOx stone formation; decreased urine concentrations of these substances may lead to CaOx precipitation. Most dogs that form CaOx stones have urine calcium and oxalate concentrations similar to those of healthy dogs, suggesting other risk factors exist for CaOx precipitation.7 Male dogs and toy and small-breed dogs are at increased risk for forming CaOx stones.8

Treatment
CaOx stones are not amenable to medical dissolution; however, their recurrence may be somewhat prevented with appropriate therapy. Increased water intake is likely the most important factor to help prevent recurrence. CaOx stones recur in approximately 50% of dogs within 3 years. The solubility of CaOx is not greatly influenced by urine pH, but, because of the potential for acidosis-promoting hypercalciuria, the currently recommended target urine pH is 6.5 to 7. Urine pH greater than 7.5 may promote formation of calcium phosphate uroliths and should be avoided.9

Dietary therapy is very important in the prevention of CaOx stones. Switching to a canned diet or adding water to food increases water intake and dilutes urine. Dilute urine decreases the concentration of calculogenic substances and increases the frequency of urination, helping remove crystals from the bladder. Prescription diets designed to help prevent CaOx stones include Hills c/d (Hills, hillspet.com), Royal Canin SO (Royal Canin, royalcanin.com), and Purina UR St/Ox (Purina, proplanvetdirect.com); however, not all of these diets have been evaluated for their efficacy in preventing stone recurrence.

Medical therapy may be required in patients with stone recurrence despite appropriate dietary intervention. Thiazide diuretics may reduce calcium excretion in dogs with CaOx urolithiasis; therefore, hydrochlorothiazide (2 mg/kg PO q12h) is the drug of choice.10 Potassium citrate is also commonly used to increase urine pH, potentially increasing urine citrate excretion (citrate is an inhibitor of CaOx precipitation). Vitamin C and D supplementation should be avoided, as vitamin C is converted to oxalate and vitamin D may increase gastrointestinal absorption of calcium, increasing urine concentrations of oxalate and calcium. Lactobacillus species have been demonstrated to degrade oxalate in vitro; however, the usefulness of these supplements in preventing CaOx stones has yet to be evaluated in vivo.11

Struvite

Risk Factors
Struvite is composed of magnesium ammonium phosphate (MAP; also known as triple-phosphate). In dogs, struvite stones are almost universally caused by urinary tract infection (UTI) with urease-producing bacteria; hence these stones are commonly called infection stones. Urease-producing bacteria include Staphylococcus, Proteus, Pseudomonas, Klebsiella, Corynebacterium, and Ureaplasma species.

Urease converts urea into ammonia and carbon dioxide (which is metabolized into bicarbonate). The ammonia combines with magnesium and phosphate, forming MAP crystals. Both bicarbonate and ammonia (which scavenges H+ to become ammonium) increase urine pH, which decreases the solubility of struvite crystals. Bacteria may become trapped within layers of the stone, yet remain viable. Thus, as the stone is dissolved, live bacteria may be released. Struvite nephroliths and ureteroliths may cause obstructive pyonephrosis and urosepsis.12

Treatment
Struvite stones are amenable to medical dissolution. Appropriate therapy includes antibiotic therapy and a
calculolytic diet. Abdominal radiographs and urinalysis should be routinely performed during dissolution. Antibiotic therapy should be based on urine culture and susceptibility results. Although some suggest that only a short course of antibiotic therapy may be needed, most experts suggest antibiotics should be administered throughout the entire dissolution period while live bacteria are being released from the stone. Antibiotics are typically continued for 2 to 4 weeks beyond radiographic/ultrasonographic resolution of the stone. Struvite solubility is maximized at a urinary pH less than 6.4.

Several prescription calculolytic diets are available, including Royal Canin SO, Purina St/Ox, and Hill’s c/d and s/d. Not all diets have been evaluated via clinical trials. The average time for dissolution of canine struvite stones is approximately 1 to 3 months. Clinical signs of dysuria typically resolve within 1 to 3 days of starting appropriate antibiotic therapy despite the prolonged time required for stone dissolution.

Purine Stones (Urate and Xanthine)

Risk Factors
Purine stones are made of either ammonium urate or xanthine and typically represent abnormal purine metabolism. Formation of purine stones is promoted by high dietary intake of purines as well as acidic urine, which decreases uric acid solubility. Rarely, urate stones are secondary to UTI caused by urease-producing bacteria, as the hydrolysis of urea increases the urine ammonium concentration.

Dalmatians, bulldogs, and black Russian terriers can have a predisposition for formation of urate stones due to a defect in urate transport. Affected dogs have reduced transport of uric acid into hepatocytes, resulting in accumulation of uric acid in serum. Concurrent decreased renal proximal tubular reabsorption of uric acid results in hyperuricosuria.

Hepatic dysfunction may also result in urate urolithiasis. This is most commonly seen in dogs with portosystemic vascular abnormalities. Hepatic failure leads to hyperammonemia, and subsequently hyperammonuria and hyperuricuria.

Xanthine stones are most common in dogs that are receiving allopurinol therapy for prevention of urate stones. High dietary purine consumption increases the risk in these dogs even further. Cavalier King Charles spaniels and dachshunds have been reported to have xanthine urolithiasis unattributable to allopurinol therapy.

Treatment
Urate stones are amenable to medical dissolution. Dietary modification and medical therapy are the cornerstones of treatment. Calculolytic diets decrease urinary excretion of uric acid and ammonium ions, alkalinize urine, and increase urine volume. To minimize purine content, these diets are significantly protein restricted and contain proteins with low amounts of purine (e.g., egg, dairy). These diets are not suitable for growing, pregnant, and lactating animals; they are also not recommended for Dalmatians. The target urine pH is 7; urine that is too alkaline (pH >7.5) may increase the risk of calcium phosphate stone formation. Only dogs that have formed purine stones should be fed these diets.

Allopurinol, a xanthine oxidase inhibitor, reduces the risk of urate stone formation. This decreases uric acid production but may increase serum concentrations of hypoxanthine and xanthine, increasing the risk of xanthine stone formation. This medication is renally excreted; therefore, the dose must be reduced in patients with decreased renal function (normal dose, 15 mg/kg PO q12h). Allopurinol should not be used in dogs that have developed urate uroliths secondary to portosystemic vascular anomalies.

Xanthine stones forming secondary to allopurinol therapy are likely amenable to medical dissolution; however, stones formed in the absence of allopurinol (primary xanthinuria) are unlikely to be dissolved. Allopurinol should be discontinued in patients receiving it.

A calculolytic diet that promotes urinary alkalinization and contains low amounts of purines should be administered (canned Hill’s u/d is preferred; some prescription renal diets may be acceptable). The target urine pH is greater than 7 and most stones will dissolve within 1 to 2 months.

Cystine

Risk Factors
Cystine is composed of 2 molecules of cysteine, an
amino acid. Cystine has low solubility in urine, where it is typically present in low concentrations. It is freely filtered across the glomerulus and is actively reabsorbed in the proximal tubule. Newfoundlands, Labradors, Australian cattle dogs, and miniature pinschers have genetic mutations causing defective carrier proteins in the tubule, increasing urinary excretion of cystine, ornithine, lysine, and arginine. Genetic tests are available for these mutations. Other breeds have cystinuria dependent on androgen production; neutering these animals may have a profound effect in reducing the degree of cystinuria. Nearly all dogs that form cystine stones are male (98%).

**Treatment**

Cystine stones are amenable to medical dissolution and may be prevented with appropriate dietary and medical therapy. The propensity to form cystine stones diminishes with age, so medications may be discontinued in some older patients. Protein-restricted diets that encourage alkaluria (pH 7 to 8) and a low USG are recommended. Currently, Hill’s u/d is the preferred diet. Food high in methionine (a precursor to cystinuria), such as dairy products, should be avoided.

If diet fails to prevent cystine crystalluria or stones, medical therapy can be implemented. Thiol-containing drugs react with cystine, increasing solubility by replacing one of the cysteine molecules. Tiopronin has been shown to be effective in dissolving uroliths in 60% of dogs (average time between 1 and 3 months) and preventing cystine urolith recurrence in 86% of dogs.

**MEDICAL DISSOLUTION OF UROLITHS**

When possible, uroliths should be medically dissolved rather than surgically removed. An exception is when stones cause nephroureteral obstruction, as the time required for dissolution may result in permanent kidney dysfunction. Minimally invasive procedures, such as ureteral stenting, are recommended over nephrotomy or ureterotomy to relieve obstruction.

Obstructive urethroliths should be retropulsed back into the urinary bladder and dissolution therapy initiated. Recurring obstruction is possible; however, many patients undergo successful dissolution without another episode of obstruction. Patients with multiple obstructive events may benefit from stone removal.

**Dietary dissolution therapy is fundamental for all stone types. Generally, the urine should be dilute (USG <1.025) to encourage dissolution of all stone types.**

Failure of uroliths to dissolve is common when urine targets are not met. Urinalysis should be rechecked 1 month after starting the dissolution diet. If the target pH and USG are not met and appropriate client compliance has been confirmed, the diet may need modification or medications may be required.

- **USG above 1.025:** If the patient is being fed a dry diet, switch to a canned diet. If a canned diet is already being fed, gradually add water to food until target is met. Rarely, subcutaneous fluids may be needed for patients that will not eat a slurry diet.

- **pH above target:** This is uncommon unless dietary compliance is poor, as dissolution diets are acidifying. Treating UTI will normalize urine pH. Methionine or ammonium chloride are rarely needed.

- **pH below target:** Potassium citrate may help alkalinize urine, but the effects are small. Switching to another dissolution diet or oral bicarbonate therapy may be needed.

**MINIMALLY INVASIVE TECHNIQUES FOR UROLITH REMOVAL**

American College of Veterinary Internal Medicine consensus guidelines on the management of urolithiasis suggest that minimally invasive methods for stone removal are preferred over traditional cystotomy. Cystotomy has been shown to result in incomplete stone removal in 20% of dogs. Suture within the urinary bladder may be responsible for 9% of recurrent cystoliths. Minimally invasive methods of stone removal may decrease surgical pain, lower the rate of incomplete stone removal, and decrease risk of suture nidus.
Voiding Urohydropropulsion
Voiding urohydropropulsion (VUH) is a very useful technique for removing small stones from dogs; the size of stone likely able to be removed can be estimated from the urethral width (FIGURE 3).26,27 If a 10 Fr catheter can be passed through the urethra, stones up to ~3 mm are likely able to be voided (3 Fr = 1 mm). The patient should be anesthetized to allow complete muscular relaxation. The bladder is filled with sterile saline via a urethral catheter, the patient positioned vertically to allow stones to fall toward the trigone while the bladder is agitated, the catheter is removed, and the bladder is manually expressed with the patient in the vertical position. Urine is collected and stones are submitted for analysis.

Intracorporeal Lithotripsy
Intracorporeal lithotripsy is performed via a cystoscope.

Mechanical (electrohydraulic) or photothermal (laser) energy is transferred to the stone, resulting in fragmentation. The stone fragments are then removed via VUH or basket retrieval. This technique has been successful in removing 100% of urethroliths and 87% of cystoliths.28,29 In one study, laser lithotripsy resulted in shorter hospitalization but longer procedure time than cystotomy in dogs.30

Extracorporeal Shockwave Lithotripsy
Extracorporeal shockwave lithotripsy is typically reserved for fragmenting uroliths in the kidneys and ureter.31 Patients are anesthetized and positioned so the urolith is within the focal zone of the machine. High-energy shockwaves are generated and focused on the urolith. The resulting fragments are left to pass naturally through the urinary system. Temporary ureteral stenting is often used to decrease the chance of fragments causing obstruction. Few hospitals in the United States offer this therapy; they are listed at asvnu.org.

Transvesicular Percutaneous Cystolithotomy
In transvesicular percutaneous cystolithotomy, the bladder is isolated through a keyhole midline incision and a laparoscopic trocar is inserted. Small stones can be flushed out of the bladder through this trocar, and a cystoscope can be advanced through the trocar for larger stones to be removed via basket retrieval. The cystoscope allows for confirmation of complete stone removal. This procedure is typically performed on an outpatient basis, and the average procedure time is 66 minutes.32 TVP

References


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**JD Foster**

Dr. Foster directs the nephrology, urology, and extracorporeal therapies services at Friendship Hospital for Animals in Washington, DC. He is a past president of the American Society of Veterinary Nephrology and Urology. He has lectured throughout the world on renal and urinary topics and is one of the founding faculty of the Hemodialysis Academy.