### CYSTIC AND URETHRAL CALCULI: BASIC TO ADVANCED THERAPEUTIC OPTIONS. WHY WE DO THE THINGS WE DO.

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Cystic and urethral calculi are a common cause of lower urinary tract signs in dogs and cats. Clinical signs can vary from mild dysuria, pollakiuria, and stranguria, to urethral obstruction. In some cases, cystic and/or urethral calculi are clinically silent.

Multiple types of uroliths can be found in dogs and cats. Struvite (magnesium ammonium phosphate) and calcium oxalate are the most urolith types, comprising 85.3% of all calculi. Calcium phosphate, urate, cystine, xanthine, silica, and mixed composition uroliths comprise the remaining 14.7%, with 6.5% being of mixed composition.

# **Diagnostic Evaluation**

Multiple diagnostic tests are used to diagnose cystic and urethral calculi. Conventional radiographs are excellent for the detection of radiopaque calculi, but urate, cystine, and xanthine stones are typically minimally radiopaque to radiolucent and therefore are often not detected via conventional radiography. Ultrasonography is excellent for the detection of cystic and proximal urethral calculi (including radiolucent calculi), but is a poor technique for the detection of distal urethral calculi. Additionally, ultrasonography will sometimes underestimate the number of calculi as several small calculi can sometimes cast a single shadow. Radiolucent calculi in the mid and distal urethra can be challenging to diagnose, and are best detected via positive contrast radiography or urethroscopy.

In addition to the diagnostic tests recommended to detect uroliths, routine bloodwork (complete blood count, chemistry profile), urinalysis, and urine culture are recommended in patients with lower urinary tract signs. These diagnostic tests can detect alternate or concurrent processes causing lower urinary tract signs, and can also help diagnose a disease process responsible for urolith formation.

# Treatment of Urethral Calculi

In order to prevent urinary obstruction and urethral stricture due to chronic urethritis, urethral calculi should be removed from the urethra once detected. Urolith dissolution is not an appropriate technique for the treatment of urethroliths, as dissolution requires that the stone is bathed in urine on all sides, and requires a significant length of time (median of 3 months) to be effective.

### Catheterization and Retropulsion

In the emergent setting, urethral calculi can be passed from the urethra into the bladder by retropulsion in order to relieve a urethral obstruction. Once they are in the urinary bladder, they can be treated as cystic calculi. First, pass a red rubber urinary catheter of appropriate size in a retrograde fashion until it meets resistance. Compress the proximal urethra by passing a finger per rectum and pressing ventrally. While occluding the urethra, distend the urethra with saline that has been passed from the urethral catheter. This increases the pressure within the urethra beyond that which can be obtained via passage of saline alone. Then, release the digital pressure on the urethra and forcefully instill saline into the urethral catheter in order to flush the urethral stones retrograde into the bladder. Document successful retropulsion of the urethral calculi by repeating abdominal radiographs including the entire perineal urethra (for radiopaque calculi), or by ultrasounding the urinary bladder to confirm the presence of calculi in the bladder that had not been present previously (for radiolucent calculi).

### Cystoscopic-guided Laser Lithotripsy

This option is used for calculi that cannot be retropulsed from the urethra into the urinary bladder. This procedure is appropriate for female dogs with urethral diameter large enough for passage of at least a 1.9 mm cystoscope with sheath (7.8 French), or male dogs large enough for passage of a flexible cystoscope (2.7 mm, 8.1 French). Because the cystoscopes used in female patients are rigid, with a relatively large field of view and excellent image quality, lithotripsy can be performed in female dogs even if there are a several urethral calculi as well as cystic calculi. For male dogs, we only perform retrograde cystoscopic-guided laser lithotripsy if there are very few calculi in the urethra, and no cystic calculi. Otherwise, we perform a percutaneous cystolithotomy (PCCL, see below).

The patient is placed under anesthesia in dorsal recumbency. The cystoscope is passed into the urethra and the urethrolith is visualized. A Holmium:YAG laser fiber is passed through the instrument channel of the cystoscope and placed in contact with the urethrolith. The laser is then activated using a foot pedal and the urolith is fragmented. Once the fragments are small enough to pass through the urethra, they are removed with a nitinol stone basket, which is also passed through the instrument channel of the cystoscope. They may also be retropulsed into the bladder and removed via voiding urohydropulsion.

Thorough removal of calculi is documented with post-procedural conventional radiographs which include the perineal urethra (radiopaque calculi), or a combination of ultrasound and positive contrast urethrography (radiolucent calculi).

### Percutaneous Cystolithotomy (PCCL)

We use this procedure for urethrolith removal in the vast majority of male patients, in small female patients, and in female patients with a large number of cystic calculi in addition to urethroliths. The antegrade approach to the urethra enables access to calculi that could not be accessed via a retrograde approach, because the proximal urethra is significantly larger in diameter than the distal urethra.

The patient is placed under general anesthesia in dorsal recumbency. A 1.5 cm ventral midline incision is made just cranial to the prepuce in males, and caudal to the umbilicus at the apex of the bladder in females. The apex of the urinary bladder is identified and exteriorized, and is held in position using stay sutures. A stab incision is made on the

ventral aspect of the bladder apex and a Ternamian Endotip port is passed through the stab incision. It is helpful to pass a urethral catheter at the start of the procedure, so that saline can be instilled retrograde in order to dislodge fragments that are adherent to the wall, and to flush debris from the urethra if lithotripsy is necessary (see below). A flexible cystoscope is passed through the port and down the urethra in an antegrade fashion. The urolith is identified. A stone basket is passed through the instrument channel of the cystoscope and is used to grasp the stone, then pull it retrograde from urethra through the port. If the stone is lodged in the urethra to the extent that it cannot be removed with the stone basket, then laser lithotripsy is used to fragment the stone. The fragments are then removed via stone basketing. Following complete urethrolith removal, the urinary bladder is assessed using a rigid cystoscope, which is also passed through the Ternamian Endotip port. This provides a better field of view and image quality for complete assessment of the urinary bladder. Any calculi or fragments that are found in the bladder can be removed with a stone basket, passed through the instrument port of the cystoscope.

Thorough removal of calculi is documented with post-procedural conventional radiographs which include the perineal urethra (radiopaque calculi), or a combination of ultrasound and positive contrast urethrography (radiolucent calculi).

# Treatment of Cystic Calculi

### **Urolith Dissolution**

Some stone types (struvite, urate, cystine) can be dissolved using a dissolution protocol. This is an appropriate approach for patients that have cystic but not urethral or ureteral calculi, as cystic calculi are bathed on all sides by urine, and cystic calculi do not result in outflow obstruction unless they are passed into the urethra. Urolith dissolution is minimally invasive, and when successful may be less expensive than urolith removal. Dissolution is often ineffective for calculi of mixed composition. The average time for struvite urolith dissolution is 3 months, whereas the length of treatment necessary for dissolution of urate and cystine calculi is not well documented.

### 1. Struvite Calculi

Struvite calculi are formed in urine of alkaline pH. In dogs, 90% of struvite uroliths are formed due to urinary tract infections involving urease-producing bacteria (e.g. *Staphylococcus spp., Proteus spp.*). Dissolution of these uroliths involves clearance of the infection with appropriate antibiotic therapy (based on urine culture and sensitivity), and ideally diet change to a diet that creates a relatively acidic urine pH (approved diets for this purpose are Royal Canin's Urinary SO diet and Hill's s/d diet). Increasing water intake to create relatively dilute urine (USG <1.020 in dogs, <1.025 in cats) is an important aspect of the dietary management of uroliths.

Note that, because there are typically bacteria embedded within the calculi, which will shed into the urine as the calculi dissolve, antibiotic therapy is necessary for the duration of the dissolution protocol—we typically treat with appropriate antibiotic therapy until 2 weeks after complete stone dissolution is documented. Due to the risk of antimicrobial

resistance, urine cultures are performed frequently (every 2-3 weeks) throughout the duration of the dissolution protocol.

In cats, approximately 50% of struvite uroliths are formed in association with a urinary tract infection. The treatment protocol for the dissolution of feline infection-associated struvite uroliths is identical to the canine protocol. For cats with sterile struvite urolithiasis, there is more reliance upon diet change to one of the aforementioned dissolution diets.

Note that the Hill's s/d diet is not formulated for long term use. Thus, if Hill's s/d is used, the diet should be altered to an appropriate stone prevention diet (e.g. Royal Canin Urinary SO, Hill's c/d multicare) for prevention of stone recurrence.

### 2. Urate Calculi

Urate uroliths are also potentially amenable to dissolution protocols, dependent upon the cause of urolith formation. Urate uroliths that form due to a breed associated genetic defect in the uric acid transporter (e.g. Dalmatians and English Bulldogs) can sometimes be dissolved with a combination of a low purine diet (Hill's u/d diet, Royal Canin Urinary Low Purine diet) and the xanthine oxidase inhibitor allopurinol, used at a higher dose than is used for prevention of stone formation. There are also anecdotal reports of diet change alone resulting in urate stone dissolution. Urate uroliths that form due to hepatic insufficiency or portosystemic shunt formation are less amenable to dissolution protocols, though there are anecdotal reports of urate urolith dissolution following portosystemic shunt attenuation. Allopurinol is not recommended for patients with portosystemic shunts due to alterations in drug metabolism. Allopurinol may be used in low dosages for patients with hepatic insufficiency, though there are undoubtedly alterations in drug metabolism in these patients as well. At a minimum, a protein restricted diet that is low in purines should be administered to dogs with portosystemic shunts that are not attenuated, or in dogs with urate urolithiasis due to hepatic dysfunction. As is the case with all types of uroliths, increasing water intake to create relatively dilute urine is essential.

# 3. Cystine Calculi

Cystine calculi form due to a genetic mutation in cystine metabolism, and certain breeds (Newfoundland, English Bulldog, Dachshund, Chihuahua, Miniature Pinscher, Welsh Corgi, Bullmastiff, Labrador Retriever, Scottish Deerhound) are predisposed. These calculi can sometimes be effectively dissolved by feeding a diet that is low in sulfur amino acids (e.g. Hill's u/d diet, Royal Canin Urinary UC Low Purine, Royal Canin Vegetarian diet, Purina HA diet, Hill's d/d egg and rice diet), and administering Thiola, which is a drug that metabolizes cystine to a more soluble compound. Cystine excretion may be androgen dependent in some male dogs, therefore castration may be beneficial for stone dissolution and/or prevention. As is the case with all types of uroliths, increasing water intake to create relatively dilute urine is essential.

# Voiding Urohydropulsion

Voiding urohydropulsion is a non-invasive procedure which requires general anesthesia. The procedure is performed to remove small calculi from the lower urinary tract. It is essential that patient selection is careful, as this procedure could result in bladder rupture if attempted in a patient with calculi of excessive diameter for passage through the urethra. Please see the table at the end of the voiding urohydropulsion section, which shows the maximum diameter of uroliths obtained via voiding urohydropulsion in male and female dogs and cats of various sizes. Voiding urohydropulsion is typically easier in male dogs than in females, due to the relative ease of catheterization of males, but it can be performed in patients of either sex, and it can be performed in cats or in dogs.

The patient is placed under general anesthesia. A urinary catheter is passed retrograde into the urinary bladder. The urinary bladder is filled with saline until it is large and firm. Typical filling volumes are between 5 and 10 ml per kilogram of body weight. The catheter is removed. The patient is held upright and the bladder is palpated and agitated while holding the vulva or prepuce closed. The bladder is then expressed and the vulva or prepuce is released, creating a jet of urine. The urine is collected in a sterile bowl so that any calculi can be collected and submitted for analysis. We typically repeat the procedure until no calculi are expelled for three consecutive attempts. Thorough removal of calculi is documented with post procedural conventional radiographs which include the perineal urethra (radiopaque calculi), or a combination of ultrasound and positive contrast urethrography (radiolucent calculi).

MAXIMUM UROLITH SIZE PASSED DURING VOIDING UROHYDROPULSION			
SPECIES	SEX	BODY WEIGHT	MAXIMUM UROLITH SIZE
Canine	Female	7.4 kg	7mm
	Male	9 kg	5 mm
Feline	Female	4.6 kg	5 mm
	Male	6.6 kg	1 mm

Maximum diameter of uroliths passed through the urethra via voiding urohydropulsion

From: Lulich JP, Osborne C.A. Voiding Urohydropulsion: A Nonsurgical Technique for Removal of Urocystoliths. In: Bonagura JD, ed. Kirk's Current Veterinary Therapy Small Animal Practice, 12 ed. Philadelphia: W.B. Saunders Company; 1995:1008-1010.

### Cystoscopic-Guided Stone Basketing

This procedure is an appropriate approach for the removal of relatively small (<10) numbers of cystic calculi of small size. Success relies upon the ability of the urolith to pass through the urethra, thus the guidelines for case selection should be similar to those used to determine if voiding urohydropulsion is appropriate for an individual case. In fact, we will often use a combination of cystoscopic stone basketing and voiding urohydropulsion in patients who have many small calculi. Cystoscopic stone basketing is used for the calculi that are larger and require more guidance for successful passage through the urethra, while voiding urohydropulsion is used for the smaller calculi (1-2 mm in diameter) that present less cause for concern for possible urethral obstruction.

The cystoscope (rigid for females, flexible for males) is passed retrograde from the urethra into the urinary bladder. The calculi are visualized. A nitinol stone basket is passed through the cystoscope's instrument channel and used to grasp the calculi. The calculi are then pulled through the urethra along with the cystoscope, and collected for urolith analysis. This procedure is repeated until no further calculi are visualized, and a post-procedural routine or contrast radiograph is performed to confirm complete removal of all cystic calculi.

### Cystoscopic-Guided Laser Lithotripsy

Cystoscopic guided laser lithotripsy is an appropriate approach to the removal of cystic calculi in female dogs, as long as there are not excessive quantities of large calculi (>1.5 cm). In male dogs, we rarely perform cystoscopic-guided laser lithotripsy for cystic calculi, because of the inherent challenges associated with flexible cystoscopes (fiber optic scope, very narrow field of view), and resultant prolonged procedure times and increased risk of incomplete stone removal. Please see the previous section regarding cystoscopic guided laser lithotripsy for the removal of urethroliths for procedural notes.

### Percutaneous Cystolithotomy (PCCL)

This procedure is the approach that we use for male dogs with relatively small calculi (<1 cm), for small female dogs and cats with relatively small cystic calculi (<1 cm), and for larger female dogs with a larger number (>20) of cystic calculi that are up to 1 cm in diameter. The benefit of this approach is that it is less invasive than a cystotomy, allows well magnified visual assessment of the urinary bladder, thus reducing the chance of leaving calculi behind, and allows visual assessment of the urethra. Please see the previous section regarding PCCL for the removal of urethroliths for procedural notes. We will typically use the rigid cystoscope and address calculi in the urinary bladder prior to assessment of the urethra if we do not suspect urethrolithiasis prior to the procedure.

### Cystotomy

We typically perform cystotomies in patients with very large calculi (>2 cm), particularly if there are large numbers of large calculi. Even in these patients, we frequently pass a flexible cystoscope down the urethra in an antegrade fashion, to ensure that no urethroliths are present. Even experienced surgeons leave behind calculi in 15% of cases in which a cystotomy is performed. Thus, it is essential that the urinary tract be assessed to the best of one's ability during the procedure, and that post-surgical routine radiography/contrast radiography be performed while the patient is still anesthetized to document the absence of uroliths. If uroliths are still present, they should be removed during the same anesthetic event.

Please call us anytime at Cornell University Veterinary Specialists (CUVS) at 203.595.2777 if you have questions about management options for your patients. The best way to access us for questions emergently is surgery@cuvs.org or internalmedicine@cuvs.org.