FLUTD: STRUVITE RELATED DISEASES IN CATS
Jody P. Lulich, DVM, PhD
Minnesota Urolith Center, College of Veterinary Medicine, University of Minnesota
St Paul, MN 55108

Struvite was first described in the medieval sewer systems in Hamburg Germany in 1845 and named after the geologist who characterized it, Heinrich von Struve. It is ironic that this mineral composed of magnesium, ammonium, and phosphate also precipitates in and clogs the urinary systems of animals. In the following sections, we describe three clinical syndromes in which struvite affects the lower urinary tract of cats and dogs.

STRUVITE CRYSTALLURIA
Increasing ionic concentrations of urinary minerals are the driving forces underlying crystal formation. As the mineral concentrations increases, urine becomes thermodynamically unstable as it struggles to keep its contents in solution. Finally, a concentration is reached at which minerals can no longer remain dissolved. Minerals are forced out of solution into a solid phase (crystals), subsequently decreasing their concentrations in solution. Now that the concentrations of minerals are lower, urine re-establishes a more favorable thermodynamic equilibrium necessary to retain its fluid properties.

The urine concentrations of magnesium, ammonium, and phosphorus are the building blocks for struvite crystalluria. In addition, urine pH and its influence on the concentration of trivalent ionic phosphate (PO$_4^{3-}$) play a key role underlying struvite crystallization. As urine pH increases, H$_3$PO$_4$, H$_2$PO$_4^{-1}$ and HPO$_4^{-2}$ are rapidly deprotonated (i.e. removal of hydrogen ions) increasing the concentration of PO$_4^{3-}$, a principal component and driving force for struvite crystal formation.

Diagnostic Considerations
• Be skeptical of the clinical importance of crystalluria from samples improperly collected (e.g. from the floor), or improperly stored (greater than several hours or refrigerated prior to analysis). These in vitro phenomena may not represent what is occurring in the patient.
• Interpret the severity and persistence of crystalluria in light of urine pH and specific gravity. Increasing alkalinity and increasing urine specific gravity promote struvite crystal formation.
• Crystalluria is a marker for urine supersaturation and a risk factor for urethral plug and urolith formation. Therefore, consider medical imaging of the abdomen of cats and dogs with lower urinary tract signs and struvite crystalluria.
• Persistent urine alkalinity and subsequent struvite crystalluria may be an indication to culture the urine for urease producing bacteria including Staphylococcus sp., Proteus sp., and Ureaplasma sp.

Therapeutic Strategies:
• In the absence of uroliths, the ability of crystalluria to cause urinary signs is likely based on status of the bladder and the magnitude of crystalluria.

However, struvite crystals have been observed in cats that are apparently normal, have sterile struvite uroliths, have infection-induced struvite uroliths, have non-struvite uroliths, and have urinary tract disease without uroliths. If no other causes for clinical signs are detected, it is possible that struvite crystals can contribute to clinical signs in cats with sensitive bladders and possibly dogs.

• In male cats with persistent struvite crystalluria, feed therapeutic foods that increase urine solubility of struvite to prevent life-threatening urinary obstruction caused by struvite crystalline-matrix plugs. Between 2004 and 2005, the Minnesota Urolith Center analyzed urethral plugs from 906 cats; 84% of the cats were between 1 and 7 years old (31% were 2 to 3 years old, 26% were 4 to 5 years old, and 19% were 6 to 7 years old; 9% of cats were 8 to 9 years old and 6% were 10 to 11 years old). On the basis of these data, we recommend feeding struvitolytic foods to male cats with persistent struvite crystalluria through, at least, their 7th year of life.

**STRUVITE UROLITHS**

Although surgery plays an important role in the management of uroliths in some animals, the detection of uroliths is not always an indication for surgery. For example, struvite uroliths can be managed by medical therapy alone. In contrast, all cases that undergo surgical intervention also require medical management. If surgery is the only form of therapy, uroliths are likely to recur.

Only two dissolution foods have been evaluated in cats with struvite uroliths. Radiographic disappearance of sterile struvite uroliths was achieved within a mean of 36 days when cats were fed Hills Prescription Diet s/d. In a similar study, radiographic disappearance of struvite uroliths was achieved within a mean of 30 days feeding Medi-Cal Dissolution Formula. In both of these prospective studies, visible hematuria and dysuria subsided prior to complete urolith dissolution (usually within 2 weeks), and urethral obstruction was not reported in any study (in one study 52% were male (10 of the 13 had a perineal urethrostomy with 2 forming post-surgical urethral strictures), in the other study 31% were male). Some veterinarians prefer to remove all uroliths surgically because of perceptions that surgical management is more effective, is less expensive, controls clinical signs quicker, and will not be associated with urethral obstruction as uroliths decrease in size. These perceptions are not supported by published evidence. Medical dissolution is a compassionate, safe, effective, and rapid method for eradicating struvite uroliths.

**Diagnostic Considerations**

• Bladder palpation is not reliable to diagnosis struvite urolithiasis. In two studies, 10% or less of cases were identified by palpation because stones are often larger in dogs, palpation is likely to be associated with a higher diagnostic yield.
• Ultrasonography of the bladder is a sensitive method for detecting stones; however, survey radiography affords the advantage of providing urolith characteristics for predicting their mineral composition. Moderately radio-opaque, discoid uroliths are consistent with a mineral composition of struvite.
• Perform a urinalysis. Struvite crystalluria is helpful in predicting the mineral composition of uroliths.
• Culture urine for aerobic bacteria of cats with suspected urinary tract infection to differentiate sterile struvite uroliths from those that formed as a consequence of urinary tract infection. The most common bacteria associated with infection-induced struvite uroliths is Staphylococcus sp.

Therapeutic Strategies:
- Feeding canned formulations of struvitolytic foods have been associated with quicker dissolution times compared to dry formulations.
- Antimicrobial therapy is unnecessary for dissolution of sterile struvite uroliths (which commonly occur in cats); consumption of the struvitolytic diet is all that is required.
- To dissolve infection-induced struvite uroliths, calculolytic diet and antimicrobics need to be administered throughout the entire period of dissolution. Longer antimicrobial therapy is necessary because bacteria remain viable within the matrix of uroliths.
- To assess dietary effectiveness and owner compliance in cats, assess radiography and urinalysis results every 2 to 3 weeks.
- When feeding Hills Prescription Diet s/d Canine® to dogs, owner/patient compliance is easily and rapidly determined with a urine specific gravity (mean = 1.008 ± 0.003) and pH (mean = 6.2 ± 0.7). If urine is inaccessible, the serum concentration of urea nitrogen is also a reliable marker (mean = 3.5 ± 2.4 mg/dl) of dietary compliance.
- Hills Prescription Diet s/d Canine® is relatively high in fat in order to maintain calorie intake while providing lower quantities of protein to reduce urolith precursors (e.g. phosphorus and urea) important for dissolution. High dietary fat is a risk factor for pancreatitis. Likewise, female Miniature schnauzers (and other breeds) and dogs with hyperadrenocorticism are also risk factors for pancreatitis and urinary tract infections that include urease-producing uropathogens. Be aware of these associations and know how to respond (e.g. discontinue struvitolytic diet, maintain hydration) to adverse events (vomiting/pancreatitis) if they occur. Then consider low-fat alternatives that also acidify urine (e.g. canned Prescription diet w/d) to assist correction of both diseases.
- Urethroliths are less amenable to dietary dissolution because they are not continually surrounded by medicated urine. Therefore, urethroliths need to be flushed back into the urinary bladder and their position periodically monitored to successfully dissolved urethroliths.
- Candidates for urolith removal (e.g. surgery) include those with 1) persistent or recurrent urolith-induced obstruction despite appropriate urolith repositioning into the urinary bladder, 2) increasing urolith size or number despite medical therapy to inhibit their growth, 3) poor response because of poor compliance by the client or the patient with the
therapeutic recommendations, 4) persistent patient discomfort despite sufficient analgesia.

- To prevent urolith recurrence, foods that promote aciduria (pH less than 6.5), hypomagnesuria, and less concentrated urine are associated with the greatest success.
- When preventing infection-induced struvite uroliths, early detection and eradication of recurrent urinary tract infections is of primary importance.
- To prevent recurrence of struvite uroliths, feed diets that dissolve struvite stones for at least 1 month after stone removal. Then provide diets that abolish struvite crystalluria through, at least, the 7th year of the cat’s life. Although struvite stones have been recognized in all age groups, cats 4 to 7 years of age were at greatest risk for struvite urolith formation.
- Recent preliminary data (abstracts at ACVIM 2010) indicated that two maintenance therapeutic foods (Prescription Diet Feline c/d multicare and Royal Canin SO) also dissolved struvite uroliths.

STRUVITE URETHRAL PLUGS IN CATS

Urethral plugs are a common cause for urethral obstruction in cats; most plugs are composed of struvite. Between 1981 and 2009, the Minnesota urolith center analyzed urethral plugs from 7119 cats. During that period 84.5% were composed of struvite and 1% was composed of calcium oxalate. These findings are interesting because although the prevalence of calcium oxalate uroliths has increased dramatically in cats (of 11,697 urolith submissions in 2009, 40% were calcium oxalate and 48% were struvite), the prevalence of calcium oxalate urethral plugs has remained very low (of 415 urethral plug submissions in 2009, 1% was calcium oxalate and 93.5% were struvite).

Between 1980 and 1999, the prevalence of urethral obstructions significantly decreased from approximately 20 cases per 1000 cats evaluated to 7.4 cases per 1000 cats. We attribute this reduction in disease to the availability and use of specially formulated diets designed to minimize struvite crystalluria.

Diagnostic Considerations

- When admitting young male cats in a medical crisis, always assess bladder size. Cats with severe and prolonged urethral obstruction rarely present with signs referable to the urinary tract.
- Perform survey radiography early in the diagnostic process prior to urethral catheterization.
- Medical imaging is essential to verify bladder distension, localize disease, and recognize the underlying cause.
- Survey radiography is superior to ultrasonography for evaluating the feline urethra.
- When radiographing cats with lower urinary tract diseases, remember to include the entire urethra.
- Recognizing the underlying cause for urethral obstruction is important for selecting appropriate therapy with a successful outcome.
**Therapeutic Strategies** (see Proceedings – The S.A.F.E. Approach to Unobstructing the Safely Unobstructing the Feline Urethra):

- To minimize unrealistic expectations, informed consent is essential. Re-establishment of urethral patency is necessary, but can be associated with complications (e.g. death, bladder rupture, urethral tear, uroabdomen).
- To facilitate physical examination, radiography, and safe bladder manipulation; provide prudent amounts of analgesia (butorphenol 0.2 to 0.3 mg/kg and midazolam 0.2mg/kg administered IM or IV).
- Before correcting the urethral obstruction, first stabilize the patient (i.e. minimize hypothermia, azotemia, acidemia, hyperkalemia and hypocalcemia prior to general anesthesia).
- Place an intravenous access line.
- Perform decompressive cystocentesis using a 1.5 Inch 22 gauge needle, intravenous extension tubing, three-way stopcock, and large syringe (20 to 60cc) to avoid repeating cystocentesis in cats with large volumes of urine.
- To avoid urethral trauma, extend the urethra caudally to eliminate the flexure before inserting and advancing urethral catheters.
- Never force urinary catheters. To achieve patency, flush the urethral lumen clear before advancing a catheter.
- Avoid attaching the urinary catheter directing to the syringe. Assemble the urethral catheter, intravenous extension tubing, and syringe filled with normal saline. Evacuate air from these lines by flushing saline through the assembled supplies. To keep the urethra exteriorized caudally, have an assistant operate the syringe to flush to the urethra.
- Do not maintain transurethral catheterization, if it is not needed.
- If urine is sterile, delay antibiotic administration until indwelling urinary catheters are removed. By doing so, antimicrobial-resistant infections are minimized.3
- If hydration status cannot be monitored and maintained, avoid non-steroidal anti-inflammatory drugs to minimize iatrogenic kidney damage.
- To prevent recurrence of struvite plugs and urethral obstruction, feed diets that dissolve struvite stones for at least 1 month. Then provide diets that abolish struvite crystalluria though, at least, the 7th year of life cats life.


6. MacLeay et.al. Struvite urolith dissolution in 5 cats fed a maintenance diet with 0.06% magnesium, 35% protein and a targeted urine pH of 6.2-6.4. JVIM 2010;24:704.
