

Canine Lower Urinary Tract Disease



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KEY POINTS

- **LUTD describes a number of diseases of the bladder and/or urethra that may or may not result in obstruction of the urine outflow.**
- **Dietary management is a cornerstone in the treatment of some types of canine urolithiasis.**
- **Diet and feeding patterns can influence urinary pH, urine volume, and solute concentration, and hence urinary saturation with specific minerals.**
- **Urine pH is crucial in the treatment and prevention of struvite-related problems and should be kept constantly between 5.5 and 6.0.**
- **Most cases of struvite urolithiasis in dogs are associated with urinary tract infection and appropriate antimicrobial therapy is essential.**
- **Increasing urine volume for a given solute load has a diluting effect on the concentration of crystalloids responsible for the formation of uroliths; it can also increase the frequency of urination and therefore provides less time for crystals to form.**
- **Ensuring urinary undersaturation with specific minerals prevents crystal and urolith formation.**
- **Dietary management can help to:**
 - Dissolve and prevent the formation of struvite uroliths
 - Prevent the formation of calcium oxalate uroliths
 - Dissolve and prevent the formation of cystine uroliths
 - Dissolve and prevent the formation of ammonium urate uroliths

The term Lower Urinary Tract Disease (LUTD) describes any condition affecting the bladder and/or urethra. The range of clinical signs associated with LUTD in the dog includes **hematuria**, **dysuria**, **pollakiuria**, and **urinary incontinence**.

- **Hematuria** - presence of blood or red blood cells in the urine
- **Dysuria** - difficulty in passing urine, often associated with pain
- **Pollakiuria** - abnormally frequent passage of urine
- **Urinary incontinence** - inappropriate passage of urine resulting from loss of voluntary control

ANATOMY AND FUNCTION

The urinary bladder is responsible for the storage and the intermittent voiding of urine. Urine is produced in the kidneys and then passed into the bladder via the ureters. The urinary bladder serves as an expandable reservoir, with the bladder neck and the proximal urethra acting as an outflow valve. In order to control outflow and continence, the intraurethral resistance must be greater than the pressure within the bladder. When voiding urine, the bladder becomes a high-pressure pump, activated by the distension of its wall.

The urethra of male and female dogs varies both in length and diameter. The longer and narrower urethra in the male dog seems to predispose males to urethral obstructions.

INCIDENCE

Precise epidemiologic data for canine LUTD are not available; but in one study, lower urinary tract diseases were diagnosed in 3% of dogs admitted to North American veterinary colleges between 1980 and 1995, and urolithiasis occurred in 21.3% of these cases (Lulich and Osborne 1997). The prevalence of urolithiasis in dogs was estimated as 1% to 3% in one German study, with an incidence of 0.3% to 0.8%.

The most common type of uroliths found in dogs is struvite or magnesium ammonium phosphate. Calcium oxalate uroliths are also of significant importance, accounting for 25% of canine uroliths presented in a U.S. survey (Lulich *et al.*, 1992).

CLINICAL DISORDERS

Signs of CLUTD include **urinary incontinence**, **hematuria**, **dysuria**, and **pollakiuria**. These signs are nonspecific and give little information regarding their underlying cause. A detailed **diagnostic evaluation** should be completed to try to establish the cause of signs in an individual case.

Diagnostic Evaluation

Diagnostic evaluation of lower urinary tract disease in dogs is based on a combination of:

- History
- Physical examination
- Urinalysis and urine culture
- Radiography
- Ultrasonography

A systematic approach to establishing the cause of hematuria and/or incontinence should be adopted.

Where urolithiasis is suspected, effective therapy is dependent on identification of any predisposing urinary tract disorder and on determination of the specific mineral composition of the urolith involved.

Crystalluria

The term crystal refers to microscopic mineral precipitates. However, the presence of crystals in urine does not, in itself, cause disease. Crystalluria may occur in many healthy animals that never develop LUTD—with the exception of cystine crystalluria. Nevertheless, if crystal formation can be prevented, urolithiasis *cannot* occur. This can be an important factor in preventing the disease process in predisposed dogs.

The presence of crystals may give an indication of the type of problem present. In obtaining an accurate diagnosis of the crystal type present, the method of **sample collection and examination** is

important and the results need to be assessed in the light of other urine parameters, such as pH and specific gravity.

In dogs, the most common minerals found in urinary crystals are **struvite** (magnesium ammonium phosphate), **calcium oxalate**, **ammonium urate** and **cystine**.

Urine Sample Collection and Examination

The method of sample collection and examination is important when assessing urine for pH, the presence of crystals and bacterial infection.

For the assessment of urine pH and crystalluria, it is important to use a freshly voided sample and to examine it within 30 minutes of collection, as crystals may start to form spontaneously within the urine due to temperature and pH changes. If samples are not examined within this time span, they must be preserved. This can be done with a solution of white mineral oil and thymol powder, but it is advisable to contact the relevant laboratory for specific instructions prior to urine collection.

Always use a clean, sterile container.

The microscopic examination for crystals is best done in urine at body temperature, as urine saturation is temperature dependent. Struvite can be seen under x20 magnification, whereas calcium oxalate is best seen under x40/50 magnification.

Continuous Monitoring of Urine Parameters

The WALTHAM Centre for Pet Nutrition has developed a **noninvasive 24-hour urine monitoring system**, which allows for the collection of urine without interfering with the dog's natural urination pattern (Stevenson *et al.*, 1997). This procedure is not only animal friendly, but also ensures that the data produced are not influenced by the stress that may be associated with other methods of urine collection.

Dogs are trained to urinate in a special litter tray that is angled to allow the rapid drainage of urine and its analysis, within 30 seconds of being voided. During the trials, dogs are housed individually and using this system, their urinations may be monitored continuously (24 hours) for urine pH and urine volume. The method may also be adapted to measure urinary relative supersaturation (RSS) for a range of urolith types.

Urinary Tract Infection

Bacterial urinary tract infection (UTI) is the most common cause of cystitis in the dog and is usually associated with ascending bacterial migration from the urethra. Most uropathogens are derived from normal skin and bowel microflora. In the dog, UTI with urease-splitting bacteria, such as *Staphylococcus spp.* or *Proteus spp.*, produces an increasingly alkaline environment, which is an important predisposing factor for the formation of struvite and certain other urolith types, such as calcium phosphate (Osborne *et al.*, 1995).

Quantitative urine culture is essential to confirm the diagnosis of UTI and ideally, for this purpose, the urine sample should be obtained by cystocentesis to avoid bacterial contamination from the urethra.

Urolithiasis

Urolithiasis may be defined as the presence of macroscopic mineralization within the urinary system. Uroliths may vary in size from sand-like (sabulous) particles to larger, radiographically visible “stones.” They are polycrystalline concretions composed primarily of one or more minerals and contain only limited quantities of proteinaceous matrix.

Uroliths of a variety of mineral compositions have been found in dogs, but the most common are **struvite** (magnesium ammonium phosphate), **calcium oxalate**, **ammonium urate**, and **cystine**. Other urolith types that are found less frequently in dogs include calcium phosphate, silica, carbonate, drugs, and drug metabolites.

Mineral precipitation

The process of mineral precipitation within the urinary tract can largely be explained on a physical-chemical basis and involves a number of thermodynamic and kinetic factors. One simple approach is to consider urolith formation in two stages:

- Processes that lead to crystal formation
- Processes that lead to growth or aggregation (agglomeration) of crystals resulting in the development of a clinically significant urolith.

The key factor controlling mineral crystallization, a prerequisite for the formation of uroliths, is the degree of **saturation** of the urine with the particular mineral.

Urine Saturation

Saturation provides the driving force (free energy) for crystallization. The higher the degree of saturation, the greater the likelihood of spontaneous crystallization and crystal growth. Saturation is determined by the mathematic product of the activity (free concentrations) of individual solutes in urine (e.g., calcium and oxalate), which are determined by the:

- Absolute concentrations of the individual ions
- Interaction of these ions with other substances in urine
- Effect of urine pH
- Overall ionic strength of the solution

Solute activity (the amount that is free to react) is not synonymous with the simple concentration of a solute because individual ions may form complexes with other substances in the solution. Calcium or magnesium, for example, may form complexes with urate, citrate, or sulfate, as well as taking part in the formation of calcium oxalate or struvite. The extent to which these complexes form can be predicted from known dissociation constants, provided that the concentrations of the complexing substances are determined.

An additional complicating factor is that the freedom of movement of ions is further restricted in a nonspecific manner by the overall ionic strength of the solution containing them. The ionic strength is determined by the concentration and valency of ions in the urine sample. A high ionic strength reduces the activity of individual ions.

The product of the activities of the individual ions can be related to two values (i.e., **solubility product and formation product**) for a given crystal type; these values predict the likely crystallization processes within that solution.

The **solubility product** is a thermodynamic constant and determines the point at which the solution becomes saturated with the mineral in question. Spontaneous crystal formation is not possible in an undersaturated solution, and preformed crystals would be expected to dissolve. This has been demonstrated with struvite; however, the rate of dissolution of calcium oxalate may be very slow and not practically useful.

Formation products are usually determined empirically and are not constants.

A solution with saturation greater than the formation product will be in an unstable state (labile supersaturation) and spontaneous homogeneous crystallization, with the formation of a pure crystal of the mineral, becomes likely.

Between the formation and solubility products, a solution will be in a metastable state. Homogeneous crystallization will not occur. However, heterogeneous crystallization (aided by microscopic impurities such as cells, cellular debris, or different types of crystals) or aggregation of pre-formed crystals and slow crystal growth may occur, particularly as the formation product is approached.

Urine pH

Urine pH has been shown to be crucial with respect to struvite formation, as changing the pH has a proportionally much greater effect on struvite product activity than changing the concentration of one or more of the component crystalloids of struvite. The objective for the dietary management of struvite-related urolithiasis in dogs is to obtain a urine pH above 5.5 (to avoid metabolic acidosis) and below 6.0 (to promote undersaturation).

Increasing pH increases the concentration of the divalent anion as the monovalent anion is deprotonated.

Urine Volume and Specific Gravity

Increasing the urine volume and decreasing the concentration for a given solute has a diluting effect on the concentration of crystalloids responsible for the formation of a particular urolith. It also increases the frequency of urination and therefore provides less time for crystals to form. A number of methods may be used to help increase the dog's water intake, including:

- Feeding a canned product with a high moisture level
- Adding water to a dry diet, if necessary
- Feeding a highly digestible diet, which will ensure little water loss through the feces
- Feeding a diet with a relatively high fat level, as the breakdown of fat may produce a high level of metabolic water

- Adding moderate levels of sodium chloride (salt) to the diet to promote voluntary water intake; however, this may not be appropriate in the management of cystine urolithiasis, where dietary sodium levels should be restricted

MANAGEMENT

The management of urolithiasis is based on:

- **Relief of urinary obstruction**
- Removal of existing uroliths by **surgical removal** or by dissolution *in situ*
- Where appropriate, **treatment** of the underlying cause or associated risk factor
- **Prevention** of recurrence of uroliths

Relief of Urethral Obstruction

The initial management of obstructed dogs is similar, regardless of the cause of obstruction. Follow-up management will depend, however, on the initiating cause of the problem and may involve long-term dietary therapy.

The first consideration for dogs with urethral obstruction of less than 24 to 48 hours duration is relief of the obstruction to urine outflow, which may require anesthesia. Dogs with urethral obstruction of this duration are not usually systemically ill.

If urinary tract obstruction has been present for more than 24 to 48 hours, case management will be complicated by the effects of post-renal azotemia. Therapy is aimed at correcting these effects as well as relieving urinary tract obstruction. Thus the additional therapeutic goals are to correct hyperkalemia, acid-base imbalance, dehydration, and azotemia with appropriate fluid therapy.

Following relief of obstruction and stabilization of the patient with prolonged obstruction, consideration must be given to correction of the primary cause of disease and preventing recurrence of these cases.

Dietary Management of Urolithiasis

Dietary factors can profoundly influence urolith formation, because dietary ingredients and feeding patterns have the potential to influence the pH, volume, and solute concentration of the urine. Diet therefore has a key role in the prevention of recurrence of mineral precipitation and in some cases, may facilitate the dissolution of uroliths *in situ*. Specific dietary therapy depends on the urolith type involved, and in this respect, an accurate diagnosis, is important.

Additionally, measures to increase water intake, which help to increase urine volume and decrease solute concentration, have a role in the management of all urolith types.

Thus dietary management plays a significant role in the dissolution of uroliths composed of:

- **Struvite**
- **Cystine**
- **Ammonium urate**

and in the prevention of recurrence of uroliths composed of:

- **Struvite**
- **Calcium oxalate**
- **Cystine**
- **Ammonium urate**

Struvite Urolithiasis

Unlike cats, most cases of struvite urolithiasis in dogs are associated with urinary tract infection. Urease-producing bacteria such as *Staphylococcus spp.* and *Proteus spp.* create an increasingly alkaline environment, favoring the formation of struvite. It is therefore essential that quantitative urine culture be carried out in all dogs with suspected struvite urolithiasis. Appropriate antibiotic treatment should be given in conjunction with dietary therapy and continued until at least 1 month after dissolution of the urolith is complete or, if surgical removal of the urolith is performed, until quantitative culture results are negative. Failure to eradicate the infection will result in the continued formation of struvite.

Although antimicrobial therapy is a prime consideration where infection is present, dietary modification forms a cornerstone in the control of struvite urolith formation. Appropriate dietary

management can be used to dissolve struvite crystals and uroliths *in situ* and reduce the risk of recurrence of the condition.

Dietary Management of Struvite Urolithiasis

The principle of management of struvite-associated LUTD is to create and maintain urine that is undersaturated with struvite. The following factors can contribute to achieving this goal:

- Acidification of urine
- Enhancement of urine volume and reduction of specific gravity
- Restriction of dietary crystalloid intake

Measurements of urinary saturation provide a critical appraisal of the effects of dietary manipulation. Such calculations require computer programs and a complex series of analyses of urine samples.

Cystine Urolithiasis

Cystine urolithiasis occurs in dogs with an inherited defect in cystine metabolism, resulting in impaired reabsorption of the amino acid cystine in the proximal tubule of the kidney and hence leading to **cystinuria**. This may then lead to cystine urolith formation since cystine is relatively insoluble, particularly in acidic urine. Although many breeds may develop cystine urolithiasis, the condition is most common in the Dachshund, Bulldog, Basset hound, Chihuahua, Irish terrier, and Yorkshire terrier. Uroliths are almost exclusively seen in male dogs and are often not recognized until adult age.

The presence of cystine crystals provides strong evidence for cystinuria; however, not all dogs with cystine uroliths show concurrent crystalluria. The cyanide-nitroprusside test is a simple and reliable aid in the diagnosis of cystinuria (Hoppe 1994).

Strategies for the management of cystine urolithiasis are aimed at:

- Reducing the concentration of cystine in the urine
- Increasing the solubility of cystine in the urine

Dissolution and prevention of recurrence of cystine uroliths can be achieved through:

- Increasing water intake to increase urine volume
- Reducing dietary protein intake to reduce cystine production and excretion
- Restricting dietary sodium intake to promote tubular re-absorption of cystine
- Alkalinizing the urine (with bicarbonate or citrate) to increase cystine solubility
- Administering compounds, such as D-penicillamine or 2-mercaptopyrionylglycine (2-MPG), which convert cystine to a more soluble compound

Conversion of Cystine

D-penicillamine and 2-mercaptopyrionylglycine (2MPG) will chemically modify the cystine molecule into a more soluble form. This then leads to a lower urinary cystine concentration with a reduced risk of cystine urolith formation.

Even though D-penicillamine is effective in the prevention of urolith formation, and possibly dissolution, it can have undesirable side effects, such as vomiting and the enhanced excretion of such minerals as calcium, zinc, and copper (Hoppe 1994).

2-MPG is chemically similar to D-penicillamine but may be more effective and is usually well-tolerated.

Calcium Oxalate Urolithiasis

Potential predisposing factors for the occurrence of calcium oxalate urolithiasis include hypercalciuria and hyperoxaluria. Hypercalciuria has been found in dogs with calcium oxalate urolithiasis, usually associated with increased intestinal absorption or decreased renal tubular reabsorption of calcium. Rarely, hypercalciuria may be associated with hypercalcemia arising from, for example, hyperparathyroidism or malignant lymphoma.

While the degree of urinary saturation with calcium and oxalate is the driving force for crystallization, inhibitors or promoters in the processes of crystal aggregation and growth seem to play a much more important role in the development of uroliths than is the case in struvite urolithiasis.

Currently, it is not possible to dissolve calcium oxalate uroliths *in situ* by dietary or other means and, in dogs, surgery is required for the removal of pre-formed uroliths. Nevertheless, dietary manipulation plays a crucial role in the prevention of recurrence of the condition.

Dietary Management of Calcium Oxalate Urolithiasis

Dietary manipulation to prevent calcium oxalate urolith formation should aim to:

- Enhance urine volume, preferably by the addition of water to the food
- Undersaturate the urine with respect to calcium and oxalate

Enhancing urine volume contributes to the restricted urinary saturation with calcium oxalate and also decreases the time urine is kept in the bladder as it increases the frequency of urination.

Although restriction of dietary calcium and oxalate may be beneficial, restriction of only one of these components may increase intestinal absorption of the other.

Urine pH may also be important, and although calcium oxalate saturation can be increased in very acidic urine, studies have shown that certain diet formulations can result in the production of moderately acidic urine that is undersaturated with calcium oxalate (Stevenson and Smith 1998).

Although increased magnesium intake is sometimes recommended, care should be taken to ensure that this measure does not predispose the dog to struvite urolith formation.

Urate Urolithiasis

Urate uroliths are relatively uncommon in dogs and occur mostly in Dalmatians (although other breeds may also be affected) and in patients with portosystemic shunts. The most common salt of urate uroliths is ammonium acid urate, also known as ammonium urate. Uroliths mainly occur in young adult males of 3 to 6 years of age (Osborne *et al.*, 1986).

In affected dogs, hepatic conversion of uric acid (a product of purine metabolism) to allantoin is impaired. The defect of the uric acid metabolism in Dalmatians means that only approximately 30% to 40% of uric acid is converted due to impaired urate transport across liver cell membranes. However, the definite cause of urolith formation remains unclear, since all Dalmatians show an increased urinary excretion of urate but only a few dogs actually form uroliths. The metabolic defect therefore seems to be a predisposition rather than the primary cause of urate urolithiasis (Hoppe 1994).

Allantoin is highly soluble, while uric acid is insoluble and can precipitate to ammonium urate, predisposing to urate urolith formation.

Urate uroliths usually have a smooth surface. In Dalmatians, they are mainly located within the bladder, whereas they may also be found in the kidneys in dogs with portosystemic shunts. Urate uroliths are easily missed on plain radiographs and are best detected by ultrasonography.

Surgical relief of obstruction may be required in some cases. In others, dissolution and prevention of recurrence of urate uroliths may be achieved by:

- Controlling the dietary protein and purine intake to limit purine intake
- Supplementation with potassium citrate to promote neutral or slightly alkaline urine
- Increasing water intake
- Administration of **allopurinol**, which inhibits uric acid production

Allopurinol

Allopurinol is a xanthine oxidase inhibitor, which binds to and thus inhibits the action of xanthine oxidase. This inhibits the conversion of hypoxanthine to xanthine and xanthine to uric acid and therefore leads to a decrease in the overall production of uric acid. Effects are seen within a couple of days of administration.

SUMMARY

Dietary management forms the cornerstone in the management of some forms of canine urolithiasis. Diet and feeding patterns can affect the urine pH, the urine volume, and urinary solute concentration that, in turn, influence saturation and can reduce the risk of diseases involving mineral precipitation.

Manipulation of the diet can help to:

- Dissolve and prevent the formation of struvite uroliths
- Prevent the formation of calcium oxalate uroliths
- Dissolve and prevent the formation of cystine uroliths
- Dissolve and prevent the formation of ammonium urate uroliths

An important difference between canine and feline struvite urolithiasis is that in dogs, struvite uroliths are usually associated with urinary tract infection, whereas most feline struvite uroliths are sterile. Appropriate antimicrobial therapy is therefore essential in affected dogs.

REFERENCES

Hoppe AE: Canine lower urinary tract disease. In: The Waltham Book of Clinical Nutrition of the Dog and Cat. Eds Wills JM and Simpson KW. Pergammon. 1994 ; 335-352

Lulich JP, Osborne CA. Managing lower urinary tract disease in geriatric dogs. Proc 15th ACVIM Forum. 1997 ; 325.1997

Lulich JP, Osborne CA, Felice LJ, Polzin D, Thumchai R, Sanderson S. Calcium oxalate urolithiasis. Proc 16th Annual Waltham/OSU Symposium for the treatment of Small Animal Disases. 1992 ; 69-74.

Osborne CA, Poffenbarger EM, Klausner JS, Johnston SD, Griffith DP. Etiopathogenesis, clinical manifestations and management of canine calcium oxalate urolithiasis. *Vet Clin North Am.* 1986.*et al.*, 1986 16 : 13-170.

Osborne C.A., Lulich J.P., Bartges, J.W., Unger, L.K., Thumachai, R., Koehler, L.A., Bird, K.A. and Felice, L.J. (1995) Canine and feline urolithiasis: relationship of etiopathogenesis to treatment and prevention. In: Osborne, C.A., Finco, D.R. (eds) *Canine and Feline Nephrology and Urology* Philadelphia, Lea and Febiger pp 798-888.

Stevenson, A.E. and Smith, B.H.E. (1998) Nutritional aspects of canine struvite urolithiasis. *WALTHAM Focus — Focus on the Urinary Tract* p 59.

Stevenson, A.E., Smith, B.H.E. and Markwell, P.J. (1997) A system to monitor urinary tract health in the dog. *WALTHAM International Symposium: Pet Nutrition and Health in the 21st Century (Abstracts)* p 80.