



Nutritional management of canine urolithiasis

Peter J. Markwell BSc, BVetMed, MRCVS Abigail E. Stevenson BSc, GIBiol
WALTHAM Centre for Pet Nutrition, UK

KEY POINTS

- Certain breeds have been reported as being at increased risk of struvite urolithiasis – these include Cocker spaniels, Springer spaniels and Labrador retrievers.
- The management goal for dogs with struvite urolithiasis is to create urine that is undersaturated with struvite.
- Calcium oxalate uroliths also occur in dogs across a wide age range, although, in contrast with struvite uroliths, they tend to occur in older animals.
- Diets intended to prevent recurrence of calcium oxalate urolithiasis should result in production of urine either undersaturated with calcium oxalate, or in the lower part of the zone of metastable supersaturation.

The prevalence of urolithiasis in dogs has been reported in Sweden and Norway to be between approximately 0.25% and 0.5% (1). Proportional morbidity rates were reported as being approximately 0.5% in North American veterinary colleges, and between 0.5% and 1% in Germany (2, 3).

Uroliths composed primarily of struvite (magnesium ammonium phosphate) are the mineral type found most commonly in dogs in North America, representing approximately 50% of all canine uroliths analysed over a 17-year period at one centre (4). Calcium oxalate was the second most common mineral type found in uroliths submitted to that centre, representing approximately 30% of the total. There is some evidence that the proportion of calcium oxalate is increasing, as it represented 35% of canine uroliths submitted to that centre during 1997 (45% were struvite) (4). Comparable data from similar size studies in other countries are not available; however, preliminary data from quantitative analysis of uroliths in the UK suggest that the prevalence of the different mineral types is

broadly similar (**Table 1**) (Stevenson and Markwell, unpublished observations). Struvite uroliths are found more commonly in females than in males, whereas calcium oxalate occurs more frequently in males (4, 5).

Struvite urolithiasis

Struvite uroliths occur in dogs across a wide age range, including those under one year of age; indeed, they are the most common types of urolith found in young dogs (4, 5). In addition to the well-documented increased risk of struvite urolithiasis in female compared with male dogs, certain breeds have been reported as being at increased risk – these include Cocker spaniels, Springer spaniels and Labrador retrievers (6).

Overall, less than 30% of struvite uroliths are pure struvite, although the proportion is greater in males (38%) than in females (24%) (5). Most struvite uroliths are of mixed composition and contain one or more additional minerals including apatite, urate and oxalate (**Figure 1**) (5).



Peter J. Markwell
BSc, BVetMed, MRCVS

Peter obtained his first degree in anatomy from the University of London, and subsequently graduated with Honours from the Royal College in 1981. He entered companion animal practice for a time before joining the staff of the Royal Veterinary College as Lecturer of companion animal husbandry at the Department of Animal Health. He joined the WALTHAM Centre for Pet Nutrition at the end of 1985 as Veterinary Advisor, subsequently becoming Senior Nutritionist. He is currently Senior Clinical Nutritionist with responsibility for the research and development of WALTHAM Veterinary Diets



Abigail E. Stevenson
BSc, GIBiol

Abigail graduated from the University of Stirling with a BSc (Hons) in 1992. After working at the University of Anchorage, Alaska as a Research Assistant, Abigail was appointed as a Research Technician at the WALTHAM Centre for Pet Nutrition in 1993, to work on feline metabolism of vitamin A and taurine. In 1995, Abigail was promoted to Project Scientist within the clinical nutrition team working on the Veterinary Diets range. Her current research area covers the lower urinary tract of cats and dogs.

Table 1

Mineral composition of 86 canine uroliths analysed by infra-red spectroscopy

Mineral	% (& no) of total analysed	% found in	
		Male	Female
Struvite	36 (31)	35	65
Calcium oxalate	44 (38)	92	8
Ammonium urate/ uric acid	4 (3)	67	33
Cystine	6 (5)	100	0
Mixed*	10 (9)	55	45

* Mixed urolith – composed of less than 70% of any one mineral component
Data from (5)

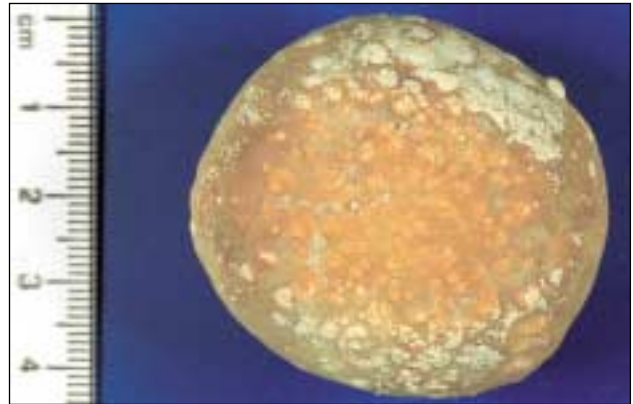


Figure 1 Infection-induced urolith of mixed composition (49% struvite, 51% calcium phosphate) from a ten-year-old female cross-breed.

Aetiopathogenesis of struvite urolithiasis

The risk of a given stone component crystallising out of solution and the rate and extent to which crystallisation will proceed are largely dependent on the level of supersaturation of that salt or acid in the urine concerned. Urine must be oversaturated with struvite for spontaneous homogeneous crystal formation to occur, although heterogeneous crystal formation, growth and aggregation of preformed crystals can occur in metastably supersaturated urine, particularly as the formation product of struvite is approached (**Figure 2**) (7). In the majority of dogs with struvite urolithiasis the key factor promoting oversaturation of urine with struvite is the presence of a urinary tract infection with urease-producing bacteria, such as *Staphylococcus intermedius* or *Proteus* spp. Hydrolysis of urea by the enzyme urease results in the formation of ammonia and carbon dioxide. The ammonia reacts with water, the result of which is an increased ammonium concentration and alkalisation of the urine. The alkaline urinary environment favours the loss of protons from H_2PO_4 , increasing the concentration of the form of phosphate necessary for struvite and calcium phosphate formation. The carbon dioxide combines with water-forming carbonic acid, which then dissociates, giving rise to bicarbonate. In an appropriate (markedly alkaline) environment this provides a source of carbonate that can substitute for phosphate giving rise to carbonate apatite. The bacterial urease thus results in an alkaline environment with a high ammonium concentration, which favours precipitation of struvite, calcium phosphate and carbonate apatite.

In a small proportion of cases, struvite uroliths develop in the absence of bacterial infection. It seems a reasonable assumption that dietary or metabolic factors that result in oversaturation of urine may be responsible for these cases.

Management of struvite urolithiasis

The management goal for dogs with struvite urolithiasis is to create urine that is undersaturated with struvite. In the majority of cases that have bacterial infections, diet alone is unlikely to achieve this aim unless the infection is controlled. It is likely that a combination of diet and antimicrobial therapy will be necessary in the management of these cases.

Selecting an antimicrobial agent

Ideally, an antimicrobial agent will be selected on the basis of antimicrobial susceptibility tests (see Vaden and Papitch), the recommended option being determination of minimum inhibitory concentrations of the antimicrobial agents excreted in urine (8). In the absence of the results of susceptibility tests, penicillin (daily dose 110,000 IU/kg divided three times a day) or ampicillin (daily dose 77 mg/kg divided three times a day) have been recommended for both staphylococcal infections and *Proteus*, with almost 100% of the former and approximately 80% of the latter expected to respond (8).

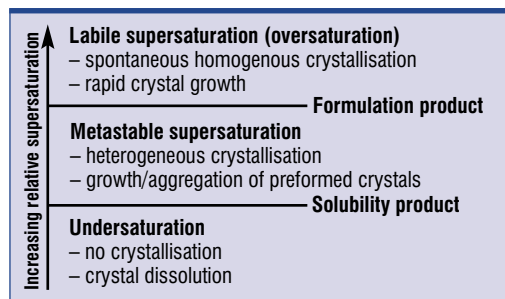


Figure 2 Crystallisation processes and regions of RSS. Modified from (8).

Dietary therapy

Diet forms an important part of the management regimen for struvite urolithiasis. Diet influences the saturation of urine with struvite, as it affects urine pH, volume and solute concentration.

Urine pH is the most important factor controlling struvite saturation (8). Reduction of urine pH through dietary manipulation is thus likely to be the most reliable means of achieving urine that is undersaturated with struvite (9). Diets designed for the management of clinical cases should thus be designed to provide an acid load to the animal and result in a urine pH in the range of approximately 5.5–6.0.

Enhancing urine volume for a given solute load will also reduce saturation, as it will decrease the concentrations of magnesium, ammonium and phosphate. In addition, increasing urine volume may influence crystal transit time through the urinary tract, thus reducing the potential for crystal growth.

The restriction of dietary crystalloid intake may also be beneficial, although changes in urinary magnesium or phosphate concentration individually have far less impact on struvite saturation than changing urine pH (8). These measures are broadly similar to those recommended for the management of struvite uroliths in cats, although the pH range is lower in dogs than would be safe in cats (7). An important additional factor for dogs with infection-induced struvite urolithiasis is restriction of dietary protein content. Restriction of protein intake reduces urea production, thus decreasing the available substrate for bacterial urease. WALTHAM Veterinary Diet PEDIGREE Low pH Control*, which is formulated to meet these recommendations, has been shown to result in the production of urine undersaturated with struvite in healthy dogs and to bring about dissolution of a struvite urolith in conjunction with antibiotic therapy in a clinical case (**Table 2**) (10).

For medical dissolution of the urolith, antimicrobial treatment in conjunction with an acidifying diet should continue until at least one month after dissolution is complete. Radiography or ultrasonography should be used to evaluate urolith dissolution. Where surgical removal of the urolith is necessary, treatment of the infection is required until quantitative culture results are negative. Failure to completely eradicate the



Table 2

Mean (\pm SD) urinary RSS (activity product/solubility product) with calcium oxalate and struvite in dogs fed WALTHAM Veterinary Diet PEDIGREE Low pH Control*

Diet formulation	Calcium oxalate RSS	Struvite RSS
Dry	2.84 \pm 1.63	0.59 \pm 0.59
Canned	0.71 \pm 0.36	0.17 \pm 0.24

infection may result in continued formation of struvite uroliths.

Supplementary therapy

Acetohydroxamic acid (AHA) is an inhibitor of urease. It has been shown to reduce urease activity, struvite crystalluria and urolith growth in dogs with experimentally induced staphylococcal infections at a daily dose of 25 mg/kg (divided twice a day) (11). Higher doses of AHA can cause a reversible haemolytic anaemia. AHA use is not routinely recommended, although it might be considered in cases that are resistant to management with a combination of diet and an appropriate antimicrobial agent (11, 12).

Calcium oxalate urolithiasis

Calcium oxalate uroliths also occur in dogs across a wide age range, although, in contrast with struvite uroliths, they tend to occur in older animals (mean age 8.69 vs. 5.79 years in one study) (5). Calcium oxalate uroliths are found more commonly in males than in females and breeds reported as being at increased risk include Cairn terriers, Pomeranians, Bichon Frises, miniature Schnauzers, and Lhasa Apsos (Figure 4) (6).

Overall, approximately 35% of calcium oxalate uroliths are pure, although, again, the proportion is greater in males (38%) than in females (29%) (5). Oxalate may be mixed with struvite, apatite or silica (5).

Aetiopathogenesis of calcium oxalate urolithiasis

The thermodynamic factors governing crystallisation of calcium oxalate are comparable to those of struvite – i.e. the risk of crystallisation can be predicted from the level of supersaturation of calcium oxalate in the urine (Figure 2) (7). In contrast with struvite, the pH does not significantly affect calcium oxalate crystallisation over the normal range of urinary pH. In humans, calcium oxalate uroliths may be formed in urine across the entire range of pH values (4.8–7.4). The main influence of pH is to determine the type of co-precipitate that may occur with the calcium oxalate; calcium phosphate is found in stones formed at high urine pH values (>6.3) and uric acid in those formed at low pH levels (<5.3). The practical importance of the lack of direct influence of urinary pH on calcium oxalate crystallisation is that urine pH targets cannot be set as a means of assessing the likely therapeutic efficacy of regimens for managing patients with calcium oxalate urolithiasis. The development of diets intended to control calcium oxalate formation thus requires techniques for the assessment of urinary supersaturation (13). Diets intended to prevent recurrence of calcium oxalate urolithiasis should result in production of urine either undersaturated with calcium oxalate, or in the lower part of the zone of metastable supersaturation (Figure 2). WALTHAM Veterinary Diet PEDIGREE Low pH Control* achieves this goal (Table 2).

Inhibitors of crystal growth and aggregation

While the degree of urinary saturation provides the driving force for crystallisation, the inhibitors and promoters of this process, and subsequently of crystal growth and aggregation (necessary for the formation of clinically significant uroliths), play a far more important role than in struvite urolithiasis (Figure 4). Crystal aggregation is likely to be the more important of these processes. The main inhibitors of crystal aggregation are

Table 3

Inhibitors of calcium oxalate crystal growth and aggregation

Inhibitor	Strength and mode of action	
	Crystal growth	Crystal aggregation
Citrate	Moderate (complexation and adsorption)	Weak (charge repulsion)
Magnesium	Moderate (complexation and adsorption)	No effect
Sulphate	Weak (complexation and adsorption)	
Non-polymerised Tamm–Horsfall mucoprotein	Weak (complexation and adsorption)	Moderate (charge repulsion)
Nephrocalcin	Moderate	Moderate–strong (charge repulsion)
Glycosaminoglycans	Weak–moderate (complexation and adsorption)	Very strong (charge repulsion)

Modified from (18)



Figure 3 Calcium oxalate uroliths from a ten-year-old miniature Schnauzer.

polyanions (Table 3) (14). Unfortunately, these are unlikely to be readily influenced by diet.

Management of calcium oxalate urolithiasis

Dietary therapy

No data are currently available that demonstrate dissolution of calcium oxalate uroliths *in vivo*. The management of clinical cases thus relies on surgical intervention, followed by dietary measures to reduce the risk of recurrence of stone formation. The goal of dietary management is to create urine that has a low saturation with calcium oxalate. Ideally urine should be undersaturated, as new crystal formation cannot occur under these circumstances, although this may be difficult to achieve in some patients. Homogeneous crystal formation will not occur, and heterogeneous crystal formation is unlikely to occur, in the lower part of the metastable zone of supersaturation. This represents a reasonable target that should reduce the risk of recurrence in patients.

Supplementary therapy

Potassium citrate has been used for the past decade in humans to prevent recurrence of calcium oxalate nephroliths (14). The beneficial effects are thought to be due primarily to the alkalinising properties of citrate, although they may be partially attributed to concurrent advice for the patient to increase fluid intake (14). In humans, oral intake of potassium citrate does not directly influence the amount of citrate excreted in the urine, as most absorbed intestinal citrate is metabolised to bicarbonate (15). This creates an alkaline tide and a resultant increase in urinary excretion of citrate, due either to increased production of citrate within the mitochondria of renal cells, or to decreased tubular reabsorption of citrate within the proximal tubular cells (16). These factors are thought to reduce calcium oxalate crystallisation in humans in a number of ways. Total urinary calcium excretion is reduced, and the availability of ionised calcium is further reduced in alkalinised urine by the increased amount and strength of binding to form soluble citrate and phosphate salts. The cumulative effect is one of reduced calcium oxalate supersaturation (14, 16).

Hypocitraturia may be a risk factor for calcium oxalate stone formation

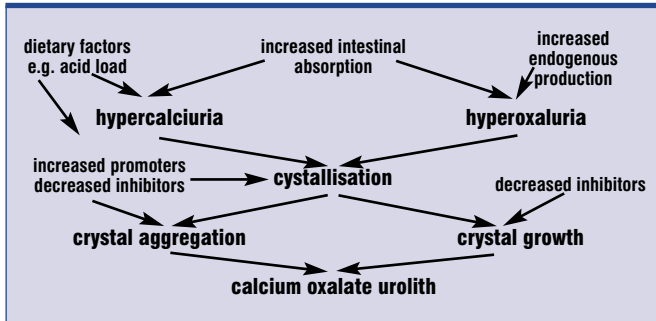


Figure 4
Theoretical schematic of factors that may promote calcium oxalate urolith formation.

in humans, with 15–50% of affected individuals reported to have very low levels of urinary citrate (15). In healthy humans citrate chelates calcium in the urine, which helps to prevent precipitation of calcium salts; as much as 70% of calcium may be bound in this way (17). When citrate excretion is reduced, less calcium is chelated and calcium urolithiasis is promoted. Most of the studies examining potassium citrate supplementation in humans have worked with individuals with hypocitraturia. Limited available data from stone-forming dogs show that hypocitraturia did not appear to be a factor contributing to stone formation in dogs (18).

The use of potassium citrate has been advocated in the prevention of recurrence of calcium oxalate urolithiasis in dogs (18). The evidence to support the use of potassium citrate is, however, inconclusive. One study

examined the effect of potassium therapy on the calcium oxalate urinary relative supersaturation (RSS) of a group of 12 healthy adult dogs (19). The dogs were fed a commercially available, nutritionally complete canned diet *solus*, or supplemented with potassium citrate powder at 150 mg/kg body weight per day in a cross-over design. A consistent increase in urinary citrate concentration was not seen with potassium citrate supplementation, nor was a decrease in urinary calcium concentration observed in this study. However, potassium citrate supplementation did result in small reductions in the calcium oxalate RSS in three of the 12 dogs. It is possible that stone-forming dogs may show a more favourable response than was observed in the healthy dogs in this study. However, the fact that hypocitraturia does not appear to be a major factor in urolithiasis-prone dogs suggests that supplementation with potassium citrate may have limited application.

A high fluid intake is still a first line of treatment for prevention of recurrence in the human field (14) and is recommended, although it may be more difficult to achieve in veterinary patients. Diets should be designed to increase urine volume, but additional measures such as the addition of water to dry foods may also be of value in some patients.

Hydrochlorothiazide has been shown to reduce calcium excretion in dogs with calcium oxalate urolithiasis (daily dose 4–8 mg/kg divided twice a day) (20). This drug may therefore be of value in selected cases with appropriate patient monitoring.

* WALTHAM Veterinary Diet; Canine Control pHFormula S/O (Americas)

PEDIGREE Low Ph Control Diet (Europe and Australasia)

WALTHAM® Canine S/O Lower Urinary Tract Support Veterinary Diet (Canada)

A feline variety of this diet is also available.

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