Nutritional Aspects of Canine Struvite Urolithiasis

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ABSTRACT

The most common component in canine uroliths is struvite (magnesium ammonium phosphate). The formation of struvite uroliths in dogs is closely linked to concurrent urinary tract infection, whereas most feline struvite uroliths are sterile. When struvite urolithiasis is suspected in dogs, urine samples should be collected via cystocentesis and quantitative urine culture should be performed. Manipulation of urine pH has long been a key component in the management of struvite urolithiasis, and diets designed to produce urine with a pH range of 5.5 to 6.0 have been identified as suitable for the dissolution and prevention of recurrence of struvite uroliths. Urine sediment should be assessed to detect and identify crystals, bacteria, and blood cells. For struvite uroliths to form, the urine must be supersaturated with magnesium ammonium phosphate; thus a determination of urinary relative supersaturation is necessary when evaluating the effect of a diet on urinary parameters. When sediment or uroliths have been removed from the urinary tract, they should be analyzed so that appropriate dietary and pharmacological management strategies can be implemented.

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Investigations into the effect of diet upon urinary parameters in the dog have been conducted for many years. Struvite (magnesium ammonium phosphate) is the most common component found in canine uroliths, and, in both dogs and cats, diet is known to contribute to the management and prevention of recurrence of struvite urolithiasis.

Work in this area has concentrated on:

- the effects of certain minerals
- the influence of diet on urine parameters including pH, volume, and solute concentration
- the effects of urinary tract infection.

In this respect, the important difference between the two species is that, in dogs, the formation of most struvite uroliths is closely linked to concurrent urinary tract infection. Most feline struvite uroliths, however, are sterile.

The WALTHAM Centre for Pet Nutrition (WCPN) has over 20 years of experience in studying the interaction of nutrition and lower urinary tract diseases, including struvite, mainly through assessment of urine pH, dietary mineral content, and, more recently, urinary relative supersaturation.

URINARY TRACT INFECTION

Approximately 70% of dogs with struvite urolithiasis have an associated urinary tract infection with urease-producing bacteria, such as staphylococci and *Proteus* spp. Hydrolysis of urea by the enzyme urease ultimately results in the formation of ammonia and carbonate, which creates an increasingly alkaline environment in the urine. These conditions are ideal for the development of struvite uroliths, but they also favor the formation of a number of other urolith types, including calcium carbonate and apatite.[1] In some cases, a urolith will form containing a combination of all three types.

Quantitative urine culture should, therefore, be carried out for any dog with suspected struvite urolithiasis. The sample should be collected by cystocentesis to avoid bacterial contamination from the urethra. Naturally voided urine samples may contain thousands of bacteria, even when fresh and collected into a sterile container, and this can lead to an inaccurate diagnosis of urinary tract infection.

If found to be infection-induced, appropriate antimicrobial agents form an essential component of therapy for struvite urolithiasis in dogs. For medical dissolution of the urolith, antimicrobial treatment in conjunction with an acidifying diet should continue until at least 1 month after dissolution is complete. Radiography or ultrasound should be used to evaluate dissolution. Where surgical removal of the urolith is necessary, treatment of the infection is required until quantitative culture results are negative. Failure to eradicate the infection completely will result in continued formation of struvite uroliths.

Dietary measures may also be employed in the control of struvite-associated urinary tract infections. Urea concentration in the urine is directly affected by the level of protein in the diet. A reduction in dietary protein intake, therefore, has a beneficial effect by reducing the amount of substrate available for the urease-producing bacteria.

Although less common, struvite uroliths may also form in alkaline urine in the absence of urinary tract infection. A reduction in urine pH is thus a prime consideration in the management of sterile struvite uroliths, and feeding a commercial acidified diet can help to achieve this goal. Under these circumstances, it is particularly important to

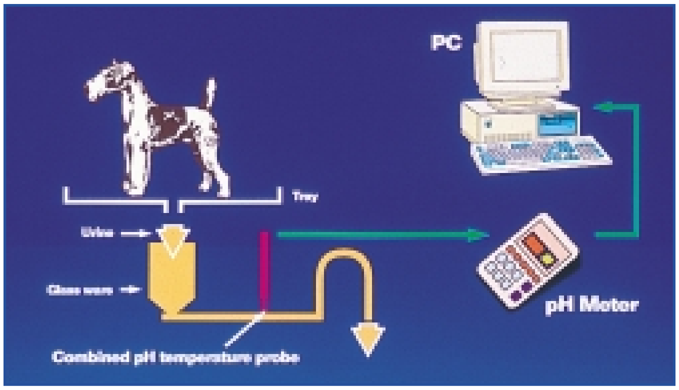

Figure 1
Diagram of the WCPN canine urine pH monitoring system.

Figure 2
The WCPN canine urine pH monitoring system.

ensure that acidification occurs and, to this end, urine pH should be closely monitored. If distinct meals are fed, measurements of urine pH should be taken 2 to 4 hours after feeding, when the urine is at its most alkaline.

URINE pH ASSESSMENT

For some years, manipulation of urine pH through diet has been a key element in the management of struvite urolithiasis. Urine pH is a much more important determinant of struvite formation than is the magnesium content of the diet.[2] This is because changes in urinary pH have a proportionately much greater effect on struvite activity product than changes in concentration of one or more of the crystalloid components of struvite.[2] Reduction of urinary pH through dietary manipulation is, therefore, one of the most reliable therapeutic strategies that can contribute to the successful management of struvite urolithiasis.

Various methods have been described for collecting urine samples from dogs, including cystocentesis[3] or catheterization under anesthesia.[4–7] Zentek *et al* kept dogs in metabolism cages that allowed for the collection of freshly excreted urine, although overnight samples could not be examined until the following morning.[8] A number of drawbacks are associated with these methods, including interference with normal urination patterns, the possible need for anesthesia, the invasive nature of the procedure, problems of urine standing for some time before analysis, and the fact that these methods do not allow for long-term or continuous measurements.

WCPN has developed a unique automated system that allows natural urinations from dogs to be analyzed within 30 seconds of urine being voided.[9] Dogs are trained to urinate in an angled litter tray. Voided urine then runs rapidly into a specially designed glass U-tube that houses a combined pH and temperature probe. These probes are linked to a personal computer via a pH meter (Figures 1 and 2). The computer software has been programmed to identify urination by a temperature increase in the urine collection tube of at least 2°C above ambient. This system has the added benefit of being non-invasive and is, therefore, suitable for both repeat and long-term testing. In addition to a mean daily urine pH, the system allows a diurnal urine pH profile to be collated to show the pattern of urine pH across 24 hours (Figure 3). Many of the methods previously mentioned may restrict the number of samples and time of day that the samples were taken. In these cases, the urine pH result obtained will depend very much on when the dog was fed and the time of day at which the sample was taken.

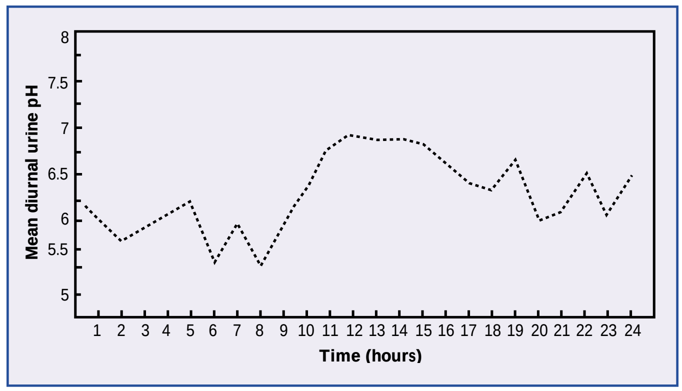

Figure 3
Mean diurnal urine pH profile of a commercially prepared dog food fed to 8 dogs for 21 days.

Although manipulation of urine pH through modification of diet is only one aspect of canine struvite urolithiasis management, the automated system described above has been used to assist in developing the WALTHAM Veterinary Diet; PEDIGREE Low pH Control Diets. In dogs, diets designed to produce an acidic urine, with a target urine pH of between 5.5 and 6.0 (Table 1), have been identified as suitable for the dissolution and prevention of recurrence of struvite uroliths. This urine pH range is known to be safe for long-term feeding and will not predispose dogs to metabolic acidosis.[5] Mixed breed panels of adult dogs were used in the development of these struvite cal-

TABLE 1

Urine pH and urinary relative supersaturation of struvite and calcium oxalate produced by feeding WALTHAM Veterinary Diet; PEDIGREE Low pH Control Diets (Dry and Canned)

	Urinary relative supersaturation		
	Struvite	*Calcium oxalate*	*Urine pH*
Dry	0.59±0.59	2.84±1.63	5.75±0.99
Canned	0.17±0.24	0.71±0.36	5.79±0.82

culolytic Diets and included miniature schnauzers, a breed known to be susceptible to forming both calcium oxalate and struvite uroliths.

While it is recognized that the automated system is not a feasible option in the veterinary practice, consideration of a number of sources of error can help to ensure a more representative assessment of urine pH. Using urinalysis reagent strips or pH indicator paper will give an indication, but not an accurate reading, of urine pH.[10] These strips tend to measure to the nearest 0.5 pH unit, and, since pH is measured on a negative logarithmic scale, this can lead to either underestimation or overestimation of the actual urine pH. In practice, the best method for measuring this parameter is to use a small portable, hand-held pH meter.

The method of sample collection is also important. When assessing urine pH, the urine should be as fresh as possible, and certainly not more than 30 minutes old. Typically, bacterial action will increase (i.e., make less acidic) the urine pH in a sample once it has been voided. It is worth emphasizing that a number of factors influence urine pH, including time of feeding pattern, presence of a urinary tract infection, stress, and type of diet.

URINE SEDIMENT ASSESSMENT

The WCPN automated system is also programmed to indicate a freshly voided urine sample by auditory and visual means and allows for immediate collection and assessment of the sample. The urine is examined for the presence and subsequent identification of crystals, bacteria, and blood cells. A 2 ml aliquot of the fresh urine sample is spun down in a minicentrifuge before removing 1.5 ml of the supernatant. The sediment is then resuspended in the remaining 0.5 ml of supernatant, and a small amount of the suspension is mounted onto a microscope slide with a coverslip. The slide is initially examined under a microscope with a heated end-stage attachment (Olympus BH2), using the x20 magnification. For certain types of crystals, and in particular calcium oxalate, x50 magnification may be necessary for correct identification. A hemocytometer slide can be used, which allows for accurate counts of crystals, bacteria, or blood cells in the urine sample.

Urinalysis reagent strips are a reliable method for initially assessing a urine sample for the presence of red blood cells. Occasional false positives may occur if the urine sample comes into contact with detergent (for example, if the sample is collected off the floor) or if the urine contains high levels of ascorbic acid (perhaps due to vitamin C supplementation).[11] If blood is not visible in the urine sample but is detected by the urinalysis reagent strips, the sample should be checked for the presence of red blood cells by microscopic examination. This technique can also be used in veterinary practice. However, great care must be taken in collecting and handling the samples. Samples must be collected into a clean container and examined within 30 minutes of voiding because, after this time, crystals start to form spontaneously within the urine. This is an important consideration when urine samples are sent via overnight delivery to an external laboratory without any type of preservative. Identification of certain types of crystals in these samples may lead to false-positive or otherwise inaccurate diagnoses. At WCPN, a 1% solution of white mineral oil and thymol powder is often used as an effective urine preservative. Provided that the initial sample was freshly voided, this method will successfully preserve samples for 24 hours and allow accurate overnight sample evaluation.

Figure 4
Canine struvite uroliths.

URINARY RELATIVE SUPERSATURATION (RSS)

Urine must be oversaturated with magnesium ammonium phosphate for struvite uroliths to form. In the dog, this may occur for a variety of reasons, including urinary tract infection, alkaline urine and genetic predisposition. Undersaturation with the components of

Case study

Lucy, an intact, 6-year-old female miniature schnauzer, was initially presented with visible hematuria and dysuria. At this time, she was being fed a mixed diet of commercially available dry and canned pet food with some additional fresh fruit and vegetables. Urinalysis and X-ray revealed the presence of calculi within the bladder, which were subsequently surgically removed, qualitatively analyzed, and found to be composed predominantly of struvite. At this stage, no bacterial culture was carried out on the urine sample, although Lucy's diet was changed to a commercially available acidified diet.

The dog was readmitted almost 1 year later, with recurrent signs of hematuria and dysuria. The presence of bladder stones was once again confirmed by radiography (Figure 5A). A sterile urine sample was also collected by cystocentesis for quantitative urine culture and sensitivity. It was suspected that, as before, the uroliths were composed of struvite so a suitable therapeutic regimen was implemented. Lucy's diet was changed to WALTHAM Veterinary Diet; PEDIGREE Low pH Control Diet (canned) to aid dissolution of the uroliths, and the appropriate antimicrobial treatment was prescribed.

Repeat X-rays were conducted at regular 6 week intervals to monitor the progress of the dissolution. After 1 month of feeding this Diet, the uroliths were already visibly smaller. The final X-ray, taken 4 months after initiating treatment, revealed complete dissolution of all uroliths (Figure 5B). In addition, quantitative bacterial culture of a sterile urine sample showed that the urinary tract was free of infection. Lucy was subsequently returned to her original diet and no recurrence of urinary tract disease has been observed in the 2 years since treatment was completed.

A

B

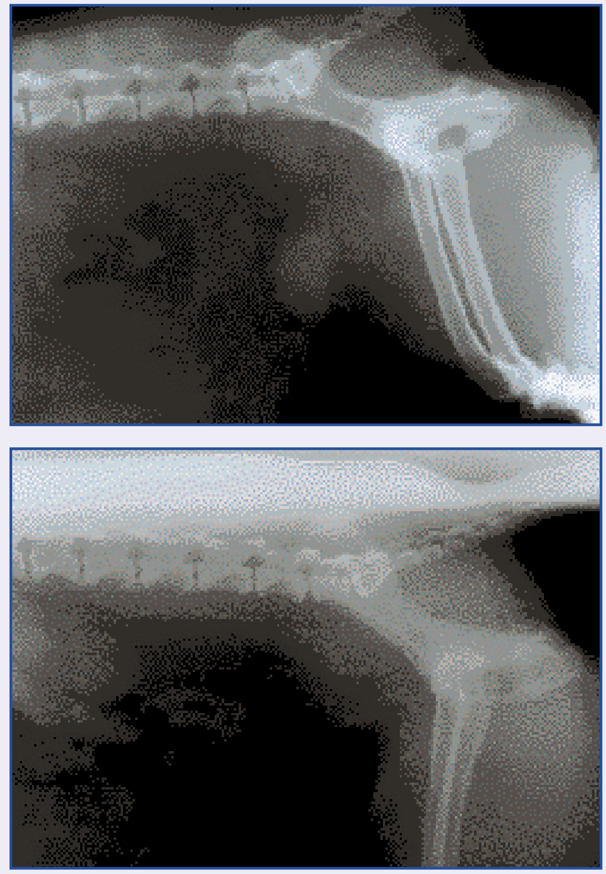

Figure 5
Abdominal radiograph of Lucy (**A**) prior to treatment, showing the presence of urinary calculi in the bladder, and (**B**) 4 months after feeding WALTHAM Veterinary Diet; PEDIGREE Low pH Control Diet, demonstrating the complete dissolution of urinary bladder calculi.

a particular urolith type is essential for dissolution of the urolith to occur (see Figure 4 on page 49), and this is the primary goal of dietary manipulation. Diets designed to produce urine that is undersaturated with struvite aim to lower urinary pH, reduce calculogenic solute concentration, and enhance urine volume.

Study of the effects of diet on urinary saturation requires determination of solute activity. Although the concentration of ions in a urine sample can be assessed relatively easily, this is not a measure of activity because it does not take into account the ion complexes that may occur. The extent to which these complexes form can be predicted from known dissociation constants, allowing free-ion concentrations to be predicted.

Urinary relative supersaturation (RSS) and urine pH are routinely measured at WCPN when assessing the effect of a diet on urinary parameters in the dog.[9] Measuring urinary RSS gives a more critical appraisal of the influence of a diet on urine than measuring urine pH alone. Dogs are trained to urinate into angled litter trays, ensuring that the urine runs rapidly into a glass bottle. This bottle is surrounded by dry ice to freeze the sample immediately after being voided. The urine is collected in this manner for 48 hours and then defrosted and titrated to pH2 with hydrochloric acid. Subsequently, the sample is analyzed for sodium, potassium, magnesium, calcium, chloride, sulfate, phosphate, oxalate, citrate, pyrophosphate, ammonia, uric acid, and creatinine using high-performance liquid chromatography. The resulting analytical values are entered into a computer program, Equil 2, that calculates urinary relative supersaturation (activity product/solubility product) for four urolith types: struvite, calcium oxalate, uric acid, and brushite (calcium phosphate). A urinary RSS value of less than 1.000 indicates that the urine is undersaturated with respect to that urolith type, whereas a value of greater than 1.000 indicates that the urine is oversaturated with respect to that urolith type.

WALTHAM has used the combined measurements of urine pH and RSS to develop the WALTHAM Veterinary Diet; PEDIGREE Low pH Control Diets (dry and canned), which are designed for the dissolution and prevention of recurrence of struvite uroliths. The data obtained (Table 1) show that both the canned and dry versions of the Diets undersaturate the urine with the components of struvite, which is highly desirable for effective management of struvite urolithiasis. These Diets have also been evaluated for calcium oxalate RSS to ensure that they do not inadvertently predispose dogs to calcium oxalate urolithiasis. The formation product of calcium oxalate is estimated to be approximately 10 times the value of its solubility product (see Figure 4 on page 49), and is equivalent to a RSS of approximately 10. Urine with a RSS value of between 1 and 10 may, therefore, be considered to be in a state of metastable saturation. Under these circumstances, calcium oxalate crystallization would not be expected to occur. This applies to the WALTHAM Veterinary Diet; PEDIGREE Low pH Control Diet (Dry), which consistently produces calcium oxalate RSS values of between 1 and 5. However, because the Canned Diet results in production of urine that is undersaturated with calcium oxalate, this Diet is also suitable for minimizing the risk of recurrence of clinically significant calcium oxalate uroliths.

UROLITH ANALYSIS

Once uroliths or urinary sediment have been removed from the urinary tract, it is important that they are quantitatively analyzed so that an appropriate dietary and pharmacological management strategy can be implemented. Figure 4 shows that struvite uroliths come in all shapes and sizes, illustrating that it is difficult to predict stone type from appearance alone. A comparison of canine uroliths analyzed using a widely available qualitative analysis reagent kit and quantitative urolith analysis by infrared spectroscopy[12] revealed that the qualitative method failed to correctly identify 62% of calcium-containing uroliths and 83% of carbonate-containing uroliths and gave false-positive results for urate in 55% of cystine uroliths. WALTHAM has recently set up a center for quantitative analysis of uroliths by infrared spectrometry. Uroliths or urinary sediment should be submitted with the appropriate paperwork to the WALTHAM Centre for Pet Nutrition, Waltham-on-the-Wolds, Melton Mowbray, Leicestershire LE14 4RT, UK.

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