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Canine Leishmaniasis and other Vector-Borne diseases.
Current State of Knowledge

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Urolithiasis is common in dogs and cats and approximately 98% of uroliths occur in the lower urinary tract. Calcium oxalate and struvite account for > 85% of uroliths and occur at approximately equal frequency in dogs and cats.1 Urolith formation is not a specific disease, but the sequelae to a group of underlying disorders. It occurs with sustained alterations in urine composition that promotes supersaturation of one or more substances in urine resulting in precipitation and subsequent organization and growth into uroliths. Urolith formation, dissolution, and prevention involve complex physical processes. Major factors include: 1) supersaturation resulting in crystal formation, 2) effects of inhibitors of crystallization and inhibitors of crystal aggregation and growth, 3) crystalloid complexors, 4) effects of promoters of crystal aggregation and growth, and 5) effects of noncrystalline matrix. An important driving force behind stone formation is saturation state of urine with calculogenic substances.2 When a solution such as urine is saturated, it refers to the maximal amount of a substance, such as calcium oxalate, that can be completed dissolved. This point is termed the thermodynamic solubility product. When calcium oxalate is present in urine at a concentration less than the solubility point, the urine is undersaturated with calcium oxalate and calcium oxalate completely dissociates and dissolves. When calcium oxalate is present in urine at a concentration that is equal to the solubility point, the urine is saturated with calcium oxalate and calcium oxalate begins to precipitate. When calcium oxalate is present in urine at a concentration above the solubility point, the urine is supersaturated with calcium oxalate and calcium oxalate precipitates. Urine contains ions and proteins that interact and/or complex with calcium and oxalic acid so as to allow them to remain in solution. This explains why calcium and oxalic acid in urine do not normally precipitate to form calcium oxalate crystals. Urine is normally supersaturated with respect to calcium and oxalic acid. But energy is required to maintain this state of calcium and oxalic acid solubility, and, therefore, the urine must constantly “struggle” to maintain calcium and oxalic acid in solution. Thus, urine is described as being metastable, implying varying degrees of instability with respect to the potential for calcium oxalate crystals to form. In this metastable state, new calcium oxalate crystals will not precipitate, but if already present, crystals can be maintained and even grown in size. If the concentration of calcium and oxalic acid is increased, a threshold is eventually reached at which urine cannot hold more calcium and oxalic acid in solution. The urine concentration at which this occurs is the formation point of calcium oxalate. Above the thermodynamic formation product, urine is oversaturated and unstable with respect to calcium and oxalic acid. Thus, calcium oxalate crystals will spontaneously precipitate, grow in size, and aggregate together. Urolith formation is erratic and unpredictable emphasizing that several interrelated physiologic and pathologic factors are often involved. Mere presence of uroliths does not necessitate their removal.

STRUVITE

Sterile struvite uroliths:1,3-5 Sterile struvite uroliths form typically in cats between 1 and 10 years of age. Risk for struvite urolith formation decreases after approximately 6-8 years of age in cats. They occur with equal frequency in male and female cats. Alkaluria is associated with increased risk for struvite formation. In a clinical study including 20 cats with naturally occurring struvite urocystoliths and no detectable bacterial urinary tract infection, the mean urinary pH at the time of diagnosis was 6.9 ± 0.4. Consumption of increased quantities of water may result in lowering concentrations of calculogenic substances in urine, thus, decreasing risk of urolith formation. Consumption of small quantities of food frequently rather than one or two large meals per day is associated with production of more acidic urine and a lesser degree of struvite crystalluria by cats. Sterile struvite uroliths can be dissolved by feeding a diet that is magnesium, phosphorous, and protein restricted, and that induces aciduria relative to maintenance adult cat foods. In a clinical study including 22 cats with sterile struvite urocystoliths, urocystoliths dissolved in 20 cats in a mean of 36.2 ± 26.6 days (range, 14 to 141 days). The cats were fed a high-moisture (canned), caloricly dense diet containing 0.058% magnesium (dry matter basis) and increased sodium chloride (0.79% dry matter basis). The diet (Prescription Diet Feline s/d, Hill’s Pet Nutrition Inc.) induced a urine pH of approximately 6.0. Prevention of sterile struvite uroliths involves inducing a urine pH less than approximately 6.8, increasing urine volume, and decreasing excretion of magnesium, ammonium, and phosphorous.
Infection-induced struvite uroliths: Infection-induced struvite uroliths occur more commonly in dogs and in cats less than 1 year and greater than 10 years of age. Infection-induced struvite uroliths form because of an infection with a urease-producing microbe. In this situation, dietary composition is not important as the production of the enzyme, urease, by the microbial organism is the driving force behind struvite urolith formation. Infection-induced struvite uroliths can be dissolved by feeding a “struvite dissolution” diet and administering an appropriate antimicrobial agent based on bacteriological culture and sensitivity. Average dissolution time for infection-induced struvite uroliths is 8 weeks; however, it is dependent on the number and size of uroliths present. It is important that the dog or cat receive an appropriate antimicrobial agent during the entire time of medical dissolution as bacteria become trapped in the matrix of the urolith, and as the urolith dissolves bacteria are released into urine. There are several case reports of medical dissolution of infection-induced struvite urocystoliths using antimicrobial therapy without changing diet. Additionally, there is a clinical trial evaluating antimicrobial therapy and urinary acidifier administration. In this study, administration of d,l-methionine (Methioform, Lloyd, Inc) effectively dissolved presumed infection-induced struvite urocystoliths in 8/11 dogs within 2 months. In the 3 dogs where attempted dissolution failed, calcium oxalate was present. Diet was not changed in this study and no complications occurred. Therefore, dietary therapy may not be required to dissolve infection-induced struvite urocystoliths in dogs if urine acidification and control of UTI is achieved. Prevention of infection-induced struvite uroliths does not require feeding a special diet as the infection causes these struvite uroliths to form. It involves preventing a bacterial urinary tract infection from recurring and treating bacterial infections as they arise.

PURINES

Urate: Urate is the third most common mineral found in uroliths in dogs and cats accounting for 5-8% of uroliths. The ammonium salt occurs most commonly, although sodium urate, sodium potassium urate, and sodium calcium urate may also occur. It is the second most common urolith occurring in dogs and cats < 1 year of age (infection-induced struvite is the most common urolith in these patients). Urate uroliths form when urine is oversaturated with urate and usually ammonium. These uroliths form because of liver disease (usually a portosystemic vascular shunt) or because of an inborn error of metabolism resulting in hyperuricosuria (e.g. Dalmatians and English bulldogs). They are more common in dogs and cats less than 5 years of age.

Dissolution is not possible in dogs and cats with uncorrected liver disease (e.g. non-surgical portocaval anomalies or microvascular dysplasia). Surgical removal, voiding urohydropropulsion, or cystoscopy ± laser lithotripsy remains the treatment of choice for symptomatic urate stones that cannot be dissolved. In dogs and cats without underlying liver disease, dissolution may be attempted. Dissolution is accomplished by feeding a purine-restricted, alkalinizing, diuresing diet and administering the xanthine oxidase inhibitor, allopurinol (15 mg/kg PO q12h). While “renal failure” diets are protein-restricted and thus lower in purines, there are 2 commercially available diets formulated to be low in purines; Prescription Diet u/d (Hill’s Pet Products) and UC Low Purine (Royal Canin). Canned diets may be better than dry diets. In one study, medical dissolution was effective in approximately 40% of Dalmatians, partial dissolution occurred in approximately 30%, and no dissolution of growth of uroliths due to xanthine formation occurred in approximately 30%.

Prevention of urate uroliths in dogs without liver disease involves continued feeding of the low purine diet. If necessary, allopurinol may be administered at a lower dose (7-10 mg/kg PO q12-24h). Periodic abdominal ultrasonography or double contrast cystography may be necessary. Determination of 24-hour urinary uric acid excretion may also be useful, although data are limited and collection of 24-hour urine samples can be difficult. The goal is to achieve 24-hour urinary acid excretion of approximately 250-350 mg/dog/24hr. Use of uric acid-to-urine creatinine ratios is not useful. Although no studies have been performed evaluating the efficacy or safety of medical dissolution of urate uroliths in cats with idiopathic urate urolithiasis, we have successfully dissolved urate uroliths in cats using a “renal failure” diet (Prescription Diet k/d, Hill’s Pet Products) and allopurinol (7.5 mg/kg PO q12hr). Until further studies are performed to confirm the safety and efficacy of medical dissolution, surgical removal remains the treatment of choice for urate uroliths in cats. Prevention of urate urolith recurrence in cats has been > 90% when using a protein restricted, alkalinizing diet (Prescription Diet k/d, Hill’s Pet Products).

Xanthine: Xanthine urolithiasis may occur with allopurinol administration to dogs especially when dietary purines are not restricted. Management involves adjusting dosage of allopurinol and changing diet. Xanthine uroliths retrieved and analyzed from cats contain pure xanthine, although a few contain small quantities of uric acid. Of 64 cats that formed xanthine uroliths in one report, none of the cats had been treated with the xanthine oxidase inhibitor, allopurinol. Sixty-one xanthine uroliths were obtained from the lower urinary tract while xanthine uroliths from 3 cats came from the upper urinary tract. Xanthine uroliths occurred in 30 neutered and 8 non-neutered males and 25 neutered females (the gender of one cat was not specified). Mean age of cats at time of diagnosis of xanthine uroliths was 2.8 ± 2.3 years (range = 4 months to 10 years). Eight of the 64 cats were less than one-year old. Urinary uric acid excretion was similar between 8 xanthine urolith-forming cats and healthy cats (2.09 ± 0.8 mg/kg/d vs 1.46 ± 0.56 mg/kg/d); however, urinary xanthine excretion (2.46 ± 1.17 mg/kg/d) and urinary
hypoxanthine excretion 0.65 ± 0.17 mg/kg/d) were higher (neither are detectable in urine from healthy cats). Xanthine uroliths have also been found in a few Cavalier King Charles spaniels. No medical dissolution protocol for naturally occurring xanthine uroliths exists. Prevention involves feeding a purine-restricted, alkalinizing, diuresing diet. Without preventative measures, xanthine uroliths often recur within 3 to 12 months following removal.

**CYSTINE**

Cystinuria occurs when there is a proximal renal tubular defect in reabsorption and often occurs with other amino acids (notably ornithine, lysine, and arginine). Cystinuria is only associated with urolith formation and is not associated with protein malnutrition or amino acid deficiency, although it can be associated with hypercarnitinuria and/or hypertaurinuria and associated dilated cardiomyopathy. Cystinuria by itself does not result in urolithiasis, however, and many cystinuric dogs and human beings do not form uroliths.

Canine cystine uroliths can be dissolved medically. Feed a diet that is low protein, alkalinizing, and induces a diuresis. While “renal failure” diets are protein-restricted and thus lower in amino acids, there are 2 commercially available diets formulated to be low in sulfur-containing amino acids: Prescription Diet u/d (Hill’s Pet Products) and UC Low Purine (Royal Canin). Canned diets may be better than dry diets. Administer 2-mercaptopropionylglycine (2-MPG, Tiopronin, Thio-Canine) to cats (neither are detectable in urine from healthy cats). Xanthine uroliths have also been found in a few Cavalier King Charles spaniels. No medical dissolution protocol for naturally occurring xanthine uroliths exists. Prevention involves feeding a purine-restricted, alkalinizing, diuresing diet. Without preventative measures, xanthine uroliths often recur within 3 to 12 months following removal.

**REFERENCES**


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