Principles of Stone Analysis
Stones can be analyzed by a variety of methods. Calculi submitted to the Gerald V. Ling Urinary Stone Analysis Laboratory at the University of California at Davis are analyzed by quantitative crystallographic analysis primarily utilizing the oil immersion method of optical crystallography using polarized light microscopy. Qualitative analyses are not recommended due to the inaccuracy of the test. When optical crystallography is insufficient to identify the mineral components present in the layers of the calculus, infrared spectroscopy (IR), x-ray diffractometry (XRD), scanning electron microscopy (SEM) with energy dispersive x-ray (EDX), and electron probe microanalysis (microprobe) can be utilized.

For most specimens submitted to the laboratory, the oil immersion method of optical crystallography is sufficient to identify the crystalline mineral components of the calculi. Because the refractive indices for the common mineral components of urinary calculi have been established, a comparison of the refractive indices of the crystals in the unknown calculus specimen can be compared with the established reference indices and a match for the crystals can be determined. In addition to optical crystallography, IR is routinely utilized to process all calculus specimens suspected of containing uric acid crystals and/or salts of uric acid crystals in order to identify the presence of xanthine, hypoxanthine, allopurinol, or oxypurinol, a metabolite of allopurinol, which may be present in the specimen. Polarized light microscopy alone is insufficient to identify xanthine, hypoxanthine, allopurinol and its metabolites so these additional methodologies are utilized. The other methods listed above can be utilized for individual stones when optical crystallography and IR are insufficient at identifying the minerals present in the specimen. For more information on how to properly submit a calculus to the UC Davis Stone Analysis Laboratory for a quantitative crystallographic analysis, please visit our website at: http://www.vetmed.ucdavis.edu/usal/index.cfm.

Stone Removal
Some uroliths such as struvite, urate and cystine may be amenable to medical dissolution. In the author’s opinion, dissolution protocols for urate and cystine are often unrewarding. It is important when attempting dissolution of struvite stones in dogs, that, in addition to dietary therapy (see below); appropriate antimicrobial therapy must also be administered. Although surgery is still the most common form for urolith removal in dogs and cats, newer, less invasive techniques are now available. These include laparoscopic assisted cystotomies, voiding urohydropropulsion (VUH), and basket retrieval of the stone via the cystoscope, laser lithotripsy and extracorporeal shock wave lithotripsy. VUH can be performed when small cystic calculi are present in the bladder. Holmium: YAG laser lithotripsy is becoming more widely available at referral institutions and uses laser energy to fragment stones; after fragmentation, the pieces can be removed using a basket inserted through the scope and VUH for the smaller pieces that remain.

Feline Struvite and Calcium Oxalate (CaOx) Containing Calculi
When evaluating stones from cats that were submitted to our laboratory over the past 25 years, the ratio of CaOx stones to struvite stones significantly increased (Figure 1). We have noted a change in feline urolithiasis trends beginning in 1993, when 53% of the stones contained CaOx, while only 47% contained struvite. CaOx containing uroliths continued to increase over the next eight years, while the struvite containing uroliths decreased during that same time period. No change was noted in other stone types submitted to our laboratory. It is theorized that the diets used to promote urine acidification may have contributed to the increase in CaOx urolithiasis. Previous studies in cats evaluating this change suggested that breed, age, sex or reproductive status did not contribute to the apparent reciprocal relationship between the prevalence of CaOx and struvite uroliths in cats over the years. When evaluating the more recent data we have at UC Davis (2003-2009), it appears that another change in the urolithiasis trend may be taking place and struvite and CaOx are now submitted in almost equal proportions. While there are several factors that could be contributing to this observed increase in struvite containing stones, it is possible that the changes in formulation of adult maintenance feline diets to minimize the occurrence CaOx
uroliths and/or a decreased use of highly acidifying diets may be influencing the composition of the stones recently submitted from the cat.

In our study, the most common location for both types of uroliths was the bladder. However, a significant increase in the number of upper urinary tract calculi (kidneys and ureters) was found for CaOx containing calculi (p=0.03). Moreover, the total number of struvite containing uroliths reported to have been removed from the upper urinary tract during this same time period was only 8 samples, six of which occurred in or prior to 1991. Lekcharoensuk et al., 5 also reported a similar trend for upper tract CaOx calculi over this time period. Himalayan and Persian cats had a higher risk ratio (RR) for CaOx (RR=4.39 and 2.82 respectively) as compared with their expected breed frequency based on UCD Veterinary Medical Teaching Hospital data. Furthermore, these two breeds also had a higher RR for struvite stones (RR=2.30 and 2.14, respectively). With regards to gender, we reported more CaOx containing stones than struvite containing stones from male cats (most were neutered but that data could not be accurately reported). CaOx urolithiasis has been reported to occur in older cats as compared with struvite urolithiasis which occurs in younger cats.

Canine Struvite and CaOx Containing Calculi
The incidence of CaOx stones appears to have increased over the past 20 years (with a reciprocal decrease in the proportion of struvite uroliths) in stones submitted from dogs. 6,7 In the early 1980’s CaOx containing uroliths comprised approximately 15% of the uroliths we analyzed; by the late 1990’s this had increased to over 50% and this mineral type is now the most common mineral submitted to our laboratory from dogs (Figure 2). The reasons for the long term changes in this trend are likely multifactorial and could include demographic and nutritional changes that occurred during this time period. Some factors might include feeding a more acidified diet, changes in mineral content of the diets, increase in canine obesity and possibly a trend favoring ownership of breeds that are more prone to CaOx. CaOx calculi appear to be more common in older, castrated male dogs; in our study, several small breed dogs (e.g. Bichon Frise, Miniature Schnauzer, Pomeranian, Cairn terrier, and Maltese) have a higher risk of CaOx urolith formation. Although not a small breed dog, we also found the Keeshond was considered clinically at substantially higher risk for forming CaOx stones. 8 This breed is predisposed to primary hyperparathyroidism which may be one reason for its increased risk.

Struvite stones occur in approximately 70-80% of female dogs as compared to male dogs. In dogs, unlike cats, virtually all struvite calculi are infection-induced, usually by Staphylococcus Pseudintermedius or, less commonly, by Proteus mirabilis. These bacteria have the ability to hydrolyze urea to form ammonia and carbon dioxide. This reaction increases the urine pH and makes ammonium available to form magnesium ammonium phosphate crystals. Occasionally, the urine can be supersaturated with the minerals that compose struvite uroliths and stone formation can occur without an infection present. If the urine culture is negative in dogs with struvite uroliths, the stone and/or bladder mucosa can also be cultured to be certain a bacterial pathogen is not present. 9

Struvite Management for Cats
If the urine of a cat with a stone is consistently alkaline (>6.8) or the cat has a history of a struvite stones, it is possible the current urolith present is composed of struvite. Struvite stones often occur as single, smooth stones
when viewed on radiographs. Dissolution of the stone can be attempted by feeding a calculolytic diet (e.g. Royal Canin® Feline Veterinary S/O or Hill’s Prescription Veterinary® Diet s/d®) and monitoring the cat periodically with radiographs. Calculolysis can occur as soon as 8 days in cats, but can take up to several weeks. Therefore, the author performs abdominal radiographs on the cat approximately 3-4 weeks after beginning dietary therapy. If the stone appears smaller, the urine is dilute (<1.016) and the pH appropriate (at least <6.5), the diet can be continued and the cat monitored in another 3-4 weeks. If the stone is not smaller with dietary intervention, the owner should be questioned about what other food and treats the cat is receiving. If the urine pH and specific gravity are not in the desired range with the calculolytic diet chosen, owner compliance should be questioned. If compliance was good, then the stone likely contains minerals other than struvite.

To help prevent recurrence of struvite urolithiasis, a high moisture diet that produces a urine pH<6.8 is advised. Urine acidifiers should only be given to cats with a persistently alkaline pH measured under ad libitum feeding conditions at home. A number of veterinary diets to help prevent the recurrence of struvite stones are available and may be of benefit. A discussion of the current diets marketed for struvite prevention will be presented in lecture. Increased dietary moisture is very important to help dilute the mineral precursors, therefore feeding a canned diet, if the cat will consume one, is advised. The moisture intake of the cat can be evaluated by periodically assessing the urine specific gravity; ideally it should be consistently <1.025. Abdominal radiographs (including the entire urinary tract) of the cat should be performed to assess for new urolith formation. If no stones are present, radiographs should be repeated periodically (every 2-3 months initially, then less often as the disease is managed). If small stones recur, voiding urohydropropulsion may be an option for removal.

To Salt or Not to Salt?
After utilizing strategies to increase the moisture content of the diet in the cat, if the urine is still too concentrated, and/or the urine sediment findings remain abnormal, one can try the addition of sodium chloride (table salt) to the diet to increase the urine volume produced daily. According to the 2006 NRC publication, “Nutrient Requirements of Dogs and Cats”, the upper safe limit of normal sodium intake by cats with unfettered access to water has not been determined, but is greater than 15 gm per kilogram diet, or about 40 grams of salt. Most commercial diets contain less than 1% salt, so cautious addition of a few hundred milligrams per day (1/8 teaspoon of table salt weighs ~300 mg) should not be dangerous in otherwise healthy cats with free access to water. Current recommendations for appropriate salt intake in animals with prior CaOx uroliths are controversial, but sodium chloride supplementation has been reported to increase urinary calcium excretion and increase the risk for CaOx uroliths in humans. In dogs, the calcium excretion was increased when consuming a higher sodium diet, however the calcium concentration and relative supersaturation for CaOx was decreased. Similar studies have not been performed in cats. Caution should be practiced if using dietary salt supplementation to manage lower urinary tract signs, particularly in animals with reduced renal function, cardiac disease or hypertension. No adverse affects of added sodium chloride have been noted in short term published manuscripts and abstracts in healthy cats ingesting diets containing up to 1.1% -1.3% sodium on a dry matter basis.

Struvite Management for Dogs
As mentioned above, struvite-containing stones occur in approximately 70-80% of female dogs as compared to male dogs and are usually caused by urease producing bacteria. Dissolution of canine struvite uroliths can be done in the same manner as described for cats, but proper antimicrobials also need to be given to the dog throughout the entire dissolution protocol. Two diets are currently marketed for struvite dissolution in dogs (Royal Canin® Canine Veterinary S/O or Hill’s Prescription Veterinary® Diet Canine s/d®). If the stones are not decreasing in size upon reevaluation, and owner compliance has been investigated, the stone may have layers of calcium phosphate in the form of apatite, which makes dissolution difficult and the stone should be removed by another method mentioned above.

For preventing recurrence of infection induced struvite stones in dogs, management should be focused on preventing future urinary tract infections. No dietary changes are indicated, but frequent urine cultures are often warranted. The urine should be cultured 5-7 days after completing the antibiotic and then again in another month. If the culture remains negative, subsequent evaluations should be done 2-4 times a year, depending on the case. For more details on diagnostics for dogs with recurrent infections, please see the section entitled, “UTIs in Small Animals: Updates on Antibiotic Protocols.” Abdominal radiographs (including the entire urinary tract) of the dog should be performed to assess for new urolith formation.

Management of CaOx Containing Calculi for Cats and Dogs
Prevention of CaOx containing calculi is similar for both cats and dogs. Once a urolith has been removed, it is recommended to increase the moisture content in the diet for both cats and dogs by feeding a canned diet, if possible, to decrease the urine concentration of stone mineral precursors. There is no dissolution protocol for CaOx uroliths, so removal and quantitative mineral analysis of the stones should be performed if they are growing or causing clinical disease. Animal related factors should be addressed initially to ascertain that no intrinsic predisposing problems are present (e.g. hypercalcemia). After utilizing strategies to increase the moisture content of the diet, if the urine is still too concentrated, or the urine sediment findings remain abnormal, one can try the addition of sodium chloride (table salt) to the diet to increase the urine volume produced daily.

A diet that is restricted in both calcium and oxalate seems logical for animals prone to CaOx urolithiasis, but to the author’s knowledge, no evidence-based studies in dogs and cats with naturally occurring disease are available. Higher intake of dietary calcium (with food) appears to decrease the risk for symptomatic CaOx kidney stones in humans. However, reducing the dietary content of only one of the CaOx precursors could potentially increase the intestinal absorption and urinary excretion of the other. As with excess calcium, foods rich in oxalate or oxalate precursors should also be avoided. For a list of the oxalate content of foods, please see the Oxalosis and Hyperoxaluria Foundation website: http://www.ohf.org/diet.html. High moisture lower calorie, low oxalate treats that are appropriate for dogs and cats may be used for owners who also wish to provide treats for their pet.

Other nutrients to consider in the dietary management of CaOx urolithiasis include magnesium and phosphorus. Urinary magnesium and phosphate (and citrate) are thought to act as inhibitors of CaOx urolith formation and therefore should not be restricted in the diet. Dietary phosphorus should not be excessively restricted because reduced serum phosphorus could result in increased activation of vitamin D₃ to calcitriol by 1-α-hydroxylase in the kidney under the action of PTH and result in increased intestinal absorption of calcium. In contrast Vitamin C supplementation is not recommended, because ascorbate is a metabolic precursor of oxalate. Lastly, dietary fats have been speculated to be involved in CaOx stone formation in rats and humans. Although the pathogenesis of CaOx stone formation in animals may differ, it may be prudent to feed animals with elevated triglycerides a diet restricted in fat (less than 2 gm/100 kcal diet). When choosing a diet, the patient’s entire history and medical conditions need to be considered.

If dietary manipulations are unsuccessful in preventing CaOx urolith recurrence alone, drug therapy may provide additional benefit. Administration of citrate as potassium citrate (Urocit-K®; approximately 50mg/kg PO BID) and hydrochlorothiazide (dog: 2mg/kg PO BID, cat: 1mg/kg PO BID) can be administered. Serum calcium should be evaluated shortly after beginning this drug to ensure hypercalcemia does not occur. While there are no studies as to the efficacy of hydrochlorothiazide in cats with CaOx stones, reports have suggested this dose is tolerated well and did reduce the relative supersaturation for CaOx in healthy cats.

References


