

## **Session 5: Crystals, Stones and Diets, OH MY!**

### **Important Points:**

- Examination of a **fresh** urine sample within minutes of collection and before refrigeration will greatly reduce the formation of crystals during storage and transport and thus reduce misinterpretation of a urine sediment.
- The higher the urine concentration (specific gravity), the more likely crystals are to form
- The lower the temperature of the urine, the more likely crystals are to form
- The lower the concentration of inhibitor substances, the more likely crystals are to form
- The higher the excretion of calculogenic substances, the more likely crystals are to form
- pH can have an impact in the formation of SOME BUT NOT ALL crystals

### Introduction

There are many misconceptions regarding the significance of crystals found on routine urine sediment examination in dogs and cats. The purpose of this discussion is to try to cut through the information down to what we know, what we don't know, and what is "veterinary urban legend".

The precipitation of mineral (calcium oxalate, struvite, urate, cystine) into crystals or stones depends on many factors including the degree of urine saturation with the particular crystalloid, the presence or lack of promoters and inhibitors of precipitation, the diet, the pH of the urine (in some but not all cases), and volume of the urine.

*\*Note: The specific diets listed here are not a comprehensive list and in no way implies my endorsement of any particular product or company. They are examples of available diets as of July 2018.*

### **Crystals – General Information**

Form in concentrated urine (even at neutral pH)

Are dependent on urine pH and temperature as well as osmolality

Not necessarily pathogenic

Do not necessarily show up in cats and dogs with stones

Do not mean that a cat or dog will be a stone former

*Can occur ex vivo in refrigerated urine or if it evaporates. Crystals formed in this manner are not clinically significant.*

Crystals that form while urine is in the refrigerator do not necessarily dissolve if the urine is warmed back up to room/body temperature

### **Stones – General Information**

Pathogenic

More likely to form in concentrated urine

Animals with stones do not always have crystals in their urine, or even crystals of the same type

Some animals are chronic stone formers and may form different types of stones during their life (usu. struvite and calcium oxalate)

May require dietary management to prevent recurrence

### **When are crystals a problem?**

If seen in a patient who is a known stone-former

Patient with lower urinary tract signs

Male cat with history of plug formation/obstruction

Persistent, significant crystalluria noted on a fresh urine sample

### **Struvite**

- Used to be the most common type of stone in both dogs and cats, now appears to be similar in frequency to calcium oxalate in both species
- Struvite is less soluble in pH > 6.7 which is why we see struvite stones and crystals in alkaline urine
- *In dogs* usually associated with UTI of Staph. or Proteus sp. which hydrolyse urea and leads to alkaline urine
- Unlike dogs, most struvite stones in cats between 1-10 years of age are not associated with a UTI
- Struvite stones can be dissolved medically by exclusively feeding a specially designed acidifying, low protein diet (Hills' Prescription s/d or c/d, Royal Canin SO, Blue Buffalo WU, etc)
- It is important to treat dogs with antibiotics or monitor for UTI during the dissolution process since bacterial infection will prevent adequate acidification of the urine

### Diet parameters for Struvite

Increased water intake (canned diet?)

Decreased in phosphorus and Mg

*Moderately* acidifying (pH 6.0 – 6.3)

Lower carbohydrate content

### Dissolution

Royal Canin Urinary SO (high in salt and fat, there is a moderate calorie version), dog and cat

Hill's Prescription Diet s/d, (concerns about long term use due to nutritional deficiencies), dog and cat

Hill's Prescription Diet c/d, esp. feline has recently been shown to dissolve struvite stones in cats.

### Prevention

Royal Canin Urinary SO, dog and cat

Hill's Prescription c/d, dog

Purina UR, cat  
Hill's Prescription c/d Multicare, cat  
Blue Buffalo WU, dog and cat

\*Note: Some companies such as Hill's and Royal Canin have marked other diets in their product lines that meet the relative requirements to maintain low urine saturation levels of calculogenic substances.

### **Calcium Oxalate**

- Urine is oversaturated with calcium and oxalate
- Formation is inhibited by nephrocalcin, uropontin, and Tamm-Horsfall proteins in the urine (inhibit combination of Ca and oxalate)
- Increased urinary citrate (and Mg and pyrophosphate) can combine with calcium and oxalic acid (soluble) and reduce CaOx (insoluble) production
- Hypercalcemia can predispose to hypercalciuria
- *Urine pH itself has little direct effect on the formation of the CaOx crystals, but in patients who produce acidic urine (pH < 6.2), more calcium is excreted and crystal inhibitors may be negatively affected*
- Thus, metabolic acidosis can predispose to hypercalciuria
- Oxalate can be absorbed from the GI tract
- Oxalic acid is an end product of ascorbic acid metabolism (Vitamin C)
- Vitamin B<sub>6</sub> deficiency can increase urinary oxalate levels

### Treatment

CaOx uroliths cannot be medically dissolved

After removal of stones a program of reduction in urinary calcium and oxalate, decreased specific gravity, and stone surveillance needs to be put into place

### Diet parameters for CaOx

Increased water intake (canned?)

Non-acidifying (aims for a pH 6.5 – 7)

Adequate phosphorus and Mg

Adequate Vitamin B<sub>6</sub>

Supplemented with citrate (+/-)

Avoid high protein, high Ca, high Oxalate, high Na diets

### Prevention

Royal Canin Urinary SO (high in salt and fat, there is a moderate calorie version), dog and cat

Hill's Prescription u/d (but some concerns regarding it being too low in protein to be adequate), dog

Hill's Prescription Diet c/d Multicare, cat

Purina UR, cat

### **Urate**

- Associated with hepatic dysfunction, portosystemic shunts (PSS), or dysfunction of the metabolism of uric acid in dogs

- Cats only rarely have an underlying metabolic disorder associated with urate stones
- Dalmatian, English Bulldog, breeds predisposed to PSS (actually all Dalmatians have increased urate in their urine)
- Males > females, likely due to increased incidence of urinary obstruction in males

### Treatment

Low purine (low protein) diets may reduce recurrence as well as assist in dissolution on dogs (Hill's u/d). Monitor for protein defects and supplement carnitine in English Bulldogs. Medical dissolution does not appear to work well in cats.

Allopurinol is a competitive inhibitor of xanthine oxidase which converts hypoxanthine to uric acid in 2 steps. A low purine diet *must* be fed at the same time as allopurinol is used to prevent xanthine stone formation. Other adverse effects are uncommon. 15 mg/kg PO q 12h for dissolution, 5-10 mg/kg PO q 12h for prevention

### Diet Parameters

Low in protein/purines (low in organ meats)  
Mildly alkalinizing of urine (pH 7.0 – 7.5)  
Want to create a low urine specific gravity (< 1.020)

### Diet Options

Royal Canin Urinary UC, dog  
Royal Canin Vegetarian, dog  
Hill's Prescription l/d, dog and cat, but has some organ meat in it  
Hill's Prescription u/d (concerns that it is too low in protein), dog  
Hydrolyzed soy-based diets (RC HP hydrolyzed), dog  
Purina feline HA (1<sup>st</sup> choice for cats), soy-based  
Purina NF (dry only), cat  
Hill's Prescription g/d (dry only), cat

### **Cystine**

- Very rare in cats, uncommon in dogs
- Breed predispositions: DSH and Siamese cats, male dogs, Newfoundlands, Dachshunds, Bassets, English bulldogs, Yorkshire terriers, Chihuahuas, bull mastiffs, Rottweilers, many others identified
- Three types identified: Type I and II have high risk of uroliths from a young age, type III has been seen in Mastifs and related breeds and has a lower lifetime risk of uroliths. Type III cystinuria can be mitigated by castration. All types may be tested for by PennGen at vet.UPenn.edu
- Defect in renal tubular transport of cystine, orinithine, lysine, and arginine (COLA) amino acids (shared transporter) in the proximal tubule
- More likely to precipitate in acidic urine

### Treatment

Medical dissolution has not been a great success

Alkalinize urine – potassium citrate

2-MPG (Thiola) converts cystine to a more soluble compound, GI side effects common  
15-20 mg/kg PO q12h for dissolution, use low end of dose with food for prevention

D-penicillimine – more toxicity reported, mainly GI

15 mg/kg PO q 12h with food

Frequent relapse, need to keep on diet, alkaline urine

### Prevention

Neuter intact males

### Diet Options

Royal Canin UC

Royal Canin Vegetarian

Purina HA

Hill's Prescription u/d

### **General Treatment Guidelines for All Stones**

*The number one thing regardless of crystal/stone type is to reduce urine specific gravity!*

Preferably < 1.030

#### Increase water intake

Canned food

Fountains

Flavored water

More water sources

Salting food is controversial

#### Monitor Urine pH

Fresh Sample

Monitor for recurrence of stones

*Treat crystalluria only if needed*

Dissolution diets will not work unless the owner feeds them exclusively

Stone surveillance program: allows detection and potential voiding urohydropulsion of new stones before they become surgical. This involves monitoring urinalysis to keep pH and specific gravity levels in check, radiographs q 2-3 months, and watching for UTIs.

### **Common Misconceptions**

- *Crystals always need to be treated when seen on a urinalysis* – Only if the patient is a chronic stone former or a male cat at risk of obstructing. A fresh urine sediment needs to be examined to confirm the presence of crystals. Struvite and CaOx crystals can form in normal urine, especially if it is very concentrated. Crystals in and of themselves are not a pathologic process and in cats, are not necessarily a contributor to lower urinary tract

signs. They may be, however, a signal that the cat's urine is very concentrated, and thus may be at risk for lower urinary tract problems.

- *Diet is the only way to manage crystals and stones* – not entirely true. Increasing water intake is one of the most important things that can be done in patients who are stone formers to reduce the saturation of the urine. Simply switching diets alone may not do the trick.
- *Dogs and cats who form one type of stone will generally only form that type of stone* – In fact, many of these animals will form struvite stones once, then form CaOx stones the next time.
- *All cats should start out on an acidifying diet* – this may actually exacerbate the propensity for CaOx stone formation. The growth of acidifying diets on the pet food market may have contributed to the rise in CaOx stones over the last 20 years.
- *Stone analysis is not always necessary* – While we can often make an educated guess regarding the type of stone, it is still important to have the stone analyzed so that appropriate therapy can be instituted. There is little excuse not to analyze the stone when the Minnesota Urolith Center does it at NO CHARGE if you provide history on the patient. The client only has to cover the shipping costs.
- *Calcium Oxalate stones can be dissolved* – not true. These stones must be removed by surgery, voiding urohydropulsion, or lithotripsy.

## References

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