Urolithiasis

Urinalysis for animals with calculi

- Ideal USG
  - <1.020 for dogs
  - <1.030 for cats
- Crystalluria
  - NOT a disease
    - Need to differentiate *in vivo* vs *in vitro* (evaluate sediment within 1 hr)
  - Crystal typed does NOT always predict stone type
- Urate and cystine crystals
  - Warrant further diagnostics/discussion with owners

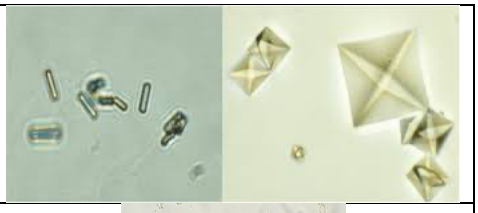
Tips for urine storage

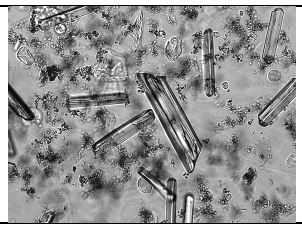
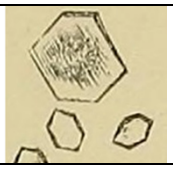
- Do
  - Evaluate within 30-60 min of collection
  - Plate for culture within 60 min of collection
  - Leave at room temp for crystal evaluation
  - Refrigerate if unable to culture immediately
- Don't
  - Send out to reference lab if interested in crystal formation
    - Artifact interference
  - Underutilize free catch urine sample
    - This can be a great way to obtain a sample

Radiographic Density of Calculi

*Radiodense/radiopaque = can be seen on a radiograph (appear white/grey)

*Radiolucent = cannot be seen on a radiograph (appears dark or black)

CaOx	Radiodense	
CaP	Radiodense	

Struvite	Generally Radiodense	
Silica	Radiodense	
Purine	Generally not radiodense	
Cystine	Generally not radiodense	
Mixed/Compound	Varies	

Stone Removal

- Dissolution – struvite and possibly urate
  - No dissolution protocols for CaOx
- Voiding urohydropropulsion
  - Small calculi (2-3 mm)
  - Female
- Baske retrieval
- Laser lithrotripsy
- Surgery
- Radiographic measurements are more accurate than ultrasound
  - Ultrasoudn overestimates the urolith diameter by ~ 50% depending on the size (overlapping edges)

Laser lithotripsy guidelines

Location	Sex	Size limit	Number limit
Urethra	Male dogs	> Urethral diameter	<4
Urinary Bladder	Male dogs	5 mm	<2
Urethra	Female dogs	> Urethreal diameter	<4
Urinary Bladder	Female dogs	10 mm (?)	<4

Canine and Feline Calcium Oxalate

- Signalment
  - Middle aged
  - Male predisposition
    - Anatomic differences, but can also vary by breed
  - At risk dog breeds

        - Standard poodle, Pomeranian, Brussels Griffon, Lhasa Apso, Miniature Schnauzer, Bichon
    - At risk cat breeds
        - Burmese, Persian
- Urolithiasis
    - Monohydrate and dihydrate forms
    - Does not change treatment strategy
    - Most often occur in the bladder
    - If ureteral stones are seen in a cat, they are usually CaOx
- Risk factors
    - Genetics
    - Hypercalciuria (idiopathic)
    - Decreased urine intake
    - Acidified urine (?)
    - Increased protein diet (type)
    - Promotors and inhibitors
    - Ca, Na, vitamin C, Vitamin D

Urine monitoring for CaOx crystals

- Dip strip
    - Read each pad at the designated time
    - Spot reading – interpret values with caution
    - pH: variability of 1 unit (cats)
    - Protein – most sensitive to albumin
- Sediment
    - In vitro crystalluria can occur
    - Analyze within 60 min
    - Increased storage time and decreased temperature is associated with crystals

Nutritional Principles for CaOx

- Specific dietary factors have not been shown to reduce recurrence rate of CaOx
- Overall approach for any urolith
    1. Reduce precursors
    2. Modify pH
    3. Dilure urine
- Goals
    - Reduce dietary excretion of calcium oxalate
    - Dilute urine, more urine volume
    - Increase solubility of urinary Ca
- Not as pH dependent as other uroliths

        - Most diets used are usually acidic enough to dissolve struvite yet can be successfully used to manage CaOx
- Calcium/Creatinine spot samples may allow us to predict/monitor CaOx urolithiasis and response to treatment
- Prevention: High Moisture Diet
    - Most important intervention
        - At 75% moisture diet, drinking stops, at 85%, total intake increases and diuresis results
    - Canned food
    - Dry food with additional water
        - At lease 1:1 volume ratio
    - Increase frequency of urination
        - USG suggestion
            - <1.030 in cats
            - < 1.020 in dogs

Calcium Oxalate and Sodium

- Stimulates thirst and increases urine volume
- Most vet diets are supplemented but some lower sodium options (use KCl instead, which might also decrease hypercalciuria)
- Caution with high sodium and concurrent diseases
    - CHF
    - Renal disease
    - Hypertension
- Studies in both dogs and cats (although short-term) show
    - Urinary calcium concentrations remained constant despite increased excretion
        - Due to increased urine volume
    - RSS (relative supersaturation: measure of risk based on urinary parameters) was unchanged
- Long-term studies are still needed
    - Need to correlate RSS with recurrence

Effects of dietary acidification

- Feline diets formulated to prevent struvite
    - Increase in urine acidity, reduced precursors, encouraged dilution if too extreme, increased urinary calcium excretion (skeletal mobilization)
- Change in trends
    - Moderate pH diets
    - CaOx pH dependent?

- Urinary pH
    - Alters function of urinary inhibitors
        - Decreases urinary citrate (urinary citrate binds to calcium which reduces its activity and prevents crystal growth, it also has an alkalinization effect)
        - May impair protein inhibitors
    - Systemic acidification – increased calcium excretion from bone
    - Likely small influence for CaOx
        - Slightly decreased saturation CaOx pH > 7.2
        - Slightly increased saturation for CaOx pH < 6.5

Controlling precursor excretion

- Oxalate
    - Avoid calcium restriction
    - Avoid oxalate-rich foods
        - Green leafy (kale, spinach), things grown in ground (beets, potatoes) most pulses and nuts, chocolate
        - Stick to berries, melon, dairy, meats, fats
    - Avoid increased intake of oxalate precursors
        - Ox is a byproduct of glycine, serine, hydroxyproline and vitamin C metabolism
        - Hydroxyproline is a structural AA important in collagen

Calcium Oxalate Crystals and Lipids

- Possible role of atherosclerosis in human CaOx disease
- No prospective studies in dogs
- Preliminary work in cats: no increase in calcium or oxilate in urine – contrast to rats
- Consider low fat diet especially in dogs with
    - Hyperlipidemia
    - Obesity
    - History of pancreatitis
- Screening dogs for triglycerides
    - Urolithiasis increased 3.3x for each mmol increase in triglycerides
    - Urolithiasis increased 2.4x per unit increase in BCS
    - Must tailor dietary therapy

Summary for CaOx

Diagnostics

- Evaluate serum calcium and iCa in patients with suspected CaOx uroliths
- Consider calcium:creatinine ratio

- Consider fasting triglycerides
- Monitor for urolith recurrence
    - Radiographis and clinical signs

Prevention

- Urinalysis: USG, sediment
    - Remove stones if recur
- Radiograph animal prior to recovery
    - Stones can be missed during surgery
- Choose a diet
- Monitor environment

Nutritional Management

- High mosture diet
- Moderate/low fat diet
- Low oxalate diet
- Moderate mineral content

Avoid

- High protein diets (>40% ME) or treats (rawhides)
- Poor protein quality
- Vitamin C supplementation
    - Gets metabolized to oxalate
- Excessive vitamin D or Ca^{2+}
- Low calcium diet

Tailored nutritional management

- Most feline and some canine options are dual purpose for both struvite (dissolution and prevention) and CaOx (prevention)
- Make sure to consider the entire pet and check for co-morbidities

Continued recurrence of CaOx

- Potassium citrate
    - Citrate is a weak alkalinizing agent but it forms soluble salts with calcium (calciu citrate is more soluble than calcium oxalate)
- Thiazide diuretics (hydrochlorothiazide)
    - Decreased Ca excretion in the urine
    - Weak diuretic
    - Dogs 2 mg/kg PO BID

    - Cats: 1 mg/kg PO BID

A note on Calcium Phosphate Uroliths

- Rarely occur as a primary stone "tag along mineral"
- Two forms
    - Apatite and brushite
- Can precipitate out with increasing pH (apatite)
- No dissolution protocol; if large component may prevent struvite from dissolving
- Manage the primary stone
- Management similar to CaOx

Canine vs Feline Struvite Urolithiasis

- MAP: Magnesium, ammonium, phosphate
- Most common in the LUT
- Can be seen in the upper urinary tracts of dogs
- Almost always associated with urease-producing bacteria in dogs
    - Staphylococcus pseudintermedius
    - Proteus mirabilis
    - Klebsiella
    - Pseudomonas
    - Providencia
- Urease > hydrolysis of urea forming NH_3 and CO_2
- Usually sterile in cats
- Consider secondary UTI for both species

Why do some dogs fail dissolution?

- Stones are too large
- Another mineral is present
    - CaOx
    - CaP
    - Urate

Antimicrobial duration

- Throughout dietary dissolution
- Considerations
    - Antimicrobial alone without diet?
    - Diet without antimicrobials?
    - Shorter course of antimicrobials?

- Concern for resistance
- Reevaluate and tailor therapy to patient

Contraindications for dissolution

- Urethral obstruction
- Growing animals
- Pregnant/lactating animals
- Fat intolerance
- Large stones that take up bladder capacity

Dissolution of Struvite

- Low in precursors: protein, P, Magnesium
- Acidifying
- Diluting
- Keep dogs on antibiotics
- Radiograph cats @ 2 weeks and dogs @ 4 weeks
- Urinalysis
- USG should be dilute
- Urine pH should be acidic

Struvite prevention in dogs

- No dietary change is often warranted
    - Obese
    - Comorbidity
- Monitor for UTI
    - Urease producing bacteria
- If recurrent UTI
    - Evaluate comorbidities
    - Look at conformation
    - Struvite prevention diet?

Struvite prevention in cats

- Precursors, pH, dilution
- Control intake of protein, P, Mg
- Target urine pH <6.5
- Ad libitum or multiple meal feedings
    - Avoid post-prandial tide?
- High moisture diet
    - USG < 1.030

Urate

Canine Urate Urolithiasis

- Third most common stone in dogs
- 15-20% of stones submitted to our lab
- Must confirm with infrared spectroscopy

Genetic vs. Hepatic dysfunction

- Dalmatians
    - Genetic defect in the uric acid transporters
        - Liver and kidney
    - Simple autosomal recessive trait
        - Decrease hepatic conversion to allantoin
        - Decrease proximal renal tubular reabsorption
    - Mutation in the SLC2A9 gene
        - Many other breeds have the same mutation

Management of Canine Urate

- Precursors, pH, dilution
- Reduced purine intake
    - Low purine protein sources
        - Dairy, egg, many plant sources
        - Avoid organ meat, seafood
    - Low total protein
- Dilute, alkaline urine
    - Water
    - Plant protein sources
    - +/- K citrate

Management for Urate in HUU breeds

- Dissolution usually not very effective
- Low purine diets (based on ingredients)
- Monitor urine, clinical signs, and imaging
    - USG < 1.020
    - Lack of crystalluria
    - pH > 7.5
- Normal ultrasound
    - Not radiographs because these are usually radiopaque
- Allopurinol

    - Xanthine oxidase inhibitor
    - Ideal to titrate dose based on uric acid excretion
        - Clinically not done often
        - If dose is too high, may see xanthine stones
    - Never administer this drug unless feeding a purine restricted diet
        - Xanthine stones!

Management in other breeds (non-HUU)

- Young dogs of non-predisposed breeds
- Clinical signs suggestive for PSS/PVH
    - Search for underlying liver disorder
    - Increase urinary uric acid excretion
- Tx the disorder if possible

Feline Urate Urolithiasis

- 3rd most common urolith
    - Reported recurrence ~13% but variable
    - Egyptian Mau and Siamese are over-represented breeds
- Many cats have LUTS
- No gender predilection
- Poorly understood etiopathogenesis
    - Most do not appear to have underlying liver disorders
    - PVH, portovascular shunt

Urate prevention: Cats

- Most do not have underlying liver disorder
- High moisture, low protein, less acidifying diet
    - Diets for CKD or Soy-based diet
- Monitor USG
- Ultrasound periodically
- Further dx in recurrent cases

Cystine

Cystine Urolithiasis

- 4-7 years of age, with most <7 years of age
- Genetic defect – testing not available for all types
- Mutation in SLC3A1
    - Type I-A: Autosomal recessive (Newfoundlands and Labs)
    - Type II-A: Autosomal dominant

- Mutation in SLC7A9
    - Type IIB: Autosomal dominant
- Androgen dependent Type III
    - English Bulldog, French Bulldog, English Mastiff

Treatment and prevention

- Precursors, pH, dilution
    - Diet low in protein (methionine, cystine precursors)
    - Alkaline, dilute urine
    - Same diets as used/marketed for urate
- Monitor ultrasound and urinalyses
    - Dilute, alkaline urine (USG <1.020, pH >7.5)
    - K citrate preferred over NaHCO3
        - Sodium bicarbonate increases cystine excretion (unwanted)!
- Neutering males (androgen-dependent form of disease, and genetic disease)
- Drug option?
    - Thiola
        - Acts by thiol disulfide exchange reaction
        - Forms disulfide with cysteine and decreases cystinuria
        - Expensive $$$
        - Side effects
            - GI and aggression
        - D-penicillamine
            - GI side effects are usually more severe

Silica

Silica Urolithiasis

- Uncommon in dogs, not reported in cats
- “Jack-like” appearance
- Most often in bladder/urethra
- Primarily larger, male dogs
- Role of diet is unclear
- Rule our dirt/sand eating, water content
- People: Beer and supplements
- Older study: high corn gluten feed or soybean hulls
- Plant breeding for drought tolerance = more silica in plants
- Breeds: GSD, Labs, Goldens, Old English Sheepdog – often older, male

Silica Management

- Precursor, dilution (not pH responsive)
- Consider a diet low in carbohydrate (high in fat and protein) if tolerated, avoid high silica foods
    - Banana, dates, whole grains, pineapple, mango, legumes, spinach, beer
    - Tropical fruits? Maybe because they grow in sand??
- Increase moisture intake
- Monitor with radiography and urinalyses
- Recurrence rates are usually low

Mixed compound stones

- Mixed urolith
    - Mineral mixed throughout
- Compound urolith
    - Core and shell different mineral composition
- Both can result due to change in urine composition during stone growth
- Preventive measures targeted to core composition
    - Urolith nucleus