Canine Urolithiasis

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Urolithiasis Outline

- Signs to watch for
- How formed
- How diagnose
  - Imaging brief
- General treatments
- Identification
  - Including “guess”
- The Stones
  - CaOx
Clinical Signs at Home

- Straining
- Frequent urination
- Unsuccessful urination
- +/- blood
  - Importance of UA
- +/- smell

- Pain
- Appetite change
- Signs of kidney involvement
- No signs
Oversaturation

- Intermittent
- Thermodynamic solubility product ($K_{sp}$)
  - Stable, crystals don’t form
- Formation product ($K_f$)
  - Cannot stay in solution
Nucleation

- Takes a higher conc if homogenous
- Crystal precipitation
  - Matrix: proteins, Gag’s
  - Mineral lattice
  - Casts, epi cells, heterogenous, suture
Nucleation Significance

- Most important for
  - Struvite
  - Cystine
  - Urate
- Treatments aimed at decreasing crystal concentration
  - pH
  - Specific gravity
Growth

- Once nucleation
  - Just need supersaturation
  - Less than for nucleation
- Aggregation > Growth
  - Nephroliths
Significance of Growth

- CaOx
- CaPO₄
- Decreasing crystal presence in the urine difficult
  - Tx to stop the combination
    - Citrate
    - Tamm-Horsfall mucoproteins
Retention

- Key to allow growth and nucleation

Nucleation
- Requires high concentration
- Kf met

Growth
- Aggregation
- Lower concentration

Retention
- If keep material in
Underlying Disease

- Liver disease
  - Urate
- Hypercalcemia
  - Calcium oxalate, Calcium Phosphate
- Infection
  - Struvite in dogs
- Iatrogenic
  - Allantoin, xanthine
Underlying Deficiencies?

- Decreased inorganic inhibitors in urine
  - Decreased citrate
    - Metabolic acidosis causes
  - Magnesium
    - Both this and citrate important for CaOx
  - Phosphate
    - Dietary pyrophosphate
Deficiencies of Anti-aggregate

- Nephrocalcin
  - Product of proximal tubule and thick asc limb
  - Potent aggregate inhibitor
- Tamm-Horsfall mucoproteins
  - Damaged with ammonia (struvite)
  - Made in thick ascending limb and distal tubule
Why Identify?

- Analysis because
  - Look similar
  - Mixed stones
  - Changes treatment
  - Changes prognosis
Techniques

- Quantitative methods best
  - Optical crystallography
  - X-ray defraction
  - Infrared Spectroscopy
Once Identified- Treat

- Treatments
  - Treat underlying cause
  - Decrease sp gravity
  - Complete any cycle
  - Stop aggregation
    - Decrease crystals (some)
  - Medical dissolution
Crystal inhibit

- Best for these stones:
  - Struvite
  - Cystine
  - Urate

- Crystal inhibitors
  - Complexing ions
  - Mucoproteins (GAGS)
  - Aggregation inhibitors
  - Specific gravity
When Crystals are Important

- **Type**
  - Struvite and urate have association
  - Cystine, xanthine, urate (not dalmation)

- **Medical history**
  - Not predictive of stone- 50%
  - Previous tx?

- **Signalment**
  - Juvenile dalmations
  - Male dogs and cats have increased obstruction
  - Increased risk in some breeds for urolith formation

- **Known/prior urolithiasis**

- **Obstruction**

- **Persistent or particularly heavy crystalluria**
<table>
<thead>
<tr>
<th>Composition</th>
<th>Density</th>
<th>Surface</th>
<th>Urine pH</th>
<th>UTI</th>
<th>Other</th>
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</thead>
<tbody>
<tr>
<td>CaOx</td>
<td>+++-</td>
<td>Sharp, mulberry, smooth</td>
<td>Acid to neutral</td>
<td>+/- 2°</td>
<td>Hypercalcemia, multiple, upper urinary</td>
</tr>
<tr>
<td></td>
<td>+++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Struvite</td>
<td>+++-</td>
<td>Single- sm to spicules Mult- smooth or pyramid</td>
<td>alkaline</td>
<td>1°</td>
<td>&gt;10 cm, rarely nephrolith but irregular</td>
</tr>
<tr>
<td></td>
<td>+++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urate/ Xanthine</td>
<td>0--</td>
<td>Mult smooth</td>
<td>acidic</td>
<td>+/- 2°</td>
<td>PSS, liver Dz, yellow green</td>
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<tr>
<td>Cystine</td>
<td>++++</td>
<td>Mult smooth</td>
<td>acidic</td>
<td>+/- 2°</td>
<td>Urine cyanide-nitroprusside; metab. screen</td>
</tr>
<tr>
<td>CaPO4 Hydroxyapatit</td>
<td>+++-</td>
<td>H: multi, sm, shape vary B: mult sm round or pyramid</td>
<td>H: alk to Nuetral B: acidic</td>
<td>+/- 2°</td>
<td>hypercalcemia</td>
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<tr>
<td>Brushite</td>
<td>++++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silica</td>
<td>+++-++++</td>
<td>jacks</td>
<td>Acid to N</td>
<td>+/- 2°</td>
<td>M&gt;&gt;F</td>
</tr>
<tr>
<td>Calcium Oxalate</td>
<td>Struvite</td>
<td>Urate/Xanthine</td>
<td></td>
<td></td>
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<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lhasa Ahpso</td>
<td>Mini Schnauzer</td>
<td>Dalmation (+/- juvenile)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miniature Schnauzer</td>
<td>Shi Tzu</td>
<td>English Bulldog</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Bichon Frise</td>
<td>Bichon</td>
<td>Mini Schnauzer</td>
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<td></td>
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<tr>
<td>Chihuahua</td>
<td>Mini poodle</td>
<td>Shi Tzu</td>
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<tr>
<td>Maltese</td>
<td>Cocker spaniel</td>
<td>Yorkie</td>
<td></td>
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<tr>
<td>Cairn</td>
<td>Lhasa Apso</td>
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<tr>
<td>Yorkshire</td>
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<td></td>
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</tr>
<tr>
<td>Pomeranian</td>
<td></td>
<td>Any liver disease though</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mini Poodle</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Shih Tzu</td>
<td></td>
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</tbody>
</table>
## Stone Breeds Cont’d

<table>
<thead>
<tr>
<th>Cystine</th>
<th>Calcium Phosphorous</th>
<th>Silica</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastiff</td>
<td>Same as CaOx</td>
<td>German Shepherd</td>
</tr>
<tr>
<td>Australian shepherd</td>
<td>-except NOT Chihuahua</td>
<td>Labrador retriever</td>
</tr>
<tr>
<td>English Bulldog</td>
<td>Cocker spaniel</td>
<td>Golden Retriever</td>
</tr>
<tr>
<td>Staffordshire terrier</td>
<td></td>
<td>Mini Schnauzer</td>
</tr>
<tr>
<td>Newfoundland</td>
<td></td>
<td>Shi Tzu</td>
</tr>
<tr>
<td>Dachsund</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Stones

- Brief review of most common
- Focus on CaOx
Urate/Xanthine

- Xanthine Oxidase
  - Metabolite 3 and 4
  - Allopurinal Tx (inhibits)
- Uricase
  - Uric acid to Allantoin
- Dalmation
  - Normal amount
  - Defective
  - Low TammH.

Allantoin ➔ Uric Acid (4) ➔ Xanthine (3) ➔ Hypoxanthine (2) ➔ Purine ➔ Uric acid to Allantoin
Cystine

- Breeds have cystinuria
  - Rarely young, decreases as age
- Freely filtered, absorbed at proximal tubule
  - Defective transporter
  - Autosomal recessive in Newfie
- Prevention
  - Previously mentioned
    - Test= negative cyanide nitropruside in urine
Top Two Stone Types

- **Struvite**
  - Dog = infection
  - Urease producing bacteria
  - Often younger dogs
  - Can medically dissolve

- **Calcium Oxalate**
  - Almost number 1
  - Breed specific
    - Often no underlying hypercalcemia
  - Older age
  - Surgical removal
  - 50% recur 4-6 months
Struvite

- Canine often infected
- Urease breaks down urea
  - Ammonium
  - Bicarb- makes pH change
- Cause of medical treatment failure
  - Don’t control the UTI
  - Ca++ or >20%
  - Not struvite at all
- Prevention- reculture
  - Acidifiers not needed
Calcium Oxalate Stones
Focus on Early Recognition

- Breed and sex predilection
- Previous stone
  - Recheck radiographs 4-6 months
  - Lower urinary tract signs important
- Removal
  - Surgery
  - Lithotripsy or basket
  - hydropulpulsion
Ions of Interest

**Calcium**
- Freely filtered
- Hypercalcemia causes
  - Rule these out, treat
- Hypercalciuria
  - Absorption- jejunum
  - Renal leak
  - Resorptive
- PTH, vit D

**Oxalate**
- Freely filtered
  - Bidirectional tub. transport
- Greater effect on crystallization
- Liver metabolism
  - Ascorbic acid
  - Glycine
  - Glyoxylate
- Gut- Oxalobacter formigenes
- Genetic
Miniature Schnauzer

- 5/6 hypercalciuria

- Three with hyperoxaluria
  - Had stones, no further evaluation
  - Tubular reabsorption
    - Na or bicarb linked transporter
Hepatic Path

- HepG₂ cells in humans
  - contain oxalate, glyoxylate, and glycolate as intracellular metabolites
  - excrete oxalate and glycolate
- 2 suspect enzymes for glycolate → oxalate
  - lactate dehydrogenase in peroxizomes
  - alanine:glyoxylate aminotransferase (AGT)₂
    - Vitamin B₆ co-factor
      - Deficient in people, rats, and cats
What about other Species?

- Others are deficient in vitamin B6
- Humans get supplemented

Can this be true in Dogs?
- Time to explain the yellow pages in the hospital
Literature Search

- Can find minimal information on dogs
  - Hyperoxaluria in Schanuzers
    - Not further evaluated
  - Only one source for vitamin B6 and dogs
- We can measure Vitamin B12
  - Similar- absorbed GI, used in many places, water soluble
- Leads to the question- why not?
The Why Not

- No method for evaluation
- High Powered Liquid Chromatography
  - Developed a method to recognize B6 in water
  - Extraction from canine serum
The Plan

- Sample dogs with confirmed CaOx stones
  - ISU VMC
  - Stone Center, University of Minnesota
  - Predisposed
- Compare to healthy, non affected dogs
  - Non-predisposed
- Fasted serum samples
- “Healthy”
Preliminary Findings

- HPLC- Up and running
  - Validated this summer
- Pilot study
  - 3 stone formers
  - 2 predisposed but unaffected
  - 4 non-predisposed breeds, unaffected
Bichon Frise Study

- Goal: 16 each
- Preliminary findings
- Interesting not-age
  - Changes how genetics would be evaluated
Future Evaluation

- Oxalate source
- Urine oxalate in Bichon Frise
- Affect of B6 on Oxalate in urine
  - And on recurrence
References

Thank You!