* Urolithiasis is common in dogs and cats
  * 99% of uroliths occur in the lower urinary tract
  * Urolith formation is not a specific disease, but the sequelae to a group of underlying disorders
  * Urolith formation 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 is erratic and unpredictable emphasizing that several interrelated physiologic and pathologic factors are often involved
  * Mere presence of uroliths, however, does not necessitate their removal
  * Approximately 98% of uroliths occur in the lower urinary tract

* Composition of uroliths
  * Approximately 80% of canine uroliths and 90% of feline uroliths are either struvite or calcium oxalate
  * Calcium oxalate and struvite occur at approximately even frequency although struvite occurs more commonly now (slightly)
  * The third most common type of mineral is urate
  * Other types – including compound uroliths (uroliths composed of more than 2 minerals) occur less frequently

* Urolith formation is dependent on a combination of many factors
  * Urine pH
  * State of saturation – related to concentrations of minerals in urine
  * Inhibitors and promoters of urolith formation
  * Complexors
  * Macrocristalline matrix

**Determination of urolith composition**
* Uroliths that are voided or removed may be submitted for quantitative analysis, which is best.
* A “guesstimate” of urolith composition can be made using readily available information
  * This may help to determine whether to attempt medical dissolution or not

* Urine pH
Urine pH values commonly associated with formation of uroliths in dogs and cats.

<table>
<thead>
<tr>
<th>Urolith Type</th>
<th>pH in Dogs</th>
<th>pH in Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sterile Struvite</td>
<td>&gt; 6.5</td>
<td>&gt; 6.5</td>
</tr>
<tr>
<td>Infection Induced Struvite</td>
<td>&gt; 7.0</td>
<td>&gt; 7.0</td>
</tr>
<tr>
<td>Calcium Phosphate Apatite</td>
<td>&gt; 7.0</td>
<td>&gt; 7.0</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>&gt; 7.0</td>
<td>&gt; 7.0</td>
</tr>
<tr>
<td>Brushite</td>
<td>&lt; 7.0</td>
<td>&lt; 7.0</td>
</tr>
<tr>
<td>Urate</td>
<td>&lt; 7.0</td>
<td>&lt; 7.0</td>
</tr>
<tr>
<td>Calcium Oxalate</td>
<td>&lt; 7.0</td>
<td>&lt; 7.0</td>
</tr>
<tr>
<td>Cystine</td>
<td>&lt; 7.0</td>
<td>&lt; 7.0</td>
</tr>
<tr>
<td>Silica</td>
<td>&lt; 7.0</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
**Crystalluria**

Characteristics of some urine crystals

<table>
<thead>
<tr>
<th>Type</th>
<th>Appearance</th>
<th>pH where commonly found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ammonium urate</td>
<td>Yellow-brown spherulites, thorn apples</td>
<td>+</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Reddish-brown needles or granules</td>
<td>+</td>
</tr>
<tr>
<td>Cal Ox dihydrate</td>
<td>Small colorless envelopes (octahedral form)</td>
<td>+</td>
</tr>
<tr>
<td>Cal Ox monohydrate</td>
<td>Small spindles, &quot;hemp seeds&quot; or dumbbells</td>
<td>+</td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>Amorphous, or long thin prisms</td>
<td>±</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Flat colorless plates with corner notch</td>
<td>+</td>
</tr>
<tr>
<td>Cystine</td>
<td>Flat colorless hexagonal plates</td>
<td>+</td>
</tr>
<tr>
<td>Hippuric acid</td>
<td>4 to 6-sided colorless elongated plates or prisms</td>
<td>+</td>
</tr>
<tr>
<td>Leucine</td>
<td>Yellow-brown spheroids with radial and concentric laminations</td>
<td>+</td>
</tr>
<tr>
<td>Struvite</td>
<td>3 to 6-sided colorless prisms</td>
<td>-</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>Fine colorless or yellow needles arranged in sheaves or rosettes</td>
<td>-</td>
</tr>
<tr>
<td>Uric acid</td>
<td>Diamond or rhombic rosettes, or oval plates, structures with pointed ends. Occasionally six-sided plates.</td>
<td>+</td>
</tr>
</tbody>
</table>

+ = Crystals may occur at this pH, but are more common at the other pH.
**Bacterial urinary tract infection**
* Certain bacteria cause uroliths to form while other bacteria are present because uroliths are a break in host defenses
  * Bacteria that produce urease (primarily Staphylococcus spp and Proteus spp; rarely Mycoplasma/Ureaplasma or other bacteria) result in struvite formation – we will discuss later

**Radiographic characteristics of uroliths**

<table>
<thead>
<tr>
<th>Mineral Type</th>
<th>Degree of Radiopacity</th>
<th>Shape</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystine</td>
<td>+ to ++</td>
<td>Smooth; usually small; round to oval</td>
</tr>
<tr>
<td>Calcium Oxalate Dihydrate</td>
<td>++++</td>
<td>Often rough; round to oval (occasionally jackstone).</td>
</tr>
<tr>
<td>Calcium Oxalate Monohydrate</td>
<td>+++</td>
<td>Often smooth, round (occasionally jackstone).</td>
</tr>
<tr>
<td>Struvite</td>
<td>+ to +++</td>
<td>Smooth; round or faceted; sometimes assume shape of renal pelvis, ureter, bladder, or urethra; sometimes laminated.</td>
</tr>
<tr>
<td>Calcium Phosphate</td>
<td>++++</td>
<td>Smooth; round or faceted.</td>
</tr>
<tr>
<td>Ammonium Urate and Uric Acid</td>
<td>0 to ++</td>
<td>Smooth but occasionally irregular; round or oval.</td>
</tr>
<tr>
<td>Silica*</td>
<td>++ to +++</td>
<td>Typically jackstone.</td>
</tr>
<tr>
<td>Mixed and Compound</td>
<td>+ to +++</td>
<td>Varies with composition. May have detectable nucleus and shell.</td>
</tr>
<tr>
<td>Matrix</td>
<td>0 to +</td>
<td>Usually round, but may be influenced by location.</td>
</tr>
</tbody>
</table>

* Not observed as a primary mineral in cats.

- Intravenous urography should be considered for patients with renal and/or ureteral uroliths
- Double contrast cystography may be necessary for radiolucent urocystoliths
- Contrast urethrogram may be necessary in some cases of urethral obstruction

**Serum and urine biochemical analysis**
* Serum calcium concentration should be checked in cases of calcium oxalate uroliths because hypercalcemia is a risk factor
* Hyperadrenocorticism increases risk of calcium oxalate urolith formation (due to hypercalciuria) and struvite formation (due to bacterial urinary tract infection)
* Infection-induced struvite uroliths may form in animals with other immunosuppressive diseases (eg Feline leukemia virus or feline immunodeficiency virus infections) or in those receiving immunosuppressive drugs
* Urate uroliths may form in animals with liver disease (eg portosystemic shunts)

**Signalment**
* Any type of urolith may form in any animal; however, certain breeds are known to have higher risk for forming certain types of uroliths
  * Dogs
    * Miniature schnauzers have increased risk for calcium oxalate, struvite and urate (due to portosystemic shunts)
    * Dalmatians have increased risk for urate (due to difference in metabolism of uric acid)
    * English bulldogs have increased risk for urate and cystine
    * Cystine uroliths are commonly found in Dachshunds, Newfoundland dogs, and Scottish terriers
    * Calcium oxalate uroliths typically form in small breed dogs such as Miniature schnauzers, Yorkshire terriers, and toy poodles
    * Struvite uroliths tend to occur in female dogs more often than in male dogs
    * Metabolic uroliths tend to occur in male dogs more often than female dogs
  * Cats
    * Longhaired cats (eg Burmese and Himalayans) have a higher risk for calcium oxalate formation
Struvite stones (not associated with bacterial urinary tract infection) typically form in cats less than 10 years of age

Table. Checklist of factors that suggest the probable mineral composition of uroliths.

1. Urine pH
   a. Struvite and calcium apatite uroliths - usually alkaline (Table). Sterile struvite uroliths may be observed with urine pH is 6.5 or higher.
   b. Ammonium urate uroliths - acid to neutral.
   c. Cystine uroliths - acid*
   d. Calcium oxalate - often acid to neutral*
   e. Silica - acid to neutral* (only in canine)
2. Identification of crystals in uncontaminated fresh urine sediment, preferably at body temperature.
3. Type of bacteria, if any, isolated from urine.
   a. Urease-producing bacteria, especially staphylococci and less frequently Proteus spp, are typically associated with canine struvite uroliths. Ureaplasma may cause struvite uroliths in dogs.
   b. Urinary tract infections often are absent in patients with calcium oxalate, cystine, ammonium urate, and silica uroliths.
   c. Calcium oxalate, cystine, ammonium urate, and silica uroliths may predispose patients to urinary tract infections; if infections are caused by urease-producing bacteria, struvite may precipitate around metabolic uroliths.
4. Radiographic density and physical characteristics of uroliths (Table).
5. Serum chemistry evaluation
   a. Hypercalcemia may be associated with calcium-containing uroliths.
   b. Hyperuricemia may be associated with uric acid or urate uroliths.
   c. Hyperchloremia, hypokalemia, and acidemia may be associated with distal renal tubular acidosis and calcium phosphate or struvite uroliths.
6. Urine chemistry evaluation
   a. Patient should be consuming a standardized diagnostic diet, or the diet consumed when uroliths formed.
   b. Excessive quantities of one or more minerals contained in the urolith are expected. The concentration of crystallization inhibitors may be decreased.
7. Breed of dog and history of occurrence of uroliths in patient's ancestors or littermates.
8. Quantitative analysis of uroliths fortuitously passed during micturition, or collected via catheter technique.

* Concomitant infection with urease producing microbes may result in formation of alkaline urine.

STRUVITE UROLITHIASIS

* Infection-induced struvite are the most common form occurring in dogs; whereas sterile struvite is the most common form occurring in cats
* However, any animal that develops a bacterial urinary tract infection with a urease-producing microorganism can develop infection-induced struvite uroliths
* Sterile struvite uroliths have been documented to occur in dogs, but it is very rare

* Dogs:
* Struvite uroliths typically, but not always, form in female dogs (because of their higher risk for development of a bacterial urinary tract infection), and in dogs with immunosuppressive diseases or receiving immunosuppressive therapy because of their increased risk for bacterial urinary tract infections.
* They can occur at any age, but are more common in young adult dogs.
* They are the most common type of urolith in puppies (dogs < 1 year of age)

* Cats:
* Sterile struvite is the most common type of struvite urolith occurring in cats.
* It typically occurs in young adult cats.
* In older cats (>10 years) and in kittens (<1 year), infection-induced struvite urolith formation is more common than formation of sterile struvite uroliths because of their increased risk for development of a bacterial urinary tract infection
* Remember, crystalluria is not synonymous with urolithiasis.
* In healthy dogs, more than 50% of urine samples will contain struvite crystals without a bacterial urinary tract infection and without subsequent urolith formation
* Likewise, some animals with active stone disease will not have crystals; however, most animals with active struvite stone disease will be crystalluric
* “Guesstimation” that is consistent with struvite uroliths
  * Urine pH: alkaline
  * Crystals: struvite
  * Bacterial urinary tract infection:
    * Yes, if infection-induced struvite uroliths
    * Should be a urease-producing micro-organism
      * Typically Staphylococci spp
      * Occasionally Proteus spp
      * Rarely other bacteria such as Klebsiella and Streptococcus
      * Rarely Mycoplasma/Ureaplasma
      * Never Escherichia coli
    * No, if sterile struvite
      * Unless a secondary bacterial urinary tract infection has occurred
  * Radiographic appearance
    * Density: radiodense
    * Size:
      * Infection-induced: typically variable sized including some fairly large stones
      * Sterile: typically small (<5-10 mm)
    * Surface contour: typically smooth
    * Shape:
      * Infection-induced: often pyramidal shaped, similar to river rocks
      * Sterile: usually round, but can be wafer-like
    * Number:
      * Infection-induced: usually many dozen
      * Sterile: usually small number (perhaps 1-a dozen or so)
  * Serum and urine biochemical analysis
    * Often normal, especially in cats
    * In animals with infection-induced struvite, predisposing metabolic causes for bacterial urinary tract infection may be present
      * Cushing’s disease
      * Diabetes mellitus
      * FeLV/FIV
* Signalment
  * Infection-induced:
    * Young to middle-aged adult female dogs
    * Pediatric or geriatric dogs and cats (due to predisposition to bacterial urinary tract infection
    * More common in females than males
  * Sterile:
    * Usually young adult cats (same is true in the few reported cases of dogs)
    * No gender or breed predisposition

Etiologic and Pathophysiologic Points:
* Infection-induced struvite
  * A urinary tract infection with urease-producing bacteria (usually Staphylococci and Proteus spp; rarely other bacteria and Ureaplasma/Mycoplasma) occurs
  * Results in urease-mediated metabolism of urea to ammonium and carbonate
* Ammonium comes from the ammonia liberated from urea buffering hydrogen ion in urine
  * Results in an alkaline pH
  * Changes ionization state of phosphorous
* Magnesium is typically present in low amounts in urine
* Phosphorous is present in high amounts and is a strong and important buffer (in acid-base metabolism) called “titratable acid”
* These conditions favor formation of uroliths containing struvite (Mg$^{2+}$NH$_4^+$PO$_4^{3-}$), with some “contaminant” minerals: calcium apatite and carbonate apatite
* Struvite is less soluble (more likely to precipitate) when the urine pH is > 6.8, and is more soluble (more likely to stay in solution) when the urine pH is < 6.8
* REMEMBER: these are called infection-induced struvite stones

**Bacteria and struvite**

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* **Sterile struvite**
  * Sterile struvite typically forms in cats; however, it has been reported to occur rarely in dogs
  * Sterile struvite uroliths are typically composed of 100% struvite and do not contain “contaminant” minerals
  * The mechanism(s) for sterile struvite formation is not clear, although an alkaline urine pH is necessary
    * Persistent or recurrent alkaluria is a predisposing risk factor for sterile struvite formation
    * Because of the carnivorous nature of cats, a “post-prandial alkaline tide” occurs and can be profound
      * It is thought that with a high protein intake, a large amount of HCl is produced and excreted into the gastric lumen to begin digestion of protein (acid-mediated proteolysis)
      * This results in a metabolic alkalosis
      * Kidneys respond by excreting less acid and more base
      * This results in alkaluria
      * This is the reason most cat foods are “acidifying” – to minimize the post-prandial alkaline tide and prevent struvite formation
  * Other factors have a role
    * Highly concentrated urine resulting in retention of urine and concentration of calculogenic minerals
    * High levels of magnesium and phosphorous in urine

**Therapeutic Points:**
* Overview of therapy
  * Eliminate existing uroliths
  * Eradicate or control bacterial urinary tract infection
  * Prevent recurrence of uroliths
* **Surgical removal** – Will be discussed in surgery section
* **Minimally invasive procedures** – Will be discussed in next lecture
* **Medical dissolution**
Infection-induced struvite

- Can be dissolved medically, or removed physically (surgery or voiding urohydropropulsion) – or combinations
- Protocol:
  - Control and/or eradicate the bacterial urinary tract infection
  - Choose appropriate antibiotic
  - Must be administered during entire time of medical dissolution. Bacteria are trapped in matrix of urolith and released as the stone dissolves from the outer layers inwards (similar to an ice cube melting in a glass of water)
  - The struvite dissolution diet induces a diuresis, which may decrease efficacy of antimicrobial (although rarely are changes in dosage necessary)
- Calculolytic diet (struvitolytic diet)
  - Currently, only 1 diet has data documenting its efficacy in medical dissolution of struvite – Hill’s Prescription Diet s/d
- Diet is:
  - Lower in protein (source of urea and therefore ammonia)
  - Lower in magnesium
  - Lower in phosphorous
  - Acidifying
  - Diuresis (to stimulate thirst and urine output)
- Although infection-induced struvite stones may dissolve with antibiotic therapy alone, it takes much longer than the combination of antibiotic and struvitolytic diet, and is less successful
- Average time for dissolution is 8 weeks
  - Monitor animal every 4 weeks
  - Urinalysis – should find aciduria, no crystalluria, no inflammation
  - Urine culture, if necessary
  - Survey abdominal radiography (at least a lateral view) to monitor dissolution
- Dissolution therapy should continue for 2-4 weeks beyond radiographic evidence of dissolution of uroliths to ensure all stones are dissolved
- Complications of medical dissolution
  - Recurrent urethral obstruction
  - Continued clinical signs of lower urinary tract disease (although signs typically resolve, except for polyuria/polydipsia, within 3-5 days of starting dissolution therapy)
  - Reaction to antimicrobial
  - Problems with diet
    - A very low protein diet – protein malnutrition may develop
    - Prolonged feeding of diet – it is not intended for long term consumption
    - Use cautiously if at all in pediatric patients, especially those in rapid growth phase
    - Contra-indicated in pregnant animals
    - Usually see an increase in alkaline phosphatase activity and a decrease in blood urea nitrogen concentration because of the low protein content
    - In addition to pregnant animals, contra-indicated in:
      - Hypertensive patients or those that cannot tolerate a sodium load
      - Those with renal failure – acidifying, hypokalemia
      - Animals that cannot tolerate a high fat intake – diet is high in fat

- An alternative dissolution protocol has been shown to be effective in > 80% of dogs
  - In this protocol, the diet is not changed; instead a urinary acidifier (d,l-methionine) is administered in combination with an appropriate antibiotic for the organism responsible for struvite formation (typically Staphylococcus)
  - Dissolution occurs in 4-8 weeks
  - Advantage is that the diet does not require changing and the acidifier is safe
  - Disadvantage is that in the one study, 2 dogs had a shell of calcium phosphate that appeared to impede dissolution – this could be due to “over” acidification
Sterile struvite
* Can be dissolved medically or removed physically
* Protocol:
  * Feed struvitolytic diet
  * Antimicrobials are not necessary unless a secondary infection is present (one that would not be associated with struvite formation)
  * Other aspects are similar to management of infection-induced struvite uroliths
  * Sterile struvite uroliths typically dissolve in 2-4 weeks; therefore, at recheck at 4 weeks, uroliths may no longer be visible on survey abdominal radiographs
  * Feed diet for 2 to 4 weeks beyond medical dissolution

Prevention of struvite uroliths
* Successful prevention of struvite uroliths involves modifying risk factors to decrease risk of re-formation
* Infection-induced struvite:
  * Most important component of prevention is preventing the bacterial urinary tract infection
  * REMEMBER: these are called infection-induced struvite
  * If predisposing risks for recurrent bacterial urinary tract infections cannot be modified, then treat the animal as having a complicated bacterial urinary tract infection, and take appropriate prophylactic steps (see notes on urinary tract infections)
  * Dietary modification for prevention of infection-induced struvite uroliths is not warranted, and often not successful
* Sterile struvite:
  * Dietary modification is often required to decrease risk of recurrent sterile struvite urolith formation
  * Specific struvite preventative diets are modified to decrease risk

URATE UROLITHIASIS
* Urate comprises 5-8% of uroliths retrieved from dogs and cats
  o Most commonly, ammonium urate is the primary salt
  o It is the second most common mineral found in uroliths from dogs and cats < 1 year of age behind infection-induced struvite
* Normally, non-primate mammals have allantoin as end-product of purine metabolism
  o Purines are nitrogen-containing compounds involved in nucleotide bases (adenine and guanine) – y’know DNA and RNA
  o Sources of purines include diet (highly cellular) and endogenous turnover of cells as well as de novo synthesis (production of purines from non-purine precursors)
    • Related compounds are methylxanthine (bronchodilators), caffeine, and theobromine (found in chocolate)
  o The purine pathway eventually terminates in allantoin, which is highly soluble and excreted in urine
    • Hypoxanthine is converted to xanthine and xanthine to uric acid by xanthine oxidase
    • Uric acid is metabolized by hepatic uricase to allantoin
For urate uroliths to form, urine must be oversaturated with ammonia and uric acid, which can occur associated with:

- **Liver disease** – particularly portovascular anomalies
- **Genetic predisposition** – e.g. Dalmatians and English bulldogs

**Clinical Diagnostic Points**

- Ammonium urate is the third most common occurring mineral found in uroliths from dogs and cats
- Urate uroliths may form secondary to liver disease, especially portovascular anomalies, or in genetically predisposed breeds (e.g. Dalmatians).
- Guesstimation that is consistent with urate uroliths
  - Urine pH: acidic
  - Crystals: urate or amorphous urates
  - Bacterial urinary tract infection – secondary to uroliths, if present
  - Radiographic appearance:
    - Density: radiolucent
    - Size: small
    - Surface contour: smooth
    - Shape: round
    - Number: numerous
  - Serum and urine biochemical analysis
    - With liver disease
      - Possibly increased liver enzymes
      - Decreased BUN
      - Microcytosis (with portovascular anomaly)
      - Hyperammonemia
    - Without liver disease
      - Usually normal
  - Signalment
    - With liver disease
      - Small breed dogs
      - Usually < 1 year of age
      - Possibly decreased growth and signs of hepatoencephalopathy
    - Without liver disease
      - Between 1-4 years of age typically
      - Males > females
      - Dalmatians, English bulldogs
Etiologic and Pathophysiological Points

- Uric acid is a metabolic product of purine metabolism
- Purines originate endogenously from cell turnover (nucleic acids) and exogenously from diet
- In most dogs and cats, the final endpoint of purine metabolism is allantoin
- For urate urolith formation, uric acid is the metabolic endpoint
  - Uric acid is converted to allantoin by hepatic uricase
  - With liver disease, this conversion does not occur
  - Without liver disease, there is a transport defect where this conversion does not occur
    - Dalmatians have adequate hepatic uricase
    - They lack a necessary transporter encoded by the SLC2A9 gene
      - This results in slightly higher serum uric acid concentrations when compared to most non-Dalmatian breeds of dogs (but lower than found in human beings) and high urine uric acid concentrations
        - Serum uric acid concentrations:
          - Non-Dalmatian dogs: 0.2-0.3 mg/dl
          - Dalmatians: 0.8-1.2 mg/dl
          - Humans: 3.0-6.0 mg/dl
        - Urine uric acid concentrations
          - Non-Dalmatian dogs: 20-30 mg/dl/24h
          - Dalmatians: 600-1200 mg/dl/24h
      - High uric acid excreting (HUA) Dalmatians are homozygous recessive for the SLC2A9 gene; therefore, all excrete higher levels of urinary uric acid
        - However, incidence of urate urolithiasis is 10-30%
      - The Dalmatian back-cross project, where a Dalmatian was bred to an English setter and then offspring back-bred resulting in dogs that outwardly look like Dalmatians, has resulted in Dalmatians that excrete low uric acid (LUA). These dogs are either heterozygous or homozygous dominant for the SLC2A9 gene
      - We have found several other genetic differences between sibling urate urolith forming Dalmatians and non-urate urolith forming Dalmatians

Treatment

- **Without liver disease - dogs**
  - Dissolution can be attempted with an “ultra low protein”, alkalinizing diet that induces a diuresis and administration of allopurinol
  - Allopurinol is a xanthine oxidase inhibitor that blocks conversion of xanthine to uric acid
  - This results in decreased concentrations of uric acid and ammonia in urine and alkaluria
  - Dissolution usually occurs in 4-8 weeks, if it does not occur by then, it won’t
  - Dissolution is successful in approximately 1 out of 3 dogs; in 1 out of 3 dogs, stones decrease in size but do not dissolve and most can be retrieved non-surgically; and in 1 out of 3 dogs, stones increase in size or number associated with xanthine formation
  - Preventative measures include feeding the “ultra low protein” diet – this is successful in > 80% of dogs
    - There is also a “vegetarian” based diet available
    - Protein hydrolysate diet has been shown to aid in prevention
    - Occasionally, a low dose of allopurinol is also required

- **Without liver disease – cats**
  - No published protocol for medical dissolution exists
  - There is no “ultra low protein” diet available in cats
  - Urate uroliths have been dissolved using “renal failure” diets and administering allopurinol at ½ of dog dose

- **With liver disease**
  - Dissolution therapy is not typically successful (see below)
Surgical removal may be required
Correction of a portovascular anomaly or medical treatment of underlying liver disease helps with prevention

**Cystine urolithiasis**
- Cystine urolithiasis occurs due to abnormally increased levels of cystine in urine
- In dogs, this occurs as a familial disease
- Represents a proximal renal tubular defect of cystine reabsorption – often in association with loss of other amino acids – COLA (cystine, ornithine, lysine, arginine)
- **Guesstimation**
  - Urine pH: acidic
  - Crystals: cystine
  - UTI: none unless secondary infection
  - Radiography: small, round, smooth, marginally radiodense, usually not more than 1-2 dozen
  - Laboratory evaluation: usually normal
  - Signalment
  - Breeds of dogs
  - Young adult
  - Males > females

**Treatment**
- **Dietary protein restriction**
  - Dogs
    - Prescription diet u/d
    - Royal canin UC
    - Vegetarian diet
  - Cats
    - Renal failure diet
- Thiol-containing drugs
  - **2-mercaptopyroionylglycine (2-MPG)** and D-penicillamine
  - Bond to the individual cysteine molecules at the sulfur groups
  - Prevents di-sulfide bond formation and cystine formation
  - DO NOT use in cats as it causes hemolysis
- **pH**
  - Cystine is more soluble in alkaline pH > 7.2
  - Low protein diets are typically alkalizing
  - May administer an alkalinating agent as well (e.g. K citrate)
- Inducing a diuresis decreases concentration of urinary cystine and therefore urinary saturation for cystine

**Prevention**
- Low protein or vegetarian-based diet that induces diuresis and alkaluria
  - Effective in > 90% of dogs
- Alkaluria
- ± thiol-containing drugs
  - Note: some people do not modify diet but only administer thiol-containing drugs at a higher dosage for prevention