Feline Struvite Urolithiasis

Abstract: Feline urolithiasis represents 15% of all cases of nonobstructive lower urinary tract disease in cats. Approximately 50% of feline uroliths are composed of struvite. Struvite urolithiasis commonly recurs, but optimal management may decrease its frequency. The pathophysiology and management of struvite urolithiasis are different in cats and dogs. This article focuses on struvite urolithiasis in cats, highlighting important aspects of pathophysiology, treatment, and prevention.

Pathophysiology
The pathophysiology of struvite urolithiasis is different from that of other forms of urolithiasis. In general, the factors that influence the formation of a calculus include urine pH, renal mineral excretion, the presence of promoters, the absence of inhibitors, and the presence of infection or inflammation. In struvite urolithiasis, the concentration of struvite crystals free to react with other solutes in a solution, called the *struvite activity product* (SAP), also influences calculus formation. When the SAP increases to the point at which the urine becomes supersaturated, the crystals aggregate, forming uroliths. With further increases in SAP, spontaneous crystallization can occur.1

Most canine struvite uroliths are caused by urinary tract infections. However, struvite uroliths are sterile in approximately 95% of feline cases. In cats, the formation of struvite uroliths is influenced by metabolic factors, including urine concentration, pH, and excess consumption or excretion of calculogenic minerals.2 An epidemiologic study3 that evaluated dietary risk factors for struvite and calcium oxalate urolithiasis found that increased magnesium, phosphorus, calcium, chloride, and fiber concentrations favored struvite formation in cats with existing urolithiasis compared with control animals without urolithiasis. As dietary fat content increased, struvite urolith formation was reduced. However, the interactions of minerals within the body may be more important than individual factors in altering the formation of struvite uroliths.5 It has been suggested that the dietary protein source may alter nitrogenous waste production, urinary acidification, and struvite formation. Additionally, protein may provide organic material that can act as a nidus for stone formation.4 Natural inhibitors such as citrate may reduce relative urinary supersaturation with struvite, similar to their suggested mechanism for reducing calcium oxalate formation.5

Urinary pH is the most important factor in determining the SAP. Acidification of urine causes deprotonation of phosphates and increases the total proportion of urine phosphate existing as trivalent anions, reducing the SAP.6 Urinary pH and SAP have been reduced with both dietary modification and administration of urinary acidifiers.7 The solubility of struvite is maximized when the urinary pH is <6.4.5

Other factors may contribute to struvite urolithiasis. Recently, it was shown that soluble proteins in feline urine act as pro-

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moters of struvite crystallization independent of SAP. The authors of this study suggested that reducing urinary protein excretion would be helpful in decreasing struvite crystallization and urolithiasis formation.

Occasionally, infection can increase urinary ammonium concentration and pH, both of which may contribute to struvite urolithiasis, through urease production. Urease acts to convert urea to ammonia (NH₃), which, through buffering of hydrogen ions, can result in formation of ammonium (NH₄⁺). Ammonium directly contributes to struvite formation and indirectly facilitates nidus formation through local urothelial damage.

Dietary moisture content has been reported to influence calcium oxalate urolith formation and the incidence of feline idiopathic cystitis, for which increased moisture may reduce supersaturation of crystallogenic substrates and urine concentration, respectively. Dietary moisture content has not definitively been shown to influence struvite calculus formation in cats.

**Signalment**

There is no clear sex predilection. Although any breed can be affected, several breeds have an increased risk of struvite calculus formation, including the foreign shorthair, ragdoll, Chartreux, Oriental shorthair, domestic shorthair, and Himalayan (odds ratio: >2). Breeds noted to have a decreased risk include the rex, Abyssinian, Burmese, Russian blue, Birman, and Siamese, as well as mixed-breed cats (odds ratio: <0.5). Cats of all ages may develop struvite urolithiasis. The median age of cats with struvite calculi was 5.75 years in one study, which was significantly younger than cats with calcium oxalate calculi. Cats older than 4 years

**QuickNotes**

Urolithiasis is the second most common cause of lower urinary tract disease in cats.

**FIGURE 1**

Struvite crystals in urine. Note the characteristic coffin shape. (1000x magnification)

**FIGURE 2**

Radiograph of typical radiopaque struvite cystic calculi.

**FIGURE 3**

Feline struvite calculi. Note the variation in gross appearance.
Algorithm for management of struvite urolithiasis in cats. 

**FIC** = feline interstitial cystitis, **UTI** = urinary tract infection
are 2.5 times more likely to develop struvite calculi compared with cats younger than 4 years. The highest incidence was seen in cats between 4 and 7 years of age, with a 10-fold greater risk compared with cats between 1 and 2 years of age. Infection-induced calculi were most common in cats younger than 1 year or older than 10 years.11

Incidence
Worldwide, urolithiasis has been reported in 15% to 23% of all cats with diseases of the lower urinary tract, and 22% to 50% of those uroliths are composed of struvite.2,9,12,13 Over the past 20 years, the ratio of calcium oxalate stones to struvite stones increased significantly, but it has recently reached a plateau. Struvite and calcium oxalate stones currently occur in almost equal proportions.14 Percentages of struvite submissions may not accurately reflect the true incidence of struvite calculi because of effective dissolution therapy without quantitative analysis. While most cases of lower urinary tract disease in cats are idiopathic cystitis, the management of this condition is different from urolithiasis.2,12

Diagnosis
Hematuria, pollakiuria, stranguria, and dysuria are common clinical signs of lower urinary tract disease and are not specific for cystic calculi. Most cats aged 1 to 10 years with lower urinary tract disease have idiopathic cystitis (55% to 64%). Urolithiasis accounts for 15% to 23% of cases of feline lower urinary tract disease; up to 11% of cases are due to anatomic defects; and 1% to 8% are urinary tract infections.12,13,15,16 In cats older than 10 years, 46% of lower urinary tract disease cases are related to infection and 17% to concurrent infection and calculi.17

Alkaline urine increases the SAP and is commonly found in association with struvite urolithiasis. Crystalluria (FIGURE 1) without stone formation is not pathologic and can be found in healthy animals. In vitro crystal formation can occur as a result of prolonged storage, refrigeration, and alkalinization.18,19 Crystalluria can be confirmed by evaluation of fresh urine samples. Pyuria may result from concurrent infection. Urine culture via cystocentesis is recommended to evaluate for bacterial infection.

Radiography is a sensitive test for detection of struvite calculi, which are radiopaque (FIGURE 2). If the calculi are small (<3 mm), ultrasonography or double-contrast cystography is superior to radiography for detection.2 Struvite uroliths tend to have smooth contours, but they vary in gross appearance (FIGURE 3).

A history of struvite urolithiasis, struvite crystalluria, alkaline urine, and compatible radiographic features increases the suspicion for struvite urolithiasis, but definitive diagnosis is based on quantitative stone analysis. An algorithm for management of struvite urolithiasis is presented in FIGURE 4.

Treatment
Therapy can be divided into stone dissolution and stone removal. Dissolution therapy has the benefits of avoiding major surgery, perioperative complications, and general anesthesia. Its disadvantages include treatment failure, reliance on owner and patient compliance, and

QuickNotes
Struvite calculi are common in the feline lower urinary tract, and their prevalence may be rising.
The costs associated with monitoring efficacy. **BOX 1** lists patient selection criteria and other considerations for dissolution therapy. The potential for urethral obstruction as calculi become smaller exists; however, no literature supports dissolution as a risk factor for obstruction at this time.

Dissolution therapy is effective in management of sterile feline struvite calculi. The key goals of dissolution diets include reduction in urine pH to ≤6.3 and reduction of dietary magnesium.20 One study21 found a mean dissolution time of 36 days (range: 14 to 141 days) for sterile uroliths and 44 days (range: 12 to 92 days) for infected uroliths when Hill’s Prescription Diet s/d (Hill’s Pet Nutrition) was used. Another commercially available dissolution diet (Medi-Cal Dissolution Formula, Veterinary Medical Diets, Guelph, Ontario) was effective in 79% of cases with clinical suspicion for sterile struvite.21 Treatment failure has been noted with mixed-composition calculi, owner noncompliance, and food refusal.22 Dissolution diets are not recommended for growing cats or for cats that are acidemic, pregnant, or hypervolemic because these diets are protein restricted and acidifying and can result in volume expansion from increased sodium concentration.20 Additionally, male cats may not be ideal candidates for dissolution therapy because of the chance of urethral obstruction.

The selected diet should be fed exclusively. Radiographic evaluation at 3- to 4-week intervals is used to quantify changes in stone size and number (**FIGURE 5**). These diets should be continued for 2 to 4 weeks beyond radiographic resolution to ensure complete dissolution of calculi <3 mm, which are not radiographically visible.

If a calculolytic diet is contraindicated (e.g., pregnancy, immaturity) or obstruction is present, physical removal of stones via surgical or nonsurgical techniques is recommended. Additionally, if infection is present, dissolution therapy is ineffective without antibiotic therapy. It is recommended that antibiotics be continued 1 month beyond radiographic dissolution, as bacteria can be released from calculi during therapy or can persistently colonize the urothelium and result in relapse.20,21 Infection-induced struvite uroliths generally take longer to dissolve than sterile struvite uroliths.21 In cats, nephroliths and ureteroliths are rarely composed of struvite and mostly composed of calcium oxalate. However, unlike feline struvite cystoliths, which are predominantly sterile, most feline struvite nephroliths (80%) are associated with urine culture results positive for urease-producing organisms.23,24

**Monitoring**

After definitive therapy, routine monitoring with urinalysis and abdominal radiography is recommended. Early detection of recurrence may allow nonsurgical therapies to be used. Cats with risk factors for urinary tract infections (i.e., chronic kidney disease, polyuria,
diabetes mellitus, hyperthyroidism, perineal urethrostomy) should have urine samples cultured every 3 to 6 months. Monitoring urine pH is recommended to assess dietary compliance and efficacy. Values between 6.0 and 6.5 may reduce the incidence of calcium oxalate and struvite crystal formation. Monitoring urine specific gravity has been recommended to assess water consumption. A urine specific gravity <1.030 has been recommended as a goal.1,28

Prevention
A general recommendation for prevention of urolithiasis is to increase water consumption to encourage diuresis and reduce time for aggregation and crystallization (Box 2). This may be most effectively completed with a transition to a moist diet; however, providing flavored or running water may encourage increased water intake.1

Dietary therapy may reduce calculi recurrence, although clinical studies on recurrence rates are lacking. Epidemiologic studies suggest that a urine pH of approximately 6.0 to 6.3 and consumption of a low-magnesium diet reduce recurrence of naturally occurring sterile struvite urocystoliths.21,29 However, acidification of the urine to <6.29 may increase the risk of calcium oxalate urolith formation.30 Dietary analysis and quantification of “alkalogenic” and “acidifying” components may aid in predicting urine pH but cannot be recommended at this time.30

Urinary acidifiers (dl-methionine, ammonium chloride) should be considered only when the urine pH is >6.5 with ad libitum feeding conditions.1 Urinary acidifiers alter the urine pH and SAP but cannot reduce the organic fraction responsible for the matrix formation.7

Commercial diets designed to prevent struvite recurrence have not been critically evaluated in randomized, controlled studies. These diets may or may not influence the recurrence rates in clinical patients.

Conclusion
Struvite cystic calculi are common; dietary therapy is the mainstay of prevention. Diets with reduced magnesium that maintain a urine pH between 6 and 6.3 are recommended despite lack of evidence of efficacy. Struvite uroliths can be effectively medically dissolved or physically removed. C
References


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1. Feline struvite cystoliths are most commonly associated with
   a. urease-producing organisms.
   b. high dietary fat content.
   c. low dietary protein.
   d. alkaline urine.

2. The SAP is defined as the
   a. concentration of struvite crystals free to react with other solutes in solution.
   b. concentration of magnesium in the diet.
   c. mathematical product of dietary phosphorus and magnesium.
   d. point at which crystal aggregation occurs.

3. The most important factor in feline struvite formation and in determining SAP is urine
   a. phosphate concentration.
   b. magnesium concentration.
   c. pH.
   d. ammonium concentration.

4. Which statement regarding the signalment for urolithiasis is true?
   a. Abyssinians and Burmese are at an increased risk for struvite urolithiasis.
   b. Cats aged 4 to 7 years are at increased risk for struvite urolithiasis.

5. What percentage of lower urinary tract disease in cats is caused by urolithiasis?
   a. 2% to 5%
   b. 15% to 23%
   c. 34% to 53%
   d. 60% to 65%

6. Which statement regarding diagnosis of feline struvite urolithiasis is true?
   a. Conventional radiography can detect only calculi ≥5 mm.
   b. Struvite crystalluria is always associated with urolithiasis.
   c. Ultrasonography and double-contrast cystography are the most sensitive means of detection.
   d. Urease-producing organisms are usually present on urine culture.

7. Dissolution therapy for struvite uroliths
   a. takes approximately 35 to 45 days.
   b. is more rapid in patients with infected uroliths.
   c. uses a diet supplemented with magnesium and designed to reduce the urine pH to ≤6.3.
   d. uses a diet restricted in magnesium and designed to maintain a urine pH ≥6.3.

8. In cats, upper urinary tract struvite calculi are
   a. more common than calcium oxalate calculi.
   b. more likely to be associated with infection than calculi of the lower urinary tract.
   c. often associated with chronic progressive renal failure.
   d. more common than in dogs.

9. Which of the following is not associated with urinary tract infections in cats?
   a. diabetes mellitus
   b. hyperthyroidism
   c. chronic kidney disease
   d. highly concentrated urine

10. Which of the following is not recommended for prevention of feline struvite urolithiasis?
    a. increasing water consumption
    b. maintaining a urine pH between 6.0 and 6.5
    c. avoiding excessive magnesium intake
    d. routinely adding d-l-methionine to the diet