Dietary Management of Feline Lower Urinary Tract Disease
At Nestlé Purina, we have a long heritage of respecting cats and the characteristics that make them unique. A successful nutrition program involves more than just combining effective dietary ingredients. We also need to formulate diets that fit cats’ physiology and discriminating nature.

Feline lower urinary tract diseases (FLUTD) can be challenging conditions to diagnose and manage. When developing our new Purina Veterinary Diets® UR URinary™ St/Ox brand Feline Formula, our team of nutrition scientists and veterinarians was committed to finding a way to safely increase fluid intake and urine volume in cats to help minimize the risk of FLUTD. UR St/Ox also provides a high level of protein—and moderate levels of fat and calories—to help manage ideal body condition. With UR St/Ox, we’ve met these criteria and created a highly effective diet that cats will love.

This monograph provides the information you need when managing patients affected by FLUTD. With the right tools, you can make a difference in the lives of your patients and their owners. We’re proud to play a part in making it happen.

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Approximately 3.0% of all cats presented to private veterinary practices suffer from feline lower urinary tract disease (FLUTD). Because FLUTD encompasses a number of diseases, its pathogenesis has not been well defined. Regardless of cause, FLUTDs are characterized by common clinical signs that may include inappropriate urination, pollakiuria, straining, hematuria and/or partial or complete urethral obstruction. These signs are uncomfortable for patients and distressing to pet owners. Even more concerning is the fact that obstructive FLUTD can be life-threatening.

While the cause(s) of FLUTD are not known, predisposing risk factors for different manifestations of FLUTD have been recognized. Feline idiopathic cystitis, urethral plugs and urolithiasis are the most common types of FLUTD (Figure 1). Less common are those caused by anatomical defects, infection, neoplasia and neurological disease.2,3

Initial diagnostics for FLUTD patients include assessment for urinary tract obstruction. If no obstruction is found, abdominal radiography, serum biochemistry and urinalysis with sediment examination of fresh urine should be performed.

For first-time episodes, urine culture may be a low-yield test; however, it is indicated for cases with suspected pyelonephritis, urinary catheter placement, immunosuppression, bacteriuria or repeat occurrences. Nearly half (44%) of male cats with one episode of urethral obstruction have early recurrence.4 Advanced imaging techniques such as cystoscopy, ultrasound and contrast imaging should be utilized if no cause has been identified in patients with repeated presentation.

Feline Idiopathic Cystitis

For the majority of cats presented for clinical FLUTD signs, no specific reason for the signs can be identified. These cats are classified as having feline idiopathic cystitis (FIC), a painful, sterile, chronic inflammatory disease. While FIC is suspected to have a complex pathophysiology, no definitive cause has been identified. Stress has been implicated for exacerbating FIC clinical signs. A recent
study identified a link between development of FLUTD and cats that display fearful, nervous and aggressive behavior. Dysfunction of the cardiovascular, endocrine and nervous systems also have been associated with the disorder.

Some studies have shown an association between incidence of FIC and exclusive consumption of dry foods. This should not be interpreted as dry foods causing FIC, since the vast majority of millions of cats fed dry foods do not develop this condition. However, in cats otherwise predisposed to FIC, exclusive consumption of dry foods has been proposed to contribute to inadequate water intake and subsequent suboptimal urine volume, although this theory has not been confirmed.

Traditional FIC treatment has been directed at reducing the frequency of episodes by addressing underlying stressors with environmental management and initiating drug therapy. Increased urine production also may be beneficial in the management of FIC due to dilution of inflammatory mediators and shorter contact time of irritating substances with the bladder mucosa as a result of more frequent voiding.

Urethral Plugs

Up to 21% of cats with signs of FLUTD had urethral plugs, according to historical research. These plugs cause partial or complete urinary obstruction, predominantly in male cats.

Plugs are typically composed of mucus and/or cellular debris, along with a mineral substance. Despite a shift in the distribution of urolith types over the past two decades, the mineral composition of urethral plugs has remained primarily struvite.

The underlying causes of urethral plugs are unknown, but cats with urethral obstructions may have concurrent urinary tract disorders, including FIC or cystic uroliths. All of these types of FLUTD can involve inflammation of the bladder wall and secondary plug formation due to increased cellular sloughing, increased mucus production and increased urinary pH caused by leakage of plasma proteins from localized vasculitis.

The significant role inflammatory mediators appear to play in the development and perpetuation of both FIC and urethral plugs points to the potential value of increased urine volume in managing cats with a history of these conditions and helping to minimize the risk of recurrences. Increasing urine volume is a means of increasing the frequency of voiding and helping to reduce contact time of inflammatory mediators with the bladder mucosa.

Urolithiasis

Most uroliths in cats are composed of struvite or calcium oxalate mineral complexes (Figure 2). Although the incidence of calcium oxalate urolithiasis has dramatically
increased in the last two decades, struvite uroliths remain an important type of FLUTD. Moreover, a reverse in this trend may be occurring, with data collected since 2001 showing increased incidence of struvite uroliths relative to calcium oxalate uroliths.  

**Struvite Urolithiasis**

While urolith formation is a complex, multifactorial process, there are well-documented risk factors for feline struvite urolithiasis. Cats that are neutered, middle-aged and/or of certain breeds, such as Himalayan, Ragdoll and Oriental Shorthair, appear to be at increased risk for urolith development.

In contrast to dogs, struvite urolithiasis in cats is rarely associated with bacterial urinary tract infection, but instead is heavily influenced by urine pH (Figure 3). Struvite crystals are more soluble at pH conditions below 6.5, and crystallization is unlikely at a urine pH below 6.3.

Studies in the 1970s evaluated dietary magnesium as a contributing factor for struvite urolithiasis. Subsequently, it was found the magnesium salts used in these studies had an alkalinizing effect on urine. When a different source of magnesium that resulted in acidic urine was used, crystalluria did not develop. This and other research confirmed urine pH is more important to struvite urolith formation than is the concentration of dietary magnesium. Furthermore, magnesium...
combines with oxalic acid in urine, preventing it from combining with calcium, and is therefore considered an inhibitor of calcium oxalate urolith formation and growth.

**Calcium Oxalate Urolithiasis**

Although sterile struvite uroliths historically have been the most common urolith type in cats (Figure 2), calcium oxalate uroliths have grown more common in the past two decades.\(^{11,13}\) The reason for this shift is unknown; however, increased use of dietary strategies to control struvite urolithiasis is a likely contributor.\(^{21-22}\)

In some patients with calcium oxalate urolithiasis, a risk factor such as hypercalcemia can be identified. But the factors associated with calcium oxalate urolithiasis are complex and not completely understood, so in most cases, a causative factor is less apparent.

Epidemiological data has identified links between the risk of calcium oxalate urolithiasis and various lifestyle, nutritional, physiologic, genetic and gender differences. For instance, inactivity, obesity and being a certain breed (suggesting a genetic or metabolic etiology) all were associated with increased risk for developing uroliths.\(^{13}\) However, most of the epidemiologic associations have not been confirmed in controlled, prospective research. For example, although epidemiological data has identified an association between calcium oxalate urolithiasis and use of acidifying diets,\(^{11,21}\) prospective research demonstrated that urinary pH of 5.85 to 6.81 did not increase the risk for calcium oxalate urolith formation, at least under the conditions studied.\(^{23-24}\) Such conflicting data contributes to questions about the best ways to manage cats with urolithiasis.

**The Role of Water Intake and Urine Volume**

Increasing water intake is a highly recommended strategy to help reduce the risk of urolith formation and recurrence. Increased water intake typically results in increased urine volume and more dilute urine. This dilution helps decrease the concentration of various urolith-forming components of urine and minimizes the likelihood of urolith formation.\(^{25}\)

In humans, reduced urine volume is a significant risk factor for calcium oxalate urolithiasis.\(^{26}\) Increased urine volume encourages frequent urination and dilutes precursors within the bladder, which decreases the likelihood of crystal formation and aggregation (Figure 4).

Consequently, increased urine volume may help reduce the risk of calcium oxalate recurrence, as well as other types of FLUTD, including FIC, urethral plugs and struvite urolithiasis.

**Key Points**

- For most cats presented for clinical FLUTD signs, no specific cause is identified.
- Inflammatory mediators appear to play a significant role in development of FIC and urethral plugs.
- Controlling urinary pH and dietary precursors helps minimize the risk of struvite urolithiasis. These pH levels do not increase the risk of calcium oxalate urolith formation in cats.
- Increased urine volume helps minimize the risk of urolithiasis and other types of FLUTD.
Methods for Quantifying Risk of Urolithiasis

Uroliths form in environments where crystals precipitate out of solution and aggregate. This process happens microscopically and involves many interacting factors, so it has historically been very difficult to predict whether urine has been altered to a urolith-favorable or urolith-unfavorable environment due to the patient consuming a particular food. Fortunately, we now have quantifiable methods to determine the likelihood of crystal formation. These methods are relative supersaturation and activity product ratio (Figure 5).

Relative supersaturation (RSS) values provide an index of the risk of urolith formation by quantifying the soluble mineral (solute) load as well as urine pH and urine volume. For a particular urolith type, the relationship between a solution (urine) and solute concentration (minerals in solution) is calculated and expressed numerically as RSS.

A high RSS value means the equilibrium of the urine is in favor of precipitates when that diet is fed, while a low value means the equilibrium is in favor of minerals staying in solution rather than precipitating out as crystals. Minerals in solution are safely voided in the urine. RSS is determined by measuring pertinent minerals, inhibitors and promoters in urine, then calculating the RSS value using one of several software programs that consider the relative contribution of all factors.

The resulting RSS values are divided into ranges for undersaturation, metastability and oversaturation.27 The specific value depends on the software used to calculate the RSS value. For example, using EQUIL software:

- An RSS value for struvite or calcium oxalate of less than 1 means the urine is undersaturated with mineral solutes; new crystals or uroliths will not develop.
- An RSS value for struvite between 1 and 2.5 means the solution is metastable and will not promote the development of struvite crystals or uroliths. The metastable range for calcium oxalate is not precisely known, but is thought to be between 1 and 10 (personal communication, J W Bartges, University of Tennessee).
- An RSS value for struvite of more than 2.5 and for calcium oxalate of more than 10 means the urine is oversaturated with mineral solutes and there is increased risk of urolith formation.

The greater the number above this point, the more likely uroliths may form. Another technique for determining the risk of crystal and urolith formation is the activity product ratio (APR). Like RSS, APR involves measurement of solutes in urine and calculations, but APR also looks at the effects of unmeasured inhibitors and promoters. APR is determined by analyzing the urine sample before and after incubating the sample with pure seed crystals of struvite, calcium oxalate or other uroliths of interest.

With APR, the crystal of interest is added to a urine sample, and the concentrations of solutes before and after incubation are measured. Solute concentrations decrease in urine samples that allow seed crystals to grow during incubation, since the soluble minerals crystallize. These urine samples have APR values greater than 1, which indicates increased risk of urolith formation.

Conversely, APR values less than 1 indicate the seed crystals did not grow, which suggests decreased risk of urolith formation. APR values less than 1 also suggest crystal and uroliths in that urine environment may dissolve.
Urolith type cannot reliably be assessed by radiographic appearance or urinalysis, which makes initial treatment decisions more difficult. Therapeutic dissolution is an option for struvite uroliths, but not for calcium oxalate uroliths, which must be removed if present in the bladder or urethra.

Cystic uroliths of any type can be removed surgically or, if they are small enough in size, with urohydropropulsion. Given the potential variable effectiveness of initiating dissolution with uroliths of unknown type, some clinicians prefer surgical removal of all uroliths too large for urohydropropulsion. However, surgical removal is typically a more costly approach and involves the risks associated with anesthesia and surgery. Dissolution protocols for struvite uroliths require frequent monitoring with abdominal radiography and urinalysis, matching the overall costs of surgical removal, although there are fewer treatment risks.

Struvite urolith dissolution generally can be accomplished by feeding a diet that promotes increased urine volume with a pH in the range of 6.0 to 6.3, although dissolution is possible with an average urine pH of up to 6.45. Due to the compound mineral composition of some uroliths, if dissolution is not accomplished within 6 to 8 weeks, surgical removal and urolith analysis should be considered. It is suggested that complete removal of all uroliths be confirmed radiographically regardless of removal method.

Monitoring FLUTD Patients

Monitoring urine of FLUTD patients helps ensure dietary compliance as well as dietary efficacy. Unfortunately, RSS and APR measurements are currently not clinically available. Instead, monitoring FLUTD patients requires repeat urinalysis of freshly collected urine samples.

Examining fresh urine is important because crystals will develop in urine samples over time. It is not uncommon to observe in vitro crystallization, especially struvite crystals, in urine that has been refrigerated and/or sent to a laboratory for analysis. These in vitro crystals are of no clinical significance.29

Crystalluria is typically not important in cats without urinary tract disease, and there is no association between urinary struvite crystals and the presence or number of struvite uroliths.28 However, in cats with histories of uroliths, crystalluria may be a useful indicator of treatment efficacy and/or risk of recurrence. Therefore, in some cats, crystalluria can be a useful monitoring parameter, and a goal of therapy should be to avoid crystalluria in fresh urine.

Several factors should be included in ongoing assessment of at-risk patients:

- Urine pH. Strive to reach the goal of <6.5. Causes for significantly higher urinary pH should be explored to ensure the client is complying with feeding recommendations, especially avoiding feeding food or treats outside the recommended therapeutic diet.
- Urine volume. Cat owners should be instructed to note the size and number of urine deposits in the litter box, with the goal of increasing both factors.
- Abdominal radiography and serum biochemical analysis. These measures may be indicated in some patients.

**Key Points**

- Relative supersaturation (RSS) values indicate the risk of urolith formation by considering soluble mineral load, urine pH and urine volume.
- Activity product ratio (APR) measures solutes in urine and other factors, before and after incubation of sample urine with seed crystals.
- Fresh urine must be examined, since crystals in vitro may develop in urine over time and may not be clinically significant.
- Monitoring cats with FLUTD should involve urine pH and volume, and sometimes radiography and serum biochemistry analysis.
FLUTD signs tend to recur in patients, highlighting the importance of using management strategies that can help minimize the risk of FLUTD. Fortunately, some FLUTDs can benefit nutritionally from feeding Purina Veterinary Diets® UR URinary™ St/Ox brand Feline Formula. The following information outlines current knowledge on FLUTD and how UR St/Ox can help successfully manage cats with this syndrome.

**Struvite Urolithiasis**

If struvite urolithiasis is confirmed by analyzing retrieved uroliths or successful medical dissolution, long-term nutritional management strategies should be instituted. Purina Veterinary Diets UR URinary St/Ox brand Feline Formula provides effective dietary management of cats with struvite urolithiasis by increasing urine volume, maintaining urine pH in the optimal range to promote struvite solubility and controlling dietary levels of struvite precursors.

**Calcium Oxalate Urolithiasis**

Management strategies for calcium oxalate urolithiasis include promoting increased urine volume, reducing urolith precursors and providing a balanced level of dietary minerals such as magnesium and calcium.

While the interacting risk factors for calcium oxalate urolithiasis are complex and control strategies are not completely understood, dietary intervention has been shown to reduce the recurrence rate. Specially formulated foods, including UR St/Ox, address all known risk factors for calcium oxalate urolith formation. Decreasing urolith precursors is a generally recommended management strategy with calcium oxalate urolithiasis patients, but dietary calcium restriction is not appropriate for patients with calcium oxalate urolithiasis. Suppling adequate dietary calcium to complex with dietary oxalate in the intestinal lumen reduces oxalate absorption and subsequently decreases urinary oxalate concentration, since the luminal calcium oxalate complex is lost in the feces. However, calcium supplementation should not be used, as this may increase the risk for calcium oxalate urolith recurrence.

In humans, it is well established that low calcium intake is associated with increased urinary oxalate excretion and increased risk of calcium oxalate urolithiasis. Diets lower in calcium were associated with an increased risk for calcium oxalate urolith formation in dogs and cats when compared to a control group. Note that oxalate is found in many common human foods, including vegetables, fruits and beans, and avoiding foods that contain high oxalate levels helps decrease the level of urinary oxalate.

UR St/Ox helps minimize the risk of calcium oxalate formation by promoting increased urine volume and providing low-oxalate-containing ingredients and balanced levels of minerals involved in development of calcium oxalate uroliths.

**Urolithiasis Management**

Since the underlying cause(s) of urolithiasis are unknown and cannot be eliminated, it is common for uroliths to recur. Therapeutic strategies for struvite and calcium oxalate urolithiasis have often focused primarily on immediate treatment more than long-term management. An integrated approach to providing long-term management to reduce controllable risk factors is now possible. UR St/Ox incorporates complementary nutritional strategies for long-term management of both struvite and calcium oxalate urolithiasis, as well as dissolution of sterile struvite uroliths.

Several therapeutic strategies can concurrently address the common causes of FLUTD. In particular, urine characteristics that influence urolith formation and can be affected by diet include:

- urine pH,
- urolith precursor concentration, and
- urine volume.
Urine pH
Studies have shown that feeding UR St/Ox produces average urine pH in the beneficial range of 6.0 to 6.4 to help minimize the risk factors associated with struvite urolithiasis, while not increasing the risk of calcium oxalate crystal formation.

Urolith Precursor Concentration
UR St/Ox has been shown to help minimize the risk factors associated with struvite and calcium oxalate crystal formation by providing appropriate amounts of key mineral precursors such as magnesium, phosphorus and calcium.

Urine Volume
Environmental changes to increase water intake and urine volume (e.g., water fountains, flavored water, providing more water bowls, maintaining higher water levels) are unproven. The only interventions that have been repeatedly shown to increase water intake and urine volume are dietary modifications.

Canned vs. Dry Food Considerations
Purina Veterinary Diets UR Urinary™ St/Ox brand Feline Formula is available in both canned and dry forms to accommodate individual preferences.

A common recommendation for cats with FLUTD is to feed a food with increased moisture, and canned UR St/Ox is ideal for patients and clients who prefer this type of product. However, dry cat foods now consistently exceed canned foods in popularity (AC Nielsen market data, 2006), and many cats refuse to consume canned foods due to a fixed texture preference for dry food. Consequently, UR St/Ox was developed to suit this preference while promoting increased water intake and urine volume.
Increasing dietary protein, feeding dry food free choice, increasing moisture content of food and adding sodium to food are all effective means of increasing water intake and urine volume. Increasing dietary protein increases urea formation, which results in an osmotic diuresis and subsequent increase in urine volume.

Increasing dietary moisture by feeding canned foods often helps increase urine volume by increasing water intake compared to cats fed maintenance-type dry food. Increasing dietary sodium increases water intake by increasing the osmolality of plasma, which is sensed by osmoreceptors in the hypothalamus and results in the sensation of thirst.

Concerns have been raised regarding detrimental effects of increased dietary sodium on systemic blood pressure and renal function. However, the levels of dietary sodium in UR St/Ox do not affect systolic arterial blood pressure in clinically normal cats. Anecdotal reports of higher dietary sodium causing adverse effects on renal function have been limited to cats with evidence of existing renal dysfunction and have not been supported by published studies. Since the reason to place patients on a higher-sodium food is to increase urine volume, patients with preexisting low urine specific gravity and polyuria do not require this therapy, so a higher-sodium diet is not indicated in such patients. However, in patients with a high urine specific gravity and a preference for dry food, a higher-sodium food may be beneficial.

The team of scientists at Nestlé Purina has used the strategies described here to develop UR St/Ox, which promotes increased urine volume and lower urine specific gravity to address the most common types of FLUTD, including FIC, urethral plugs and urolithiasis (Figure 8).

These benefits allow clinicians to use a single therapeutic food to manage patients at risk for the most common causes of FLUTD. In addition, UR St/Ox provides complete and balanced nutrition for maintenance of healthy adult cats, so clients with multi-cat households can feed the same food to healthy cats and those at risk for struvite or calcium oxalate urolithiasis.

Key Points
- Effective dietary management of cats with struvite urolithiasis includes increasing urine volume, maintaining urine pH in the optimal range and controlling dietary precursors.
- Effectively managing calcium oxalate urolithiasis involves increasing urine volume, reducing urolith precursors and balancing dietary minerals such as magnesium and calcium.
- UR St/Ox uses complementary nutritional strategies for long-term management of struvite and calcium oxalate urolithiasis, plus dissolution of sterile struvite uroliths.
Purina Veterinary Diets® UR URinary™ St/Ox brand Feline Formula

- Formulated for the dietary management of adult cats with FLUTD
- Reduces the risk of both struvite and calcium oxalate uroliths
- Promotes increased urine volume
- Contains moderate fat and calories

**Indications**

UR St/Ox is formulated for cats with these conditions:

- Struvite-associated FLUTD
- Sterile struvite uroliths
- History of calcium oxalate uroliths
- Feline idiopathic cystitis (FIC)

**UR St/Ox Helps minimize the risk of both struvite and calcium oxalate urolith formation**

- Promotes the production of urine undersaturated (RSS <1.0) for struvite to minimize the risk of struvite urolith formation and encourage dissolution of existing struvite uroliths
- Promotes production of urine metastable (RSS 1-10) for calcium oxalate to reduce risk of calcium oxalate urolith formation

**Helps increase urine volume to dilute urine**

- UR St/Ox dry is formulated to promote increased water intake
- UR St/Ox canned contains high moisture content to facilitate water intake; increased urine volume helps flush out irritants and urolith precursors

**UR contains moderate fat and calorie levels**

- Because obesity is a predisposing factor for FLUTD, it is important to maintain ideal body condition in cats that are at risk
- UR St/Ox contains moderate levels of fat and calories to help achieve ideal body condition

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1. Adjustments must be made for environmental conditions, activity level and body condition. Provide fresh water in a clean container daily.
2. Kilocalories of metabolizable energy (ME).
3. This daily amount should be divided among several small meals throughout the day.
4. For each additional pound of body weight, feed an additional 24 kilocalories.
Ingredients (Dry)

Corn gluten meal, chicken, poultry by-product meal, brewers rice, whole grain corn, oat fiber, wheat gluten, animal fat preserved with mixed-tocopherols (from Vitamin E), salt, phosphoric acid, dried egg product, calcium carbonate, brewers dried yeast, potassium chloride, animal digest, fish oil, tetra sodium pyrophosphate, chlorine chloride, taurine, zinc sulfate, Vitamin E supplement, ferrous sulfate, manganese sulfate, niacin, Vitamin A supplement, calcium pantothenate, thiamine mononitrate, copper sulfate, riboflavin supplement, Vitamin B-12 supplement, pyridoxine hydrochloride, folic acid, Vitamin D-3 supplement, calcium iodate, biotin, menadione sodium bisulfite complex (source of Vitamin K activity), sodium selenite.

Ingredients (Canned)

Meat by-products, liver, chicken, water sufficient for processing, poultry by-products, brewers rice, calcium gluconate, oat fiber, guar gum, sodium bisulfate, potassium chloride, caramel color, carrageenan, salt, taurine, Vitamin E supplement, calcium phosphate, zinc sulfate, thiamine mononitrate, ferrous sulfate, manganese sulfate, Vitamin A supplement, pyridoxine hydrochloride, copper sulfate, niacin, Vitamin B-12 supplement, riboflavin supplement, calcium pantothenate, menadione sodium bisulfite complex (source of Vitamin K activity), Vitamin D-3 supplement, folic acid, potassium iodide, biotin.
References


For More Information

Cats with most types of feline lower urinary tract diseases may benefit from long-term dietary management with Purina Veterinary Diets® UR URinary® St/Ox brand Feline Formula. For additional assistance with nutritional management of FLUTD patients, contact our Veterinary Resource Center toll-free at 1-800-222-VETS (8387) Monday-Friday, 8:00 a.m. to 4:30 p.m. CT or at purinavets.com.