

Multimodal Management of Feline Lower Urinary Tract Disease

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Feline lower urinary tract disease (FLUTD) is not a single disease but rather an umbrella term for several disorders, the most common being feline idiopathic cystitis (FIC), uroliths and urethral crystalline-matrix plugs. Regardless of the underlying cause, FLUTD is characterised by dysuria (painful or difficult urination), pollakiuria (frequent and/or prolonged attempts to urinate), stranguria (straining to urinate), haematuria (blood in the urine), excessive licking of the genital area and/or periuria (voiding outside the litter box). FLUTD leads to inappropriate urination, which is a common reason for owners to relinquish cats to shelters.¹ A multimodal approach is recommended for the management of FLUTD. Appropriate dietary therapy, providing environmental enrichment and behavioural management all play important roles in managing these patients, and will be explored in these notes.

Causes

The most common cause of feline lower urinary tract disease is FIC, which is present in up to 64% of cats with lower urinary tract signs.²⁻⁵ The diagnosis of FIC is dependent on exclusion of other known causes of lower urinary tract signs.³ FIC appears to be associated with complex interactions between the nervous system, adrenal glands and the urinary bladder. It is characterised by recurrent episodes of cystitis that usually resolve with or without treatment within 3-5 days.

Urinary stones, also known as uroliths, are another common cause of FLUTD, accounting for 15-23% of cases.²⁻⁵ Uroliths can form if the urine is supersaturated, causing formation and growth of urinary crystals which can ultimately coalesce to form stones. The most common types of uroliths in cats are struvite and calcium oxalate. Uroliths and matrix-crystalline plugs can also cause blockage of the urethra, which is diagnosed in approximately 10-21% of cats with FLUTD.²⁻⁵ However, since urethral plug formation occurs almost exclusively in male cats, the true prevalence in the population at risk is much higher (> 40%).⁴ In 2010, 90% of urethral plugs analysed at the Minnesota Urolith Centre were composed of struvite while < 1% were calcium oxalate.⁵

In contrast to dogs, urinary tract infection is rarely diagnosed in young to middle-aged cats. It is, however, more common in older cats, especially those with chronic kidney disease or diabetes. Urinary tract infections are also more common in cats that have had urinary tract procedures such as perineal urethrostomy or catheterisation, and those with immunosuppressive diseases such as Feline Leukaemia Virus (FeLV) or Feline Aids (FIV).

Risk Factors

It is likely that many factors (genetic, environmental and nutritional) play a role in urinary tract disease and individual cats are usually exposed to more than one risk factor. Patient risk factors include age, breed, gender, neuter status and body condition. Identified environmental risk factors include living in a multi-cat household, living indoors (or having

restricted access to outdoors) and/or having to use a litter tray.^{6,7} Cats with one or more of these risk factors are at an increased risk for lower urinary tract disease.

Diagnostic Tests

Urinalysis and medical imaging should be performed in every cat with FLUTD.

Urinalysis

Urinalysis on fresh urine is an important diagnostic tool. If the urine sample is allowed to sit for more than 30-60 minutes, *in vitro* changes are likely to occur. The urine sample should not be refrigerated and should be stored in an enclosed container. Cooling or refrigeration may enhance crystal growth, while evaporation can increase urine specific gravity and bacterial contamination can affect pH. If the urine is to be sent to a laboratory, it is advised that an 'in-house' urinalysis on a fresh sample be completed first. The result can then be compared with the result from the laboratory, particularly if there is a delay in getting the sample to the lab. A small sterile aliquot of urine should be decanted and stored in the refrigerator in case culture is indicated.

Urinalysis includes measuring urine pH, determining urine specific gravity (USG), sediment exam ± culture & sensitivity.

- The pH should ideally be measured with a pH meter as the test strips can provide variable results.
- Specific gravity measures the urine concentration and is an indicator of hydration and the concentrating capacity of the kidneys. The presence of large amounts of protein and glucose may alter the USG and should be considered when interpreting the USG results. A wide range of USGs are encountered in healthy animals, however, values for normally hydrated cats are typically in the vicinity of 1.035 to 1.060.
- After centrifugation, a sediment exam should be undertaken to determine the presence or absence of crystals, blood, bacteria or any abnormal cells or casts. Crystalluria may be normal in asymptomatic cats and thus the presence of crystals DOES NOT always contribute to, or cause, LUTD clinical signs. Crystalluria is not equivalent to urolithiasis and is not irrefutable evidence of stone-forming tendency - it simply indicates that the urine is sufficiently saturated that it *could* support the growth of uroliths. While crystalluria is an indication to check for uroliths, some cats may have uroliths without crystals being present. If sufficient numbers of crystals are present with a concomitant inflammatory process, male cats are at risk for matrix-crystalline plug formation. Consideration should also be given to whether the crystals may have formed *in vitro*.

Medical Imaging

Survey radiographs are valuable diagnostic tools and should be performed on every cat with LUTD signs. It is important to ensure the entire urethra is visible on the film. Radiolucent uroliths or urethroliths are difficult to detect on survey radiographs, as are radiopaque uroliths which are < 2-3 mm in diameter. Abdominal ultrasound is a useful tool to diagnose uroliths in the bladder, assess bladder wall thickness and to differentiate blood clots from uroliths.

Multimodal Management

Management of feline lower urinary tract disease must be addressed from a multimodal standpoint. This approach includes identifying and controlling underlying medical disorders, utilising dietary management, modifying the cat's home environment where appropriate and addressing behavioural issues.

Nutrition

Prescribing an appropriately formulated food is a key element of the complete approach to long-term management of the most common types of LUTD in cats. Dietary management involves:

- Controlling urine pH
- Minimising the mineral constituents of crystals and uroliths in the urine
- Adding inhibitors of crystal and urolith formation
- Managing inflammation and reducing free radical damage
- Increasing urine volume, thus diluting the urine.

To understand how to control urine pH, it is important to understand what is normal in cats. Urine is considered neutral at pH 7, acidic if less than 7 and alkaline if greater than pH 7. Cats typically produce acid urine, that is, they have 'normally' acidic urine with a pH between 6.0 and 6.4.⁸ A study of 10 healthy and 11 stone-forming adult cats demonstrated the relationship between urine saturation (for struvite and calcium oxalate) and urine pH.⁹ The data showed that a urine pH of 6.2 to 6.4 was ideal for managing urine saturation for both struvite and calcium oxalate, and that urine pH in this range was not as significant a factor for calcium oxalate urine saturation. In contrast, in another study, feeding cats a diet designed to produce a urine pH of 5.8 to 6.29 was associated with increased risk of calcium oxalate uroliths.¹⁰ In a third study, cats fed foods designed to produce urine pH of 5.99 to 6.15 were three times more likely to have calcium oxalate uroliths than cats fed foods to maintain a urine pH of 6.5 to 6.9.¹¹

Increasing water intake leads to an increase in urine volume and production of more dilute urine. The concentration of minerals in dilute urine is lower, which is beneficial for minimising the risk of urolithiasis. Increased urine volume creates the need to urinate more frequently, and urine will be less likely to be retained in the bladder, which is also beneficial for FIC. Less time in the bladder also means less time for crystals to form.

Feeding canned food is an easy way to increase water intake. Normally, cats consuming dry foods will drink more water than cats consuming canned foods, but total water intake can be greater in cats fed canned foods.¹² Canned food may also be beneficial by enhancing behavioural enrichment via factors such as mouth feel and increased owner interaction with the cat. It is important to ensure that switching to a new food does not cause stress to the cat as this may exacerbate FIC. While canned foods are frequently recommended as a means of increasing water intake in cats, some cats will not eat canned foods, and some owners prefer not to feed canned foods. In such cases increasing water intake must be approached by other means.

One proposed method of increasing water intake and urine volume is to increase dietary sodium to greater than 1% on a Dry Matter Basis (DMB). However, a study in normal cats fed a diet high in salt (1.11% sodium, DMB) versus a control (0.55% sodium, DMB) for a period of 6 months showed that, if there is an effect of salt intake on urine specific gravity, it

is short lived.¹³ By 3 months, there was no difference between the specific gravity of urine of cats fed the control and test diets and this was true at 6 months as well. If the benefit of high salt diets in controlling recurrence of uroliths is dependent on diluting the urine specific gravity, these results suggest this benefit is transient.

Despite evidence in short-term studies in healthy cats that increased salt intake appears to be safe,^{13,14} a 2006 study revealed some negative consequences of feeding high salt foods.¹⁵ The study evaluated the effect of feeding high salt (1.2% sodium, DMB), and low salt (0.4% sodium, DMB), diets to 36 cats with varying degrees of renal insufficiency over a 3 month period. In cats with subclinical kidney disease, the high sodium diet resulted in progression of their disease as measured by significant increases in serum creatinine, urea nitrogen and phosphorous. This is relevant because not only is chronic kidney disease an important consideration in older cats, it is also a significant disease in younger animals, with just under 1/3 of cases occurring in cats less than 10 years of age (Purdue University USA Database, 1990-2000). Given that early kidney disease often goes undetected, care should be taken adding salt to food or feeding high salt diets to cats.

As has been previously reported, the high salt diet in this 2006 study also caused increased urinary calcium excretion,¹⁵ The incidence of calcium oxalate nephroliths is increasing and 25% of cats with chronic renal failure have stones in the upper urinary tract, 70% of which are calcium oxalate,¹⁶ giving further reason for caution. Many over-the-counter foods and some foods designed to manage feline urinary tract disease contain similar or higher levels of salt to the test food in this study. Thus, to avoid excess calcium excretion and the possibility of formation of calcium oxalate crystals while feeding these types of foods, a sodium range of 0.3 to 0.6% DMB is recommended in foods intended for struvite dissolution and management and in cats at risk of calcium oxalate uroliths.¹⁷

Other safer methods of increasing water intake include flavouring the drinking water with low-salt tuna liquid or chicken broth, splitting the daily feed intake into 2-3 meals, leaving some water in the bottom of the sink or bath, providing wide, shallow water bowls (cats don't like their whiskers to touch the sides of the bowl) and the use of water fountains.

The inflammatory effects of FLUTD are associated with "oxidative stress", resulting in increased production of free radicals which in turn contribute to the progression of the disease. FIC in particular is an inflammatory (neurogenic) condition and stress is a big 'flare' factor. Feeding a food high in omega-3 fatty acids helps with reducing bladder wall inflammation – ingested omega-3 fatty acids are incorporated into all cell membranes of the body, where they exert anti-inflammatory effects.¹⁸ Antioxidants such as vitamin E and beta-carotene are incorporated into FLUTD diets to help protect against free radical damage associated with inflammation. Antioxidants also help protect against calcium oxalate deposition.

A recent year-long study evaluated the effects of an antioxidant and omega-3 fatty acid enriched diet in the management of FIC.¹⁹ Compared to a control food, feeding the test therapeutic urinary food (Hill's Prescription Diet™ c/d™ Multicare Feline Bladder Health) was associated with a significant reduction in recurrent episodes of FIC signs over a 12-month period. This is the first study to definitively show that foods of different nutritional profiles impact the expression of FIC in cats.

Dissolution of Struvite

At the time of writing, three struvite dissolution diets are available in Australia. The times to dissolution of uroliths range from a mean of 13 days (Hill's Prescription Diet™ s/d™ Feline dry formulation),²⁰ a median of 18 days (Royal Canin® Urinary S/O LP34 wet and dry formulations)²¹ and a mean of 27 days (Hill's Prescription Diet™ c/d™ Multicare Feline dry formulation).²⁰ During the dissolution period, it is advised to take radiographs and perform urinalysis every 2 weeks.

Management of Struvite Uroliths

After dissolution or surgical removal of struvite stones, cats should remain on, or be transitioned to, a struvite management diet formulated with controlled magnesium and phosphorous and with a target urinary pH of 6.2-6.4. Excessive sodium should be avoided. Diets currently marketed to manage struvite uroliths include Hill's Prescription Diet™ c/d™ Multicare Feline, Royal Canin® Urinary S/O LP34 and Eukanuba® Veterinary Diets Urinary Struvite Formula. A USG of 1.030 to 1.035 is ideal and may be achieved by increasing water intake by feeding canned foods or other methods described in this review. At this point, it should never be a case of 'set and forget' - ensure urinalysis is performed 3 to 6-monthly on fresh, non-refrigerated urine. Overweight cats suffering from struvite FLUTD may be maintained on a higher fibre weight management diet such as Hill's Prescription Diet™ w/d™ Feline.

Management of Calcium Oxalate Uroliths

Calcium oxalate stones cannot be dissolved with diet and thus need to be removed surgically or, if the stone is small enough, by voiding hydropropulsion. Lithotripsy, while available overseas, is not yet an option for cats in Australia. Unfortunately, no treatment or diet has been shown to completely prevent recurrence of calcium oxalate uroliths in cats. At best, the hope is to minimise the risk and delay the recurrence. All cats diagnosed with calcium oxalate uroliths should be assessed for hypercalcaemia by measuring serum ionised calcium. They should be placed on a calcium oxalate management diet formulated with controlled calcium, oxalate and sodium, increased calcium oxalate inhibitors such as citrate which forms soluble salts with calcium (making it unavailable for absorption), and a target pH of 6.2 to 6.4. Over-acidification should be avoided. Increasing antioxidants (vitamin E and beta-carotene) is advantageous as damage caused by free radicals can contribute to progression of the disease by increasing calcium oxalate crystals and stone growth.²² In addition, increased insoluble fibre decreases calcium absorption from the gastrointestinal tract, which is useful in cats with idiopathic hypercalcaemia.

Diets currently marketed to manage calcium oxalate urolithiasis include Hill's Prescription Diet™ c/d™ Multicare Feline, Royal Canin® Urinary S/O LP34 and Eukanuba® Veterinary Diets Urinary Oxalate Formula. If the urine remains too acidic, consider adding potassium citrate (alkalinises the urine and binds calcium) and/or dividing the daily ration into three meals and feeding three times per day (encourages postprandial alkalosis). Overweight cats can also be fed higher fibre diets such as Hill's Prescription Diet™ w/d™ Feline with the addition of potassium citrate if the urine is too acidic. Urinalysis should also be performed 3 to 6-monthly on a fresh, non-refrigerated urine sample and twice yearly survey radiographs are advised.

Management of Urate Uroliths

Urate uroliths make up approximately 5% of the uroliths submitted for analysis from cats.²³ Cats with urate uroliths often have an underlying hepatic or metabolic disorder but frequently the nature of the disorder cannot be identified. These cats should be assessed for liver disease and fed a liver management diet if indicated. If no underlying disorder is detected, they should be fed a urate management diet formulated to avoid excessive dietary protein, particularly avoiding proteins with high purine content such as liver, kidney, sardines, anchovies or tuna. Diets currently marketed to manage urate uroliths include Hill's Prescription Diet™ k/d™ and Royal Canin® Renal RF23 (dry). Aim for a target urine pH of 6.6 to 6.8 and a reduced USG, increase dietary antioxidants and perform a urinalysis every 3 to 6 months.

Environmental Enrichment and Behavioural Management

Environmental enrichment and behavioural management are critical pieces of the FIC management puzzle and are especially appropriate for decreasing stress in indoor cats with FIC. One 10 month prospective observational study showed that multimodal environmental modification (MEMO) resulted in significant improvement of lower urinary tract signs in cats with FIC.²⁴ MEMO recommendations included increasing the amount of time spent by the owner interacting with the cat, changing to a canned diet, increasing litter box number, location and cleaning frequency as well as specific efforts to reduce inter-cat conflict. Educating owners about the importance of environmental enrichment is thus a vital component of FIC management. Important suggestions are as follows:

- Provide outlets for typical cat behaviour such as scratching poles and elevated resting perches. This is particularly important in multi-cat households.
- Make sure litter boxes, food, water and resting perches are available in several areas of the home to make it easier for the cats in multi-cat households to avoid confrontation
- Provide a water fountain, which has the added benefit of encouraging play and activity
- Place food in a feline Kong® or hide a portion of the daily food around the house, thus creating a 'treasure hunt' and helping to stimulate normal hunting behaviour
- Ensure cats are fed in stress free eating locations, away from dogs, kids and noisy appliances

Providing toys and play that mimic chasing and pouncing behaviours, such as a fishing pole with a feathered or tailed toy on the end, are beneficial. Placing cardboard boxes and paper bags around the house encourages cats to explore, play and hide. Increased contact between owners and affected cats may also reduce stress. Examples of stress-reducing human-cat contact included petting, grooming, feeding canned cat food and playing games that simulate hunting behaviour.

Litter box management is essential for indoor cats. To minimise stress associated with accessing the litter box, it is generally advised to have as many litter boxes as cats in the house, plus one. In a multi-storey home there should be at least one litter box on each floor. Litter boxes should be accessible and have at least two exit points to avoid dead ends. They should be located away from noisy appliances and dogs. Clean, clumping clay-based litter is preferred by cats. Clean the litter boxes at least once a day and thoroughly once per month. Cats which have suffered pain and discomfort urinating may associate this with the litter box,

with resulting litter box aversions and periuria. It is important not to punish periuria as this just adds to the stress. To address this problem, the litter box must be modified so that it is no longer associated with the painful experience. Moving the box to a different location, changing the physical characteristics of the box (covered to uncovered, different style box, etc) or changing the litter type may all help.

Pharmacological

Pharmacological treatments such as analgesics, facial pheromones and glycosaminoglycans (GAGS) have also been used to manage FLUTD. Feline synthetic facial pheromone (Feliway®) has been shown to improve grooming and food intake, both indicators of decreasing stress.²⁵ One hypothesis for the development of FIC is damage to the glycosaminoglycan (GAGs) layer lining the bladder. Glucosamine is an important intermediate for the formation of GAGS, however, in a study of 40 cats with spontaneous non-obstructive FLUTD given 125mg glucosamine/day or placebo, no significant difference in the number of days with clinical signs of cystitis was found.²⁶

The efficacy of amitriptyline, a tricyclic antidepressant with anticholinergic, antihistamine, anti-alpha-adrenergic, anti-inflammatory, and analgesic properties, has been investigated. In one non-controlled study, nine of 15 cats with chronic FIC had decreased clinical signs, as observed by their owners, after amitriptyline administration for 12 months.²⁷ However cystoscopic abnormalities persisted in these cats, suggesting the possibility of a placebo effect. In a further two, separate, controlled studies, cats with FIC received either a placebo or amitriptyline for 7 days. In both studies no difference in clinical signs was observed between the two groups.^{28,29} Amitriptyline may be useful when given long-term in chronic, recurrent cases (although further studies are needed to establish efficacy) but is not helpful in acute episodes.

In cats presenting with acute FIC, the primary treatment objectives are to reduce stress and to provide pain relief. Treatment with sublingual buprenorphine (0.01–0.03 mg/kg orally every 6–12h) may reduce clinical discomfort from FIC while waiting for the disease to resolve.

Summary

Feline lower urinary tract disease can, and does, have a big impact on the family-cat bond as well as affecting the quality of life for cats and their owners. Cats suffering from FLUTD need to be suitably managed both in the acute phase of their disease as well as through appropriate long term management. Recommending the right dietary therapy, counselling owners about environmental enrichment and behavioural management are all important components of the multimodal management of cats with FLUTD.

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[JE-VA-AUS-01/14]

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